The Total Synthesis of (±)-15,16-Dimethoxyerythrinan-3-one. A Further Application of the Methyl Vinyl Ketone Annelation of Endocyclic Enamines

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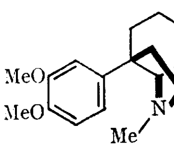
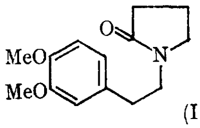
WE recently reported[1] a total synthesis of (±)-mesembrine (I) which featured the annelation of an endocyclic enamine with methyl vinyl ketone. The success of these experiments has prompted additional work in our laboratory to expand the role of this unique annelation as a general method of alkaloid synthesis. We now report a simple three-step synthesis of the *Erythrina* alkaloid[2] model (±)-15,16-dimethoxyerythrinan-3-one (V; X = H).[3]

The endocyclic enamine (IV; X = H) required to test the crucial annelation sequence had been previously prepared by Wiesner.[4] We employed a modified procedure. Condensation of homoveratrylamine and butyrolactone gave a mixture of pyrrolidone (II) and hydroxy-amide (III), which was treated with hot POCl$_3$ and the desired enamine (IV; X = H) was obtained by subsequent base work-up. The lability of this enamine required its isolation and storage as a hydrobromide salt, m.p. 196—197° (lit.,[4] 201—203°).

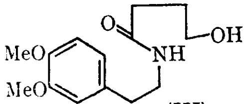
Admixture of the enamine (prepared *in situ* by treatment of the hydrobromide salt with an equivalent amount of sodium ethoxide) and a 20% molar excess of methyl vinyl ketone in refluxing ethanol provided an orange oil from which the desired base (V; X = H) was secured through preparative chromatography, m.p. 143—144°. In addition to the expected n.m.r. spectrum and a correct combustion analysis, confirmation of the structural and stereochemical assignment was easily made by comparison of the i.r. spectrum with that of an authentic sample.† Further corroboration was provided by conversion into a picrate whose i.r. spectrum as well as m.p. and mixed m.p. were in agreement with the previously synthesized material.†



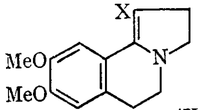
(I)



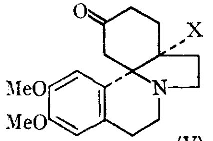
(II)



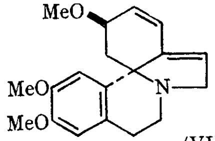
(III)



(IV)



(V)



(VI)

The remarkable simplicity of this method of approach to the *Erythrina* skeleton has prompted its further study in the elaboration of certain unsaturated bases such as erysotrine (VI). The nature of the X function in (IV) and (V) is expected to play a decisive role in this study.

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[1] R. V. Stevens and M. P. Wentland, *Tetrahedron Letters*, 1968, **2613**; R. V. Stevens and M. P. Wentland, *J. Amer. Chem. Soc.*, in the press; *cf.* also T. J. Curphey and H. L. Kim, *Tetrahedron Letters*, 1968, **1441**; S. L. Keely, jun., and F. C. Tahk, *Chem. Comm.*, 1968, **441**.

[2] For a recent review see R. H. F. Manske, 'The Alkaloids,' Vol. IX, p. 483, Academic Press, New York, 1967.

[3] For an additional synthesis and leading references see V. Prelog, A. Langemann, O. Rodig, and M. Ternbah, *Helv. Chim. Acta*, 1959, **42**, 1301.

[4] K. Wiesner, Z. Valenta, A. J. Manson, and F. W. Stonner, *J. Amer. Chem. Soc.*, 1955, **77**, 675.