Experimental[17]

O-Methylsarpagine (Ib).—Trimethylanilinium iodide (0.40 g.) in 10 ml. of hot ethanol was stirred with excess silver oxide for a few minutes, centrifuged and the supernatant evaporated. To the sirupy residue was added 200 mg. of sarpagine (Ia) and 0.45 ml. of dimethylaniline. After heating this mixture to 165° for 1.5 hours, it was poured into dilute acetic acid and extracted with ether. The aqueous layer was then made alkaline with sodium hydroxide and extracted with dichloromethane–ether. The residue of the organic layer was chromatographed on alumina (neutral, II); chloroform eluted 49 mg.; after recrystallization from ethanol–water 32.6 mg. of O-methylsarpagine, m.p. 201–203° (lit.[8] 202–202.5°), was obtained.

O-Methyldeoxysarpagine.—O-Methylsarpagine (29.3 mg.) was tosylated[8] using 25 mg. of toluolsulfochloride in 0.5 ml. of pyridine. The crude amorphous product (Ic) was divided into several parts and reduced: (a) With lithium aluminum hydride.—Half of the above product Ic was reduced with 32 mg. of $LiAlH_4$ in 2 ml. of tetrahydrofuran yielding 7.8 mg. of O-methyldeoxysarpagine, m.p. 248–250° (lit.[8] 248–250°), mol. wt. 308 (by mass spectrometry). (b) With lithium aluminum deuteride.—One-quarter of the crude tosylate Ic was reduced in the same way, using 18 mg. of $LiAlD_4$. The crude product 5.4 mg. was recrystallized, giving 2.0 mg. of O-methyldeoxysarpagine-d_1, m.p. 247–249°, mol. wt. 309 (by mass spectrometry).

O-Methyldeoxydihydrosarpagine (V).—Two milligrams of O-methyldeoxysarpagine were hydrogenated in ethanol, using platinum as a catalyst. After 20 min. the product was isolated and sublimed at 0.1 mm. and 200° (bath); m.p. 237–240°. The mol. wt. of 310 (by mass spectrometry, see Fig. 1a) indicated the formation of a dihydro derivative.

O-Methyldeoxydihydrosarpagine-d_1 was prepared in the same manner by catalytic hydrogenation of O-methyldeoxysarpagine-d_1; mol. wt. 311 (by mass spectrometry, see Fig. 2b).

O-Methyldeoxydihydrosarpagine-d_0-d_6.—When O-methyldeoxysarpagine (1.5 mg.) was catalytically deuterated, using D_2–MeOD–Pt and worked up as described for the hydrogenations above including repeated evaporation with ethanol, the mass spectrum indicated a mixture of species containing up to seven deuterium atoms per molecule, the major component having a mol. wt. of 313 (-trideuterio derivative). Equilibration of this "mixture" with H_2–EtOH–Pt gave rise to the apparent loss of one deuterium atom. The mass spectrum of this material is shown in Fig. 2c.

(17) The spectra were determined with a CEC 21-103C mass spectrometer, equipped with heated inlet system, operated at 140°. Samples of 50–250 micrograms were employed. Melting points were determined on a Kofler micro-hot-stage.

Acknowledgments.—The author is greatly indebted to Prof. R. B. Woodward for a sample of compound IV, to Dr. A. Hofmann for sarpagine, and to the National Science Foundation for financial support (Grant G5051).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE 39, MASS.]

Application of Mass Spectrometry to Structure Problems. V.[1] Iboga Alkaloids[2]

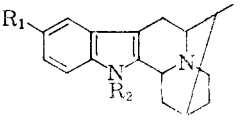
BY K. BIEMANN AND MARGOT FRIEDMANN-SPITELLER

RECEIVED JULY 10, 1961

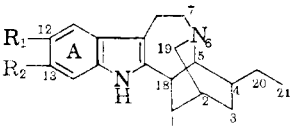
The mass spectra of the indole alkaloids ibogamine (III), ibogaine (IV) and tabernanthine (V) have been determined and are discussed in detail. The usefulness of mass spectrometry for the determination of the structure of such compounds is illustrated by two examples. Ibogaline was shown to have structure VI and iboxygaine to have structure VIII. The replacement of a hydroxyl group by deuterium and locating its position in the molecule by mass spectrometry proved useful for deciding between two previously proposed structures.

In a previous paper[1] we have correlated a degradation product of sarpagine with one of ajmaline (I and II) on the basis of their characteristic mass spectra, which exhibited almost identical peaks shifted 16 mass numbers, the difference between CH_3O and CH_3. It was concluded that both compounds must have the same carbon skeleton, the fragmentation of which gives rise to these characteristic peaks in the spectrum.

