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LYCOCLAVANOL AND SERRATRIOL

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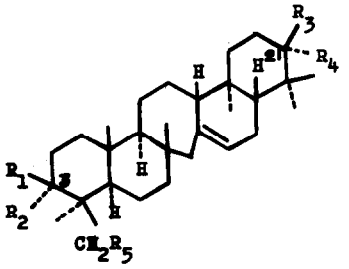
THIS communication is concerned with the constitution and the stereochemistry of two stereoisomeric triterpenoid-triols, lycoclavanol and serratriol, the former being obtained from Lycopodium clavatum[1] and the latter from Lycopodium serratum[2].

Lycoclavanol (I), m.p. 308-310°, and serratriol (II), m.p. 335-336°, have the same composition $C_{30}H_{50}O_3$, and form the triacetates, $C_{36}H_{56}O_6$, (III) m.p. 197-198°, and (IV) m.p. 245-247°, respectively. The NMR spectra*1 of the triacetates (III: $-\overset{|}{C}-CH_3$, 0.70 (3H), 0.85 (9H), 0.95 (6H); $-OCO\underline{CH_3}$, 2.05 (3H), 2.08 (6H); $-\overset{|}{C}-\underline{CH_2}-OAc$, 4.09 (2H, ABq., δ_{AB}=18 cps. J=12 cps.); $>\underline{CH}-OAc$, 4.70 (1H, broad s.), 4.94 (1H, broad s.); $>C=\underline{CH}-$, 5.37 (1H, m.). IV: $-\overset{|}{C}-CH_3$, 0.70 (3H), 0.85 (9H), 0.90 (3H), 1.00 (3H); $-OCO\underline{CH_3}$, 2.03 (3H), 2.05 (6H); $-\overset{|}{C}-\underline{CH_2}-$OAc, 4.24 (2H, ABq. δ_{AB}=19 cps., J=12 cps.); $>\underline{CH}-OAc$, 4.51 (2H, m.); $>C=\underline{CH}-$, 5.35 (1H, m.)) indicated that the parent triterpenoids contain six C-methyl, two secondary and one primary hydroxyl groups, and one trisubstituted double bond. The similarity of the spectra with that of serratenediol diacetate[3] except that they have six instead of seven C-methyls and one its oxidative

*1 NMR spectra were taken on 60 Mc machine as $CDCl_3$ solutions and chemical shifts are presented by δ(ppm) from an internal tetramethylsilane.



LC series (R_1=R_4=H)

(I) R_2=R_3=R_5=OH

(III) R_2=R_3=R_5=OAc

(V) R_2=R_3=OH , R_5=OAc

(VI) R_1,R_2=R_3,R_4=O , R_5=OAc

(VIII) R_2=R_3=H , H for CH_2R_5

(XVII) R_2=R_3=OAc , R_5=OH

(XVIII) R_2=OH , R_3=R_5=OAc

(XIX) R_2=R_3=OAc , CHO for CH_2R_5

(XX) R_1,R_2=O , R_3=R_5=OAc

(XXI) R_2=R_3=OAc , R_5=H

ST series (R_2=R_3=H)

