

CRYSTALLOGRAPHIC STUDIES OF AN ANTHRAQUINONE DERIVATIVE
OBTAINED FROM KIDAMYCIN

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Kidamycin (I) is a metabolite of *Streptomyces phaeoverticillatus* possessing antitumor and antibacterial activities(1). Attempts to determine the structure of I by X-ray analysis have proceeded simultaneously with the chemical studies. Preliminary chemical and NMR experiments(2) indicated the presence of several functional groups in I such as tert., sec. and aromatic methyls, dimethylamino groups, sec. alcoholic hydroxyls, carbonyl group(s) resistant to reduction, carbonyl(s) with a chelated hydroxyl group and ethereal oxygens. Evidence for the presence of a glycosidic linkage was not obtained and the molecular formula was assumed as $C_{39}H_{48}O_9N_2$ or its duplicate form. Acetylation of I followed by alkylation with methyl iodide and crystallization of the product from methanol and ethyl acetate gave an acetate methiodide (II) of I as very fine needles, and a compound (III) which is presumably derived from II by methanolysis as rather large prisms. The latter has been used for the present X-ray analysis.

The compound (II) dissolved in a mixed solution of methanol and ethyl acetate was kept in a sealed flask at room temperature in an attempt to obtain a crystal large enough to carry out X-ray analysis. Large elongated prismatic crystals of III were grown from the solution after several months.

Weissenberg and precession photographs indicated that the crystal belongs to the orthorhombic system with the lattice constants $a=15.55_9$, $b=39.4_9$, $c=10.18_2$. The space group was determined to be $P2_12_12_1$. The elemental analysis for the dried sample indicated the chemical formula, $C_{48}H_{64}O_{13}N_2I_2 \cdot H_2O$.

Found : C 50.17 : H 5.86 : N 2.36 : I 21.99. Calculated : C 50.18 : H 5.79 : N 2.44 : I 22.09. The density of the crystal measured by the flotation method using a mixed solution of carbon tetrachloride and ethyl acetate was 1.36 g cm^{-3} which is in agreement with the value 1.356 g cm^{-3} assuming four structure units of $\text{C}_{48}\text{H}_{64}\text{O}_{13}\text{N}_2\text{I}_2 \cdot \text{H}_2\text{O} \cdot 4\text{CH}_3\text{OH}$ are contained in the unit cell. The presence of the methanol molecules as a solvent of crystallization was confirmed later by the X-ray analysis. The lattice constants and the three dimensional intensity data were derived from the measurement using a Rigaku computer controlled four circle X-ray diffractometer. The crystal specimen was sealed in a thin-walled glass capillary since it immediately deteriorated due to loss of the solvent of crystallization.

A total of 1425 independent structure factors having net intensities above three times of their standard deviations, were obtained with Ni-filtered $\text{CuK}\alpha$ radiation by use of a ω -2 θ scan method.

The crystal structure was solved by the heavy atom method. Successive use of Fourier and difference Fourier syntheses coupled with least-squares calculations enabled us to assign the locations of all the seventy four atoms. Refinement of the structural parameters was carried out by the method of block-matrix least-squares, in which anisotropic thermal parameters were allowed for each atom. The final R value was 0.125. The absolute configuration was determined by the anomalous dispersion method. Dispersion corrections for the scattering factors of the iodine atom for $\text{CuK}\alpha$ radiation were taken as $\Delta f' = -1.1$, $\Delta f'' = 7.2$. Intensities of 200 Friedel pairs of reflexions were measured on the diffractometer using $\text{CuK}\alpha$ radiation and they were compared with the calculated value.

The molecular structure determined by the present analysis is shown in Fig. 1-a excluding the molecules of methanol and water which are contained in the crystal as the solvents of crystallization. A stereoscopic drawing of the structure is given in Fig. 1-b which shows the three dimensional absolute structure of the molecule. The figure was drawn by the ORTEP (Oak Ridge Thermal Ellipsoid Plot) program by Johnson(4) in which the atoms were drawn by the

spheres of varying radius with increasing order of atomic numbers.

