Tetrahedron Letters No.15, pp. 9-14, 1960. Pergamon Press Ltd. Printed in Great Britain

THE DETERMINATION OF CARBON SKELETON OF SARPAGINE BY MASS SPECTROMETRY

K. Biemann

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Mass.

(Received 25 May 1960)

SOME time ago several groups of investigators[2-4] simultaneously suggested structure I for sarpagine, isolated from Rauwolfia serpentina Benth. This alkaloid had been shown to possess a 5-hydroxy indole chromophore and the functional groups present in formula I. The alicyclic carbon skeleton, however, was arrived at largely by biogenetic considerations. Its rigorous proof by direct chemical intercorrelation of sarpagine with another indole alkaloid of established constitution, e. g., ajmaline,[5,6] though promised in one of the papers[3], was not presented.

---

[1] K. Biemann, C. Lioret, J. Asselineau, E. Lederer and J. Polonsky, Biochem. et Biophys. Acta in press.

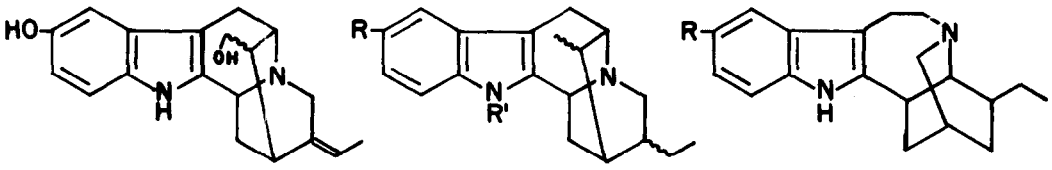
[2] D. Stauffacher, A. Hofmann and E. Seebeck, Helv. Chim. Acta 40, 508 (1957)

[3] W. Arnold, W. von Philipsborn, H. Schmid and P. Karrer, Helv. Chim. Acta 40, 705 (1957).

[4] J. Poisson, J. Le Men and M.-M. Janot, Bull. Soc. Chim. France 1957, 610.

[5] R. B. Woodward, Angew. Chem. 68, 13 (1956).

[6] R. Robinson, Angew. Chem. 69, 40 (1957).



I

II R = CH_3O R' = H
III R = H R' = CH_3

IV R = CH_3O
V R = H

It seemed to us that the correctness of the proposed structure could be checked by the comparison of the mass spectra of compound II (from sarpagine) and III (from ajmaline)[7], employing a minimum of chemical conversions and very little material.

These two compounds differ in the substitution of the indole nucleus but have an identical alicyclic carbon skeleton, apart from possible differences in the relative stereochemistry at two carbon atoms. Fragmentation on electron impact in a mass spectrometer of an aromatic molecule bearing an aliphatic or alicyclic substituent, in general, leaves the aromatic segment intact, which also retains the positive charge, whereas certain bonds in the nonaromatic part are preferentially broken. We would, therefore, expect structures II and III to have very similar spectra, in particular at the region of higher masses, which consists of the peaks due to the loss of fragments from the alicyclic moiety of the molecule. These peaks should be found at mass numbers sixteen units higher in the spectrum of II compared with III, since the net mass difference of the aromatic entities is due to one oxygen atom.

---

[7] R. B. Woodward and K. Schenker, unpublished.

Sarpagine was converted *via* phenol-O-methylation[4], tosylation and reduction with lithium aluminium hydride to desoxy-methylsarpagine[3], m.p. 248-250°, mol. wt. 308 (by mass spectrometry). Two milligrams of it were hydrogenated in ethanol using platinum as a catalyst. After 20 min. the product, II, was isolated and sublimed at 0.1 mm. and 200° (bath); m.p. 237-240°. The mol. wt. of 310, exhibited by the mass spectrum, indicated the formation of a dihydro derivative, eliminating the necessity for elemental analysis.

The partial mass spectra of II and III, shown in Figure 1, clearly exhibit a very close similarity and the shift of 16 mass units, demonstrating the identity of their alicyclic carbon skeletons and confirming structure I for sarpagine. The main difference is the peaks at m/e 279 (M-31) and m/e 280 (M-30) in the spectrum of II which, however, are due to the loss of the methoxy group, either as such (mass 31) or, with rearrangement of one hydrogen atom, as formaldehyde (mass 30). It is of interest to note that there are no characteristic peaks below mass 198 in II and 182 in III, respectively. These latter peaks are considered to be due to the β-carboline skeleton, after loss of ring D and the one carbon bridge, followed by aromatization.

To exemplify the validity of the tacit assumption that indole alkaloids with different alicyclic carbon skeletons in fact give rise to quite dissimilar mass spectra, the spectra of ibogaine (IV)[8] and ibogamine (V)[8] are shown in Figure 1. Here again the high mass parts are very similar (in ibogaine 30 mass units higher, because of the additional methoxyl group), but definitely different from the spectra of II and III. There is, however,

---

[8] M. F. Bartlett, D. F. Dickel and W. I. Taylor, J. Amer. Chem. Soc. 80, 126 (1958).

