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CRYSTAL AND MOLECULAR STRUCTURE OF GRAYANOTOXIN - I, $C_{22}H_{36}O_7$

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Grayanotoxin-I, $C_{22}H_{36}O_7$, is one of the toxic substances in the plants of Ericaceae. The stereochemistry of it has been established, except the A/B ring junction (1, 2). Kakisawa and Khumazawa proposed the A/B ring junction to have cis-configuration. However, from chemical evidence Iwasa and Nakamura (3) concluded that the configuration of the C1-hydrogen and the C5-hydroxyl are α and β, respectively. The present X-ray structure analysis has been undertaken to resolve the ambiguity of the A/B ring junction. The crystals, crystallised from ethyl acetate solution, have been kindly supplied to us by Prof. F. Zymalkowski, (Pharmazeutisches Institut der Universität Bonn, West Germany.)

The crystallographic data are: a = 26.760, b = 11.682, c = 6.544 Å; d_m = 1.34 gcm^{-3} d_{cal} = 1.34 gcm^{-3}; z = 4; the space group is orthorhombic $P2_12_12_1$. The three dimensional X-ray diffraction intensity data were measured on a Siemens on-line four-circle diffractometer, using Cu$K\alpha$ radiation. All the independent (2239) reflections with $\Theta \leq 70^\circ$ were collected (mode of measurement: Θ / 2Θ scan, 5-point measuring procedure), 437 reflections had intensities below the significance level. The structure was solved by a direct method (4, 5, 6), programmed by one of us, which does not require any initial information about the stereochemistry of the molecule. This procedure is based on a cyclic application of the statistical triple product phase relationships (7) and the Sayre equation (8). The free choice of the origin in the unit cell and of either of the two enantiomorphic structures allows the phases of four two-dimensional reflections to be arbitrarily fixed in the space group concerned here. For the analysis of the present structure, however, one of the four starting reflections was three-dimensional. The phase of this three-dimensional reflection was continually refined during the cyclic procedure. In order to extend the initial phase set two more two-dimensional reflections were included. All the four resulting phase sets were cycled until the phases of all the unitary structure factors used (300 reflections) were determined. U-Fourier synthesis of the first best set (having 296 reflections of high values out of cycled 300 reflections), revealed non-hydrogen atoms of the molecule immediately; 28 atoms were represented by the highest peaks of the Fouriersynthesis. A Fourier

synthesis using all the 2239 phases calculated from the positions of these 29 atoms with an over-all temperature factor 3.5 $Å^2$ gave an R index of 22.2 %. The R factor after few cycles isotropic and anisotropic refinements is 8,6 %.

Grayanotoxin-I is a tetracyclic diterpene having a trans-junction between the five membered ring A and the seven membered ring B and a cis-junction between ring B and the six membered ring C. The configuration suggested by Iwasa et. al. is correct.

Figure 1. shows the molecule along c-axis and figure 2. is a sketch of the molecule.

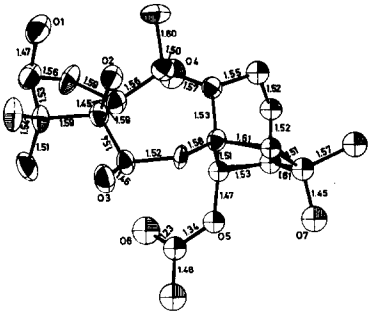

Fig. 1

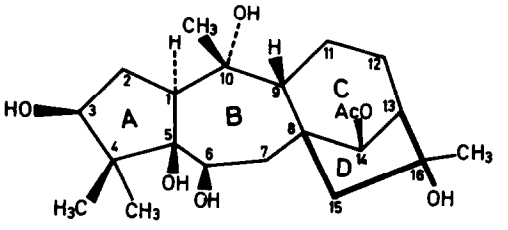

Fig. 2

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