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THE CRYSTAL AND MOLECULAR STRUCTURE OF BROMOANHYDROTETRODOIC LACTONE HYDROBROMIDE, A DERIVATIVE OF TETRODOTOXIN

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Bromoanhydrotetrodoic lactone hydrobromide, hereafter (I), is a derivative of tetrodotoxin, a poisonous animal alkaloid isolated from swellfish (Puffer). The properties of tetrodotoxin and the relationship among the derivatives are discussed by Y. Hirata et al., Nagoya University, in the following letter. In cooperation with the organic chemical investigation of Hirata et al., the crystal structure of (I) has been studied by the X-ray methods to elucidate the molecular structure of tetrodotoxin. Before the X-ray investigation was performed the chemical formula of (I) was supposed to be $C_{11}H_{16}O_8N_3Br.HBr$ or its dimer from the chemical analysis. However, the present work

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led to a revision of the formula to $C_{11}H_{14}O_7N_3Br.HBr$ as shown later.

Small single crystals of (I), suitable for the structure determination, were kindly supplied by Prof. Hirata. It has been revealed from our X-ray study that the crystal is orthorhombic with the unit cell of the dimensions, a = 10.88, b = 15.95, c = 8.55 A, the space group being $P2_12_12_1$. Since the four-fold general positions are required for this space group, it is concluded that four molecules of the monomer are in a unit cell to explain the observed density, 2.20 g/cm^3.

The intensities of the three-dimensional reflections were measured visually from integrating Weissenberg photographs around c and a axes taken with filtered Cu K_α radiation. Relative values of the observed structure factors of 1860 reflections were converted into absolute scale by Wilson's method [1]. The positions of the two bromine atoms were derived from the two-dimensional Patterson functions P(uv) and P(vw). A three-dimensional minimum function method[2] and a modified heavy-atom method for the non-centrosymmetrical structure with consideration of phase angle distribution [3] were carried out for the elucidation of the positions of light atoms. The structure thus obtained was refined by

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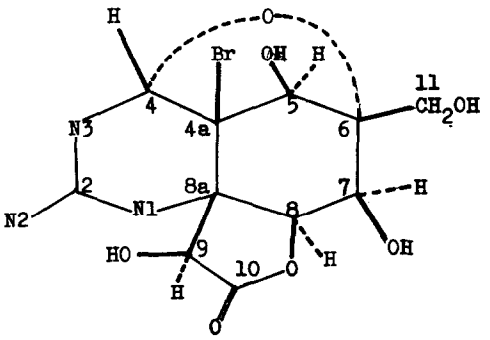
1) A. J. C. Wilson, Nature 150, 152 (1942).

2) M. J. Buerger, Acta Cryst. 4, 531 (1951).

3) G. A. Sim, Acta Cryst. 12, 813 (1959).

a three-dimensional Fourier synthesis and the least-squares method. The R factor is 15.4 per cent at the present stage.

FIG. 1 shows the molecular framework projected along the c axis. The bond lengths and angles together with intermolecular contact are reasonable considering the present stage of refinement. The structural formula corresponding to FIG. 1 is thus,



In the course of the present investigation, the calculations of the minimum function, Fourier synthesis, structure factors, the interatomic distances and bond angles were carried out on an electronic computer NEAC-2203 using our programs and the least squares method on IBM 7090 using ERBR 1 programmed by van den Hende.

Acknowledgement - We wish to thank Prof. Hirata and his colleague for sending us samples and for discussion. We are grateful to the Takeda Pharmaceutical Company for facilities for using NEAC-2203, and to Dr K. Osaki and Mr Y. Ueki for their help on programming.

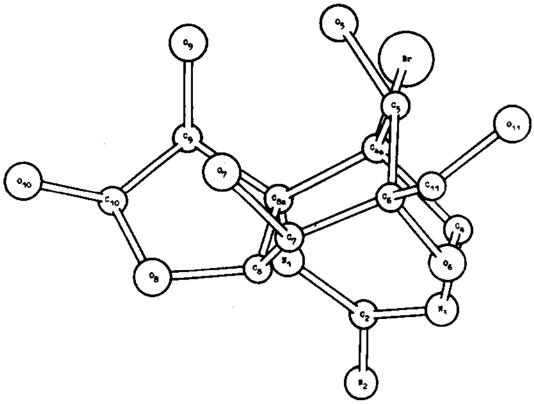


FIG. 1