Revised Structure of the Triterpene Polygalacic Acid: Configuration of the C-16 Hydroxy-group

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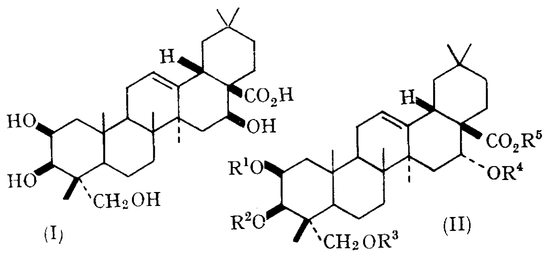
POLYGALACIC acid is the triterpenoid tetrahydroxy-acid isolated from *Polygala paenea* L.[1] and its structure has been assigned as 2β,3β,16β,23-tetrahydroxyolean-12-en-28-oic acid (I).[2] In our study on saponins of the roots of *Platycodon grandiflorum*, we isolated polygalacic acid,† together with platycodigenin [m.p. 250—252°, $[\alpha]_D$ +46·5° (EtOH)] which is an unidentified penta-hydroxy-acid $C_{30}H_{48}O_7$, isolated previously[3] as a sapogenin of this plant. We report evidence which suggests that the structure of polygalacic acid should be revised to 2β,3β,16α,23-tetrahydroxyolean-12-en-28-oic acid (IIa).

Polygalacic acid, $C_{30}H_{48}O_6$, m.p. 295—300°, $[\alpha]_D$ + 47·1° (pyridine) and its methyl ester, m.p. 235—241°, $[\alpha]_D$ + 44·5° (EtOH), were identified with authentic samples.‡ Acetylation of the methyl ester (IIb) with acetic anhydride and pyridine at room temperature followed by t.l.c. separation on silica gel G (toluene–ethyl acetate, 3 : 1) gave, in addition to the tetra-acetate (IIc),[2] m.p. 169—174°, an amorphous triacetate (IId). The mass spectrum of (IId) (M^+ 644) shows *m/e* 278, attributable to the retro-Diels–Alder fragment[4] (A), as observed in the spectrum of the methyl ester (IIb), but no peak of *m/e* 320 for an acetoxy-group. This fact reveals that, of the four hydroxy-groups in polygalacic acid, the one located at C(16) is the most difficult to acetylate and therefore it may be axial 16α-hydroxyl. In the n.m.r. spectra (60 Mc./sec., $CDCl_3$), a signal at τ 4·33 (poorly resolved triplet, $W_{\frac{1}{2}}$ 8 c./sec.)[2] observed for the tetra-acetate (IIc) shifts to τ 5·47 for the tri-acetate (IId). These chemical shifts and signal shapes are in good agreement with those assigned for the 16β-H in the di- and mono-acetates of quillaic acid methyl ester (III)[5] which has an axial 16α-hydroxy-group.

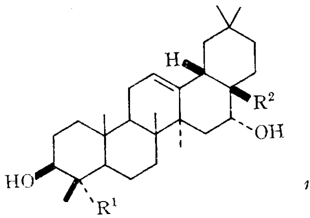
These results were supported by the following experiment. Treatment of the methyl ester (IIb) with acetone and toluene-*p*-sulphonic acid gave the 2β,3β-acetonide (IIe),[2] m.p. 204—206°, $[\alpha]_D$ +66·4° ($CHCl_3$), and the amorphous 3β,23-acetonide in a 3 : 2 ratio. The 2β,3β-acetonide (IIe) on acetylation with acetic anhydride and pyridine on a steam bath afforded the acetonide-diacetate



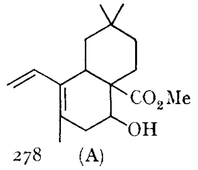
(I)

(II)

	R¹	R²	R³	R⁴	R⁵
a;	H	H	H	H	H
b;	H	H	H	H	Me
c;	Ac	Ac	Ac	Ac	Me
d;	Ac	Ac	Ac	H	Me
e;	Me_2C		H	H	Me
f;	Me_2C		Ac	Ac	Me
g;	H	H	Ac	Ac	Me
h;	H	Ac	Ac	Ac	Me
i;	$MeSO_2$	Ac	Ac	Ac	Me



(III; R^1=CHO, R^2=CO_2Me)
(IV; R^1=R^2=CH_2OH)



m/e 278 (A)

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† O. Tanaka *et al.* have recently reported an independent isolation of polygalacic acid from the same source. (See abstract of the 88th Annual Meeting of the Pharmaceutical Society of Japan, April 1968, p. 216.)

‡ We thank Dr. Rondest for these samples.

(IIf), m.p. 121—124° (from MeOH), $[\alpha]_D + 30{\cdot}6°$ ($CHCl_3$), which on hydrolysis with 70% aqueous acetic acid yielded the amorphous 16,23-diacetate (IIg). Partial acetylation of (IIg) with acetic anhydride–pyridine–chloroform (1 : 5 : 25) at room temperature for 40 hr. gave predominantly the 3β,16α,23-triacetate (IIh), M^+ 644, [n.m.r. ($CDCl_3$) τ 7·95, 7·92, and 7·89 (3H each of acetyls, s), 6·38 (3H of CO_2Me, s), 6·25 (2H at C-23, bs), 5·78 (1H at C-2, m), 5·10 (1H at C-3, d, *J* 3·7 c./sec.), 4·57 (1H at C-12, bt), and 4·35 (1H at C-16, bt). Treatment of (IIh) with methanesulphonyl chloride in pyridine afforded the triacetyl-methanesulphonate (IIi) [ν_{max} ($CHCl_3$) 1345, 1173, and 912 cm.$^{-1}$; no OH]. Reduction of (IIi) with lithium aluminium hydride in boiling tetrahydrofuran yielded a tetraol, $C_{30}H_{50}O_4$, m.p. 256—260°, $[\alpha]_D + 47{\cdot}6°$ ($CHCl_3$), which was identified with authentic olean-12-ene-3β,16α,23,28-tetraol (IV) derived from lithium aluminium hydride reduction of quillaic acid methyl ester (III).

From the above chemical correlation, the structure of polygalacic acid has been shown to be (IIa), in which it has the 16α- not 16β-hydroxy-configuration, as previously suggested from circumstantial evidence.[2]

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