phan residues, it is compelling to consider these two phenomena may be related. In this connection Hayashi, *et al.*,[12] have shown that a tryptophan residue is involved in the formation of the enzyme–substrate complex between lysozyme and poly-N-acetylglucosamine (glycol chitin). Further, it has been reported by Hartdegen and Rupley[13] that an inactive derivative, altered only in a single tryptophan residue, may be obtained by oxidation of lysozyme by iodine in acidic solution. This modification and loss of activity were prevented by the presence of N-acetylglucosamine.

Further improvement in instrumentation will be necessary before more accurate measurements of the small aromatic Cotton effects can be obtained. Efforts in this direction are now being made and further results will be published in due course.

(12) K. Hayashi, T. Imoto, and M. Funatsu, *J. Biochem.* (Tokyo), **54**, 381 (1963).

(13) F. J. Hartdegen and J. A. Rupley, *Biochim. Biophys. Acta*, **92**, 625 (1964).

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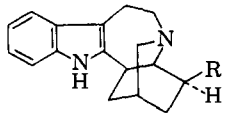
The Synthesis of Desethylibogamine

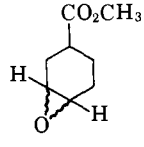
Sir:

We wish to report the synthesis of desethylibogamine (Ia), the first totally synthetic compound containing the carbon skeleton of the iboga alkaloids of which ibogamine (Ib) is a typical example.[1]

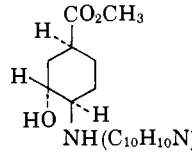
Oxidation of methyl 3-cyclohexene-1-carboxylate with *m*-chloroperbenzoic acid gives a mixture of the *trans* and *cis* epoxides (IIa and IIb,[2] b.p. 60–62° (0.1 mm.)).[3] Reaction of this mixture of epoxy esters with tryptamine in refluxing ethanol gave a mixture of amino alcohols[4] which was, without separation, heated at 190 to 200° to effect cyclization of III to the N-indolylethylisoquinuclidone (IV). Under these conditions, the amino alcohol from the *cis* epoxide would give either a



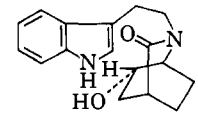
Ia, R = H
b, R = C_2H_5



IIa, *trans* epoxide
b, *cis* epoxide



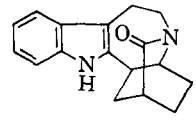
III



IV

δ-lactone and/or polymeric amide, and to separate the isoquinuclidone from these undesired compounds the crude mixture was heated with 5% methanolic sodium hydroxide[5] to give IV (m.p. 178–179°, λ_{max}^{KBr} 6.05 μ) in an over-all yield of 68%. The tosylate of this isoquinuclidone (m.p. 149–150°, 84% yield)[6] on treatment with aluminum chloride or aluminum bromide in toluene affords desethylibogamine lactam (V, m.p. 313–315°, λ_{max}^{KBr} 6.10 μ) in 38% yield. This compound gives a negative Ehrlich test, has a typical indole ultraviolet spectrum (λ_{max} 225, 283, and 291 mμ), and the n.m.r. spectrum is similar to that of ibogaine lactam.[5] The attempted use of a variety of other acids to effect this cyclization led to either gross decomposition or gave recovered starting material.

Reduction of desethylibogamine lactam with lithium aluminum hydride gives desethylibogamine (I, m.p. 186–187°, λ_{max} 226, 283, and 290 mμ) in 85% yield. The n.m.r. spectrum of this compound shows a series of peaks equal to approximately eight protons in the region from τ 6.6 to 7.2. Ibogamine and ibogaine both show a series of peaks in this general region which may be assigned to the protons adjacent to the indole and the tertiary nitrogen.



In addition to providing a synthetic pathway to the iboga alkaloid ring system in relatively few steps, this work constitutes a new isoquinuclidine synthesis which has been used to prepare the unsubstituted and N-benzyl analogs of V.[7]

Acknowledgments. This work was supported by Grant NB-04589 of the National Institute of Neurological Diseases and Blindness. We wish to thank Dr. Neville Finch of Ciba Pharmaceutical Company for samples of ibogamine and N-benzylisoquinuclidone which were used as spectral references.

(1) J. P. Kutney, R. T. Brown, and E. Piers, *J. Am. Chem. Soc.*, **86**, 2287 (1964), have obtained a compound containing the ibogamine ring system from the mercuric acetate oxidation of carbomethoxydihydrocleavamine.

(2) Vapor phase chromatography of this mixture indicates that there is a predominance of one isomer (probably IIa), but the degree of separation was insufficient to permit a quantitative evaluation of the relative amounts of each isomer. H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 221 (1959), report that the oxidation of methyl 3-cyclohexene-1-carboxylate with perbenzoic acid gives exclusively the *trans* epoxide (IIa).

(3) Satisfactory analytical data were obtained for all new compounds reported, and all compounds were characterized by infrared and nuclear magnetic resonance spectroscopy.

(4) The infrared spectrum of this mixture indicates that a negligible amount of conversion to the amide was obtained.

(5) M. F. Bartlett, D. F. Dickel, and W. I. Taylor, *J. Am. Chem. Soc.*, **80**, 126 (1958), have pointed out the resistance of ibogaine lactam to basic hydrolysis.

(6) A second compound, $C_{31}H_{32}N_2S_2O_6$, m.p. 245–246°, is obtained if a large excess of tosyl chloride is used. The nature of this compound will be discussed in the full paper.

(7) J. W. Huffman, C. B. S. Rao, and T. Kamiya, unpublished work.

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Chemical Evidence for the Occurrence and Temperature Independence of Ion–Molecule Reactions at Atmospheric Pressures

Sir:

Abundant physical evidence for the occurrence of ion–molecule reactions in mass spectrometers has been