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THE STRUCTURE OF THE BROMODILACTONE FROM JACOBINE AND THE CONFORMATION OF THE LACTONE GROUP

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With regard to the evidence for the structures of the Senecio jacobaea alkaloids, considerable importance attached to the structure assigned to the dilactone [1, 2, 3] obtained by acid hydrolysis of jacobine. Because of the critical role of this derivative, an X-ray analysis of the bromodilactone of jacobine was initiated [4]. Subsequent chemical [5, 6] and X-ray [7] evidence

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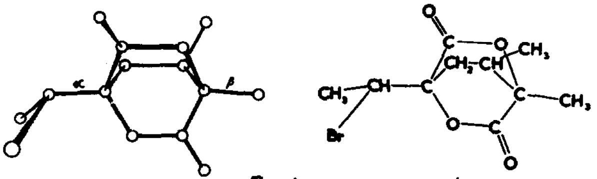
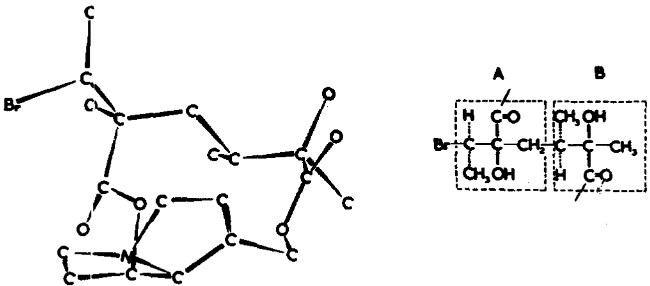
has provided a complete and detailed picture of the structure and absolute configuration of the parent compound, jacobine. The evidence presented here gives further confirmation regarding the jaconecic acid component of jacobine and also provides information on the conformation of the lactone group.

The needle-shaped crystals of the bromodilactone, $C_{10}H_{13}O_4Br$, belong to the monoclinic system, $\underline{a} = 8.70$, $\underline{b} = 6.34$, $\underline{c} = 10.44$Å, $\beta = 98.2°$, the space group being $P2_1$ with two molecules in the unit cell. Intensity data were collected at -150°C for the 0 - 4 layers about the $\underline{b}$ axis (947 measured reflections of 1125 possible). With zero-layer normal and first-layer generalised projections, phased first by the Br atoms and then with additional atoms as these were located, the spatial location of all atoms (except H) constituting the molecule was achieved in a few cycles. The atomic coordinates were then refined by least-squares procedures using the complete set of data. At this stage, the overall reliability index is 0.14.



(a) Fig. 1 (b)

The molecular skeleton as viewed at a slight angle to the $\underline{b}$ axis is shown in Fig. 1a (correct absolute configuration) and the conventional formulation in Fig. 1b. The structure is in complete agreement with that proposed by Geissman [3] and is in accord with the structure of jacobine [5]. The relative configurations of the four asymmetric centres in the dilactone are in agreement with those in the jaconecic acid component of jacobine [6, 7] Fig. 2a, and by reference to the absolute configuration of jacobine defined by chemical and X-ray evidence were placed on an absolute basis, Fig. 1a. The antipodal relationship, noted earlier [7], between the A and B units of the jaconecic acid component in jacobine bromhydrin, Fig. 2b, is a concomitant of the formation of the dilactone from jacobine.



(a) Fig. 2 (b)

With regard to the structure of the dilactone, the bicyclic part is composed of the backbone carbon chain and the two lactone functions, the small difference between the $-\mathrm{C}-\mathrm{C}-$ and $-\mathrm{C}-\mathrm{O}-$ bond lengths causing a deviation from collinearity of the bonds α and β, Fig. 1a. The lactone group exhibit two points of more general interest, each group $-\mathrm{C}-\underset{\substack{\| \\ \mathrm{O}}}{\mathrm{C}}\overset{x}{-}\mathrm{O}\overset{y}{-}\mathrm{C}-$ being coplanar within the accuracy of the analysis and the bonds y longer than the bonds x by approximately 0.1 Å. These conditions were noted first with respect to the γ-lactone group in himbacine hydrobromide[8] and have received further support in the analysis of iso-iridomyrmecin[9]. Combined with the evidence for the two δ-lactone groups in the present analysis, these factors would appear to be sufficiently consistent to be regarded as characteristic of lactone groups.

The coplanarity of the lactone group brings it into accord with the known characteristics of the related amide[10] and ester[11] groups. Conditions of this type constitute further useful conformational restrictions in assessing the validity of molecular models.

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c) Supporting evidence for coplanarity of ester groups is evident in the structure of jacobine bromhydrin Fig. 2a.