(II) R_1=R_4=R_5=OH

(IV) R_1=R_4=R_5=OAc

(VII) R_1,R_2=R_3,R_4=O , R_5=H

(XIII) R_1=R_5=OAc , R_3,R_4=O

(XIV) R_1=R_5=OAc , R_4=OH

(XV) R_1=OH , R_4=R_5=OAc

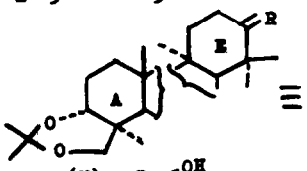
(XVI) R_1,R_2=O , R_4=R_5=OAc

(XXIII) R_1=R_5=OH , R_4=OAc

(XXIV) R_1=OH , R_4=OAc , R_5=OTs

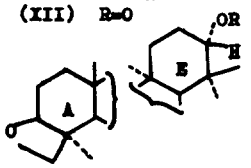
(XXV) R_1=R_5=OTs , R_4=OAc

(XXVIII) R_1=R_4=OH , R_5=H



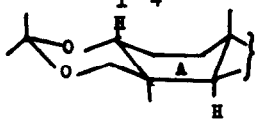
(X) R=$\lessgtr^{OH}_{H}$

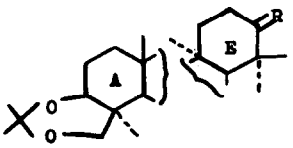
(XII) R=O



(XXVI) R=Ac

(XXVII) R=H





(IX) R=$\lessgtr^{OH}_{H}$

(XI) R=O

(XXII) R=$\lessgtr^{OAc}_{H}$

equivalent implies that they are derivatives of serratene.

That lycoclavanol and serratriol differ only in the stereochemistry of either or both the secondary hydroxyl groups was demonstrated by the following transformations. Lycoclavanol, when acetylated with acetic anhydride in pyridine at 5° for 30 min., gave a mono-acetate (V), $C_{32}H_{52}O_4$, m.p. 252-254°, NMR: 1 OAc, 2.04, which was oxidized to a diketo-acetate (VI), $C_{32}H_{48}O_4$, m.p. 242-244°, ORD: $[\phi]_{320m\mu}$ -2400°(trough), $[\phi]_{290m\mu}$ +120°(peak). Lithium aluminum hydride reduction of (VI) gave a triol whose triacetate was identical with serratriol triacetate (IV) in all respects.

Here we elaborate the further argument by assuming that serratriol is a hydroxy-serratenediol because the ORD curve of (VI) showed the similar pattern with that of serratenedione (VII)[3], the assumption being proved by conversion of serratriol into serratenediol (see later).

Wolff-Kishner reduction of the diketo-acetate (VI) gave, with loss of CH_2OAc group, a nor-hydrocarbon (VIII), $C_{29}H_{48}$, m.p. 179-182°. Hence the primary hydroxyl group must be at either C 23, 24, 29 or 30.

Serratriol, when allowed to react with 2,2-dimethoxypropane in DMF, formed an acetonide (IX), $C_{33}H_{54}O_3$, m.p. 250-252°, NMR: $(CH_3)_2C<^{O}_{O}$, 1.38 (3H), 1.45 (3H); -C-CH_2-O-C, two doublets at 3.16 and 3.95 (J=12 cps.), >C<u>H</u>-O-C and >C<u>H</u>-OH, 3.38 (2H, m.). Lycoclavanol gave, with some difficulty, an analogous acetonide (X), $C_{33}H_{54}O_3$, m.p. 200-204°, NMR: $(CH_3)_2C<^{O}_{O}$, 1.51 (6H); -C-C<u>H</u>$_2$-O-, 3.74 (2H, ABq., δ_{AB}=18 cps., J=10 cps.), >C<u>H</u>-O-C, 4.41, (1H, t. J=8.5 cps.), >C<u>H</u>-OH, 3.50 (1H, broad s.). Oxidation of the acetonides (IX) and (X) with chromium trioxide-pyridine gave different keto-acetonides of $C_{33}H_{52}O_3$, (XI) m.p. 213-215°, and (XII) m.p. 197-201°, respectively. The negative Cotton effects of both the keto-acetonides, (XI) ($[\phi]_{316m\mu}$ -2240° (trough), $[\phi]_{280m\mu}$ +1170°(peak)) and (XII) ($[\phi]_{316m\mu}$ -1080°(trough)) define

the position of the ketonic function as at C_{21} in each compound, since serraten-21-on-3β-ol acetate gave a negative Cotton effect but serraten-3-one gave a positive one[3]. Hence we can conclude that C_3-hydroxyl groups of serratriol and lycoclavanol are similarly concerned with the acetonide formation, though their stereochemistry is different.