To provide experimental proof for the validity of such arguments, we have determined the spectra of two indole alkaloids of unambiguously proven structure[3]—ibogamine (III) and ibogaine (IV). Both contain the same carbon skeleton and differ merely in the presence of a methoxy group in ring A in IV, which is absent in III. These spectra, shown in Fig. 1, permit a number of important conclusions to be drawn. First of all, the spectrum (Fig. 1b) of ibogaine (IV) is very different from the one[1] of the isomeric compound I obtained from sarpagine (VII) and verifies our conclusion that compounds of different carbon skeleton, in fact, give different mass spectra. Secondly, a comparison of the spectra (Figs. 1a and 1b) of ibogamine (III) and ibogaine (IV) reveals the presence of two groups of peaks: one set which is of identical mass number and comparable intensity in both spectra (for example, mass 122



I, $R_1 = CH_3O$, $R_2 = H$
II, $R_1 = H$, $R_2 = CH_3$



III, $R_1 = R_2 = H$
IV, $R_1 = CH_3O$, $R_2 = H$
V, $R_1 = H$, $R_2 = CH_3O$
VI, $R_1 = R_2 = CH_3O$

124, 135, 136, 149) and must therefore arise from the isoquinuclidine moiety in the molecules, identical in both compounds. The peaks of the second group are also comparable in intensity in both spectra but appear in the spectrum of IV 30 units higher than in the one of III (mass 156, 195, 251, 265, 280 in III). These fragments must, therefore, contain the indole nucleus. The mass of these fragments alone is already an indication of their origin as the first group fits best the type of

(1) Part IV, K. Biemann, *J. Am. Chem. Soc.*, **83**, 4801 (1961).

(2) Presented in part at the 138th Meeting of the American Chemical Society, New York, N. Y., September, 1960. Another part was the subject of a preliminary communication: K. Biemann and Margot Friedmann-Spiteller, *Tetrahedron Letters*, No. 2, 68 (1961).

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

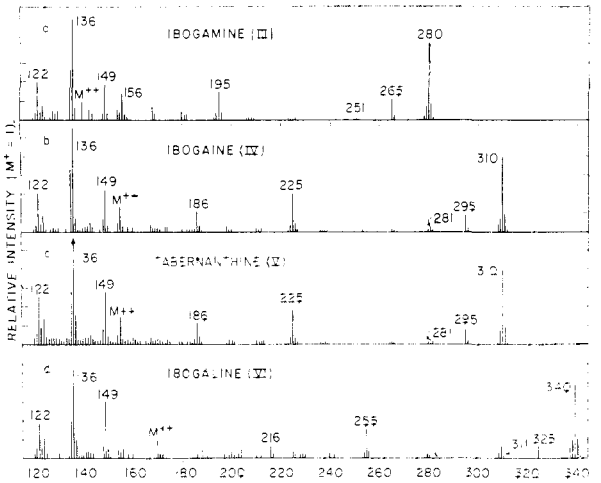


Fig. 1.—Mass spectra of four iboga alkaloids in the mass region from *m/e* 120 to 350. All peaks which are ≥2% as intense as the molecular ion are shown. The peak at *m/e* 136 in part is 1.7 times as intense as the one at *m/e* 310.

partly unsaturated alkylpiperidines, while the masses of the fragments belonging to the second group point to highly unsaturated systems.

It follows that any alkaloid of the ibogamine type should exhibit these two groups of peaks, partly shifted to other mass numbers if an additional substituent is present, unless the latter greatly alters the path of fragmentation of the initially formed molecular ion for reasons discussed previously.[1] The spectrum of tabernanthine (Fig. 1c) indicates the rather small effect of a change in position of the methoxyl group. The spectra of ibogaine (IV) and tabernanthine (V)[3] are very similar. The characteristic peaks are all of the same mass and of comparable intensity but still permit a differentiation between the two compounds if the spectra are determined with the same instrument and under comparable conditions.

Ibogaline.—It was then of interest to use these correlations to determine the structure of related alkaloids of this group. Recently a new alkaloid, ibogaline, was isolated from *Tabernanthe iboga* Baill in a very small yield.[4] Its ultraviolet spectrum indicated the presence of a 5,6-dimethoxyindole chromophore, a conclusion also supported by its infrared spectrum, and the analyses were in agreement with $C_{21}H_{28}N_2O_2$ containing two methoxyl groups. On the basis of these data and the fact that ibogamine (III), ibogaine (IV) and some related alkaloids occur in the same plant, structure VI, 12,13-dimethoxyibogamine was suggested,[4] for ibogaline. Verification of this proposal by conversion into a known iboga alkaloid or a common degradation product was impossible because of the scarcity of the material.

