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LYCOPODIUM ALKALOIDS*

SAUROXINE

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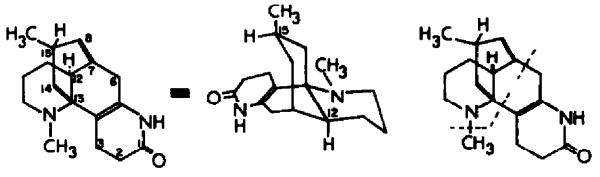
Abstract—On the basis of UV, IR, NMR and mass spectral data structure I is proposed for sauroxine. The dehydrogenation of sauroxine to give 7-methylquinoline and 6-methyl-α-pyridone is described.

DEULOFEU and De Langhe reported[1] an examination of the alkaloids of *Lycopodium saururus*, a plant which is widely distributed in South America and in Africa. *L. saururus* contained none of the commonly occurring Lycopodium alkaloids[2] but afforded two alkaloids, named saururine and sauroxine, unique to this species. We now wish to report a study of the physical and chemical properties of sauroxine which shows that it has structure I.



I Iα II

The molecular formula $C_{17}H_{26}ON_2$ originally assigned to sauroxine[1] was confirmed by mass spectrometric determination of the mol. wt. Sauroxine is thus isomeric with α-obscurine (II),[3] and a comparison of the spectral data obtained from sauroxine with that from α-obscurine[3] suggested that they are in fact stereoisomers. In the UV sauroxine shows a maximum at 257 mμ (log ε 3·70) compared with 255 mμ (log ε 3·73) for α-obscurine. The IR spectra of the two in carbon tetrachloride were almost superimposable in the region above 1500 cm^{-1}, both showing amide NH absorption at 3415, 3220, 3160 and 3100 cm^{-1}, and N-methyl CH stretching[4] at 2800

* This paper represents Part IX in the series Lycopodium Alkaloids by the Alberta group. Part VIII, *Canad. Jour. Chem.* **43**, 328 (1965).

[1] V. Deulofeu and J. De Langhe, *J. Amer. Chem. Soc.* **64**, 968 (1942).
[2] H. G. Boit, *Ergebnisse der Alkaloid-Chemie bis* 1960, pp. 916, 1011. Academie-Verlag, Berlin (1961).
[3] W. A. Ayer, J. A. Berezowsky and G. G. Iverach, *Tetrahedron* **18**, 567 (1962).
[4] K. Nakanishi, *Infrared Absorption Spectroscopy, Practical*, pp. 40, 190. Holden-Day, San Francisco (1962).

cm^{-1}. Sauroxine absorbed at 1690 (medium intensity) and 1665 cm^{-1} (strong) in the carbonyl region, somewhat lower than α-obscurine (1700, 1675 cm^{-1}). The fingerprint regions of the spectra were distinctly different.

The NMR spectrum of sauroxine showed, among others, a one proton signal at τ 1·36, attributed to the lactam NH, an N—CH_3 signal at τ 7·64, and a secondary C-methyl signal at τ 9·12 (splitting 5 c/s). The corresponding peaks in α-obscurine are found at τ 1·99, 7·55 and 9·14 (splitting 5 c/s).

Even more striking proof of the similarity of sauroxine to α-obscurine (II) was obtained from an examination of the mass spectra (Fig. 1) of the two substances. In both spectra the base peak appears at m/e 217 and as can be seen in Fig. 1 the fragmentation pattern is very similar.* These results strongly suggest that both compounds have the same skeleton and differ only in stereochemistry. Because of the nature of the fused ring system present this difference can only be at C-12 or C-15. We favour C-12 as the point of difference for the following reasons: First, if the difference were at C-15 the methyl group at C-15 would be in the shielding region of the dihydropyridone system[6] (conformational drawing Ia) and would be expected to appear at higher field than in α-obscurine, which is not the case. Secondly, it has been shown[7] that with Lycopodium alkaloids a cis arrangement of the C-12 hydrogen and the C-7 to C-13 bridge is more favourable than a *trans* arrangement for the loss of the bridge and the C-12 hydrogen on electron impact (a process[5] which leads to the base peak

