The Structure of Platycodigenin, a 4,4-Di(hydroxymethyl)-triterpene

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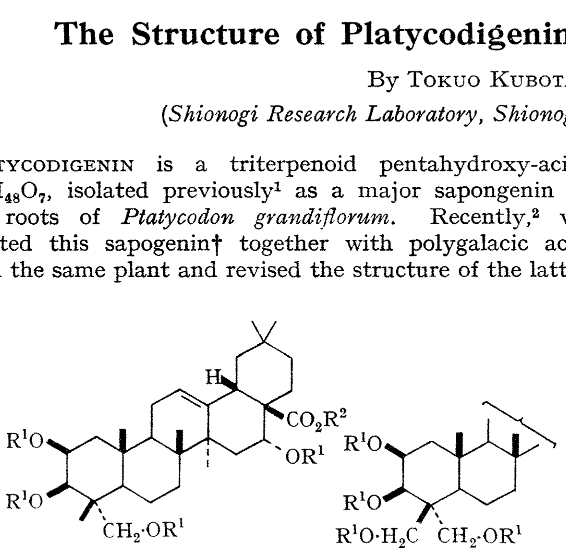
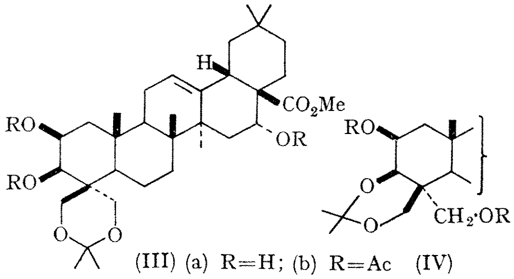
PLATYCODIGENIN is a triterpenoid pentahydroxy-acid, $C_{30}H_{48}O_7$, isolated previously[1] as a major sapongenin of the roots of *Ptatycodon grandiflorum*. Recently,[2] we isolated this sapogenin† together with polygalacic acid from the same plant and revised the structure of the latter to 2β,3β,16α,23-tetrahydroxyolean-12-en-28-oic acid (Ia). We now present evidence that platycodigenin is 2β,3β,16α-23,24-pentahydroxyolean-12-en-28-oic acid (IIa).



(I) (II)

(a) $R^1=R^2=H$
(b) $R^1=H$, $R^2=Me$
(c) $R^1=Ac$, $R^2=Me$



(III) (a) R=H; (b) R=Ac (IV)

Platycodigenin, $C_{30}H_{48}O_7$, m.p. 250—252° (decomp.), $[\alpha]_D$ +46·5° (EtOH), on treatment with diazomethane afforded the methyl ester, $C_{31}H_{50}O_7$, m.p. 246—250° (decomp.), $[\alpha]_D$ +44·7° (EtOH). The mass spectrum of the ester (M^+ 534) exhibited intense fragment peaks at *m/e* 278, 260, and 201, suggesting that the functional groups in rings D and E are the same as those of methyl polygalacate (Ib).[2] On treatment of the ester with acetic anhydride and pyridine at room temperature, one hydroxy-group resisted acetylation but, on heating, was acetylated to give the penta-acetate, which was amorphous but homogeneous on t.l.c. The n.m.r. spectrum of the penta-acetate resembles that of (Ic) except that one methyl group (τ 8·97) in (Ic) is replaced by $AcOCH_2$ (IIc) (τ 5·45) and the acetoxy-group brings about some additional shift of the protons at C-3 and C-23 to lower field. The results suggest a close relationship between the structures of polygalacic acid and platycodigenin.

Treatment of platycodigenin methyl ester [*i.e.*, (IIb)] with acetone and toluene-*p*-sulphonic acid gave an amorphous diacetonide, M^+ 614, the constitution of which was further confirmed by the n.m.r. spectrum of its acetylated derivative. Acetonide formation under more gentle conditions, carried out in a mixture diluted with benzene, afforded mainly two monoacetonides, $C_{34}H_{54}O_7$, m.p. 153—157°, $[\alpha]_D$ +63·0° ($CHCl_3$) (IIIa) and m.p. 247—249°, $[\alpha]_D$ +39·0° (EtOH) (IVa). The former acetonide (IIIa) on acetylation yielded an amorphous acetonide triacetate (IIIb). On comparison of the n.m.r.

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† O. Tanaka, T. Akiyama and S. Shibata [Abstracts of the 88th Annual Meeting of the Pharmaceutical Society of Japan, April 1968, p. 216 and *Chem. and Pharm. Bull.* (*Japan*), in the press] have recently reported an independent isolation of platycodigenin from the same source. We thank Dr. Tanaka for confirming the identity of the two specimens.

spectra of (IIIb) and the penta-acetate (IIc), the two oxygen-bearing methylene groups in (IIIb) appear at significantly higher fields, τ 6·52 (2H, s), and τ 6·09 and 5·81 (2H, AB q, J 11 c./sec.). This suggests that the two primary hydroxy-groups of (IIb) relate to the acetonide linkage of (IIIa) and treatment of (IIIa) with phosgene and pyridine formed a five-membered-ring cyclic carbonate [ν_{max} ($CHCl_3$) 1805 cm.$^{-1}$] between C–2 and C–3. Acetylation of the other monoacetonide (IVa) afforded an acetonide triacetate (IVb), $C_{40}H_{60}O_{10}$, m.p. 237—240°, $[\alpha]_D$ $+2\cdot7°$ ($CHCl_3$). Comparison between the n.m.r. spectra of (IVb) and (IIc) showed transposition of the peaks at τ 5·45 (2H, s) and 4·97 (1H, d, J 4c./sec.) in (IIc) to τ 6·18 (2H, s) and 6·07 (1H, d, J 8·5 c./sec.) in (IVb), respectively, and suggested that the acetonide linkage was formed between the 3β- and 24-hydroxy-groups.

From the above chemical results, the structure of platycodigenin is 2β,3β,16α,23,24-pentahydroxyolean-12-en-28-oic acid (IIa),‡ the first example of a geminal di(hydroxymethyl) group at C–4 in naturally occurring triterpenes. Unusual chemical properties result from the crowded hydroxy-groups of (IIa), which will be described in a full publication.

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‡ Just before this communication was submitted, T. Akiyama, Y. Iitaka, and O. Tanaka (*Tetrahedron Letters*, 1968, 5577) have reported that their group reached the same conclusion as ours by *X*-ray diffraction studies of a derivative of platycodigenin.

[1] M. Tsujimoto, *J. Agric. Chem. Soc. Japan*, 1940, **16**, 613 and earlier papers.
[2] T. Kubota and H. Kitatani, *Chem. Comm.*, 1968, 1005.