The mass spectrum of ibogaline (Fig. 1d) provides unambiguous proof for the correctness of the proposed structure VI. It shows the group of isoquinuclidine peaks characteristic for this group of alkaloids while the indole peaks are now shifted 60 mass numbers in comparison with the spectrum of ibogamine, indicating the presence of two methoxy-groups and the iboga carbon skeleton.

(4) N. Neuss, *J. Org. Chem.*, **24**, 2047 (1959).

It is of interest to note that the type of information obtained from elemental and methoxyl analysis is in this case also borne out by the mass spectrum: The exact molecular weight is 340. Since it is an even number, it has to contain an even number of nitrogen atoms, most probably two; the intensity of the isotope peak at mass 341 indicates the presence of a maximum of 21 carbon atoms; finally, the shift of 30 mass numbers *vs.* ibogaine and 60 mass numbers *vs.* ibogamine shows the presence of two methoxyl groups. Structure VI of ibogaline is, therefore, uniquely determined by its ultraviolet and mass spectra, which together require less than half a milligram of material.

Even the stereochemistry of the attachment of the ethyl group in ibogaline must be the same as in ibogamine and ibogaine[5] because the intensity of the peak at mass 325 is comparable to the one at 295 and 265 in the other alkaloids, which indicates a similar degree of stabilization in the fragment formed by loss of the methyl group. The stereochemical implications of this fact are discussed in a later section of this paper.

The relatively high intensities of the peaks at mass 309 and 310 may be due to a higher probability of the loss of the methoxyl group in the form of CH_3O or CH_2O in the dimethoxy compound. On the other hand, a small amount of ibogaine present in ibogaline would also add to the intensity of mass 310. Such a contamination of ibogaine by a trace of ibogamine (approx. 3%), which could only be removed by repeated recrystallization, similarly gave rise to a more intense peak at 280 in the spectrum of ibogaine determined earlier.[5a] Mass spectra may thus be used for the determination of the purity of an alkaloid, once the spectrum of a highly purified specimen is available.

Iboxygaine.—In addition to some of the alkaloids discussed above, another one had been isolated[6,7] from *Tabernanthe iboga*. Its elemental composition, $C_{20}H_{26}N_2O_2$, and its infrared spectrum suggested it to be a hydroxy derivative of ibogaine.[6] It was named iboxygaine[6] or kimvuline.[7] Iboxygaine was shown to contain one C–CH_3 group and to give a positive iodoform reaction. It could be oxidized to a ketone as suggested by the infrared spectrum of the crude product. On the basis of these findings and the ultraviolet spectrum, which revealed a 5-methoxyindole chromophore, iboxygaine was assigned structure VIII.[6] In the attempt to prepare an O-tosylate of this alkaloid it underwent internal cyclization and only the ionic tosylate of the quaternary compound could be isolated. Because of the presence of only one C-methyl group in the quaternary tosylate, structure X was suggested[6] for this salt without any further comments on its formation.

At about the same time, two other groups[8,9]

(5) The stereochemistry of the attachment of the ethyl group *cis* with respect to N_6 had been established by X-ray crystallography: G. Arai, J. Coppola and G. A. Jeffrey, *Acta Cryst.*, **13**, 553 (1960).

(5a) K. Biemann, *Tetrahedron Letters*, No. **15**, 9 (1960).

(6) R. Goutarel, F. Percheron and M.-M. Janot, *Compt. rend.*, **246**, 279 (1958).

(7) D. F. Dickel, C. L. Holden, R. C. Maxfield, L. E. Paszek and W. I. Taylor, *J. Am. Chem. Soc.*, **80**, 123 (1958).

(8) U. Renner, *Experientia*, **13**, 468 (1957).

(9) D. Stauffacher and E. Seebeck, *Helv. Chim. Acta*, **41**, 169 (1958).

obtained a new iboga alkaloid from *Voacanga africana* Stapf., given the names voacristine[8] and voacangarine,[9] respectively. They were later found to be identical and recognized as the carbomethoxy derivative of iboxygaine.[10] Stauffacher and Seebeck[9] also obtained the quaternary tosylate in the reaction of decarbomethoxyvoacangarine with toluolsulfochloride in pyridine. The reduction of this product with sodium in ethanol gave, among other substances, ibogaine (IV); this reaction constituted the first and only correlation of this alkaloid with a compound of known structure. Assuming that only a tosyl group at C_{21}[11] would be prone to facile cyclization, decarbomethoxyvoacangarine was assigned structure IX, while the tosylate was thought to be represented by X.[9]