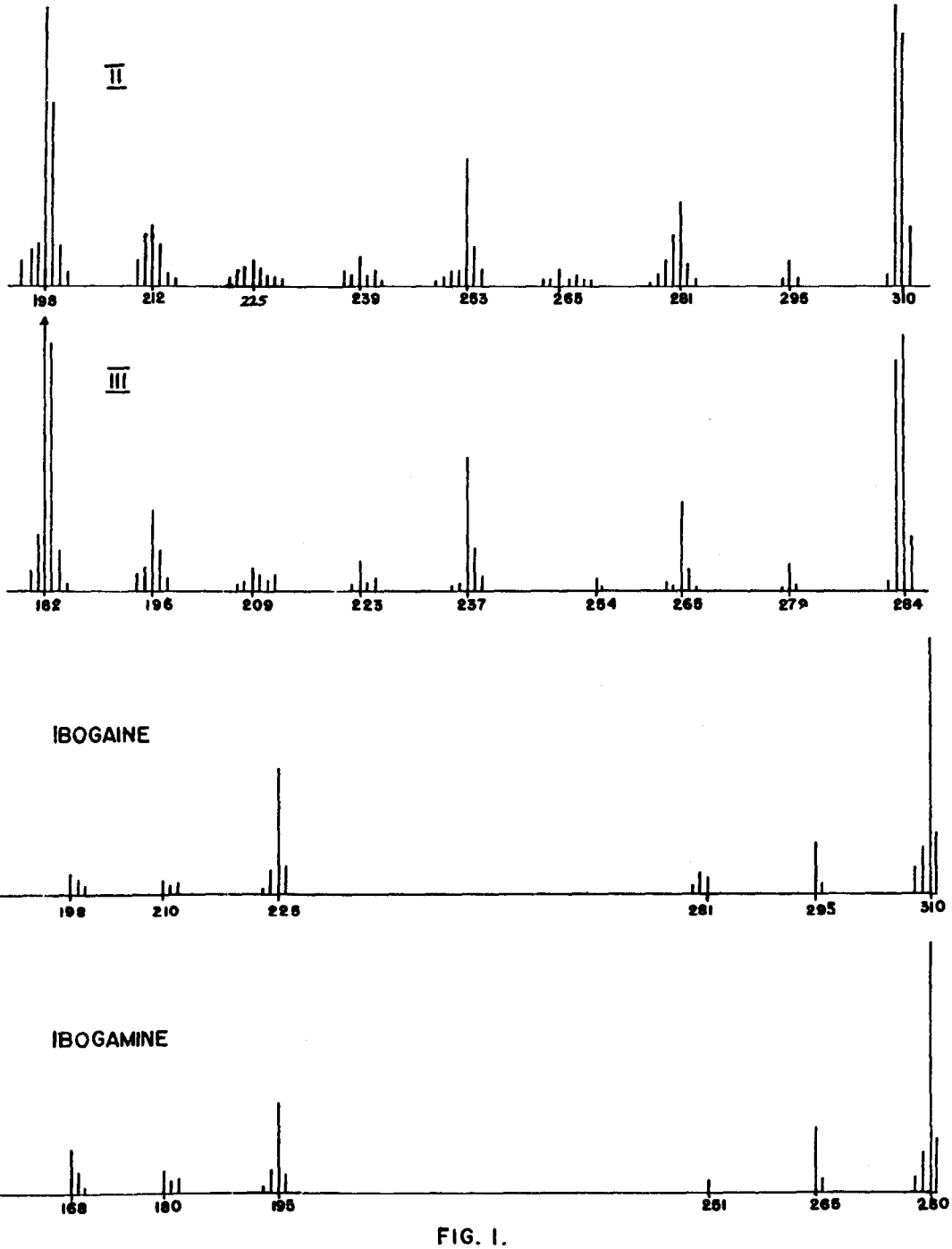

II
198
212
225
239
253
268
281
295
310
III
182
196
209
223
237
254
268
279
284
IBOGAINE
186
198
210
225
281
295
310
IBOGAMINE
156
168
180
195
251
265
280

FIG. 1.

clearly present a group of peaks (at m/e 122, 123, 124, 135, 136, 148, 149, 154, not shown in Figure 1 for lack of space) which are identical in the spectra of both ibogamine and ibogaine, and therefore arise from the alicyclic parts. This points out that the molecular ion formed originally can also decompose into highly stabilized fragments not containing the indole grouping, probably because the seven-membered ring C prevents decomposition to a β-carboline. This behavior on electron impact is somewhat paralleled by the fact that the alkaloids of the ibogaine family, in contrast to sarpagine, yield 3-ethyl-5-methylpyridine under various pyrolyti conditions.[9,10]

We feel that this investigation points out some of the potentialities mass spectrometry has in this field. It might well become very useful for the relatively facile and speedy comparison of aliphatic or alicyclic carbo skeletons attached to similar aromatic nuclei in these more complicated cases where the structure of this part of the molecule cannot be deduced by direct interpretation of the spectrum of the unknown compound itself. The relative insensitivity of mass spectra to differences in the stereochemistr of certain groups, which lead only to differences in the intensity but not in the mass numbers of the peaks, is an added advantage in this case.

---

[9] R. Goutarel, M.-M. Janot, F. Mathys and V. Prelog, Compt. rend. 237, 1718 (1953).

[10] R. Goutarel, F. Percheron, J. Wohlfahrt and M.-M. Janot, Ann. pharm. franc. 15, 353 (1957).

Furthermore, it should be noted that all the spectra discussed above have been obtained with samples ranging from 30-100 micrograms.*

A more detailed discussion of the spectra and deuteration experiments, which further corroborate the position of the alcoholic hydroxyl and of the double bond, will be published elsewhere.

Acknowledgments - The author is greatly indebted to Prof. R. B. Woodward for a sample of compound III, to Dr. A. Hofmann for sarpagine, to Dr. W. I. Taylor for ibogaine and ibogamine, and to the National Science Foundation for financial support (Grant G5051).

---

* The spectra were determined with a CEC 21-103C mass spectrometer, equipped with heated inlet system, operated at 140°.