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

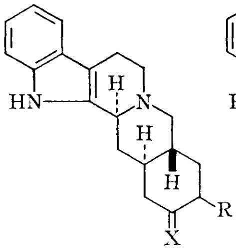
By R. L. AUTREY and P. W. SCULLARD

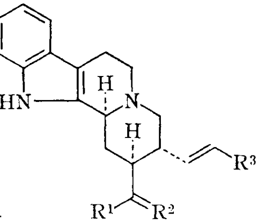
(*Department of Chemistry, Harvard University, Cambridge, Massachusetts* 02138)

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*-sulphonate[6] 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°, $[\alpha]_D$ 38 ± 3° (c = 0·14, MeOH), [lit.,[8] m.p. 170—192°, $[\alpha]_D$ 43° (c = 1·0, MeOH)]. Identity was established by comparison of infrared spectra, mass spectra, and R_f in two solvent systems.





(I) R=H, X=O
(II) R=CHO, X=O
(III) R=SMe, X=O
(IV) R=SMe, X=N·OH

	R¹	R²	R³
(V)	CN	H,H	SMe
(VI)	CN	H,H	H
(VII)	CO_2Me	H,H	H
(VIII)	CO_2Me	CH·OH	H
(IX)	CO_2Me	CH·OMe	H

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