The Structure of Pododacric Acid, a Tricyclic Aromatic Diterpene Acid

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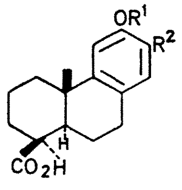
Summary Pododacric acid from N.Z. *Podocarpus* species has been formulated as (Id) and its structure confirmed by partial synthesis of its tetra-*O*-methyl derivative (IIa) from podocarpic acid (Ia).

PODODACRIC acid is a tricyclic aromatic diterpene acid, $C_{20}H_{28}O_5$, m.p. 213—214°, $[\alpha]_D + 118°$, obtained from the heartwoods of *Podocarpus dacrydioides*[1] and *P. totara*.[2] It forms a triacetate, m.p. 160—161°, $[\alpha]_D + 82°$, and a derivative, m.p. 135—136°, $[\alpha]_D + 47°$, which has been shown[3] to be a mixed anhydride of a tribenzoate and benzoic acid. On treatment with dimethyl sulphate and potassium carbonate in acetone followed by methyl iodide and silver oxide, it gives a tetra-*O*-methyl derivative, m.p. 112—113°, $[\alpha]_D + 87°$. At least one of the hydroxy-groups is phenolic since the acid gave a green colour with iron(III) chloride, coupled with diazotised *p*-nitroaniline to give a red dye, and possessed a u.v. spectrum, λ_{max} 225 (ϵ 5500) and 284 nm (ϵ 3100), similar to that of podocarpic acid (Ia).

The n.m.r. spectrum of the triacetate showed the presence of one phenolic acetate (δ 2·32, 3H), two alcoholic acetates (δ 2·05, 6H), two non-adjacent aromatic protons (δ 6·94), and C-18 (δ 1·33) and C-20 (δ 1·10) tertiary methyl groups. The absence of peaks assignable to isopropyl methyl groups but presence of a one-proton multiplet at δ 3·43 and a four-proton doublet at δ 4·26, indicated that the compound possessed a hydroxy-substituted isopropyl group, which on biogenetic grounds was tentatively assigned to the C-13 position. Like the calculated value (8·41), the experimental pK_{MCS} values[4] of 8·44 and 8·42 for pododacric acid and its triacetate were consistent with a C-4 axial carboxyl group, *cf.* (Ia) has a value of 8·39, (Ib) of 8·26, and (Ic) of 8·41. On this evidence the structure of pododacric acid was assigned as (Id).



(I) a; $R^1 = H$, $R^2 = H$
b; $R^1 = Ac$, $R^2 = H$
c; $R^1 = H$, $R^2 = Pr^i$
d; $R^1 = H$, $R^2 = CH(CH_2OH)_2$

The structure has been confirmed by conversion of podocarpic acid into the tetra-*O*-methyl derivative (IIa) of pododacric acid. The 13-ethylglyoxylate (IIb),[5] prepared from (IIc) in 94% yield with ethyl oxalyl chloride and aluminium chloride (2 mol) in 1,2-dichloroethane,[6] was converted by Clemmensen reduction into (IId, 90%) m.p. 138—139°. Compound (IId) was methylated with methyl iodide and potassium carbonate in moist methanol to the methyl ester (IIe, 96%), m.p. 113—114°. Treatment of this ester with sodium and ethyl formate in dry ether[7] gave the oily hydroxymethylene derivative (IIf) which rapidly isomerised to the formyl derivative (IIg). Reduction of the hydroxymethylene derivative (IIf) with sodium borohydride gave the diol (IIh, 64%), m.p. 118—119°, which on methylation with methyl iodide and silver oxide afforded a product (78%) identical (m.p., i.r., n.m.r.) with the tetra-*O*-methyl derivative of pododacric acid. De-esterification of the diol (IIh) with potassium t-butoxide in dimethyl sulphoxide followed by demethylation with boron tribromide gave pododacric acid (Id).

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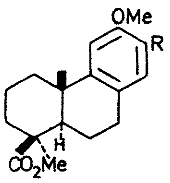

(II) a; $R = CH(CH_2OMe)_2$
b; $R = COCO_2Me$
c; $R = H$
d; $R = CH_2CO_2H$
e; $R = CH_2CO_2Me$
f; $R = C({=}CHOH)CO_2Me$
g; $R = CH(CHO)CO_2Me$
h; $R = CH(CH_2OH)_2$

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