Configuration of Echinocystic and Cochalic Acids

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Summary The structures of echinocystic and cochalic acids were confirmed as 3β,16β-dihydroxyolean-12-en-28-oic acid and 3β,16α-dihydroxyolean-12-en-28-oic acid respectively, by comparing the ease of acetonide formation of the corresponding triols.

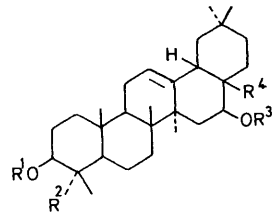
OUR recent studies,[1] based on acetonide formation by the 16- and 28-hydroxy functions of the tetrol (**1**) derived from quillaic acid (**2**), have suggested that the 16-OH is β-oriented. Since the configuration of the 16-OH in quillaic and echinocystic acids (**3**) was found to be identical,[2] we have proposed the 16β-configuration for the latter acid, *i.e.*, contrary to the currently accepted formula.[3]

Recently St. Pyrek[4] described acetonide formation from olean-12-ene-16α,28- and 16β,28-diols, claiming that the change in conformation of ring D from the chair to the boat form permits acetonide formation in the *trans*-oriented diol, *i.e.*, olean-12-ene-16α,28-diol.

These results induced us to confirm our previous assignment of the two epimers, the echinocystic and cochalic acids, by studying acetonide formation of the two isomeric triols derived from them.

Echinocystic acid (**3**) was obtained by Wolff–Kishner reduction of quillaic aid. Acetylation with equimolar acetic anhydride (room temp., 24 h) yielded the 3-acetoxy-echinocystic acid (**4**), *m/e* 514 (M^+), 496 ($M - H_2O$), 454 (M — HOAc), 452 (496-CO_2), 392 (452-HOAc), 264 (retro Diels–Alder). Methylation with diazomethane followed by Jones oxidation yielded the 16-ketone (**8**),[5] which was reduced with $NaBH_4$ in propan-2-ol, (reflux, 24 h), to a mixture of the corresponding 16α- and β-alcohols, which could not be separated by t.l.c. Methanolic KOH hydrolysis of the mixture yielded two isomeric acids, in a ratio of 10:1 in favour of the less polar isomer. Separation was done by column chromatography. The less polar acid was identified as the starting echinocystic acid (**3**). The more polar isomer was shown to be its 16-epimer, cochalic acid (**6**), m.p. 300—304°, $[\alpha]_D$ + 56° (dioxan) (lit.[3] m.p. 303—306°, $[\alpha]_D$ + 58°). The identity of the cochalic acid was further confirmed by CrO_3 oxidation of its methyl ester into diketoechinocystic acid methyl ester, which was identical in all respects with the diketone obtained from methyl echinocystate. Acetylation of the two acids followed by methylation led to the two isomeric diacetate methyl esters, which were reduced to the corresponding triols of echinocystic acid, primulagenin (**5**),[6] and of cochalic acid, longispinogenin (**7**).[7]

Primulagenin (**5**) on treatment with 2,2-dimethoxypropane in dry acetone in the presence of *p*-toluenesulphonic acid (10^{-4}M) led to the acetonide (**9**) (60%), m.p. 231—234°, $[\alpha]_D$ + 19° (chloroform); *m/e* 498 (M^+), 483 ($M - CH_3$), 440 (M-Me_2CO), 290 (retro Diels–Alder); ^{1}H n.m.r. ($CDCl_3$) δ 1·4 (6H broad s, $OCMe_2O$), 3·1—4·2 [4H, C(3)H, C(16)H,



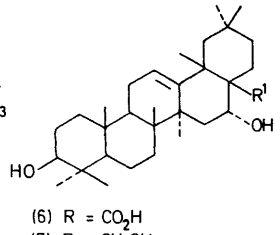
(1) $R^1=R^3=H, R^2=R^4=CH_2OH$

(2) $R^1=R^3=H, R^2=CHO, R^4=CO_2H$

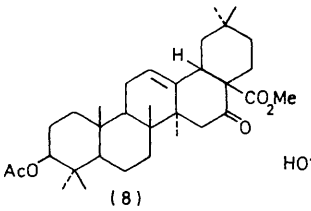
(3) $R^1=H, R^2=Me, R^3=H, R^4=CO_2H$

(4) $R^1=Ac, R^2=Me, R^3=H, R^4=CO_2H$

(5) $R^1=R^3=H, R^2=Me, R^4=CH_2OH$



(6) $R = CO_2H$
(7) $R = CH_2OH$



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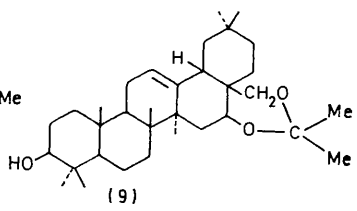

(9)

C(28)H_2], 5·4 [1H, m, C(12)H]. Acid hydrolysis of the acetonide yielded the original triol (**5**). Longispinogenin (**7**)‡ treated under similar conditions with 2,2-dimethoxypropane failed to produce any acetonide. Traces of an acetonide could however be detected when a tenfold concentration of *p*-toluenesulphonic acid was used.

These results show that primulagenin (**5**) yields an acetonide under very mild reaction conditions while longispinogenin (**7**) may form this product only when higher acid concentrations are used. These findings conform with those of St. Pyrek,[4] according to which primulagenin yields twice as much acetonide as longispinogenin. The n.m.r. data cited there, which were confirmed by us, do not support either stereochemical assignment of the 16-OH. Inspection of Dreiding models shows that olean-12-ene-16β,28-diols can easily yield acetonides in all possible conformations of ring D, while the 16α-OH epimers will form these products only *via* the boat conformation.

Since the reaction with primulagenin proceeds so much more easily than with longispinogenin, we must conclude that the former is the 16β-OH isomer and the latter has the 16α-OH configuration.

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‡ All analytical data are in accordance with those published in the literature.

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