Tetrahedron Letters No.26, pp. 2193-2194, 1969. Pergamon Press. Printed in Great Britain.

X-RAY STRUCTURE ANALYSIS OF LAPPACONINE

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(Received in USA 14 March 1969; received in UK for publication 26 April 1969)

Lappaconine is a diterpenoid alkaloid of the aconite family. It has been isolated originally from Aconitum septentrionale Koelle. The chemical structure of lappaconine has been investigated by Marion and his colleagues since 1963, but certain unusual results (see following communication) have precluded a complete elucidation of the structure. For this reason it was decided to carry out an X-ray structure analysis of lappaconine hydrobromide which was prepared by Dr. N. Mollov.

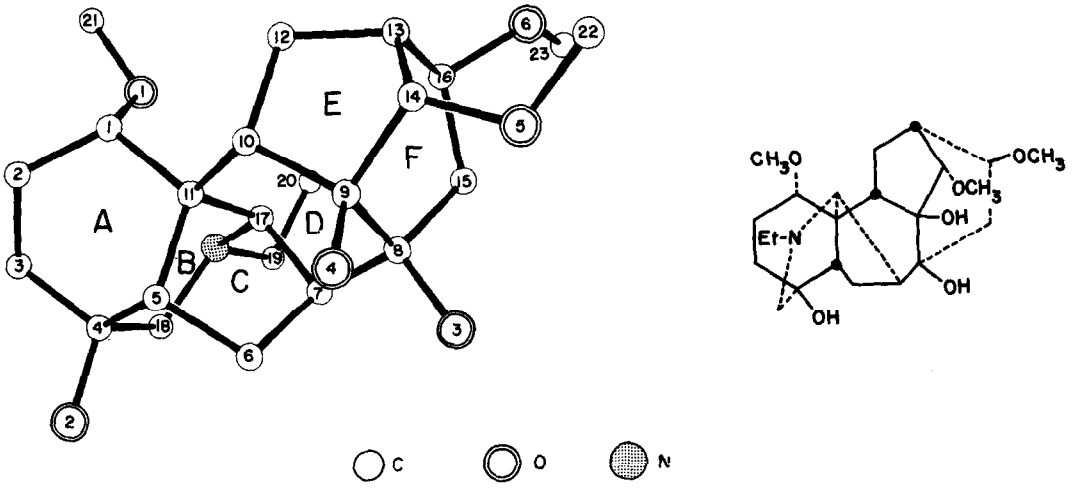
Crystals of lappaconine hydrobromide, $C_{23}H_{37}O_6N.HBr$, were obtained from a mixture of ethanol and petroleum ether. They were colorless prisms elongated in the direction of the b axis, with a diamond-shaped base. Precession photographs showed the crystals to be orthorhombic, space group $P2_12_12_1$, with 4 molecules in the unit cell. The following cell dimensions were obtained from diffractometer measurements: a = 26.194, b = 10.160, c = 8.809 Å. Three-dimensional data were collected on a Picker automatic diffractometer. It was noted that the intensities were decreasing gradually as a result of X-ray exposure. Consequently, the data were collected from two crystals. Of the 2291 accessible reflections within $2\theta = 130°$, 1888 (82%) had observable intensities.

The structure was solved by the heavy-atom method. The position of the bromide ion was easily deduced from a three-dimensional Patterson synthesis. Using the phases thus obtained, structure factors were computed followed by a three-dimensional electron-density distribution. Several rounds of this procedure revealed all the atoms in the structure. The atomic parameters are being refined by the least-squares procedure. At the present time, the reliability factor R = 8.5%.

As assumed, the carbon-nitrogen ring system of lappaconine turned out to be the same as that of delcosine[1] and lycoctonine.[2] It should be noted, however, that lappaconine presents the first example in this group of alkaloids in which one of the carbon atoms normally attached to C(4) is missing and in which there are oxygenated substituents at C(4) and C(9). These facts contributed to the difficulties encountered in the interpretation of the chemical studies of lappaconine. The six-membered ring A is in boat conformation. The same situation was encountered in delcosine although in lycoctonine the corresponding ring is a chair. As in delcosine, the boat form in this structure is

stabilized by a hydrogen bond. In the present case this involves the proton attached to the quaternized nitrogen atom being donated to the axially attached O(1). This proton is also donated to the bromide ion, thus being involved in a bifurcated hydrogen bond system. The six-membered rings B and D are in chair form, but ring F is forced into a distorted boat conformation by its substituents. Only the methoxy group attached to C(14) is axial, the other three groups being equatorial.

It will be attempted to determine the absolute configuration of lappaconine at the end of the refinement. It is reasonable to assume, however, that it is the same as that of lycoctonine, which has been determined, viz. that shown in the Figure.



Figure

Full details of this structure analysis and its results will be published elsewhere.

Acknowledgments:

I wish to thank Dr. L. Marion and Dr. N. Mollov for suggesting this problem to me and for supplying crystals of lappaconine hydrobromide. The programs of Ahmed, Hall, Huber, and Pippy were used for all crystallographic computations. Finally, I want to thank Dr. M. Przybylska for her continued encouragement and interest in this work.

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