The Structure of Lycoclavanin: Triterpenoid of *Lycopodium clavatum*

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Summary The structure and stereochemistry of lycoclavanin, a triterpenoid of *L. clavatum*, were established as (Ia).

LYCOCLAVANIN, a triterpenoid tetraol of *L. clavatum*, was isolated in 1962.[1] We have now established its structure and stereochemistry as (Ia).

The n.m.r. spectrum of lycoclavanin tetra-acetate (Ib), $C_{38}H_{56}O_9$, m.p. 238—240°, indicated the presence of six *C*-methyl groups at δ 0·86 (3H), 0·91 (6H), 0·95 (3H), 1·18 (3H), and 1·31 (3H), and of four acetyl methyls at δ 1·99 (3H), 2·05 (3H), 2·09 (3H), and 2·15 (3H). Three of four acetoxy-groups are secondary [C*H*–OAc, 4·94 (2H), 5·23 (1H)] and one is primary [C–CH_2–OAc, 4·09 (2H, ABq, δ_{AB} 18, *J* 12 Hz). The fifth oxygen function in lycoclavanin consists of a conjugated ketone chromophore [λ_{max} (EtOH): 247 nm (ε *ca.* 14,000); ν_{max} (KBr): 1665 (s), 1625 (m) cm^{-1}; o.r.d.: negative peaks at 370—380 nm] whose double bond is trisubstituted [δ 5·75 (1H, broad s.)] thus suggesting that the compound possesses the 16-oxoserratene skeleton.[2,3]

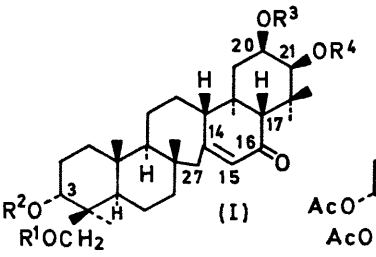
Lycoclavanin, when allowed to react with 2,2-dimethoxypropane in *NN*-dimethylformamide in the presence of toluene-*p*-sulphonic acid, formed a mixture of di- and mono-isopropylidene derivatives, (Ic) m.p. 225—227°, and (Id) m.p. 306—309°. Further reaction converted the latter into the former, and the former slowly decomposed into the latter when heated in methanol. Either compound regenerated lycoclavanin on acid hydrolysis. Acetylation of (Id) with acetic anhydride–pyridine afforded a diacetate (Ie), m.p. 307—310°, whose n.m.r. spectrum exhibited signals indicative of the presence of C–CH_2OAc (δ 4·08, 2H, ABq. δ_{AB} 18, *J* 12 Hz) and of C*H*–OAc (δ 4·96, 1H, broad s.), showing that in (Id) the isopropylidene function had been formed between two secondary hydroxy-groups. Acid hydrolysis of (Ie) with acetic acid and tosylation of the resulting diol-diacetate (If), m.p. 307—310°, by toluene-*p*-sulphonyl chloride–pyridine gave a monotosylate (Ig), m.p. 202—205°, which on slow chromatography over alumina or on heating in pyridine lost toluene-*p*-sulphonic acid to furnish a keto-diacetate (II), m.p. 280—282° [ν_{max} 1740 (OAc), 1715 (CO), 1665, and 1628 (m) cm^{-1}

(conj. CO)], thus confirming the presence of *cis*-α-glycol function in lycoclavanin. Since two of the six methyl groups of (II) appeared at low field (δ 1·35, 6H), the ketonic function formed was considered to be at C-21. The structure of (II) was established by transforming 16-oxolycoclavanol[3] to the same compound.

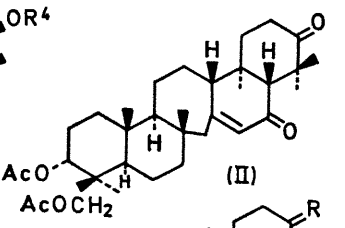
Chromium trioxide–pyridine oxidation of *OO*-isopropylidene-16-oxolycoclavanol[3] (III) gave a keto-acetonide (IV), which on hydrolysis with acetic acid and acetylation yielded the keto-acetate (II), identical with the compound obtained above.

The remaining problem, the stereochemistry of the *cis*-α-glycol function at C-20 and C-21 was elucidated as follows. (i) Diacetate-dibenzoate (Ih), m.p. 166—170°, showed a marked positive Cotton effect in its c.d. spectrum at 239 nm [$\Delta\epsilon$ +29·6 (solvent: methanol–dioxan)]. Application of the dibenzoate chirality rule[4] disclosed that the compound has the conformation (A) or (B) (depending upon whether the glycol function has the β- or α-orientation) and eliminated any contribution from boat conformations. (ii) The n.m.r. spectrum of the tetra-acetate (Ib) showed the 17-H signal at δ 2·45 which indicates that the 21-OAc group is axially oriented.[2,3] If (Ib) had conformation (B) the signal should appear at *ca* δ 2·2.

Lycoclavanin is therefore 16-oxoserrat-14-en-3α,20β,21β,-24-tetraol (Ia). This conclusion is supported by the fact that tosylation on (If) occurred exclusively at the C-20 hydroxy-group (see above).

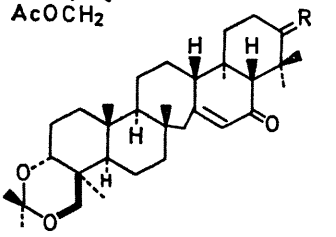


(I)

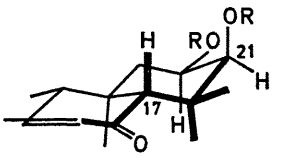


(II)

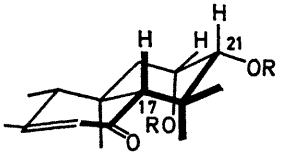
	R^1	R^2	R^3	R^4
(a)	H	H	H	H
(b)	Ac	Ac	Ac	Ac
(c)	-CMe_2-		-CMe_2-	
(d)	H	H	-CMe_2-	
(e)	Ac	Ac	-CMe_2-	
(f)	Ac	Ac	H	H
(g)	Ac	Ac	Ts	H
(h)	Ac	Ac	Bz	Bz



(III) R = β-OH, α-H
(IV) R = O



(A)



(B)

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[1] Y. Inubushi, Y. Tsuda, and T. Sano, *J. Pharm. Soc. Japan*, 1962, **82**, 1083, 1537.
[2] Y. Tsuda and T. Fujimoto, *Chem. Comm.*, 1969, 1042.
[3] Y. Tsuda, T. Fujimoto, and K. Kimpara, following communication.
[4] N. Harada and K. Nakanishi, *J. Amer. Chem. Soc.*, 1969, **91**, 3989.