THE MOLECULAR STRUCTURE AND ABSOLUTE CONFIGURATION OF THELEPOGINE METHIODIDE

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An alkaloid has been isolated from the grass, Thelepogon elegans, by Dr. W. D. Crow* of the Organic Chemistry Section of the Chemical Research Laboratories, C.S.I.R.O. and named thelepogine(1). Since only a small amount of the alkaloid was available and this X-ray analysis was proposed, no investigation of the structure by chemical or other physico-chemical techniques was initiated apart from elemental analysis of the base and its methiodide. Excellent crystals of the methiodide were provided by Dr. Crow, the microanalytical data being in closest accord with $C_{20}H_{33}ON.CH_3I$.

The crystals are monoclinic with $\underline{a} = 7.462$, $\underline{b} = 13.044$, $\underline{c} = 11.117$Å, $\beta = 109.05°$ at $-150°$C, the space group being $P2_1$ with two molecules in the unit cell. X-ray analysis (CuK_α radiation) was based on only the h0l, 0kl and 1kl data (704 reflections of 764 theoretically possible). The molecular skeleton i.e. atoms other than hydrogen, was first located three-dimensionally and then the nitrogen and oxygen atoms differentiated. From the bond lengths and stereochemical disposition within the skeleton, hydrogen atom sites

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[1] W. D. Crow — to be published.

can be allocated, the molecular formula on this basis being $C_{20}H_{31}ON.CH_3I$. With the molecular structure defined, the absolute configuration of the molecule was fixed by application of Bijvoet's(2) technique using the anomalous dispersion of the iodine atoms.

The atomic distribution of the molecular skeleton as viewed down the b axis is given in the correct absolute orientation in Fig. 1a while a more conventional chemical formulation is presented in Fig. 1b.

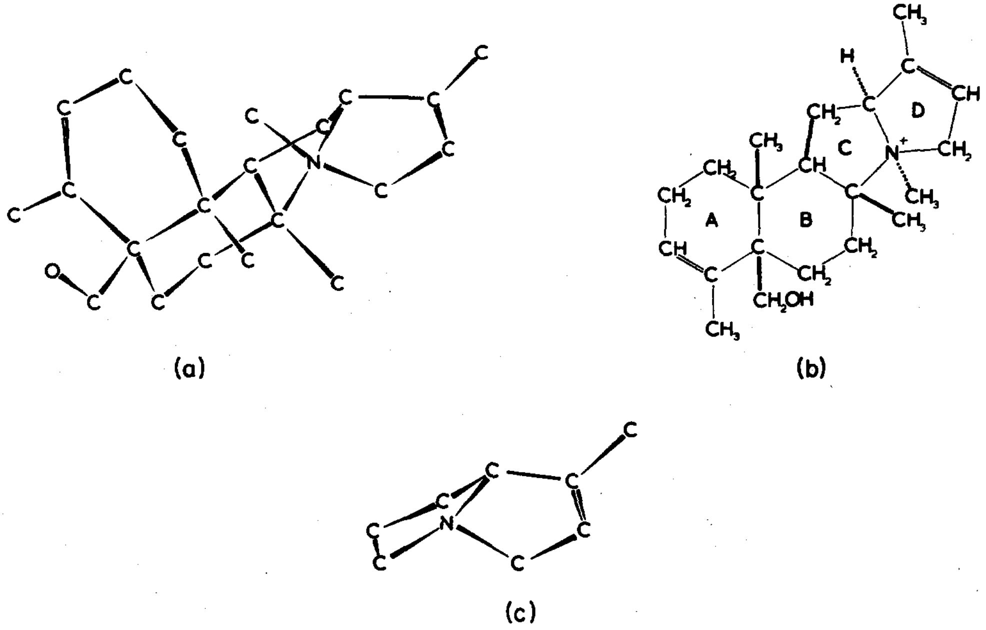

FIG. 1.

