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CONSTITUTION OF PROCERAGENIN A - A TRITERPENOID SAPOGENIN FROM ALBIZZIA PROCERA BENTH*

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The isolation of proceragenin A (Ia) $[C_{30}H_{46}O_4$ m.p.294-296°, $[\alpha]_D^{26}$ - 13° ($CHCl_3$); $\bar{\nu}$ in cm^{-1} (KBr) : 3550 (OH); 1765 (a five-membered lactone); 1360, 1380 (gem-dimethyl). Anal. calc. for $C_{30}H_{46}O_4$: C, 76.59; H, 9.78; found: C, 76.34 ; H, 9.74], a triterpenoid sapogenin, from the seeds of Albizzia procera Benth was reported in a preliminary communication[1]. This paper deals with its structure elucidation.

The ethanolic extract of the defatted seeds of A. procera furnished a good amount of saponin, which on hydrolysis with ethanolic hydrochloric acid gave acid and neutral sapogenins. The acid sapogenin fraction on treatment with ethereal diazomethane and subsequent chromatographic resolution over acid-washed alumina afforded proceragenin A as one of the constituents. Proceragenin A

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was also obtained from neutral sapogenin fraction on column chromatography over acid-washed alumina. Proceragenin A, on hydrolysis with alcoholic caustic potash, yielded an acid, which on treatment with diazomethane or on standing with alcoholic hydrochloric acid gave back proceragenin A. This is perhaps the reason why proceragenin A is encountered from both the acid and neutral sapogenin fractions during isolation.

Proceragenin A (Ia), when treated with pyridine and acetic anhydride at 0°, furnished a mixture of diacetate (Ic) $[C_{34}H_{50}O_6$, m.p. 246-248°, $[\alpha]_D^{26}$ - 38° ($CHCl_3$); $\bar{\nu}$ in cm^{-1} (KBr) : 1750 (a five-membered lactone) ; 1725, 1240 (acetate carbonyl)] and monoacetate (Ib) $[C_{32}H_{48}O_5$, m.p. 301-304°, $[\alpha]_D^{30}$ - 10° ($CHCl_3$); $\bar{\nu}$ in cm^{-1} (KBr): 3600 (OH) ; 1765 (a five-membered lactone) ; 1720, 1240 (acetate carbonyl)]. Acetylation of Ia or of Ib on steam-bath furnished only Ic. Ib on oxidation with chromium trioxide-acetic acid at room temperature afforded a neutral keto monoacetate (Id) $[C_{32}H_{46}O_5$, m.p. 296-302° (decomp.); $\bar{\nu}$ in cm^{-1} (KBr): 1765 (a five-membered lactone); 1720, 1240 (acetate carbonyl)] Thus all the four oxygen atoms in proceragenin A are accounted for as forming part of two hydroxyl groups and one lactone ring.

The ethylenic linkage in Ia, indicated by tetranitromethane colour, is very hindered. Ic did neither react with perbenzoic acid[2] nor did it react with selenium dioxide[3,4,5,6,7].

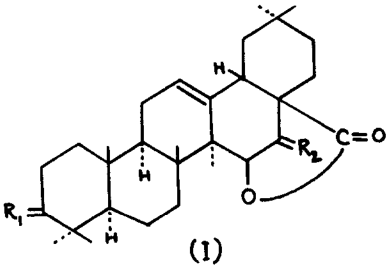
Lithium aluminium hydride reduction of Ia furnished a tetrol (IIa) $[C_{30}H_{50}O_4$, m.p.306-310°, $[\alpha]_D^{35}$ + 18.11° (pyridine);

$\bar{\nu}$ in cm^{-1} (KBr): 3400 (OH)_7 which on acetylation by pyridine and acetic anhydride on steam-bath gave a triacetate (IIb) $C_{36}H_{56}O_7$, m.p. 197-199°, $[\alpha]_D^{28}$ + 43.2° ($CHCl_3$); $\bar{\nu}$ in cm^{-1} (KBr): 3500 (OH); 1720, 1240 (acetate carbonyl)_7. This clearly indicated that one of the newly formed hydroxyl groups in the tetrol is highly hindered and cannot be acetylated under the above condition. The tetrol triacetate (IIb) consumed one mole of perbenzoic acid at a rate typical of the triterpenes of the β-amyrin group having a double bond at 12:13 position. The unusually hindered nature of the ethylenic linkage in proceragenin A must be then due to the shielding effect of the lactone ring[5]. The tetrol triacetate on oxidation with chromium trioxide-acetic acid at room temperature furnished a monoketotriacetate (IIc) $C_{36}H_{54}O_7$, m.p. 226-228°, $[\alpha]_D^{33}$ + 13.88° ($CHCl_3$); $\bar{\nu}$ in cm^{-1} (KBr) : 1720, 1240 (acetate carbonyl)_7 which on reduction with lithium aluminium hydride furnished the tetrol (IIa). Evidence for the typical 12:13 double bond of the α or β-amyrin nucleus was obtained by oxidation of either IIb or IIc with chromium trioxide - acetic acid on steam-bath to yield an α,β -unsaturated ketone (IId) $C_{36}H_{52}O_8$, m.p. 265-267°, λ_{max} 243 mμ (log ε 4.1); $\bar{\nu}$ in cm^{-1} (KBr): 1665 (α,β -unsaturated ketone)_7. The u.v. absorption maximum is slightly at a lower wave length than is usually observed for 11-keto Δ^{12}-triterpenes of the β-amyrin series[8]. Lithium aluminium hydride reduction and subsequent acid treatment of the α,β -unsaturated ketone (IId) furnished a diene showing triple ultraviolet absorption maxima at 243, 251, 261 mμ characteristic