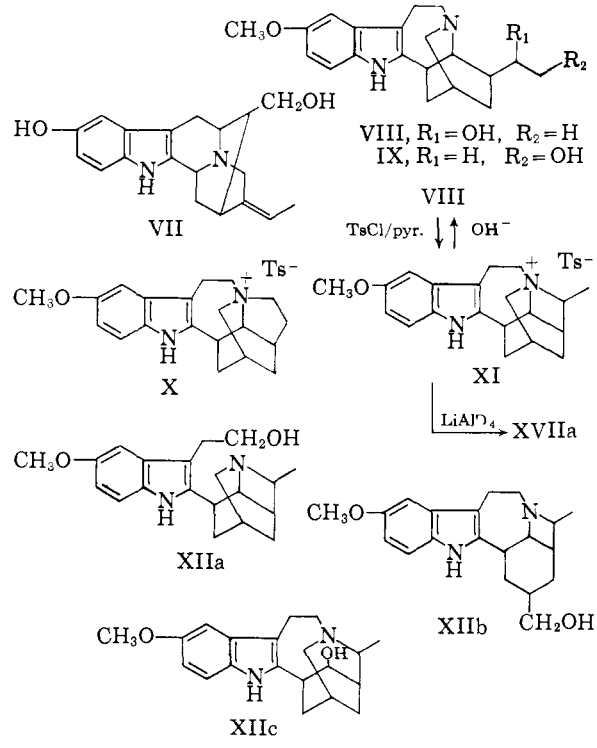
It was, however, pointed out by Renner and Prins[10] that the C–CH_3 values of the quaternary tosylate are much too high to be due to the methyl group of the tosylate anion which always gives very low values. While the earlier results of the sodium and ethanol reduction of the tosylate could not be reproduced in their hands, it was found that the tosylate is in part reconverted to iboxygaine on treatment with aqueous sodium hydroxide. Based on the findings that both iboxygaine and the cation of the tosylate contain one C–CH_3 group, structures VIII and XI were proposed for iboxygaine and the quaternary tosylate, respectively.[10]

Our first attempt to settle unequivocally the question of the position of the hydroxyl group in iboxygaine and to confirm the presence of the iboga carbon skeleton on the basis of the mass spectrum of this compound failed because the additional hydroxyl group decreases the volatility of this alkaloid considerably. Under the conditions required for volatilization of iboxygaine into the mass spectrometer with our present equipment, the molecule dehydrates and gives only a very poor spectrum.

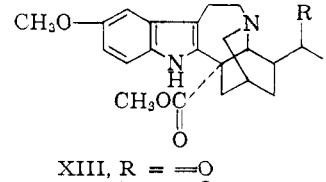
It was decided, therefore, to replace the hydroxyl group by deuterium and then to deduce the position of this deuterium atom in the ibogaine molecule from its mass spectrum. This conversion was accomplished by reduction of the quaternary tosylate with lithium aluminum deuteride. The product formed in 82% yield was almost pure deuterioibogaine according to its mass spectrum and melting point (146 to 149°). One recrystallization from ethanol–water raised the melting point to 150–151°, undepressed on admixture of authentic IV.

The principal peaks of the mass spectrum of the pure sample are shown in Fig. 2b. The molecular weight is found at mass 311 indicating the incorporation of one deuterium atom. The fragment due to loss of the methyl group is now found at mass 296 rather than 295 as in non-deuterated ibogaine and demonstrates that the deuterium atom is not located in the methyl group. Structures X for the tosylate and IX for iboxygaine are, therefore, excluded. The deuterium atom is, however, located in the ethyl group because in deuterated and non-deuterated ibogaine we find a fragment of mass 281 due to loss of the ethyl group. The latter is lost as 30 mass units in the deuterated molecule obtained from iboxygaine. It follows that this deuterioibogaine is XVIIa and the tosylate of iboxygaine is therefore represented by structure XI since obviously the bond between C_{20} and N_6 must have been opened in the lithium aluminum deuteride reduction.

