The Crystal and Molecular Structure of Demycarosyl Leucomycin A_3 Hydrobromide

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Leucomycin A_3 (I) is a basic macrolide antibiotic obtained from *Streptomyces kitasatoensis* Hata.[1] The structure of this compound has recently been reported by Hata *et al.*, Kitasato University.[2] Treatment of I with dilute hydrochloric acid yields 4-*O*-isovaleryl mycarose[3] and demycarosyl leucomycin A_3 (II). We now report the stereochemically complete molecular structure of II, including absolute configuration, from a three-dimensional X-ray diffraction study of its hydrobromide, $C_{30}H_{49}NO_{11}\cdot HBr\cdot nC_2H_5OH$.

Small single crystals of this hydrobromide, suitable for the structure determination, were grown from methanol-ethanol-ethyl ether solution. The crystal belongs to the orthorhombic system with the unit cell of the dimensions, $a=19.41$, $b=20.64$ and $c=9.29$ Å. The space group is $P2_12_12_1$ and the unit cell contains four formula units.

The intensities of reflections were visually estimated from the multiple-film equi-inclination Weissenberg photographs around the b and c axes taken with Ni filtered Cu$K\alpha$ radiation. These intensities were corrected for the Lorentz-polarization factor but not for the absorption effect. Relative values of the observed structure factors of 2450 reflections were converted into an absolute scale by Wilson's method.

The position of the bromine atom was derived from the three-dimensional Patterson function to be (0.143, 0.095, 0.182). A minimum function method was carried out for the elucidation of the positions of light atoms. The tentative structure thus obtained was refined by alternating application of the least squares method and Fourier synthesis. In the course of refinement, it has been found that the crystal contains some amount of ethanol as alcohol of crystallization, though the amount seems not to be stoichiometric. This point is under investigation. The discrepancy factor R is 17.7% at the present stage. The molecular structure of II projected along the c axis is shown in Fig. 1, the corresponding structural formula being given in Fig. 2.

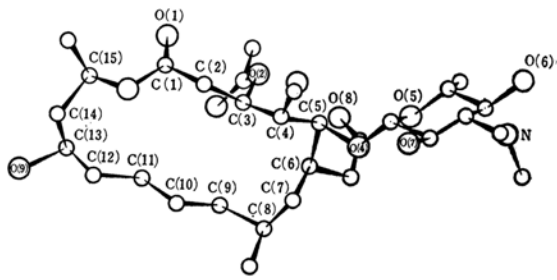

Fig. 1. Molecular structure projected along the c axis.

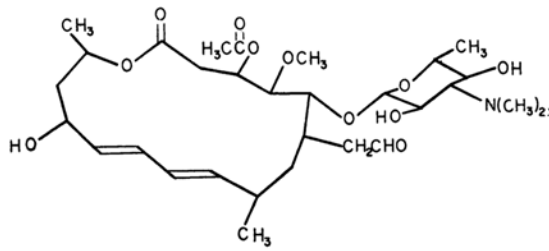

Fig. 2.

From the comparison of the intensities of twenty-three pairs of reflections ($h\ k\ l$) and ($h\ \bar{k}\ l$) on the same Weissenberg photographs, the absolute configuration of the present molecule has been determined just as shown in Fig. 1.

The bond lengths and angles together with intermolecular contacts are reasonable considering the accuracy in the present stage of refinement. The sugar component mycaminose,[4] which has an β-glycosidic linkage, is attached to C(5) of the lactone ring. The conjugated diene system, C(9)-C(10)-C(11)-C(12), has the trans-trans configuration. O(6), O(7) and O(9) form hydrogen bonds with Br, O(9) of the adjacent molecule and Br′ respectively; their lengths are about 3.28, 2.72 and 3.15 Å respectively.

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1) T. Watanabe, H. Nishida, J. Abe and K. Satake, This Bulletin, **33**, 1104 (1960).

2) S. Omura, H. Ogura and T. Hata, *Tetrahedron Letters*, **1967**, 1267.

3) T. Watanabe, H. Nishida and K. Satake, This Bulletin, **34**, 1285 (1961).

4) W. D. Celmer, *J. Am. Chem. Soc.*, **87** 1799 (1965).