

Conversion of Yohimbone into Natural (3S,15S,20R)-Corynantheine

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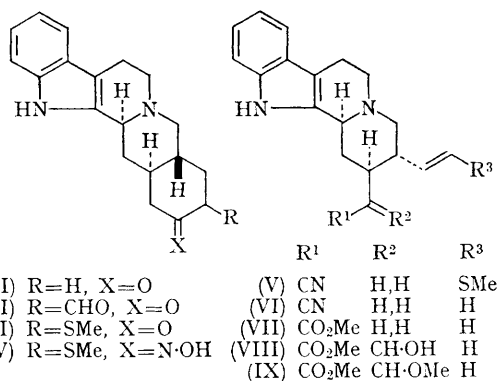
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THE structure and absolute configuration of corynantheine (IX) was established through the efforts of several groups.¹ A total synthesis of the racemic substance along lines suggested by biochemical analogy has been published.²

We report here a formal total synthesis of the natural alkaloid by a route which applies our unsymmetrical, mildly oxidative cleavage of the bond between a ketone function and an adjacent methylene.³

Yohimbone (I)⁴ was converted into 18-hydroxymethyleneyohimbone (II)⁵ and thence by the action of methyl thiotoluene-*p*-sulphonate⁶ and potassium acetate into the 18-methylthio-derivative (III). The oxime (IV) of this ketone was rearranged^{3,7} to the corynanthenitrile derivative (V), which was desulphurised by the action of deactivated Raney nickel to recrystallized corynanthenitrile (VI) in 23% yield from (I). Methyl corynantheate (VII), obtained from the nitrile (VI), was formylated^{1c,2} to desmethylcorynantheine (VIII) and the enol was methylated^{1c,2} to afford corynantheine (IX), chromatographically homogeneous in 6%

yield from (VI), m.p. of the hydrochloride, 167—188°, $[\alpha]_D^{25}$ $38 \pm 3^\circ$ ($c = 0.14$, MeOH), [lit.,⁸ m.p. 170—192°, $[\alpha]_D^{25}$ 43° ($c = 1.0$, MeOH)]. Identity was established by comparison of infrared spectra, mass spectra, and R_f in two solvent systems.



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¹ (a) M.-M. Janot, R. Goutarel, and V. Prelog, *Helv. Chim. Acta*, 1951, **34**, 1207; (b) P. Karrer, R. Schwyzer, and A. Flam, *Helv. Chim. Acta*, 1952, **35**, 851; (c) J. A. Weisbach, J. L. Kirkpatrick, K. R. Williams, E. L. Anderson, N. C. Yim, and B. Douglas, *Tetrahedron Letters*, 1965, 3457; (d) Y. Ban and O. Yonemitsu, *Tetrahedron*, 1964, **20**, 2877; and references quoted therein.

² E. E. van Tamelen and I. G. Wright, *Tetrahedron Letters*, 1964, 295.

³ R. L. Autrey and P. W. Scullard, *J. Amer. Chem. Soc.*, 1965, **87**, 3284.

⁴ Yohimbone has been totally synthesized and resolved by G. A. Swan, *J. Chem. Soc.*, 1950, 1534.

⁵ (a) P. D. Pächt, Dissertation, Harvard University, 1960; (b) J. D. Albright, L. A. Mitscher, and L. Goldman, *J. Org. Chem.*, 1963, **28**, 38.

⁶ Cf., L. G. S. Brooker and S. Smiles, *J. Chem. Soc.*, 1926, 1723.

⁷ (a) C. Schöpf, *Annalen*, 1927, **452**, 211; (b) M. Ohno, N. Naruse, S. Torimitsu, and I. Teresawa, *J. Amer. Chem. Soc.*, 1966, **88**, 3168.

⁸ M.-M. Janot and R. Goutarel, *Bull. Soc. chim. France*, 1951, 588; (The constants are those reported for the natural mixture of corynantheine and dihydrocorynantheine as the hydrochlorides).