While structure VIII is the most logical for iboxygaine, it is not strictly proved, because it could have been any one of the three remaining C–N bonds that were formed during the quaternarization, and we must briefly consider structures XIIa, XIIb and XIIc. Since it was found that the only saturated product formed on treatment of the quaternary tosylate with sodium hydroxide is iboxygaine, it was the bond formed during the quaternarization that was broken during this displacement reaction. It would be very unreasonable to assume that the deuteride should exclusively displace another bond. Structure XIIa and XIIb still contain an azetidine ring the presence of which in iboxygaine is excluded by the acid stability of the latter which can be obtained from voacangarine by prolonged heating with hydrochloric acid.[9] The free electron pair

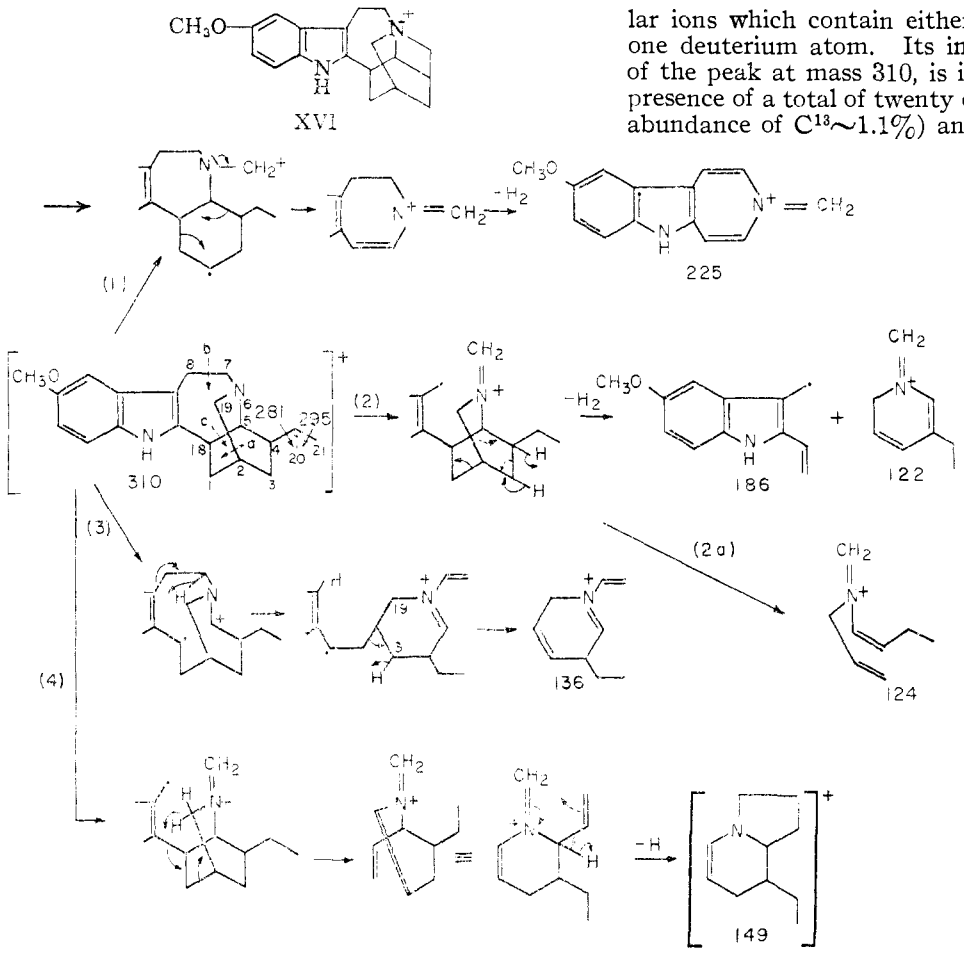


of N_6 in structure XIIc is very far away from C_5 thus precluding a facile cyclization. Molecular models of all four isomers (VIII, XII a,b,c) reveal that only in structure VIII is the hydroxyl-bearing carbon atom held in the vicinity of the tertiary



XIII, R = =O
XIV, R = —OH
XV, R = —H

(10) U. Renner and D. A. Prins, *Experientia*, **15**, 456 (1959).
(11) Numbering according to ref. 3.



nitrogen, a situation which forces the covalent tosylate to cyclize.

The formulation of iboxygaine as a C_{20}-hydroxy ibogaine has recently been corroborated by a chemical correlation.[12] Voacryptin,[8] also isolated from *Voacanga africana* Stapf., contains a carbonyl group and was converted by Wolff–Kishner reduction, which is accompanied by decarbomethoxylation, into ibogaine. Reduction by sodium borohydride, on the other hand, produced a mixture of epimeric hydroxy esters, one component of which was identical with voacristin. As voacryptin was found to have only one C-methyl group and gives a positive iodoform reaction, the carbonyl group was placed at C_{20} (structure XIII). The hydroxyl group in voacristin must then be at the same carbon atom (structure XIV).

Discussion of the Mass Spectra.—For the assignment of the structures of ibogaline and iboxygaine only a limited part of the information contained in the mass spectra was utilized. In a more detailed discussion of the spectra (Fig. 1) it will now be attempted to present a picture of the fragmentation of the ibogaine molecule (IV) on electron impact.

