

THE CONFIGURATION OF THE CARBOMETHOXY GROUP IN VOBASINE,
TABERNAEMONTANINE AND DREGAMINE

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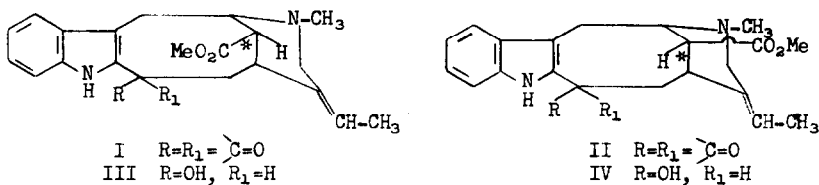
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THE alkaloid vobasine¹ belongs to the relatively new group of 2-acyl-indole alkaloids². An unusual cyclooctindole structure, I, has been advanced for vobasine on the basis of chemical transformations and



ultraviolet absorption data³. We now report the following NMR evidence, which supports the chemistry suggested at C* for vobasine and clearly

¹ U. Renner, *Experientia* **15**, 185 (1959).

² J. A. Weisbach, R. F. Raffauf, O. Ribeiro, E. Macko and B. Douglas, *J. Pharm. Sci.* in press (and references cited).

³ U. Renner and D. A. Prins, *Chimia* **15**, 321 (1961).

assigns that of II, the epimeric structure, to isovobasine. Earlier evidence relevant to this structural feature was deduced from a study of Hoffman eliminations in this series³.

The NMR spectrum of vobasine exhibits two bands attributable to O-CH₃ and N-CH₃ at $\delta=2.61$ and 2.54^4 , respectively. This remarkable shift upfield of the methoxyl band of ca. 1-1.2 ppm. contrasts sharply with the usual position of $\delta=3.6-3.8^5$ for this grouping (cf. the ca. 0.25 δ shift observed upon conversion of yohimbine into the corresponding oxindole⁶). The comparable N-CH₃ ($\delta=2.49$) and O-CH₃ ($\delta=3.50$) values in isovobasine are in accord with previous experience, the small increase in O-CH₃ shielding being caused by interaction with the basic nitrogen.

Two explanations can be advanced for the pronounced shift, namely, that the carbomethoxyl group is (i) interacting with the carbonyl group alpha to the indole ring, or (ii) is interacting with the aromatic π electron cloud and undergoing a large displacement, particularly due to the pyrrole portion of the indole. Indeed, two conformations of I which could be constructed with Drieding models corresponded to these possibilities. Upon inspection of the borohydride reduction products, vobasinol, III, and isovobasinol, IV, a verification of ii was readily obtained. The N-CH₃ ($\delta=2.50$) and C-CH₃ ($\delta=2.35$) of

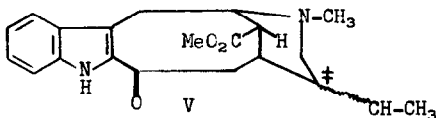
⁴ The O-CH₃ and N-CH₃ assignments have been made such that the N-CH₃ values of compounds I-IV differ at most by 0.1 ppm. It is possible that these assignments should be reversed. In either event, the fundamental conclusions of this communication retain their validity.

⁵ N. S. Bacca, L. F. Johnson, and J. N. Shoolery, High Resolution N.M.R. Spectra Catalog, 1962, Varian Associates.

⁶ N. Finch and W. I. Taylor, J. Am. Chem. Soc. 84, 1318 (1962).

III exhibited even greater diamagnetic shielding than vobasine itself, while those of IV ($N-CH_3=2.45$, $C-CH_3=3.40$) were, as expected, in the more normal range⁷.

As vobasine has been catalytically reduced⁸ to tabernaemontanine



and dresamine V, isomers at C[†], the arguments just evolved may be directly extrapolated to these other naturally occurring 2-acylindole alkaloids. It is anticipated that this diagnostic methoxyl shift will be of value in structural studies with other members of the cyclo-octindole group.

⁷ Examination of a model in the appropriate conformation for the aromatic interaction shows that the methoxyl can be exceedingly close to the plane of the pyrrole ring and can thus experience a maximum ring current diamagnetic effect. Due to the flexibility and free rotation of the methoxyl grouping there are a variety of positions it may assume without changing the basic molecular conformation, thus precluding use of the method of C. E. Johnson and F. A. Bovey, J. Chem. Phys. 29, 1012 (1958) to obtain the conformation of ring C.

⁸ U. Renner and D. A. Prins, Experientia 17, 209 (1961).