A Simple Total Synthesis of (±)-Aspidospermidine

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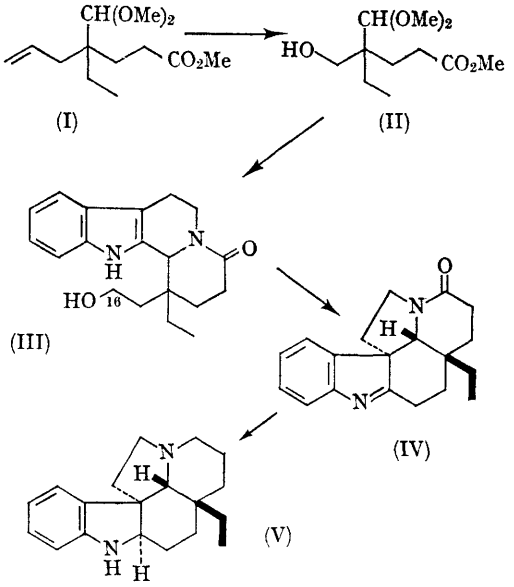
AN earlier Communication[1] from this laboratory described a total synthesis of 16-methylaspidospermidine[2] (vincadifformane) using the readily accessible methyl 4-ethyl-4-formylhept-6-enoate as a key intermediate. We have now extended this work, using the same intermediate, to furnish a simple high-yield synthesis of aspidospermidine (V) itself, the parent compound of the large family of *Aspidosperma* alkaloids.

The above ester was converted into the corresponding dimethyl acetal (I) using trimethyl orthoformate. Ozonolysis followed by borohydride reduction[3] of the crude ozonide gave the hydroxy-ester (II). This reacted smoothly with tryptamine in boiling acetic acid to give the hydroxy-lactam (III), m.p. 117—120°. Treatment with 40% sulphuric acid or boron trifluoride etherate at 100° gave the indolenine–lactam (IV),

which with lithium aluminium hydride gave (±)-aspidospermidine (V), m.p. 108—110°, whose



behaviour on layer chromatography in several solvent systems was identical with that of an authentic (optically active) specimen kindly supplied by Dr. G. F. Smith. The mass spectra were also identical. Alternatively, catalytic hydrogenation of (IV) gave an indoline–lactam, m.p. 211—213°, which with lithium aluminium hydride gave (V). The process appeared to be entirely stereospecific and no indication of the presence of isomeric products was found. The overall yield based on tryptamine was 20—25%.

In the synthesis above and the one previously described[1] we believe that the remarkable stereospecific skeletal rearrangement is initiated by the formation of a carbonium ion at C-16 of the tetracyclic lactam. We are currently endeavouring to obtain further information on the process by study of the solvolysis of the *O*-tosylate of the lactam (III).

The award of an 1851 Exhibition Overseas Scholarship (to M.K.) is gratefully acknowledged.

(*Received, July 24th*, 1967; *Com.* 758.)

[1] J. E. D. Barton and J. Harley-Mason, *Chem. Comm.*, 1965, 298.
[2] The numbering system due to J. Le Men and W. I. Taylor, *Experientia*, 1965, **21**, 508, is used here.
[3] *Cf.* J. A. Sousa and A. L. Bluhm, *J. Org. Chem.*, 1960, **25**, 108.