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# MASS SPECTROMETRIC EVIDENCE FOR THE STRUCTURE OF IBOXYGAINE AND ITS TOSYLATE

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THE structure of iboxygaine[1] and its carbomethoxy derivative voacangarin[2] (= voacristin[3]) has been investigated recently in three laboratories[1,2,3] and expressions Ia [2] and Ib [1,3] have been proposed for the former. One of the remarkable reactions of iboxygaine is the facile quaternization of its tosylate which cannot be isolated in its covalent form. This quaternary salt occupies a central position in the structural arguments for iboxygaine since its conversion[2] into ibogaine[4] (IIIa) is the only correlation with a compound of known structure. For this tosylate both structures IIa [1,2] and IIb [3] have been suggested.

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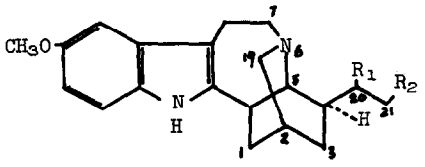
[1] R. Goutarel, F. Percheron and M. M. Janot, Compt. rend. 246, 279 (1958).

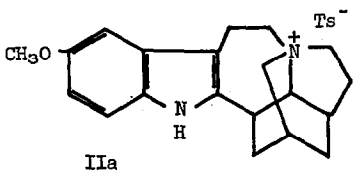
[2] D. Stauffacher and E. Seebeck, Helv. chim. Acta 41, 169 (1958).

[3] U. Renner and D. A. Prins, Experientia 15, 456 (1959).

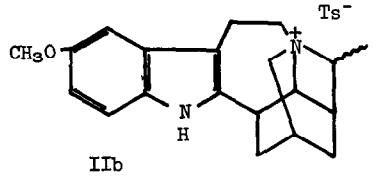
[4] M. F. Bartlett, D. F. Dickel and W. I. Taylor, J. Am. Chem. Soc. 80, 126 (1958). For stereochemistry see G. Arai, J Coppola and G. A. Jeffrey, Acta. Cryst. 13, 553 (1960).



Ia $R_1$=H, $R_2$=OH
Ib $R_1$=OH, $R_2$=H
IIIa $R_1$=$R_2$=H
IIIb $R_1$=D, $R_2$=H



IIa



IIb

We have now obtained conclusive evidence for structures Ib and IIb for iboxygaine and its tosylate, respectively, by their conversion into specifically monodeuterated ibogaine and locating the position of the deuterium atom in this molecule by mass spectrometry: On reduction of iboxygaine tosylate[2] (42 mg , m.p. 267-8° [3]) with lithium aluminum deuteride in tetrahydrofuran, ibogaine was obtained in quite pure[5] form (m.p. 146-9°; 82% yield). One recrystallization from ethanol/water raised the m.p. to 150-51°, undepressed on admixture of authentic IIIa.

The mass spectrum[6] of this product corresponded to the one[7] of IIIa

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[5] The mass spectrum of this crude material did not indicate any appreciable by-products.

[6] The spectra were determined with a CEC 21-103C mass spectrometer equipped with a heated inlet system operated at 140°; electron energy 70 eV.

[7] K. Biemann, Tetrahedron Letters 15, 9 (1960). The sample of ibogaine used in the present investigation had been recrystallized repeatedly to remove a small amount of ibogamine, the presence of which contributed to the peaks mass 279 and 280 in the spectrum published previously.

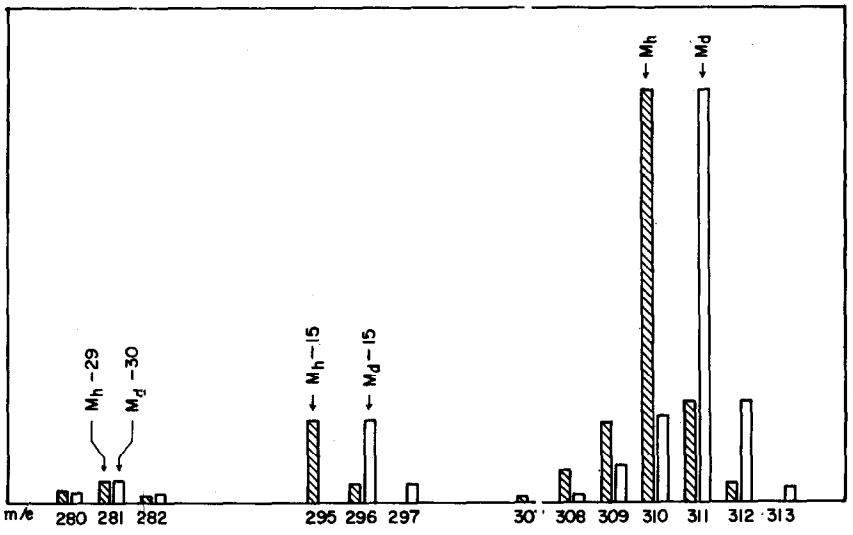


Figure 1

except that certain peaks were displaced for +1 mass unit. In Fig. 1 the spectrum of the deuterated sample (light peaks) is compared with ibogaine (shaded peaks) in the region of m/e 280-313. The presence of one atom of deuterium in the former is evidenced by its molecular weight (designated $M_d$) of 311 vs. 310 (designated $M_h$) for IIIa. The methyl group is lost in both cases as 15 mass units, and the deuterium atom is, therefore, not located in this group, thus excluding structure Ia. (The methyl group of the methoxyl cannot be responsible for the peaks at m/e 295 and 296, respectively, since also ibogamine, lacking the methoxyl, exhibits[7] the corresponding peak at m/e 265.) The deuterium atom is, however, present in the ethyl group because both spectra exhibit a peak at m/e 281; i.e. this fragment is formed by the loss of 29 mass units ($C_2H_5$) from ibogaine and of 30 mass units ($C_2H_4D$) from the deuterated compound, which is, therefore, IIIb. In the rest of the spectrum the isoquinuclidine peaks appear at m/e 123,

124, 125, 136, 137, 149, 150, 151 and are thus shifted for one mass number, whereas the indole peaks remained at 186 and 225 as in IIIa. This pattern is in agreement with a deuterium atom at $C_{20}$[8] on the basis of a more detailed interpretation of the spectrum which will be presented in the full paper.

These results demonstrate that in the deuteride reduction of the tosylate a bond between $N_6$ and $C_{20}$ was opened, and the structure of the cation must thus be IIb. Iboxygaine is, therefore, Ib and not Ia. The other isomeric structures (OH at $C_5$,$C_7$ or $C_{19}$) which conceivably could also lead to IIb are excluded for the following reasons: (a) The only saturated product isolated after treatment of the tosylate with sodium hydroxide[3] is iboxygaine itself; i.e. the bond formed in the quaternization was reopened in this displacement reaction, and there is no reason to assume that the deuteride should exclusively displace another bond. (b) The acid-stability of iboxygaine - one mode of formation from voacangarin requires prolonged heating with hydrochloric acid[2] - precludes the presence of an azetidine ring in iboxygaine, and (c) the tosylate of Ib is the only one of all four possible isomers which would be expected to quaternize so easily. The four-membered ring in IIb, the supposed strain of which led some of the earlier investigators[1,2] to discard structure IIb as impossible, is in fact part of an azapinane system and thus not unduly strained.

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[8] Numbering system according to ref. 4.