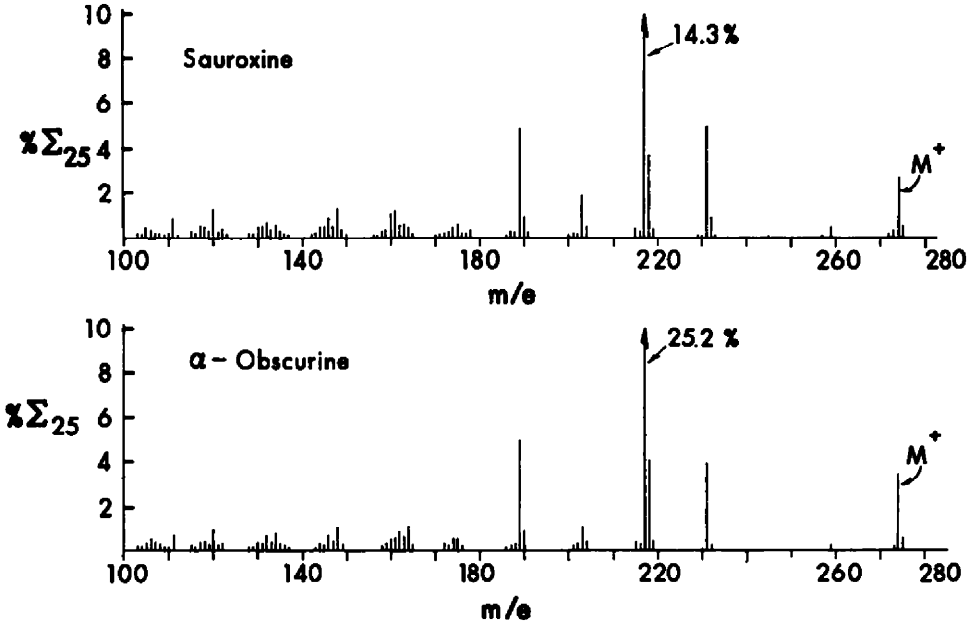


FIG. 1. Mass spectra of sauroxine and α-obscurine.

* A fragmentation scheme for α-obscurine has already been presented[5] and need not be discussed here.

[5] D. B. MacLean, *Canad. J. Chem.* **41**, 2654 (1963).
[6] F. A. L. Anet, *Canad. J. Chem.* **39**, 2262 (1961).
[7] W. A. Ayer and G. G. Iverach, *Canad. J. Chem.* **42**, 2514 (1964).

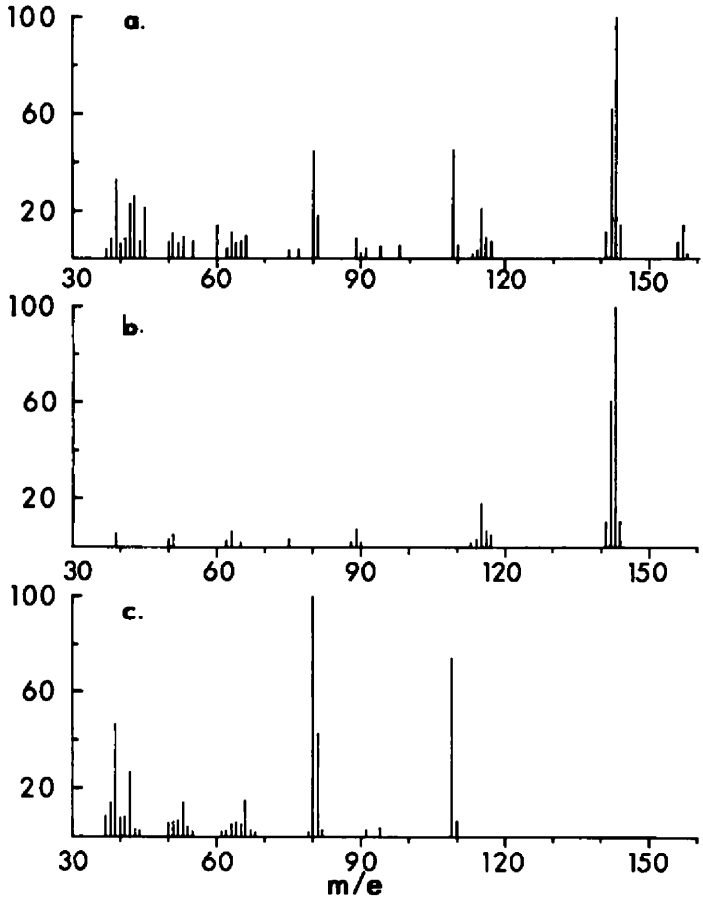


FIG. 2. Mass spectrum of (a) volatile product of dehydrogenation of sauroxine, (b) 7-methylquinoline, (c) 6-methyl-α-pyridone. Only peaks with an intensity greater than 2% of the base peak are shown.

