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THE STRUCTURE OF LYCODINE

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AYER and Iverach[1] have recently discovered the presence of an N-methyl group in the Lycopodium alkaloids α- and β-obscurine. They have suggested structures for these alkaloids on the basis of dehydrogenation experiments of Moore and Marion[2] and of a biogenetic relationship to lycopodine[3]. They have also suggested[1] a relationship of β-obscurine to lycodine, which they have recently proven[4].

We now wish to present evidence which rigorously establishes these suggested structures as correct and furthermore completely defines the relative stereochemistry of these alkaloids. This has been done by relating lycodine to lycopodine, the structure and stereochemistry of which are

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1 W.A. Ayer and G.G. Iverach, Tetrahedron Letters No. 10, 19 (1960).

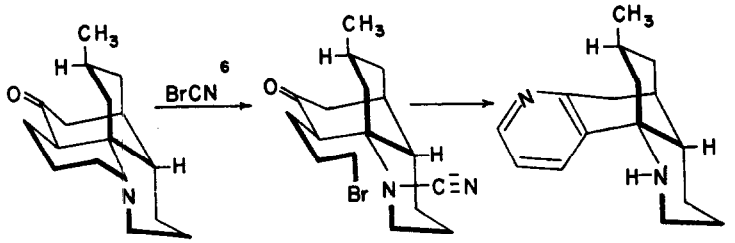
2 B.P. Moore and L. Marion, Canad. J. Chem. 31, 952 (1953).

3 W.A. Harrison and D.B. MacLean, Chem. and Ind. 261 (1950).

4 W.A. Ayer, private communication. Paper presented at the Chemical Institute of Canada Annual Conference, Ottawa, June, 1960.

known[5].

β-Cyanobromolycopodine[6] (II), available as the minor product from the reaction of lycopodine (I) with cyanogen bromide, was heated with a suspension of sodium azide in acetone. The reaction product contained intense bands at 1700 cm^{-1} (ketone), 2095 cm^{-1} (azide group), and at 2200 cm^{-1} (cyano group), and was directly reduced to a base by means of hydrogen in the presence of palladium-charcoal in acidic ethanol. This indirect method was chosen as it was known[3,6] that II underwent cyclization easily under alkaline conditions to form a very inert enol ether. The base, which partially cyclized under the isolation conditions, was dehydrogenated under mild conditions (boiling p-cymene and palladium-charcoal for 1.5 hours, conditions under which lycodine was known to be stable) and then heated with hydrochloric acid to remove the cyano group. The base, obtained in good yield, crystallized readily and was identified as lycodine by m.p., mixed m.p., ultraviolet and infrared spectra.



I II III

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[5] F.A.L. Anet, Tetrahedron Letters, No. 20, 13 (1960).

[6] D.B. MacLean, R.H.F. Manske and L. Marion, Canad. J. Res. 288, 460 (1951).

Therefore, lycodine has the relative stereochemistry shown in III and β-obscurine is the α-pyridone, and α-obscurine the 3,4-dihydropyridone analogues of III.

The structure III is completely consistent with our unpublished degradation work on lycodine. In particular, the large (0.34 p.p.m.) shift in the position (only) of the γ-proton of the pyridine ring in the NMR spectrum of lycodine on acetylation finds a ready explanation in the proximity of the γ-proton and the secondary nitrogen atom in III. This is in agreement with previous deductions[7] based on the abnormal chemical shift of the γ-proton with respect to the α- and β-protons. Unlike the results at 40 Mc., it has now been found that at 60 Mc. the methyl group of lycodine is a doublet, although poorly resolved, whilst the acetyl derivative gives a single, but broad line, for this group. The acetyl methyl group is a single very sharp line. The reasons for these effects will be discussed in a separate paper.

α-Obscurine gives[2] 7-methylquinoline and 6-methyl-α-pyridone on dehydrogenation. The cleavage into two fragments probably involves reverse Mannich-type reactions, which would not be expected to take place with lycodine. In fact, dehydrogenation of lycodine with palladium-charcoal at 250° did not give any quinoline derivatives, but a number of compounds, as shown by paper chromatography. These

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[7] F.A.L. Anet and C.R. Eves, Canad. J. Chem. 36, 902 (1958).

compounds all appear to be substituted m-phenanthrolines as shown by their ultraviolet absorption spectra. This is not unexpected for the dehydrogenation of structure III.

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