The structure consists of a tetracyclic conjugated ring system A,B,C,D, and two tetrahydropyrane moieties attached to the ring D. The presence of the geminal methoxyl and acetoxy groups with the peri hydroxyl group in the ring C

Fig. 1-a

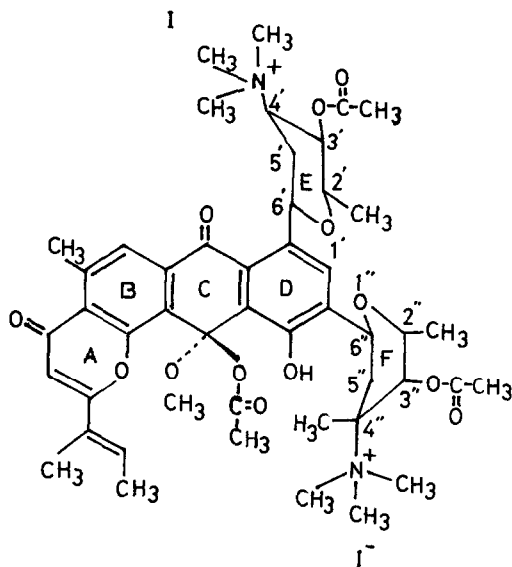
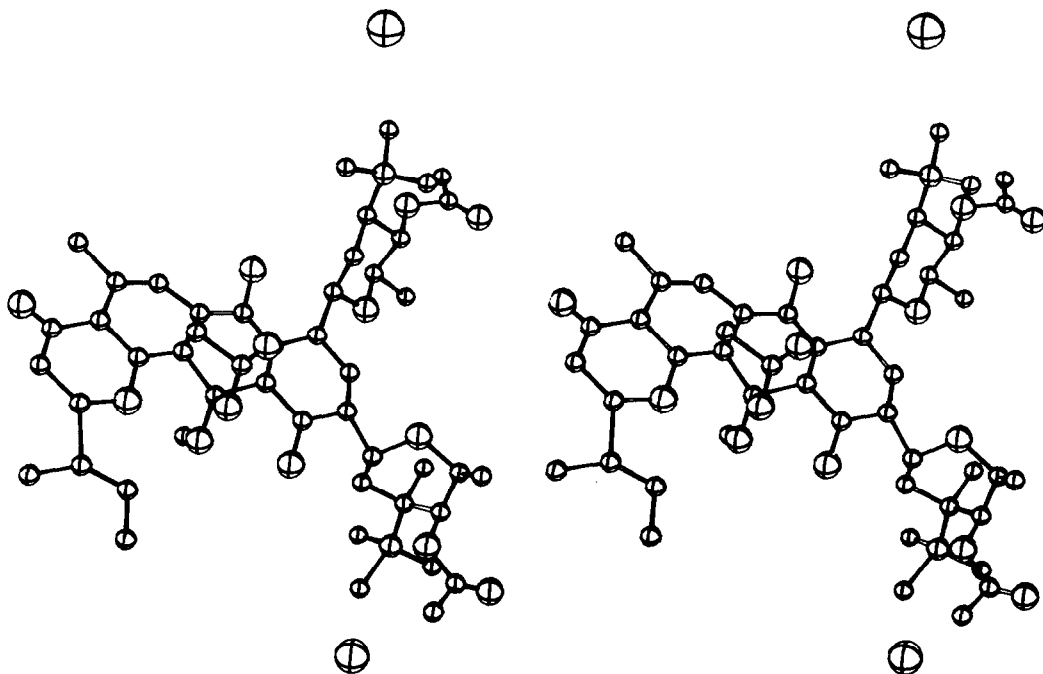


Fig. 1-b



of the present structure indicates that the compound (III) was formed by methanolysis with rearrangement.

The same ring system of the chromophore as that of III has been found in indomycinone(3) and the similarity between I and indomycins(3) should be noted. The tetrahydropyran rings E and F in III are linked to the aromatic atoms directly through the C-C bonds. The both rings have a similar conformation except for the presence of a tertiary methyl group at C-4'' in the F ring. It should be noted also that both the configurations and conformations of the tetrahydropyran rings differ from each other. The absolute configurations of the E ring are 2'R,3'S,4'R,6'R, while those of the F ring are 2''S,3''S. The conformation of the E ring is a chair form while that of F ring is a boat form. The difference in the conformations of the two rings may be caused by the differences in the configurations at C-2' and C-2'', and also at C-4'' atoms. In both rings, the bulky trimethylamino groups attached to C-2' and C-4'' are oriented in equatorial direction. If the F ring took a chair conformation, the trimethylamino group would come to the cis-1,3 diaxial position with respect to the C-2'' methyl group. Details of this study and the constitution of III will be given elsewhere.

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