(m/e 217) in the mass spectra of sauroxine and α-obscurine). In α-obscurine the peak at m/e 217 accounts for 25·2% of Σ_{25} (sum of the relative intensities of all peaks from mass 25 to the mol. wt.) whereas in sauroxine it accounts for only 14·3%. The ratio (1·76) of these percentages is very similar to that observed[7] with lycopodine–12-epilycopodine (1·71), and leads us to propose structure I (= Ia) for sauroxine.

The key reaction in the determination of the structure of α-obscurine[3] was a Pd catalysed dehydrogenation which yielded[8] 7-methylquinoline and 6-methyl-α-pyridone, formed by cleavage as indicated (broken lines) in II. Similar dehydrogenation of a small quantity of sauroxine yielded a volatile fraction which, on thin-layer chromatography (tlc) gave two spots which had the same R_f values as 7-methylquinoline and 6-methyl-α-pyridone. The mass spectrum of this volatile fraction (Fig. 2) also indicates the presence of these two components. In Fig. 2 the mass spectrum of the dehydrogenation mixture (a) is compared with that of authentic 7-methylquinoline (b) and 6-methyl-α-pyridone (c). The presence of the peak at m/e 157 suggests the presence

[8] B. P. Moore and L. Marion, *Canad. J. Chem.* **31**, 952 (1953).

of a small amount of a higher homolog of 7-methylquinoline in the dehydrogenation mixture.

Although the absolute stereochemistry of α-obscurine is as shown in II,[3] no direct correlation with sauroxine has been achieved and hence I (= Ia) does not necessarily represent the absolute stereochemistry of sauroxine. This is the first example of a naturally occurring Lycopodium alkaloid with the 12-epi configuration.

EXPERIMENTAL

Mass spectra were determined on an AEI MS2-H mass spectrometer. UV spectra were measured in 95% EtOH on a Cary Model 14 recording spectrometer. NMR spectra were determined in $CDCl_3$ on a Varian Associates Model A-60 spectrometer. IR spectra were determined on a Perkin-Elmer Model 421 spectrophotometer. Thin-layer chromatograms were carried out on aluminium oxide G (E. Merck, Darmstadt, Germany) and were developed with I_2 vapour.

Isolation of sauroxine. Finely ground *L. saururus* (collected in Argentina) was Soxhlet-extracted with MeOH, the MeOH replaced with dil. HCl and the solution filtered and washed with ether. The acid solution was then made strongly basic with NH_4OH aq and extracted with $CHCl_3$. The basic fraction was dissolved in $CHCl_3$ and subjected to chromatography over alumina (activity III). Elution with chloroform yielded non-crystalline material which has not yet been investigated. Elution with $CHCl_3$–MeOH (199:1) yielded a colourless oil which solidified on standing. Crystallization of this material from acetone yielded pure *sauroxine*, m.p. 200–201° (reported[1] 198°). The mass spectrum, determined at 200°, is shown in Fig. 1. The remaining spectral details are mentioned in the text. pK_a (50% MeOH) 8·1. The pK_a of α-obscurine, determined under the same conditions, was also 8·1.

Further elution of the column ($CHCl_3$–MeOH, 99:1 and 19:1) yielded an amorphous alkaloid, homogeneous to thin-layer chromatography, the UV, IR, mass and NMR spectra of which suggest a structure analogous to β-obscurine.[3]

Dehydrogenation of sauroxine. A mixture of sauroxine (29 mg) and 5% Pd–C (43 mg), under N_2, was heated for 30 min at 290–300° and then 30 min at 260–270°. A small amount of material (4 mg) condensed in the condenser. This material consisted, as shown by tlc, of 7-methylquinoline and 6-methyl-α-pyridone. The mass spectrum of the mixture, determined at 150°, is shown in Fig. 2a.

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