The Structure of Serratidine

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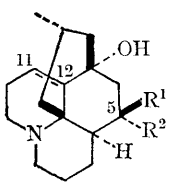
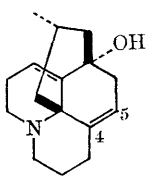
SERRATIDINE, m.p. 143—144°, has been isolated from a kind of Lycopodium plant growing in Japan, together with six other new alkaloids.[1,2] We now suggest the structure (I) for this alkaloid on the basis of chemical correlation with 12-epilycopodine and dihydrolycopodine.

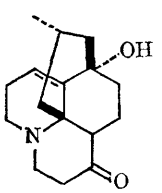
Serratidine is a tetracyclic alkaloid[2] possessing an expanded formula, $C_9H_{15}(-CH_2-CO-)(>CH-CH_3)(\geqslant C-OH)(-CH=C>)(>N-)$ and its mass spectrum shows three significant peaks at $M-43$, $M-56$, and $M-57$ which are diagnostically important for the lycopodine-type alkaloids possessing a hydroxy-group or a double bond at C-12.[3]



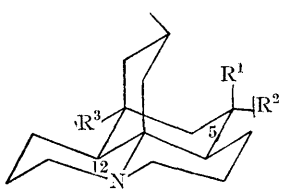
(I) $R^1=R^2=O$
(II) $R^1=OH$, $R^2=H$



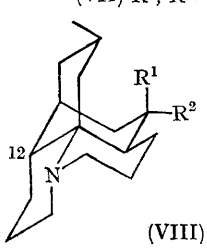
(III)



(IV)



(V) $R^1=OAc$, $R^2=H$, $R^3=OH$
(VI) $R^1=OAc$, $R^2=H$, $R^3=Cl$
(VII) R^1, $R^2=O$, $R^3=H$



lycopodine
(R^1, $R^2=O$)

(VIII) $R^1=OH$, $R^2=H$

Sodium borohydride reduction of serratidine affords an alcohol (II) and dehydration of this alcohol with thionyl chloride–pyridine gives an anhydro-compound (III), whose n.m.r. spectrum reveals a signal due to a newly introduced olefinic proton at τ 4·63 (m), together with that of the original olefinic proton at τ 4·28 (t, J 4 c./sec.), but no signal due to a proton geminal to a hydroxy-group, although the compound (III) still shows a hydroxy-band in its i.r. spectrum. The anhydro-compound on treatment with acetic anhydride–toluene-*p*-sulphonic acid gives an acetate, whose n.m.r. spectrum reveals a signal due to an acetyl methyl at τ 7·98 but no signal due to a proton geminal to an acetoxy-group.

The foregoing results show that serratidine possesses a partial structure, $>CH-CO-CH_2-$, and could have either structure (I) or (IV). The o.r.d. curve of serratidine in MeOH shows a positive Cotton effect (308 and 269 mμ) and this is reversed to a negative value on the addition of hydrochloric acid. This observation agrees with that observed for lycopodine,[4] which suggests that structure (I) is preferred to the other.

Reduction of the alcohol (II) over PtO_2 gives two isomeric dihydro-compounds, A and B, and both compounds show the molecular ion peak at m/e 265 in the mass spectra, but the Bohlmann absorption is observed only in the i.r. spectrum of the compound A. This suggests that the olefinic linkage in serratidine must be situated between C-11 and C-12. Acetylation of the compound A with acetic anhydride–pyridine gives a monoacetate (V), which shows a hydroxy-band at 3480 cm.$^{-1}$, and the n.m.r. bands at τ 7·99 (s, 3H) and 4·78 (m, 1H) are indicative of the presence of an acetoxy-group and a proton geminal to an acetoxy-group. The monoacetate on treatment with phosphorus pentachloride in methylene chloride gives a chloride (VI), which gives a positive Beilstein test. Reduction of the chloride with sodium in liquid ammonia, followed by oxidation with Jones reagent, affords a ketone (VII), m.p. 86—89°, whose i.r. spectrum is superimposable on that of 12-epilycopodine.[5] On the other hand, the compound B, when subjected to the same sequence of reactions except the last oxidation process, gives an alcohol (VIII), which is identical with dihydrolycopodine[6] in all respects.

Consequently, the absolute stereostructure of

serratidine has now been shown to be (I) and serratidine is the first example of a lycopodium alkaloid possessing a bridgehead hydroxy-group.

We are grateful to Professor W. A. Ayer for an authentic sample of dihydrolycopodine and for an i.r. spectrum of 12-epilycopodine.

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