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[2] J. M. Bijvoet, A. F. Peerdeman and A. J. van Bommel, Nature 168, 271 (1951).

As an example of structure-determination by the X-ray technique based only on knowledge of the empirical formula(3), a more complete discussion of the analysis of this grass alkaloid will be presented later but certain observations on the structure may be of more immediate chemical interest.

a) The molecule of thelepogine contains within its atomic array the skeleton of the pyrrolizidine ring systems, CD in Fig. 1b. Comparison of the three-dimensional ball model of the thelepogine methiodide structure with that for jacobine bromhydrin(4) reveals that the pyrrolizidine ring systems exhibit unexpected coincidence of structural detail e.g. location of the double bond, substitution in the 1-position (pyrrolizidine convention) and, in particular, their absolute configuration. Fig. 1c presents the retronecine component of the jacobine bromhydrin structure(4) for comparison.

b) That the molecular formula of the alkaloid involves a C_{20} component suggested the probability of a diterpenoid origin for thelepogine. Thus the carbon skeleton of thelepogine may be derived from a hypothetical precursor of the mannoöl(5) type, Fig. 2a, by a 1,2 shift of the β-methyl group from the 4-position to the 5β-position resulting in the formation of the 3,4 double bond, Fig. 2b. Ring closure of the side chain could be affected by the introduction of nitrogen in a manner analogous to that in Adams and Leonard's(6) synthesis of (–)-retronecanone. Subsequent elimination of the hydroxyl group from C_{13} could give rise to the 13,14 double bond.

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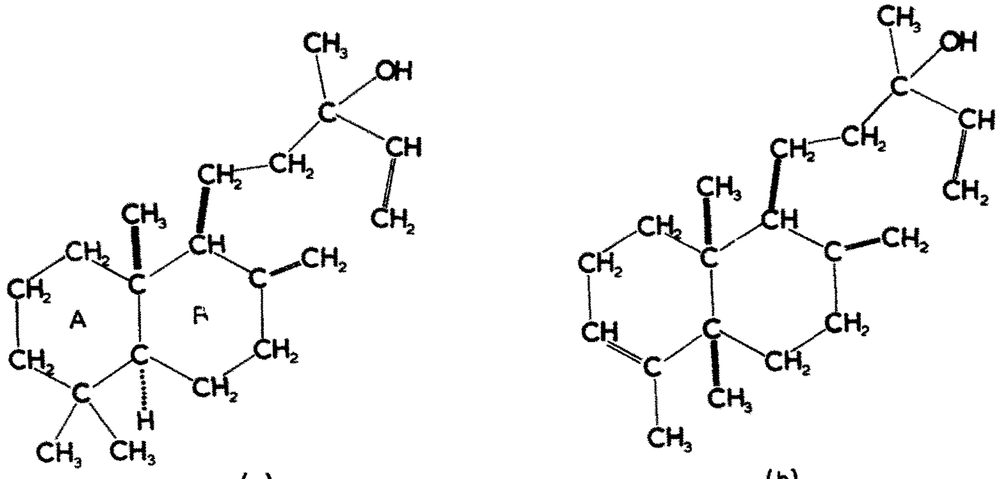
[3] A. McL. Mathieson, I.U.P.A.C. Symposium on the Chemistry of Natural Products, Australia (1960) (to be published by Butterworths Scientific Publications, London).

[4] J. Fridrichsons, A. McL. Mathieson and D. J. Sutor, Tetrahedron Letters No. 23, 35 (1960).

[5] Ann. Reports Chemical Society **60**, 243 (1958).

[6] R. Adams and N. J. Leonard, J. Amer. Chem. Soc. **66**, 257 (1944).



(a) (b)

FIG. 2.

Such a scheme would account for the identity of the asymmetric centres common to thelepogine and the mannoöl derivative *cf.* Figs. 1b and 2b. These structural relations with diterpenes have been discussed with Dr. C. S. Barnes of the Organic Chemistry Section for whose assistance we are grateful.