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THE STRUCTURE OF JEGOSAPOGENOL

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In spite of extensive studies (1,2), the chemical structure of jegosaponin, a fish poison from Styrax japonica Sieb. et Zucc., has not yet been established (3). We now wish to report that jegosapogenol should be formulated as 3β,16α,21β,22α,28-pentahydroxy-olean-12-ene (Ia).

Acid hydrolysis of jegosaponin gave two equivalents each of glucuronic acid and glucose as well as a sapogenin, which, on digestion with alkali, was hydrolyzed to jegosapogenol (Ia), $C_{30}H_{50}O_5$, mp. 326-330° (decomp.), $[\alpha]_D$ +30° (c,

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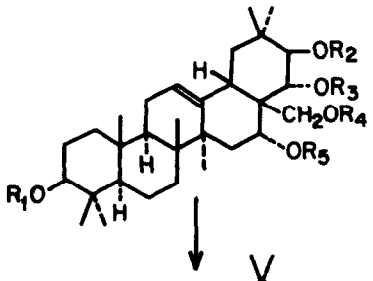
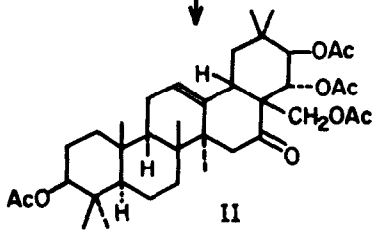
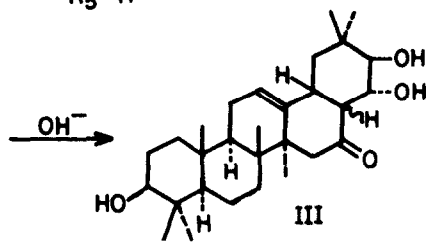


Ia : $R_1=R_2=R_3=R_4=R_5=H$
Ib : $R_1=R_2=R_3=R_4=R_5=Ac$
Ic : $R_1=R_2=R_3=R_4=Ac$, $R_5=H$
Id : $R_1=R_3=R_4=Ac$, $R_2=R_5=H$
Ie : $R_1=R_3=R_4=Ac$, $R_2=SO_2CH_3$, $R_5=H$



II



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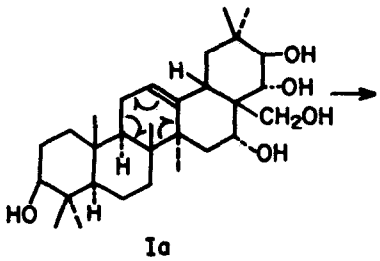
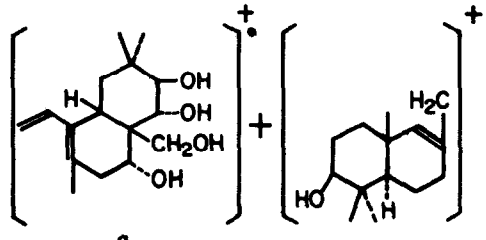
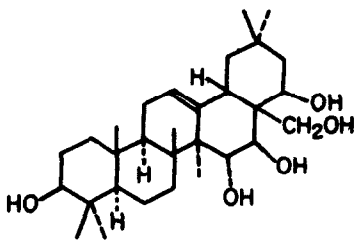


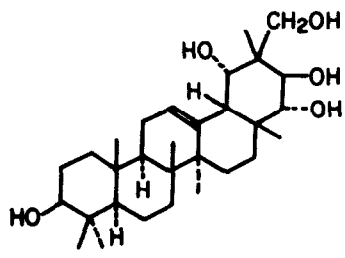
Ia



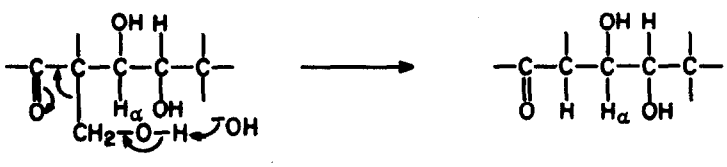
a b



IV



V



A B

0.64, in pyridine), $\lambda_{max}^{95\% \text{ EtOH}}$ 203 mμ (ε, 6000), and tiglic acid. On being refluxed with acetic anhydride jegosapogenol afforded a penta-acetate (Ib), $C_{40}H_{60}O_{10}$, m.p. 154-156°, $[\alpha]_D$ +28° (c, 1.16). Its NMR spectrum (100 Mc, in benzene) showed signals at 4.38 (2H, singlet, two $\geq$C<u>H</u>OAc), 4.50 (1H, multiplet, $\geq$C<u>H</u>OAc), 4.70 (1H, multiplet, double bond), 5.28 (1H, quartet, J = 6.5 and 12 cps, $\geq$C<u>H</u>OAc), 6.12 (2H, AB quartet, J = 13 cps, -C<u>H</u>$_2$OAc), 7.85, 8.18, 8.21, 8.22, and 8.23 (15H, singlets, five -OCOC<u>H</u>$_3$), 8.68, 8.89, 9.02, 9.10, 9.11, 9.18, and 9.21 τ (21H, singlets, seven $\geq$C-C<u>H</u>$_3$), which indicated that the oxygen functions are present as one primary and four secondary alcohols.

