The Stereochemistry of Chanoclavine-I and Isochanoclavine-I

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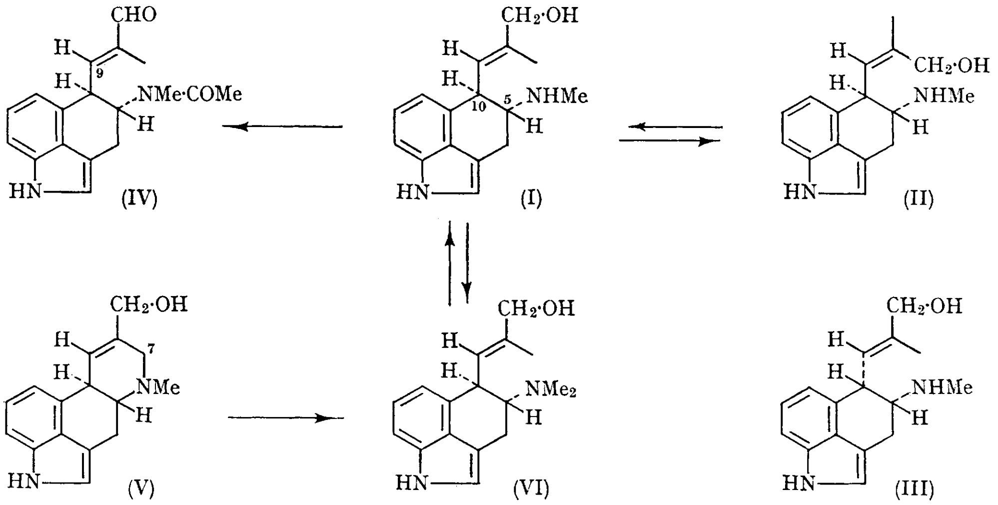
THE recent discovery[1] of two further isomers of chanoclavine,[2] together with considerations of their possible role in the biosynthesis of ergot alkaloids, has focussed attention on the stereochemistry of these compounds. The absolute configuration of chanoclavine-I (I), at C-5 and C-10, has already been defined by a correlation[2] with festuclavine.[3,4] Assignment of structures (II) and (III) for isochanoclavine-I and chanoclavine-II, respectively, as well as of the substitution pattern about the isolated double bond in (I) rests exclusively on comparison of n.m.r. data.[1] We now report experiments which establish the correctness of structures (I) and (II).

First, additional spectroscopic evidence was secured by oxidation of the *N*-acetyl derivative of (I)[2] with MnO_2 in acetone to form the aldehyde (IV), m.p. 209°, $[\alpha]_D -108°$ ($CHCl_3$), having λ_{max} 227 mμ (log ϵ 4·20 in ethanol after substraction of the indole chromophore), in which the olefinic proton at C-9, τ 3·4 ($CHCl_3$), is clearly *cis* to the carbonyl group.[5] Final proof for the substitution pattern about the double bond of (I) was obtained as follows. Cleavage of the methiodide from elymoclavine (V) with sodium in liquid ammonia[6] with or without added methanol gave, after chromatographic separation, a 70% yield of *N*-methyl-6,7-*seco*-elymoclavine (VI), m.p. 162°, $[\alpha]_D -127°$ ($CHCl_3$), identical in all respects with the monomethylation product of (I). The *O*-acetyl-derivative of (VI) afforded on demethylation with diethylazodicarboxylate in ether[7] the *O*-acetyl derivative of (I), m.p. 111°, $[\alpha]_D -160°$ ($CHCl_3$), converted by alkaline hydrolysis into a compound identical in all respects with natural chanoclavine-I. Since the geometry of the double bond is known to be preserved in the course of similar reductive cleavages,[8] a *cis*-relationship of the CH_2·OH group and the olefinic proton of (I) is established.



Irradiation of (I) in t-butyl alcohol with a low-pressure mercury lamp gave a mixture containing roughly equal amounts of (I) and (II), from which pure isochanoclavine-I (II),[1] m.p. 190°, $[\alpha]_D -208°$ (pyridine), could be isolated in 30% yield. A similar mixture was obtained on irradiation of (II). Thus, chanoclavine-I and isochanoclavine-I have the same configuration at C-5 and C-10 and differ only in the relative positions of CH_2·OH and olefinic proton. The reversible isomerisation (I) ⇋ (II) is likely to occur by an intramolecular energy transfer mechanism (*cf.* ref. 9).

(*Received, October 5th,* 1966; *Com.* 745.)

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[1] D. Stauffacher and H. Tscherter, *Helv. Chim. Acta*, 1964, **47**, 2186.

[2] A. Hofmann, R. Brunner, H. Kobel, and A. Brack, *Helv. Chim. Acta*, 1957, **40**, 1358.

[3] E. Schreier, *Helv. Chim. Acta*, 1958, **41**, 1984.

[4] H. G. Leemann and S. Fabbri, *Helv. Chim. Acta*, 1959, **42**, 2696; P. A. Stadler and A. Hofmann, *ibid.*, 1962, **45**, 2005.

[5] L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, 1959, pp. 61, 119.

[6] S. Bhattacharji, A. J. Birch, A. Brack, A. Hofmann, H. Kobel, D. C. C. Smith, H. Smith, and J. Winter, *J. Chem. Soc.*, 1962, 421.

[7] O. Diels and E. Fischer, *Ber.*, 1914, **47**, 2043; *cf.* G. W. Kenner and R. J. Stedman, *J. Chem. Soc.*, 1952, 2089.

[8] K. W. Greenlee and V. G. Wiley, *J. Org. Chem.*, 1962, **27**, 2304.

[9] A. A. Lamola, P. A. Leermakers, G. W. Byers, and G. S. Hammond, *J. Amer. Chem. Soc.*, 1965, **87**, 2322; H. Morrison, *ibid.*, p. 932.