Total Synthesis of (±)-Vincamine

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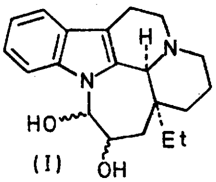
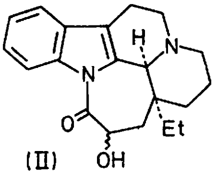
Summary A new total synthesis of (±)-vincamine is reported.

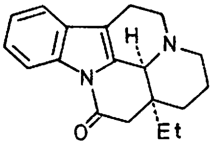
IN continuation of our experiments[1] on the synthesis of indole alkaloids we now report a new total synthesis of (±)-vincamine (V). (±)-Homoeburnamenine, prepared as described earlier,[1] was oxidised (OsO_4) to dihydroxyhomoeburnamenine (I), m.p. 155—157°, M^+ 326·199, which was then subjected to oxidation under a variety of conditions; unfortunately, the desired di-oxo-compound could not be obtained. Oxidation of (I) by means[2] of $Me_2SO:NEt_3:$pyridine–$SO_3:H_2O$(trace) afforded the two diastereoisomeric lactams (II), together with a small amount of the related unsaturated lactam obtained by dehydration. In a further attempt to obtain the di-oxo-compound, the lactams (II) were oxidised separately by copper acetate in methanol. In each case the product was (±)-eburnamonine (III), m.p. 198—201·5°(lit.[3] m.p. 200—202°), identical in i.r., u.v., and mass spectra with published data.[4]



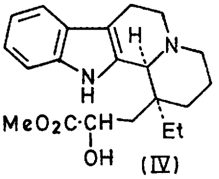
(I)



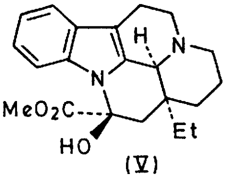
(II)



(III)



(IV)



(V)

Alkaline hydrolysis of the mixture of lactams (II) gave the corresponding hydroxy-acids (not isolated), which were esterified (CH_2N_2) to the methyl esters (IV), m.p. 194—196°, M^+ 356·2078. Finally, oxidation of the methyl esters by means of the $Me_2SO:NEt_3:$pyridine–$SO_3:H_2O$(trace) reagent afforded (±)-vincamine (V), m.p. 228—229°, M^+ 354·1926 (lit.[5] m.p. 235—236°), which was shown to be identical with authentic vincamine by t.l.c. comparison in three different solvent systems, and by comparison of i.r. and mass spectra.

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[1] K. H. Gibson and J. E. Saxton, *Chem. Comm.*, 1969, 799.

[2] J. R. Parikh and W. von E. Doering, *J. Amer. Chem. Soc.*, 1967, **89**, 5505.

[3] E. Wenkert and B. Wickberg, *J. Amer. Chem. Soc.*, 1965, **87**, 1580.

[4] N. Neuss, "Physical Data of Indole and Dihydroindole Alkaloids," Eli Lilly Research Laboratories, Indianapolis, 1966; H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structural Elucidation of Natural Products by Mass Spectrometry," Holden-Day, San Francisco, 1964, vol. I, p. 89.

[5] M. P. Cava, S. S. Tjoa, Q. A. Ahmed, and A. I. Da Rocha, *J. Org. Chem.*, 1968, **33**, 1055.