The mass spectrum of jegosapogenol (Ia) gave peaks at <u>m</u>/<u>e</u> 490 (M^+), 282 (<u>a</u>), 264 (<u>a</u>-H_2O), 246 (<u>a</u>-$2H_2O$), 215 [<u>a</u>-($2H_2O$+CH_2OH)], 207 (<u>b</u>), and 197 [<u>a</u>-($3H_2O$+CH_2OH)], a fragmentation pattern characteristic of either α- or β-amyrin derivatives (4).

The detection of seven quaternary C-methyl groups as sharp singlets in the NMR spectrum of the penta-acetate (Ib) suggested that jegosapogenol is a β-amyrin-type triterpene alcohol. Since the mass of the mass spectrometric retro-Diels-Alder fragment <u>a</u> (<u>m</u>/<u>e</u> 282) showed the incorporation of four hydroxyl groups and on the assumption that the remaining one is located at C-3, one can conclude that one primary and three secondary hydroxyl groups are located on rings D and E, as indicated in structure Ia.

Acetylation of Ia with pyridine-acetic anhydride afforded a tetra-acetate (Ic), $C_{38}H_{58}O_9$, m.p. 234°, $[\alpha]_D$ +33° (c, 1.31),

NMR (100 Mc, in $CDCl_3$), 4.39 (1H, doublet, J = 10 cps, $\rangle C\underline{H}OAc$), 4.60 (1H, doublet, J = 10 cps, $\rangle C\underline{H}OAc$), 4.61 (1H, multiplet, double bond at C-12), 5.48 (1H, triplet, J = 8 cps, $\rangle C\underline{H}OAc$ at C-3), 5.81 (1H, multiplet, $\rangle C\underline{H}OH$), 6.33 (2H, singlet, $-C\underline{H}_2OAc$), 7.94 (3H), 7.95 (3H), and 7.98 (6H) τ (singlets, four $-OCOCH_3$). Two doublet signals at 4.39 and 4.60 τ with a diaxial coupling (J = 10 cps) confirmed the presence of a diequatorial α-glycol* whose neighboring carbon atoms are both quaternary.

The unusually low field position (8.57 and 8.54 τ respectively) of one quaternary C-methyl observed in the tri-(Id) and the tetra-acetate (Ic) suggests that one methyl group is deshielded by an axial hydroxyl group in a 1,3-diaxial relationship (5) to it. An up-field shift (4 ~ 11 cps) of this methyl signal should be observed on acetylation, which indeed was the case (8.68 τ) in the penta-acetate (Ib). The axial nature (6) of the non-acetylated hydroxyl group in the tetra-acetate (Ic) was further substantiated by the fact that it was readily oxidized with chromium trioxide-pyridine complex to the ketone II, $C_{38}H_{56}O_9$, m.p. 281-285°, $[\alpha]_D$ -30° (c, 1.43), $\nu_{max}^{CHCl_3}$ 1745 cm^{-1} (OAc) and 1724 cm^{-1} (C=O).

On treatment with alkali the ketone (II) underwent a retro-aldol reaction (7) to furnish the nor-ketone (III), $C_{29}H_{46}O_4$, m.p. 245-246°, $[\alpha]_D$ -25° (c, 0.78), which showed the

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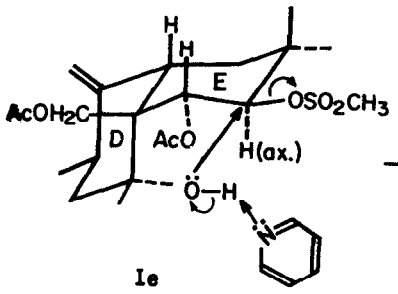
* Jegosapogenol consumed about one mole of lead tetra-acetate in acetic acid at room temperature to furnish a hemiacetal, m.p. 206-207°, which was further characterized as the keto-lactone, $C_{30}H_{42}O_5$, m.p. 290°. Details of this reaction will be reported in a full paper.

absence of a primary hydroxyl group in its NMR spectrum (60 Mc, in pyridine), 4.43 (1H, multiplet, double bond at C-12), 5.81 (1H, triplet, J = 9 cps, $\geq$C<u>H</u>OH), 6.48 (1H, doublet, J = 9 cps, $\geq$C<u>H</u>OH), 6.51 (1H, triplet, J = 8 cps, $\geq$C<u>H</u>OH at C-3), 8.71, 8.75, 8.85, 8.89, 8.94, 9.03, and 9.15 τ (21H, singlets, seven $\geq$C-C<u>H</u>$_3$). Here, one of the two protons in the α-glycol system, H_α exhibits a triplet-signal at 5.81 τ due to the coupling with an adjacent newly generated proton (see B). Thus, the moiety (A) must be present in the molecule of jegosapogenol.