Partial hydrolysis of serratriol triacetate in 3% HCl-EtOH under reflux for 30 min. gave a mixture, from which there were isolated diacetate-a (XIV), $C_{34}H_{54}O_5$, m.p. 249-251°, NMR: 2 OAc, 2.02, 2.05, and diacetate-b (XV), $C_{34}H_{54}O_5$, m.p. 235-237°, NMR: 2 OAc, 2.03 (6H). The diacetate-a, on chromic oxidation, gave the keto-diacetate-a (XIII), $C_{34}H_{52}O_5$, m.p. 245-247°, identical with that obtained from the keto-acetonide (XI). The diacetate-b (XV) gave, on oxidation, keto-diacetate-b (XVI), $C_{34}H_{52}O_5$, m.p. 252-254°, ORD: $[\Phi]_{307m\mu}$ +1220°(peak).

Zemplene's methanolysis of lycoclavanol triacetate yielded diacetate-B (XVII), m.p. 225-227°, NMR: 2 OAc, 2.08 (6H), and diacetate-A (XVIII), m.p. 243-245°, NMR: 2 OAc, 2.05, 2.09, the former being oxidized into an aldehyde-diacetate(XIX), m.p. 191-195°, NMR: 2 OAc, 2.07 (6H), -CHO, 9.73, and the latter to the keto-diacetate (XX), m.p. 235-237°, NMR: 2 OAc, 2.05, 2.14 ORD: $[\Phi]_{308m\mu}$ -550°(peak), $[\Phi]_{274m\mu}$ -1660°(trough). Though XVI and XX are the expected 3-keto-diacetates, as evidenced from their possitive Cotton effects for $n\rightarrow\pi^*$, they were apparently different; a fact which indicates that the stereochemistry of C_{21}-hydroxyl groups of lycoclavanol and serratriol is again different. Wolff-Kishner reduction of XIX gave, on acetylation of the product, diaxial epimer of serratenediol, diepiserratenediol diacetate[4],*2 (XXI), m.p. 236-239°, as expected.

*2 Diepiserratenediol was also isolated from Lycopodium clavatum. (unpublished work by the authors)

An axial orientation of $-CH_2OH$ was suggested from the NMR spectra of its acetyl derivatives which always exhibited a band attributable to $-CH_2OAc$ at 4.23-4.09 ppm. The chemical shift is in agreement with that for axial $-\underline{CH}_2-OAc$ (4.30-4.08 ppm.) rather than equatorial one (3.84-3.77 ppm.)[5]. Hence for the acetonide formation of lycoclavanol, the ring A must have been converted to boat form as depicted. The assignment was supported by changing the coupling pattern of C_3-H signal from a broad singlet (half-width ca. 5 cps.) for (III) etc, to a triplet (J=8.5 cps.) for the acetonide (X). Lycoclavanol and serratriol are therefore concluded to be serrat-14-en-3α,21β,24-triol (I) and serrat-14-en-3β,21α,24-triol (II), respectively.

Correlation of serratriol and serratenediol is as follows. Acetylation of the acetonide (IX) with pyridine and acetic anhydride yielded the acetate (XXII), $C_{35}H_{56}O_4$, m.p.> 300° which on mild acid hydrolysis gave the monoacetate (XXIII), $C_{32}H_{52}O_4$, m.p. > 300°. Tosylation of this with toluene-p-sulfonyl chloride and pyridine gave a mixture of monotosylate (XXIV), $C_{39}H_{58}O_6S$, m.p. 188-189°, and of ditosylate (XXV), $C_{46}H_{64}O_8S_2$, m.p. 185-186°. The monotosylate, on slow chromatography over alumina, was smoothly converted into an oxetane derivative (XXVI), $C_{32}H_{50}O_3$, m.p. 273-275°, NMR: 1 OAc, 2.10, $-\underline{CH}_2-O$, 4.30 (2H, ABq., δ_{AB}=22 cps., J=7 cps.). IR(Nujol): 1720 cm^{-1} (OAc), no OH absorption. The mechanistic consideration and the spectroscopic evidence of this compound clearly indicated the formation of an oxetane ring. The corresponding alcohol (XXVII), $C_{30}H_{48}O_2$, m.p. 254-256°, was also formed when XXIV was treated with lithium aluminum hydride. Prolonged reduction of XXVII with lithium aluminum hydride gave a diol which was found to be identical with serratenediol (XXVIII) by IR comparisons of the corresponding diacetates.

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