Synthesis of a Reduction Product of the Oxindole Alkaloid Vincatine and of (±)-8-Oxovincatine

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Summary The total synthesis in one step of (±)-8-oxovincatine, and its reduction to a diol identical with that obtained by reduction of vincatine, confirm the structure of the latter.

THE structure of vincatine (I) has recently been announced,[1] based mainly upon application of physical methods to the alkaloid itself and its lithium aluminium hydride reduction product, the diol (II).

We have found that reaction of 1-methyl-3-oxindolylethylamine[2] (III) (as hydrochloride) with dimethyl 4-ethyl-4-formylpimelate[3] (IV) in boiling aqueous ethanolic sodium acetate buffer gave in 70% yield the dilactam 8-oxovincatine (V) as a mixture of two racemates differing in configuration at C-5 only.† These racemates were readily separated by preparative layer chromatography giving products A, m.p. 217—218°, and B, m.p. 200—201°. These dilactams were separately reduced to the diols (II) with lithium aluminium hydride. The mass spectra of these two stereoisomers were indistinguishable and were identical with that of (II) obtained from vincatine. Comparison by layer chromatography, kindly performed by Dr. Döpke, indicated that the diol from dilactam B was identical with that obtained by him from vincatine.

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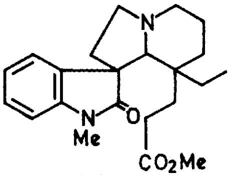
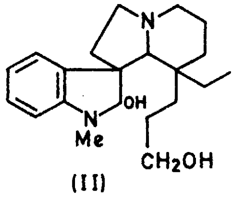


(I)



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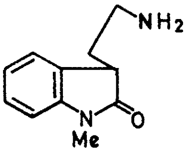

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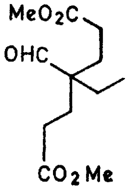

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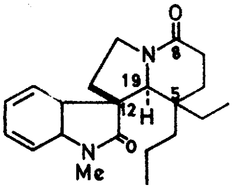

(V)

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† Examination of Dreiding models of (V) shows clearly that the relative configuration at C-12 and C-19 must be as shown since in the alternative arrangement one of the substituents at C-5 is so close to the benzene ring that its formation is most improbable. Thus the synthesis is partly stereoselective.

[1] W. Döpke, H. Meisel, and H. W. Fehlhaber, *Tetrahedron Letters*, 1969, 1701.
[2] J. Harley-Mason and R. F. J. Ingleby, *J. Chem. Soc.*, 1958, 3639.
[3] M. E. Kuehne, *J. Amer. Chem. Soc.*, 1964, 86, 2946; *Lloydia*, 1964, 27, 435.