The Pyrolysis of Diterpenoid Ester Alkaloids

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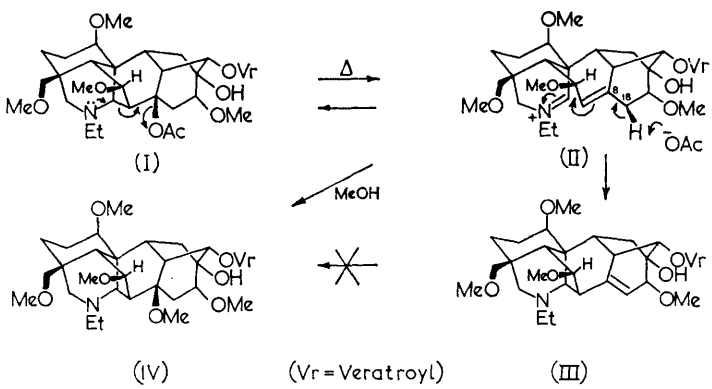
THE mild (180—220°) pyrolytic loss of acetic acid from diterpenoid alkaloids of the aconitine type (I) has been interpreted as a *cis*-1,2-elimination to give the 'pyro'-compounds (III)[1-3] despite the strained character of the resulting double bond. We re-interpret this reaction as rapid reversible formation of the ionic species (II), followed by a slower attack of acetate ion on the 18-hydrogen.



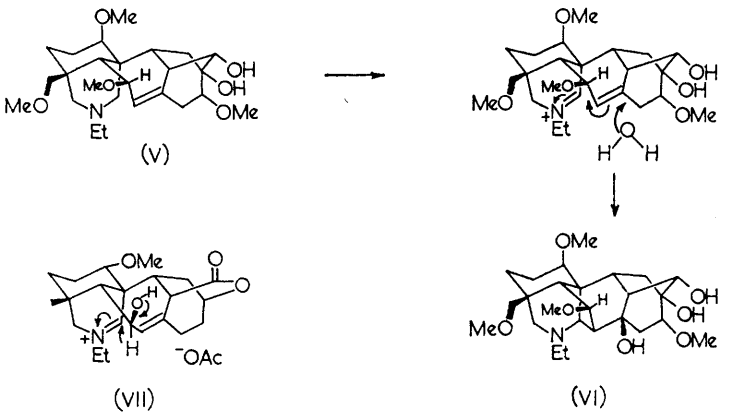
The long-known replacement of the acetoxy-group by a methoxy-group at 130° is similarly explained as attack of methanol on C-8 of (II), with re-establishment of the original skeleton (II → IV). Evidence that such reactive intermediates as (II) exist has now been provided, since the pyro-compounds are inert to methanol at this temperature. Simple ionization of the acetoxy-group, the only alternative, is most unlikely.

The elimination of acetic acid from bikhaconitine (I) has been shown to proceed to completion in 3 hours at 160° in "diglyme." The intermediate

[1] K. Wiesner, F. Bickelhaupt, and Z. Valenta, *Tetrahedron*, 1958, **4**, 418.
[2] D. J. McCaldin and L. Marion, *Canad. J. Chem.*, 1959, **37**, 1071.
[3] K. Wiesner, M. Götz, D. L. Simmons, and L. R. Fowler, *Coll. Czech. Chem. Comm.*, 1963, **28**, 2462.

(II) has been reductively trapped at this and lower temperatures using lithium tri-t-butoxyaluminium hydride. In less than 15 min. at 140° the product is largely (*ca.* 70%) the olefin (V) (amorphous, distillable at 160°, 5×10^{-4} mm. $[\alpha]_D + 26°$; correct analysis; end absorption in the ultraviolet; broad singlet vinyl hydrogen signal at τ 4·5; the methyl of the *N*-ethyl group shielded 0·07 p.p.m. by the double bond relative to bikhaconine). (V) was inert to lithium aluminum hydride in refluxing dioxan (contrast pyrobikhaconine[4]). Parallel results were obtained with the alkaloid pseudaconitine.

Mercuric acetate oxidation of (V) followed by heating in aqueous dioxan gave a 20% yield of bikhaconine (VI). This type of oxidative cyclization is suggested to be the final step in the biosynthesis of the skeleton of the aconitine group of alkaloids. In addition (V) and related bases provide valuable relays in approaches to total synthesis of these alkaloids.



Finally, in the light of the above interpretation a more plausible mechanism for the pyrolysis of heteratisine monoacetate[5] involves isomerization to the 8-acetate, fission to the ion pair (VII), and hydride transfer (see ref. 6) from C–6 to C–17.

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[4] Y. Tsuda and L. Marion, *Canad. J. Chem.*, 1963, **41**, 3055.
[5] R. Aneja and S. W. Pelletier, *Tetrahedron Letters*, 1965, 215.
[6] D. Dvornik and O. E. Edwards, *Tetrahedron*, 1961, **14**, 54.