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STRUCTURE OF PLATICODIGENIN, A SAPOGENIN OF PLATYCODON GRANDIFLORUM A.DE CANDOLLE

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Recently, the isolation of polygalacic acid (I)(1) and a sapogenin(II) with an unknown structure from the hydrolysate of saponins of the roots of Platycodon grandiflorum (Japanese name: Kikyo 桔梗) has been reported, and the configuration of the hydroxyl at C-16 of I has been revised to be α (axial) by Kubota et al.(2) and by the present authors(3). As already reported(3), the sapogenin(II), colourless needles, $C_{30}H_{48}O_7$, mp 241-242°, $/\alpha/_D^{25}$ +35.3°(pyridine), which is assumed to be identical with platicodigenin, $C_{30}H_{48}O_7$, mp 241-242°, previously isolated by Tsujimoto from the same plant source(4), formed a methyl ester(III), colourless needles, mp 246°, $/\alpha/_D^{25}$ +45.0°(pyridine), a methyl ester triacetate(IV), colourless needles, mp 189-190°, $/\alpha/_D^{15}$ +47.2°($CHCl_3$), and an amorphous methyl ester penta-acetate(V). Although the direct comparison of our sapogenin(II) with Tsujimoto's sample has not been made, the present authors wish to name II "platicodigenin". The comparison of the chemical properties and the spectral data (Mass, NMR, and IR) of II and its derivatives with those of I and its corresponding derivatives suggested that the sapogenin(II) can be represented by one of the three possible structures, 2β,3β,16α,23,24-, 2β,3β,16α,23,25-, and 2β,3β,16α,24,25-pentahydroxyolean-12-en-28-oic acids. This communication deals with the X-ray crystallographic determination of the bromolactone(VI)(vide infra), on which the structure of platicodigenin has been established as being II.

Like the known olean-12-en-28-oic acid type triterpenes (5), II yielded a bromolactone(VI), mp 203-206°, $/\alpha/_D^{30}$ +45.9°(pyridine), $IR\nu_{max}^{KBr}$ 1760cm^{-1} by the action of Br_2-NaOAc in acetic acid. The crystal of VI with an appropriate size

grown from a mixture of ethyl acetate and benzene is a colourless monoclinic needle elongated along the b-axis containing one equivalent mole of benzene as a solvent of crystallization. The composition of the crystal was therefore determined to be $C_{30}H_{47}O_7Br \cdot C_6H_6$ (mol. wt. 677.3). The lattice constants (a=16.81Å, b=7.49Å, c=13.52Å, β=103.3°) and space group($P2_1$) were determined from precession photographs taken with CuKα radiation. The density measured by the flotation method using the mixture of CCl_4 and benzene was 1.364 $g.cm^{-3}$ which agrees well with the calculated value 1.359 $g.cm^{-3}$ assuming that two structure units are contained in the unit cell. Three-dimensional diffraction data were recorded on multiple film equi-inclination Weissenberg photographs taken with CuKα radiation of the layers zero through fifth about the b-axis and zero through third about the a-axis. A total of 2205 independent observed structure factors were derived by visual estimation of the intensities using calibrated intensity scales. The structure was solved by the heavy atom method with the use of several repeated cycles of Fourier and difference Fourier syntheses coupled with the structure factor calculations. Refinement of the structural parameters was made by the block-matrix least-squares calculations to an R value of 0.16, in which anisotropic thermal vibrations of the bromine atoms were allowed for. The absolute configuration was determined by utilizing the anomalous dispersion effect of the bromine atom for CuKα radiation. The molecular structure of VI determined by the present X-ray analysis is shown in Fig. 1, which is drawn with the correct absolute configuration.

Consequently, the structure of platicodigenin(II) can be unequivocally formulated as 2β,3β,16α,23,24-pentahydroxyolean-12-en-28-oic acid, which is the first example of the naturally occurring triterpene having geminal hydroxymethyl groups at C-4 of A-ring. The NMR spectra of the derivatives(III-V)(3) are consistent with the formulations given in the chart, respectively.

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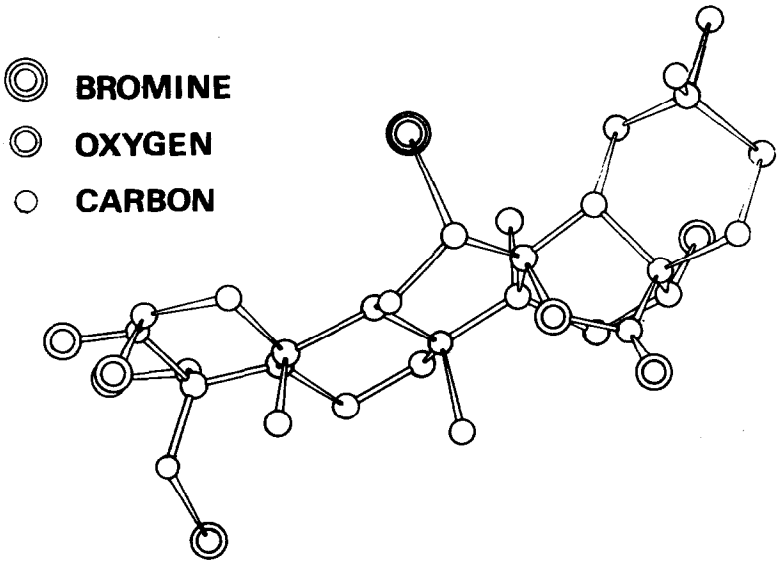
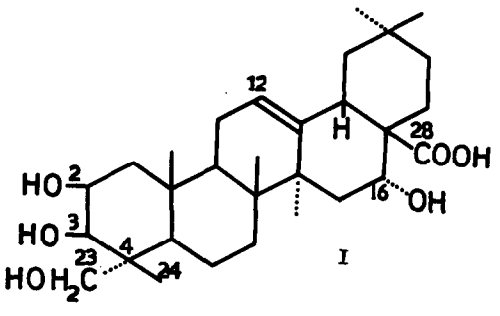
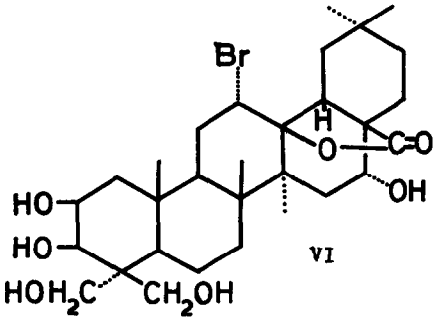


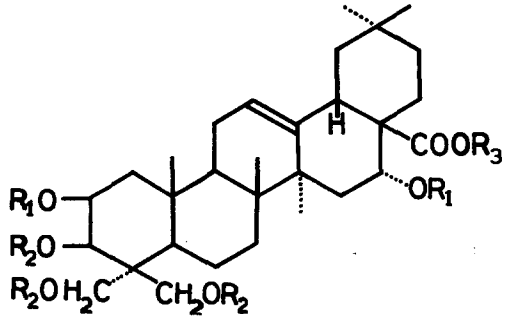
Fig. 1 The Molecular Structure of VI



I



VI



II: $R_1=R_2=R_3=H$

III: $R_1=R_2=H$, $R_3=CH_3$

IV: $R_1=H$, $R_2=Ac$, $R_3=CH_3$

V: $R_1=R_2=Ac$, $R_3=CH_3$

the early stage of the X-ray analysis. Thanks are due to the staffs of C. Itoh Electronic Computing Service Co.Ltd. for making the CDC 3600 computer available to us. This work was supported by the grants from Hohansha and Takeda Science Foundation.

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