of $\Delta^{11:12,\ 13:18}$-dienes from β-amyrin type of compounds. On the basis of above observations, it is concluded that proceragenin A is a triterpene belonging to the β-amyrin group, having a double bond at the 12:13 position.

Proceragenin A did not consume any periodic acid which showed the absence of any α-glycol system. Oxidation of Ia with chromium trioxide-acetic acid at room temperature furnished a colourless neutral diketone (Ie) $[C_{30}H_{42}O_4$, m.p. 308-312° (decomp.); $\bar{\nu}$ in cm^{-1} (KBr): 1770 (five-membered lactone); 1710 (six-membered ring ketone)$]$. Formation of this diketone clearly demonstrated that both the hydroxyl groups in Ia are secondary in nature. The absence of an α-diketone or an enolizable α or β -diketone system in the above oxidation product was shown by negative ferric chloride test. The diketone (Ie) gave positive Zimmermann colour test[9] for 3-keto group thus showing the presence of one secondary hydroxyl group at C_3 position in proceragenin A and eliminating the possibility of any substitution at C_2. Moreover, as the oxidation product was not an α- or β-diketone, the second free hydroxyl group could not be attached to C_1 or C_2.

Id and Ie on heating with alkali furnished a pale yellow product which gave violet colour with alcoholic ferric chloride and showed absorption maximum at 281 mμ (log ε 3.5). But low molecular extinction value suggested that only a very small amount of diosphenol was formed during saponification. The formation of the above diosphenol can only be explained if the



(I)

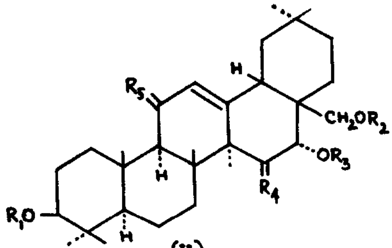
a, $R_1 = $ OH (β), H (α), $R_2 = $ OH (α), H (β)

b, $R_1 = $ $OCOCH_3$ (β), H (α), $R_2 = $ OH (α), H (β)

c, $R_1 = $ $OCOCH_3$ (β), H (α), $R_2 = $ $OCOCH_3$ (α), H (β)

d, $R_1 = $ $OCOCH_3$ (β), H (α), $R_2 = O$

e, $R_1 = R_2 = O$



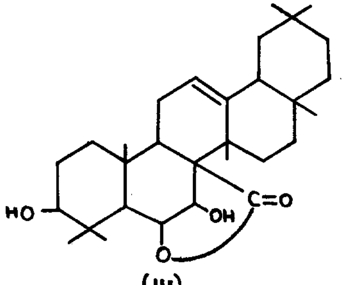
(II)

a, $R_1 = R_2 = R_3 = H$, $R_4 = $ OH (β), H (α), $R_5 = H_2$

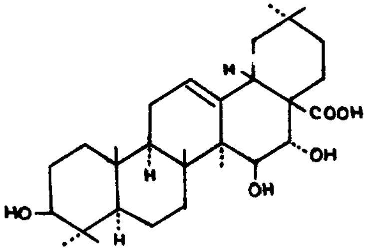
b, $R_1 = R_2 = R_3 = COCH_3$, $R_4 = $ OH (β), H (α), $R_5 = H_2$

