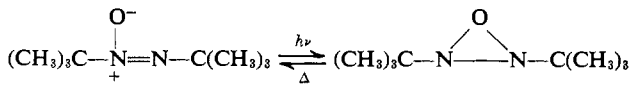
spectrum at 70 ev: *m/e* (relative intensity) 103 (1.8), 102 (3.8), 87 (6.8), 57 (100), and 41 (45).

The compound is thermally labile, reverting quantitatively to the azoxy derivative IV (at 20° $t_{1/2}$ ~8 hr in CCl_4, ~3 hr in CH_3NO_2). It is unreactive toward water and moderately stable in acidic media.[8] In carbon tetrachloride the only observed effect of dichloroacetic acid (1.7 *M*) is a fivefold increase in rate of isomerization of the photoproduct to the azoxy compound. The available physical and chemical data afford a strong basis for assignment of the three-membered ring structure V to the photoproduct.



IV V

Compound V is far less stable than corresponding oxaziridines (I, A = oxygen, B = nitrogen, C = carbon).[3] In the latter series aryl-substituted derivatives are less stable than those with alkyl groups.[3,9] On this analogy, aryl-substituted oxadiaziridines may be expected to be highly unstable species. The dependence of stability of oxadiaziridines on the nature of *alkyl* substituents, however, is a more open question.

(8) A possible open-chain isomer, RN=O⁺—N̄R (III, A = C = nitrogen, B = oxygen), is rendered unlikely by these observations.

(9) See J. S. Splitter and M. Calvin, *J. Org. Chem.*, 30, 3427 (1965), and references cited therein.

(10) National Institutes of Health Predoctoral Fellow, 1965–1967.

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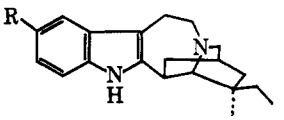
Received September 30, 1967

The Total Synthesis of *dl*-Ibogamine

Sir:

The seven-membered ring and isoquinuclidine moiety[1] of the iboga alkaloids (I) give them a unique position among the indole alkaloids.[2] Attention has been focused on them because one of the building blocks of *vincaleukoblastine*,[3] an antileukemic agent, and of *voacamine*,[4] a cardiotonic dimeric indole, also possesses the iboga skeleton.

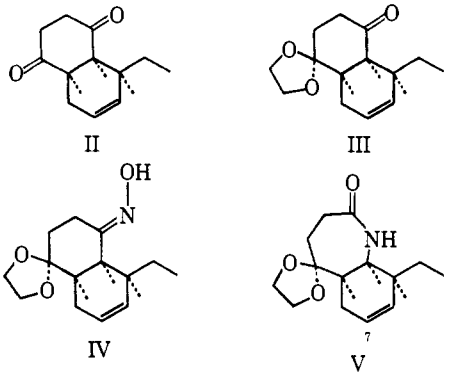
In view of the interest in structure and physiological activities[2c] of the iboga alkaloids, their synthesis was initiated in our laboratory.[5] While this work was in progress, Büchi and his co-workers[6] reported the first total synthesis of *dl*-ibogamine (Ia) and *dl*-ibogaine (Ib),[7] while others achieved partial[8a] or part structure[8b–e] syntheses.



Ia, R = H
b, R = OCH_3

The present work represents a different, completely stereocontrolled approach that is more versatile by virtue of forming the seven-membered ring first and completing the isoquinuclidine and indole ring closures at the end of the synthesis. This scheme is devoid of undesired rearrangement[6] and the several steps produce good yields.

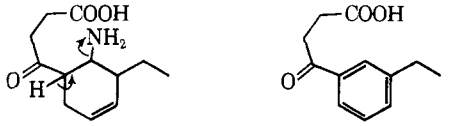
The *cis*-enedione II[5a] afforded an excellent starting point. The stereochemically unstable II was monoketalized at C_1 to III with the retention of its *cis* configuration (80%); bp 104° (0.01 mm);[9] ν_{max}^{neat} 5.83 (>C=O), 9.0 μ (ketal); nmr δ 4.10 ppm (ketal, 4 H, singlet).[10] Then the *cis,anti*-oxime ketal IV was prepared (90%); mp 126.5–127.5°; ν_{max}^{KBr} 3.1 (–OH), 5.97 (>C=N–), 6.05 μ (>C=C<); nmr δ 4.06 (ketal, 4 H, singlet), 5.65 (2 vinylic H, singlet), 8.8 ppm (hydroxyl, 1 H, broad). A Beckmann rearrangement of IV by tosyl chloride in hot pyridine readily produced the seven-membered *cis*-lactam ketal V (80%); mp 146–147.5°; ν_{max}^{KBr} 3.15 (–NH–), 6.03 μ (lactam).[11]



II III

IV V

The structure of V was proved by consecutive acidic and alkaline treatment, which cleaved the ketal and lactam groups, respectively. The intermediate β-amino ketone XVII lost ammonia and the cyclohexadiene structure aromatized to 3-(*m*-ethylbenzoyl)propionic acid (XVIII; 95%); ν_{max}^{KBr} 3.73 (–OH), 5.83 (–*C*OOH), 5.92 μ (ketone); nmr δ 7.64 ppm (4 aromatic H, multiplet). Finally, nitric acid oxidation of XVIII led to isophthalic acid, mp 334–337°.



