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THE STRUCTURE OF α-BROMO-ISOTUTINONE

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X-ray analysis of this compound was undertaken to assist in establishing the structure of tutin, the poisonous constituent of the New Zealand species of Coriaria. Tutin is similar in structure and physiological properties to picrotoxinin and coriamyrtin. The chemistry of these three bitters has been studied extensively, leading in the case of picrotoxinin to the elucidation of its structure by Conroy (1,2), while the crystal structure analysis of α_1-bromopicrotoxinin, by Craven (3) has assisted in defining many of the structural details in this group. While the present analysis of α-bromo-isotutinone was nearing completion, Dr. Craven informed us that he had carried out a three-dimensional analysis of the corresponding alcohol, α-bromo-isotutin (4). The results of the analysis of the keto compound are in essential agreement with those of the alcohol and provide corroborative evidence which should aid in defining configurational and conformational details in the isotutin and, less directly, the tutin group.

The crystallographic data for α-bromo-isotutinone are summarized as follows:

$C_{15}H_{15}O_6Br$ F.W. = 371.19

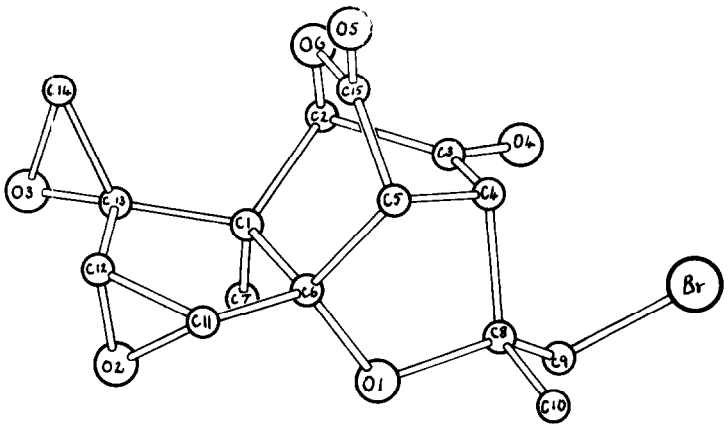
Orthorhombic Space Group $P2_12_12_1$ Z = 8

$\underline{a}$ = 7.35, $\underline{b}$ = 14.06, $\underline{c}$ = 28.06Å, U = 2910Å^3, D_m = 1.69, D_x = 1.69

Intensity data were collected at -150°C (for details, see (5)) for the 0-, 1- and 2-layers about the $\underline{a}$ axis and the 0-layer about the $\underline{b}$ axis, 1555 reflections of 1860 possible being measured.

The Br atoms were located from Patterson projections down the a and b axes. Normal and generalised projections (6) down the a axis were used to determine the three-dimensional location of the majority of the light atoms. Although the asymmetric unit consisted of two molecules and therefore involved the location of 42 light atoms, this task was alleviated by the molecular multiplicity, since the shapes of the two molecules can be regarded as identical to the first order (cf. (7)). Difference syntheses enabled the total set of atom sites to be located and the oxygen atoms differentiated from carbon. For 0kl, 1kl, 2kl and h0l, the reliability index, R, is 0.17. Refinement was not quite straightforward because of a persistent electron-density peak adjacent to one molecule of the asymmetric unit which could only be accounted for by assuming that the material from which the crystals were prepared was not pure and that a proportion (say 30%) of this one molecule corresponded to unchanged α-bromo-isotutin.*

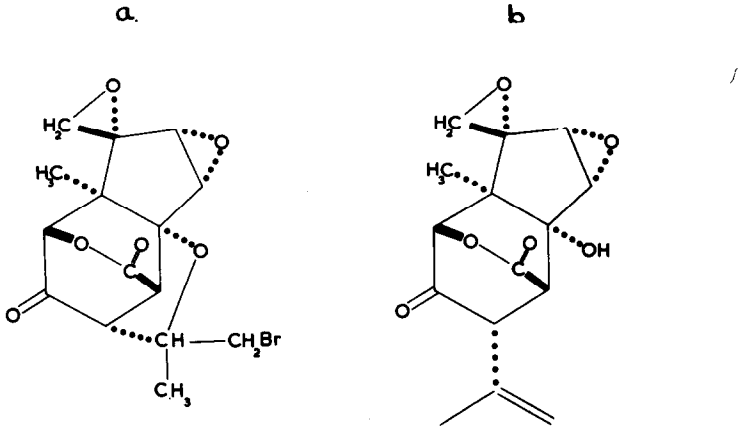
FIG. 1



*Footnote:- Our material was made from α-bromo-isotutin by an oxidative procedure which is difficult to carry to completion (see (8)). As a result, the region corresponding to the group $\diagup C = O$ is partially occupied by the group $\diagup C \diagdown^{H}_{OH}$, the remainder of the molecule being unchanged. The stereochemistry at this carbon atom with respect to the alcohol group is in accord with Craven's deductions for α-bromo-isotutin and hence the occurrence of the additional peak is consistent with the chemical evidence.

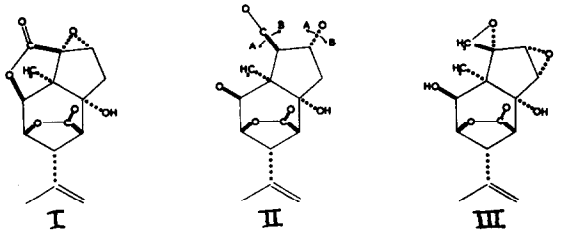
The molecular skeleton of α-bromo-isotutinone is shown in Fig. 1 and the more conventional formulation in Fig. 2a. The corresponding structure of isotutinone is given in Fig. 2b. The structure of the carbon skeleton is in accord with the earlier proposal of Johns and Markham (9) for isotutinone but the full structure differs from their more complete proposal. The oxygen atoms previously ascribed to a lactone group linking C_{11} and C_{13} are separately involved in epoxide rings, one spiro at C_{13} and the other linked 1,2 to C_{11}, C_{12}. The structural results for both α-bromo-isotutinone and α-bromo-isotutin indicate the need for caution in the interpretation of infra-red spectra with regard to the oxygen functional groups since diagnostic features for epoxide rings are not definite. Indeed, for tutin, the possible presence of epoxide rings had been carefully considered by Browne, Johns and Markham (8) as a result of structural proposals by Kariyone and Okuda (10) and they concluded that the presence of epoxide rings could not be substantiated by the available chemical and infra-red evidence. The mutual disposition of the epoxide rings probably modifies their normal chemical reactions and so conceals their existence. From Fig. 1, protection is afforded $C_{12}O_2C_{11}$ against rearward attack, but failure to detect the spiro epoxide ring is harder to explain.

FIG. 2



In the bicyclic ring system, $C_2 - - - C_5$, the lactone group $C_2O_6C_{15}(O_5)C_5$ is planar, a conformational characteristic of such groups noted earlier by Mathieson and Taylor (11). If, as appears most probable, the isotutin series arise from the tutin series by the isomerization of the lactone group $C_5 - - - C_2$ to $C_5 - - - C_3$ and no other major structural change occurs, then the close structural relationship of the picrotoxinin and tutin series can be illustrated by Fig. 3.

FIG. 3



The molecular skeleton, II, is basic to both series and can be converted by the concerted moves A to I, picrotoxinin, or alternatively B to III, tutin. If this be the case, the absolute configuration of both molecules is defined by that of α_1-bromo-picrotoxinin (3). Further, the close relationship of coriamyrtin to these groups suggests that structurally it can be ascribed to a de-oxygenated variant of II.

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