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THE MOLECULAR STRUCTURE AND ABSOLUTE CONFIGURATION OF JACOBINE BROMHYDRIN

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THE bromhydrin of jacobine, $C_{18}H_{26}NO_6Br$, crystallises from ethanol in space group $P2_1$ with cell dimensions, $\underline{a} = 9.88_9$, $\underline{b} = 15.3$, $c = 14.63_4 \text{Å}$, $\beta = 112.7°$ at -150°C. Unit cell contents are $2(2 \times C_{18}H_{26}NO_6Br + C_2H_5OH)$. X-ray analysis based on 0-10 layers about the b axis (3327 reflections of 3496 theoretically possible) has yielded the three-dimensional arrangement of the 55 atoms constituting the skeletons of the two jacobine bromhydrin molecules and the ethanol molecule[1]. The two molecules of jacobine bromhydrin which are crystallographically independent are identical to the first order, thus providing additional internal evidence of the essential correctness of the molecular structure. When the molecular structure had been determined, the absolute configuration was defined by application of Bijvoet's[2] technique using the anomalous dispersion of the bromine atoms.

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[1] 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).

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

The three-dimensional atomic distribution of the jacobine bromhydrin molecule, 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.

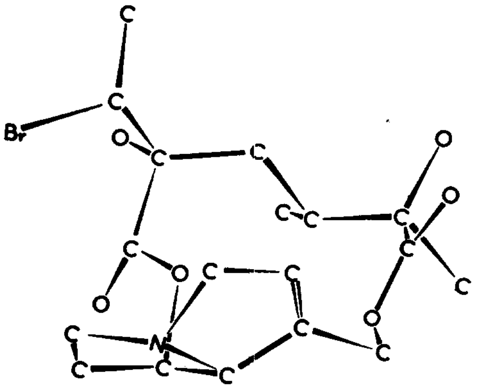

Fig. 1a.

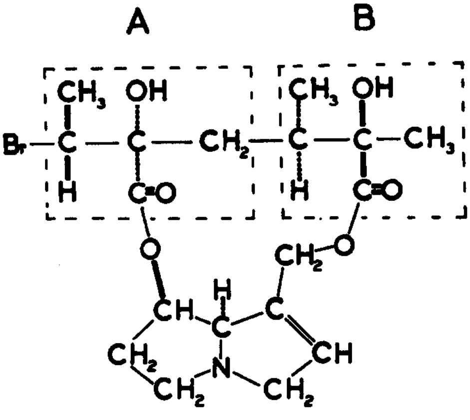

Fig. 1b.

The structure is in agreement with the reformulation of jacobine proposed by Geissman[3] on the basis of re-assessment of the available chemical and spectral evidence (see also Bradbury and Masamune[4]). Additional support for Geissman's reformulation of jacobine is also available in the X-ray analysis of its bromdilactone, $C_{10}H_{13}O_4Br$, which will be reported independently by Taylor[5].

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[3] T. A. Geissman, Austral. J. Chem. 12, 247 (1959).

[4] R. B. Bradbury and S. Masamune, J. Amer. Chem. Soc. 81, 5201 (1959).

[5] J. C. Taylor, International Symposium on the Chemistry of Natural Products, Abstracts p.43 (1960).

The analysis of jacobine bromhydrin provides independent proof of the absolute configuration of the retronecine component[6] and defines, for the first time, both the relative internal and the absolute configuration of the jaconecic acid component.

The method of structure analysis and details of the stereochemistry of the molecule will be presented later, but one aspect of the stereochemistry is worthy of note here. Inspection of the three-dimensional atom model of the crystal structure revealed that the jaconecic acid component is composed of two parts whose carbon and oxygen skeletons are identical in their spatial arrangement but antipodal in configuration. The two parts are within the dotted boxes, A and B in Fig. 1b. Their spatial arrangement can also be deduced from inspection of Fig. 1a.

It is tempting to suggest that the two units A and B are derived from an isoprenoid precursor *e.g.* angelic acid. It would appear possible that detailed configuration evidence of this type may provide an additional guide in the elucidation of the biogenetic origin of the *Senecio* alkaloids.

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[6] N. J. Leonard, *The Alkaloids* Vol. VI, Chap. 3. Senecio Alkaloids Academic Press (1960).