XVII XVIII

(1) M. F. Bartlett, D. F. Dickel, and W. I. Taylor, *J. Am. Chem. Soc.*, 80, 126 (1958).

(2) (a) L. Marion, *Alkaloids*, 2, 450 (1952); (b) J. E. Saxton, *ibid.*, 7, 143 (1960); (c) W. I. Taylor, *ibid.*, 8, 203 (1965).

(3) N. Neuss, M. Gorman, H. E. Boaz, and N. J. Cone, *J. Am. Chem. Soc.*, 84, 1509 (1962).

(4) J. LaBarre and L. Gillo, *Compt. Rend. Soc. Biol.*, **149**, 1075 (1955); A. Quevauviller and O. Blaupin, *Ann. Pharm. Franc.*, **15**, 617 (1957).

(5) (a) S. I. Sallay, *Tetrahedron Letters*, 2443 (1964); (b) S. I. Sallay, U. S. Patent 3,294,817 (1966).

(6) G. Büchi, D. L. Coffen, K. Kocsis, P. E. Sonnet, and F. E. Ziegler, *J. Am. Chem. Soc.*, 87, 2073 (1965); **88**, 3099 (1966).

(7) Shown in their absolute configuration; *cf.* footnote 11 of ref 6.

(8) (a) J. P. Kutney, R. T. Brown, and E. Piers, *J. Am. Chem. Soc.*, **86**, 2287 (1964); (b) M. P. Cava, C. K. Wilkins, Jr., D. R. Dalton, and K. Bessho, *J. Org. Chem.*, 30, 3772 (1965); (c) J. W. Huffman, C. B. S. Rao, and T. Kamiya, *J. Am. Chem. Soc.*, 87, 2288 (1965); *J. Org. Chem.*, **32**, 697 (1967); (d) Y. Ban, T. Oishi, M. Ochiai, T. Wakamatsu, and Y. Fujimoto, *Tetrahedron Letters*, 6385 (1966); (e) W. Nagata, S. Hirai, K. Kawata, and T. Okumura, *J. Am. Chem. Soc.*, **89**, 5046 (1967).

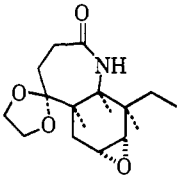
(9) Satisfactory elemental analyses were obtained for all compounds for which melting point or boiling point values are cited. These measurements are uncorrected.

(10) All samples were measured in $CDCl_3$ at 60 Mc on a Varian Model A-60 spectrometer and expressed as parts per million shift (δ) downfield from tetramethylsilane.

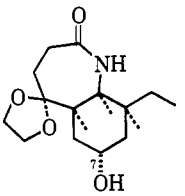
(11) The model study[5a] has shown that the related *trans*-oxime ketal does not undergo Beckmann rearrangement under the same conditions.

Because the Beckmann rearrangement proceeds with *anti* migration the structure of V retrospectively verified the stereochemistry of the *anti*-oxime IV and the assigned structure of the *cis*-monoketal III.

The double bond of V survived all the transformations and was available at this point to introduce a C_7-oxygen function into the molecule. Perbenzoic acid attacked mostly from the *convex* face[12] of the molecule, leading to the oxide VI in 65% yield; mp 170–172°; ν_{max}^{KBr} 3.17, 3.28 (–NH–), 6.02 μ (–*CO*–NH–). A selective lithium aluminum hydride reduction of VI furnished the C_7-*axial* hydroxy lactam VII (85%); mp 181–183°; ν_{max}^{KBr} 2.98 (–NH–), 3.07 (–OH), 6.13 μ (–*CO*–NH). During the next step the lactam group protected the nitrogen