The strong peak at mass 310 represents the monoisotopic molecular weight (the mass of the molecules consisting of only their lightest isotopes) while the peak at mass 311 is due to those molecular ions which contain either one C^{13}, one N^{15} or one deuterium atom. Its intensity, about 23.5% of the peak at mass 310, is in agreement with the presence of a total of twenty carbon atoms (natural abundance of C^{13}~1.1%) and two nitrogen atoms (natural abundance of N^{15}~0.36%). The very small peak at 312 is due to species containing C_2^{13}, $C^{13}N^{15}$ or O^{18}. Because of the low natural abundance of deuterium, its contribution may be neglected for such estimations of a more qualitative nature.

The origin of the peaks at mass 295 and mass 281 has already been discussed. It should be noted, however, that the loss of the methyl group is in this case much more pronounced than the loss of the ethyl group, which is in contrast to the behavior of simpler molecules like ethylcyclohexane showing a reverse behavior. Loss of the methyl group leads to a primary carbonium ion while the loss of an ethyl group leads to a secondary one, and the latter is in general more stable. In the case of ibogaine the situation is different because of the vicinity of the basic nitrogen N_6 and the *cis*-ethyl group.[5] The primary carbonium ion formed by loss of C_{21} is stabilized by the free electron pair of N_6, giving rise to the ammonium ion XVI. This behavior is, in fact, the mass spectrometric equivalent of the cyclization of iboxygaine tosylate discussed earlier. The secondary carbonium ion with a positive charge at C_4 does not receive any additional stabilization and is therefore less favored than the fragment at mass 295. The fragmentation of the side chain is here very much influenced by the stereochemistry of its attachment, making it possible to deduce in iboga alkaloids even this stereochemical detail from the mass spectrum.

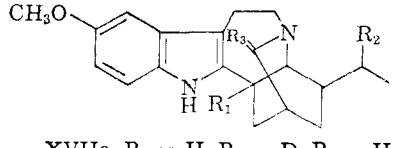
These two fragments are the only ones formed by simple cleavage of one single bond in this molecule. All other fragments arise in a more complex fragmentation involving the cleavage of more than one bond, frequently accompanied by the migration of one or more hydrogen atoms. In the following discussion two basic assumptions are made. First, the fragmentation is initiated by the breaking of a bond in such a manner that both the positive charge and also the radical formed in this process are well stabilized, and secondly that

(12) U. Renner and D. A. Prins, *Experientia*, **17**, 106 (1961).

multiple bond cleavage should proceed in a concerted manner and lead to well stabilized fragments in which most, if not all, electrons are paired. An amino nitrogen can, by virtue of its free electron pair, very effectively stabilize a positive charge on a neighboring carbon atom, and it is for this reason that bonds a, b, and c in ibogaine (IV) should have a considerable tendency to cleave on electron impact.

Fragmentation of bond a and retention of the positive charge at C_{19} followed by the loss of C_{1-4} and C_{20-21} and elimination of one hydrogen each at C_7 and C_8 in the form of a hydrogen molecule leads to the highly unsaturated ion of mass 225 (scheme 1). This mechanism is corroborated by the finding that mass 225 of ibogaine belongs to the group of peaks which do contain the indole moiety as pointed out earlier and that it does not contain C_{20} as evidenced by the fact that in the deuterated molecule obtained from iboxygaine (VIII) the deuterium atom is completely lost. Fragmentation of bond b in the initial molecular ion initiates the formation of a number of other fragments. If the positive charge is retained at C_7 and bonds C_1–C_2 and C_5–C_{18} are broken concertedly under simultaneous elimination of a hydrogen molecule from C_3 and C_4, a positive fragment of mass 122 is formed (scheme 2). If, however, the positive charge is initially retained at C_8, it will appear at the fragment of mass 186, giving rise to a peak at that mass, because a conventional mass spectrometer records only the positively charged fragments. The fragment of mass 124 of lower intensity may conceivably arise by another variation of this process involving cleavage of the C_3–C_4 bond (dotted arrow) rather than elimination of hydrogen (scheme 2a). Here again the interpretation is in agreement with the previous observation that mass 186 does contain the indole part of the molecule while mass 122 and 124 do not, but in turn retain the deuterium atom of XVIIa.