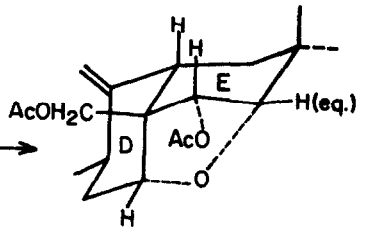
On the basis of the foregoing results, three structures (Ia, IV, and V) are possible for jegosapogenol. However, detection of seven quaternary C-methyl groups as sharp singlets in the NMR spectrum of the nor-ketone III excludes structure V.

The correctness of structure Ia for jegosapogenol was further verified by the following experiments.

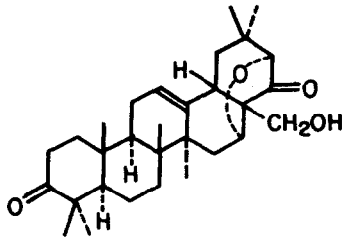
Acetylation of jegosapogenol with acetic anhydride-pyridine under controlled condition yielded a triacetate (Id), $C_{36}H_{56}O_8$, m.p. 245-247°, $[\alpha]_D$ +11° (c, 1.33), <u>m</u>/<u>e</u> 616 (M^+), NMR (60 Mc, in $CDCl_3$), 4.60 (1H, multiplet, double bond at C-12), 4.72 (1H, doublet, J = 10 cps, $\geq$C<u>H</u>OAc at C-22), 5.44 (1H, triplet, J = 8 cps, $\geq$C<u>H</u>OAc at C-3), 5.79 (1H, multiplet, $\geq$C<u>H</u>OH at C-16), 5.97 (1H, doublet, J = 10 cps, $\geq$C<u>H</u>OH at C-21), 6.30 (2H, singlet, -C<u>H</u>$_2$OAc at C-28), 7.88 (3H, singlet, -OCO-C<u>H</u>$_3$), and 7.94 τ (6H, singlet, two -OCOC<u>H</u>$_3$). The triacetate Id was transformed with pyridine-methanesulfonyl chloride at room temperature into a monomesylate (Ie), $C_{37}H_{58}O_{10}S$, m.p. 168-169°, $[\alpha]_D$ +46° (c, 0.75), NMR (60 Mc, in $CDCl_3$), 4.64



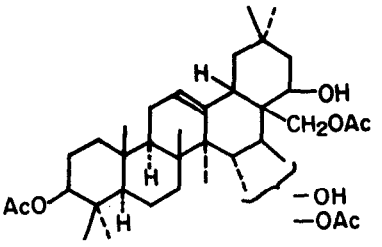
Ie



VI



VII



VIII

(1H, doublet, J = 10 cps), 4.66 (1H, doublet, J = 10 cps), and 7.00 τ (3H, singlet, $-OSO_2C\underline{H}_3$ at C-21). Refluxing of this monomesylate with pyridine led to an epoxide [$C_{36}H_{54}O_7$, m.p. 235-236°, $[\alpha]_D$ +58° (c, 1.11), m/e 598 (M^+), NMR (60 Mc, in $CDCl_3$), 4.70 (1H, multiplet, double bond at C-12), 4.70 (1H, singlet, $\geq C\underline{H}OAc$ at C-22), 5.47 (1H, triplet, J = 7 cps, $\geq C\underline{H}OAc$ at C-3), 5.72 (1H, multiplet, $\geq C\underline{H}$-O- at C-16), 6.03 (2H, AB quartet, J = 11 cps, $-C\underline{H}_2OAc$ at C-28), and 6.40 τ (1H, singlet, $\geq C\underline{H}$-O- at C-21], whose genesis is formulated by structures Ie → VI.

The constitution of the epoxide (VI)* was further supported by the fact that the derived diketone VII, m.p. 217-220°, showed a five-membered carbonyl infrared band at 1753

cm^{-1} in addition to a six-membered ketone absorption at 1703 cm^{-1}. Work to correlate jegosapogenol with a known triterpene is now in progress.

Melting points are uncorrected. All compounds described gave satisfactory elemental analyses. Unless otherwise noted, all rotations were taken in chloroform solution. The 100 Mc and the 60 Mc NMR spectra were obtained with Varian HR-100 and A-60 spectrometers, respectively, using TMS as an internal standard, while the mass spectra were determined at 70 ev with a CEC model 21-103C mass spectrometer equipped with a direct inlet system (8).

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* If strucure IV were the correct one for jegosapogenol, its triacetate would be VIII which can not yield an epoxide analogous to VI.

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