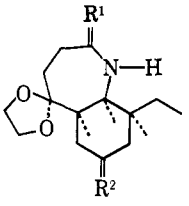


VI

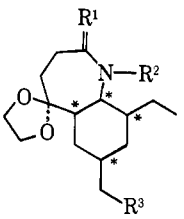


VII

function from oxidation. Thus, a Sarett oxidation of VII produced the C_7-ketone VIII in 90% yield; mp 220°; ν_{max}^{KBr} 3.0, 3.14, 3.28 (–NH–), 5.84 (>C=O), 6.03 μ (–*CO*–NH). A Wittig reaction transformed the ketone lactam VIII to the *exo*-methylene derivative IX (82%); mp 196–197°; ν_{max}^{KBr} 3.1 (–NH–), 3.3 (>C=CH_2), 6.03 μ (–*CO*–NH–); nmr δ 4.72 ppm (>C=CH_2, singlet). Hydroboration attacked the double bond on the *convex* face of IX, creating an *equatorial* hydroxymethyl derivative, X (90%); ν_{max}^{neat} 3.0 (–OH), 6.0 μ (–*CO*–NH–). A lithium aluminum hydride reduction of X produced the amino alcohol XI (90%); ν_{max}^{neat} 3.0 μ (–OH); the mass spectrum showed the molecular ion at *m/e* 269 and the most intense peak at *m/e* 168. The N-carbobenzoxylated amino alcohol XII [ν_{max}^{neat} 3.0 (–OH), 6.0 μ (>N–*CO*–)] was tosylated to XIII; ν_{max}^{neat} 5.92 (amide), 7.35, 8.50 μ (–SO_2–).



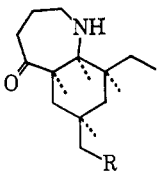
VIII, $R^1 = R^2 = O$
IX, $R^1 = O$; $R^2 = >CH_2$



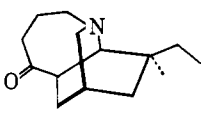
X, $R^1 = O$; $R^2 = H$; $R^3 = OH$
XI, $R^1 = H_2$; $R^2 = H$; $R^3 = OH$
XII, $R^1 = H_2$; $R^2 =$ Cbz; $R^3 = OH$
XIII, $R^1 = H_2$; $R^2 =$ Cbz; $R^3 = OTs$

The ketal and N-carbobenzoxy groups of XIII were then cleaved with HBr–AcOH and the hydrobromide of the amino ketone XIV was isolated in good yield; mp 150°; ν_{max}^{KBr} 3.7 (>NH_2^+), 5.88 (ketone), 7.60, 8.40 μ (–SO_2–). The mass spectrum of the hydrobromide salt of XIV interestingly showed peaks at *m/e* 379 (M – HBr) and another molecular ion at *m/e* 287, 289 corresponding to XV. A large peak at *m/e* 208 suggested the formation of the protonated tricyclic ketone system (XV → XVI).

The preparative equivalent of the above mass spectroscopic cyclization of XIV to *dl*-9-ethyloctahydro-1,7-methano-1H-benzazepin-5(4H)-one (XVI) was carried out in refluxing isoamyl alcohol in good yield. The tricyclic ketone XVI was successfully transformed by Fischer indolization to the racemic ibogamine (Ia); mp 128–131° (lit.[6] mp 129–132°).



XIV, R = OTs
XV, R = Br



XVI

The mass spectrum of the synthetic product was identical with that of the naturally occurring ibogamine; all the characteristic "ibogamine peaks"[13] were exhibited, including the significant peaks at *m/e* 280 (M^+), 265 (M – 15), 195, and 156 and those of other fragments which arise from the isoquinuclidine moiety[13] at *m/e* 122, 124, 135, 136, and 149. In addition, the synthetic product showed R_f values in three different solvent systems identical with those of ibogamine.

This synthesis provides the first preparative proof that the ethyl side chain of the iboga alkaloids has a cis configuration with respect to the N_6 function.[14]

Acknowledgments. The author is much indebted to the Analytical Department of Wyeth Laboratories. He especially wishes to thank Dr. Stephen Shrader for the invaluable determination and interpretation of the mass spectroscopy data, Dr. Charles Hetzel for the determination of the nuclear magnetic resonance spectra, and Dr. Norbert Neuss of Eli Lilly Company, who kindly provided the samples of natural ibogamine and epiibogamine.

(13) K. Biemann and M. Friedmann-Spiteller, *J. Am. Chem. Soc.*, **83**, 4805 (1961).
(14) See numbering in ref 2c.

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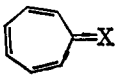
Received October 5, 1967

Tropenylidenimmonium Salts and Tropenylidenimines

Sir:

We wish to describe syntheses for, and some of the salient properties of, several members of the two classes of compounds **1**, X = R_2N^+= and RN̈=. The imines to be described have no previous direct precedent, although the related oxime and phenylhydrazone[1] of



1

tropone have been reported (**1**, X = HON= and NHPhN=), and diazatropolones have been synthesized.[2] A single tropenylidenimmonium salt (**1**, X =

(1) T. Mukaki, *Bull. Chem. Soc. Japan*, **33**, 238 (1960).
(2) (a) T. Nozoe, *et al.*, *Proc. Japan Acad.*, **29**, 565 (1953); (b) W. R. Brasen, H. E. Holmquist, and R. E. Benson, *J. Am. Chem. Soc.*, **82**, 995 (1960).

(12) R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey, and R. W. Kierstead, *Tetrahedron*, **2**, 1 (1958).