The origin of the peaks at mass 135, 136 and 149 now remain to be explained. A simple calculation shows that 135 and 136 have to contain N_6 and all the carbon atoms of the alicyclic system except two and all except one in the fragment of mass 149. In an attempt to solve these questions and also to corroborate further the correctness of the assignment made above, two specifically deuterated ibogaine molecules were prepared in addition to the one obtained during the work on



XVIIa, R_1 = H, R_2 = D, R_3 = H_2
XVIIb, R_1 = D, R_2 = H, R_3 = H_2
XVIIc, R_1 = R_2 = H, R_3 = D_2
XVIII, R_1 = R_2 = H, R_3 = O

iboxygaine. Ibogaine-18-*d* (XVIIb) was prepared by decarbomethoxylation[13] of voacangine (XV) using deuterated hydrazine. The sample of ibogaine obtained in this way consisted of 65% monodeuterioibogaine as judged from the mass spectrum (Fig. 2c). The incomplete deuteration is due to the use of not completely deuterated hydrazine and methanol. Ibogaine-19-d_2 (XVIIc) was obtained by reduction of ibogaine lactam (XVIII)[3] with lithium aluminum deuteride. The partial mass spectra of these three deuterioibogaines are compared with ibogaine in Fig. 2. All the shifts observed in these spectra are in agreement with our assignments and show, furthermore, that the fragments of mass 135 and 136 do contain the hydrogens at C_{20} and also part of the hydrogens at C_{19}, but not the one at C_{18}. The fragment of mass 149 must contain the hydrogens at C_{20}, C_{19} and C_{18}.

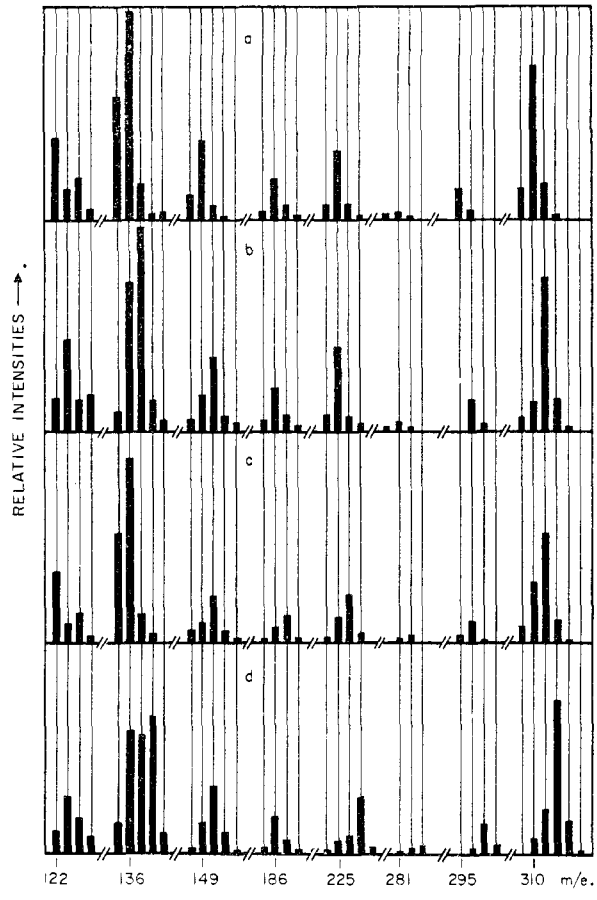


Fig. 2.—Partial mass spectra of deuterated ibogaines compared with ordinary ibogaine: a, IV; b, XVIIa; c, XVIIb; d, XVIIc. In each group the peaks which are ≥2% as intense as the peak due to the molecular ion are shown. In all four spectra the total intensity of the molecular ions (*i.e.*, in part c the peak at *m/e* 311 plus the part of peak m/e 310 due to the non-deuterated species) was made equal.

Cleavage at c initiates the fragmentation leading to the fragment of mass 136 (scheme 3). In the last step, a hydrogen may be lost either from C_3 or C_{19} which would account for the fact that the mass of this fragment shifts in part to mass 137, in part to mass 138 in the spectrum of ibogaine dideuterated at C_{19}. Elimination of a hydrogen atom from the fragment of mass 136 leads to mass 135.

(13) U. Renner, D. A. Prins and W. A. Stoll, *Helv. Chim. Acta*, **42**, 1572 (1959).

The formation of mass 149 is more difficult to visualize, as it requires cleavage of the C_{17}–C_{18} bond and the specific loss of one of the two hydrogen atoms at C_{19}. A possible path leading to this fragment is suggested in scheme 4. One of its weaker points is the required migration of a hydrogen from C_{19} to C_{17}, two centers which might be quite far apart once the C_7–C_8 bond is broken. This migration and the cleavage of the C_{17}–C_{18} bond may, however, precede fragmentation at b.