c, $R_1 = R_2 = R_3 = COCH_3$, $R_4 = O$, $R_5 = H_2$

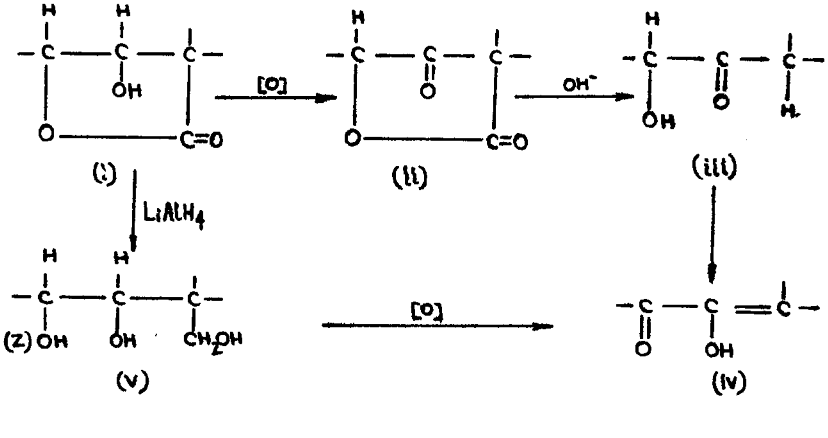
d, $R_1 = R_2 = R_3 = COCH_3$, $R_4 = R_5 = O$



(III)



(IV)



relative position of one of the hydroxyl groups and the lactone ring in Ia be as shown in (i). Thus the diketoproceragenin A should have the moiety (ii) which on saponification would furnish the α-ketol (iii). The latter being susceptible to aerial oxidation in alkaline medium, may furnish, in low yield, the diosphenol which should have the moiety (iv).

The above conclusion is further strengthened by the fact that the tetrol (IIa) did consume one mole of periodic acid whereas Ia was inert to this reagent. Thus the tetrol must have the moiety (v). The newly formed secondary hydroxyl group may for the sake of convenience be designated as Z-hydroxyl group which has previously been shown to be highly hindered. The tetrol (IIa) on oxidation with chromium trioxide-acetic acid furnished a yellow amorphous product which gave a violet colour with alcoholic ferric chloride and showed absorption maximum at 281 mμ (log ϵ 4.0).

The above observations clearly show proceragenin A to be a dihydroxy (secondary) pentacyclic (excluding the lactone ring) triterpene γ-lactone of the oleanane series with a 12:13 double bond. One of the hydroxyl groups has already been located at C_3 position and the other in the moiety (i). The moiety (i) cannot be in ring A because diketoproceragenin A (Ie) responded to Zimmermann test and it was neither an α or β diketone. None of the free hydroxyl groups of Ia can be located at C_6 (cf. sumaresinolic acid[10]), C_{15} (see paper on dumortierigenin[5]) and C_{19} (cf. siaresinolic acid[11] and tomentosic acid[12]) as the

hydroxyl groups (whether α or β) at these positions are highly hindered and cannot be acetylated by pyridine and acetic anhydride on steam-bath. Necessarily the Z-hydroxyl group in the tetrol (IIa) which could not be acetylated by pyridine and acetic anhydride on steam-bath, must be situated in any of the positions C_6, C_{15} and C_{19}. Further the potential carboxyl group of proceragenin A (Ia) must be in 1:3 diaxial position with the 'Z'-OH group to account for the spontaneous lactonisation of the acid (IV). With these evidences at hand it is possible to deduce the permissible structural expressions for proceragenin A as I and III. Of these two structures, the former (I) appears to be more probable on biogenetic ground as C_{17} is the usual site for a carboxyl function in a triterpene of the oleanane series rather than at C_8. In fact, uptil now no triterpene has been reported from nature in which there is a carboxyl or any oxygen function attached to C_8.

The carboxyl group attached to C_{17} in triterpenes of the oleanolic acid group is axial β and the 28 ⟶ 15 lactone formation requires the potential hydroxyl group at C_{15} to be axial (β). The axial nature of the C_{15} hydroxyl is further substantiated by the formation of the tetrol (IIa) from monoketo triacetate (IIc) by the expected axial reduction (Lithium aluminium-hydride) of the highly hindered 15-keto group. The ease of acetylation (at 0°) of the C_3-OH of proceragenin A suggests a normal equatorial (β) orientation. The low molecular rotation difference (+ 9.9°) of Ia and Ib is comparable to those of 3β-oriented alcohols and their acetates.

The fact that the C_{16} hydroxyl group in proceragenin A resisted acetylation at 0° suggests its axial (α) configuration. Further the high negative Δ_1 value (- 159.32°) of C_{16} hydroxyl group of proceragenin A also calls for its axial configuration (cf. methyl echinocystate and genin A).

The above discussions show proceragenin A to be 28 ⟶ 15 lactone of 15β, 16α-dihydroxy oleanolic acid (IV). IV is a new triterpene acid and is one of the constituents of the acid sapogenin fraction of A. procera. Though proceragenin A is a facile lactonisation product of IV, it is difficult to prove that it is not at all occurring in nature.

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