It is of interest to note that the C_4–C_5 bond does not appear to be cleaved in any one of the major modes of fragmentation of ibogaine. This is attributed to the fact that the resulting carbonium ion at C_5 cannot be stabilized by the free electron pair of the neighboring nitrogen because the resulting ammonium ion would violate Bredt's rule.

While in this section concrete, mostly covalent structures have been drawn for the fragments and for the intermediates, it should be remembered that the particles formed probably are not present in the ground state but in an excited state. It is, nevertheless, important to base any empirical correlation of the mass spectrum with a given structure on the basic necessity that the fragments giving rise to peaks of reasonable intensity should have an energetically favorable arrangement of the atoms. The support any such mechanistic correlations receive from the mass spectra of isotopically labeled molecules cannot be overemphasized and aids considerably in the understanding of the fragmentation of molecules as complex as the alkaloids discussed in this paper.

Experimental[14]

Reduction of Iboxygaine Tosylate (XI) with Lithium Aluminum Deuteride.—The quaternary tosylate of iboxygaine (42 mg.; recrystallized from methanol, m.p. 267–268°), prepared as described previously,[9] was suspended in 1 ml. of tetrahydrofuran. Addition of about 20 mg. of lithium aluminum deuteride in the same solvent caused dissolution of the tosylate and evolution of hydrogen. The mixture was kept in a sealed tube at 50° overnight, the cooled reaction mixture decomposed with a small amount of water and extracted thoroughly with ether–tetrahydrofuran. The organic layer was washed with water, dried over sodium sulfate and the solvent distilled. The crystalline residue, m.p. 145–148°, amounted to 22.5 mg. of XVIIa (82% yield) and was recrystallized once from ethanol–water: 14 mg., m.p. 149–150°, undepressed on admixture of authentic ibogaine (IV) of m.p. 148–150°. The mass spectrum (Fig. 2b) indicates a molecular weight of 311, demonstrating the incorporation of one atom of deuterium per molecule.

Decarbomethoxylation[12] of Voacangine (XV) with Deuteriohydrazine.—Two milliliters of deuteriohydrazine, prepared by repeated addition of D_2O to hydrazine (95%+) and removal of the water by distillation, was added to 55 mg. of voacangine (m.p. 135–136°) in 2 ml. of methanol-O-*d* and the mixture was heated in a sealed tube to 95–100° (causing dissolution of the substance). After 48 hours the cooled reaction mixture was evaporated *in vacuo*, 3 ml. of water added to the precipitate and extracted with ether–dichloromethane. The organic phase was dried over sodium sulfate and, on evaporation of the solvent, 33 mg. (74% yield) of crude material was obtained. After one recrystallization from alcohol it melted at 144–149° and was purified further by chromatography over alumina (20 mg. of XVIIb, 2.5 g. of alumina act. II, elution with a mixture of benzene and petroleum ether) raising the m.p. to 149–151°, undepressed on admixture of an authentic sample IV. The mass spectrum (Fig. 2c) indicates the incorporation of 0.7 atom of deuterium per molecule.

Reduction of Ibogaine Lactam (XVIII) with Lithium Aluminum Deuteride.—To 31 mg. of ibogaine lactam[8] (m.p. 201–203°) in 2 ml. of tetrahydrofuran was added a mixture of 40 mg. of lithium aluminum deuteride in 1 ml. of the same solvent. After heating the mixture in a sealed tube to 50° for 4 hours, it was cooled and decomposed with a few drops of water. After centrifugation the organic phase was decanted and the residue extracted with ether–tetrahydrofuran. On evaporation of the combined and dried solutions there remained 22.5 mg. of crystalline material XVIIc, m.p. 144–147°. It was chromatographed on alumina as described above and the eluted fraction melted, after recrystallization from ethanol, at 150–151°, undepressed on admixture of an authentic sample of ibogaine (IV). The mass spectrum (Fig. 2d) indicates the incorporation of two atoms of deuterium per molecule.

Acknowledgment.—The authors are indebted to Dr. W. I. Taylor for samples of ibogamine, ibogaine, ibogaine lactam, tabernanthine and voacangine, to Dr. N. Neuss for ibogaline, to Dr. D. Stauffacher for iboxygaine and voacangarine, and to the National Science Foundation (Grant G5051) and the Petroleum Research Fund of the American Chemical Society for financial support.

(14) The mass spectra were determined with a CEC 21-103C mass spectrometer, equipped with heated inlet system, operated at 140°. Ionizing potential 70 e.V., ionizing current 10 or 50 μamp., depending on sample size (approx. 30–200 micrograms). Melting points were determined on a Kofler micro-hot stage.