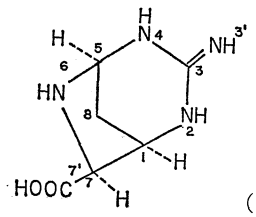
Communications to the Editors

THE MOLECULAR AND CRYSTAL STRUCTURE OF VIOMYCIDINE

Sir:

In 1966, BÜCHI and RALEIGH[1] presented the structure I for viomycidine on the basis of its n.m.r. spectrum and chemical evidence. In order to establish the absolute configuration of I, an X-ray crystal structure analysis of I was undertaken. During this crystallographic work, BYCROFT, *et al.*[2] reported the X-ray analysis of a tricyclic degradation product, viocidic acid, which supported the relative and absolute configurations at C1 and C7 in I. In the present paper, the authors report the molecular and crystal structure, including the absolute configuration, of viomycidine.*



(I)

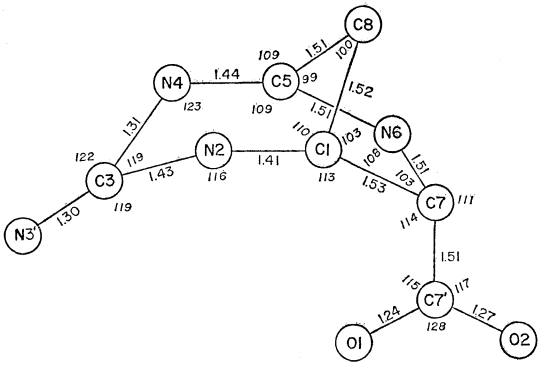
Viomycidine was isolated from the acid hydrolysate of viomycin by ion-exchange resin chromatography. Crystals of the monohydrobromide of viomycidine are colorless prisms and the analytical data coincide with the formula, $C_6H_{10}N_4O_2 \cdot HBr$; m.w. 251.1 (248 by the X-ray method), m. p. 202~204°C (dec.).

The crystal belongs to the orthorhombic system, space group $B22_12$ with eight structure units in the unit cell of dimensions of $a=12.45$ Å, $b=15.34$ Å and $c=9.35$ Å. The density measured by the flotation method using a mixed solution of bromoform and carbon tetrachloride 1.846 g/cm^3; (calculated for eight molecules in the unit cell 1.868 g/cm^3). Three-dimensional intensity data were collected from the equi-inclination WEISSENBERG photographs about the c- and a-axes. The layers $hk0 \sim hk7$ and $0kl \sim 3kl$ were taken with CuKα radiation by the multiple film technique. The intensities were estimated visually by the use of a calibrated intensity scale. Totally, 942 independent structure factors of $F_0 \neq 0$ were evaluated for the analysis.

Two- and three-dimensional PATTERSON syntheses were calculated and the position of a bromine atom was determined as (0.065, 0.120, 0.250). A three-dimensional FOURIER synthesis was then calculated, using phases determined by the bromine atom (R=41.4 %). The resulting electron density map, however, showed a false mirror plane of symmetry. Four prominent peaks were arbitrarily selected from each pair of mirror-related positions. The subsequent FOURIER synthesis calculated, based on a bromine atom and four light atoms, assuming all to be oxygens (R=37.7 %), no longer contained the above mentioned mirror plane for all peaks, and five more light atoms could be found on the basis of the formation of a bicyclo [3. 2. 1.] ring system. Another FOURIER synthesis including the contributions of a bromine and nine light atoms (R=28.5 %) enabled the positions of all 13 non-hydrogen atoms to be determined, and the last set of calculations resulted in a reduction of the reliability factor to 23.2 %. The atomic parameters of this structures were then subjected to three cycles of the least-squares refinement in which the anisotropic thermal parameters were applied only for the bromine atom and the R factor dropped to 15.9 %. The calculations of three more cycles of the least-squares refinement with individual anisotropic thermal parameters for all atoms gave the reliability factor of 13.8 %. Further refinement of the structure was carried out and the final R factor is 12.6 % for 942 independent reflections.

* Most recently, the authors were informed of the report by DYER, *et al.* of the X-ray determination on the same compound. DYER's group has not metioned the absolute configuration of the molecule, although the molecule in the Figure presented in the paper indicates the same absolute configuration as assigned in our work[3].

Fig. 1.



The crystal structure analysis of viomycidine presented here has not only confirmed the structure elucidated by BÜCHI and RALEIGH, but also has established the absolute configuration of the molecule. The absolute configuration was determined by BIJVOET's method using the anomalous dispersion of CuKα radiation due to the bromine atom. Thus, the absolute configuration at C7 is *S*, corresponding to the L configuration in the amino acid configurational notation.

The intramolecular bond distances and angles are shown in Fig. 1. The average standard deviations of the bond distances and angles are 0.024 Å and 1.48°.

The calculations in the present work were performed on the HITAC 5020E computer at the University of Tokyo and CDC 3600 computer at Itoh Chu Co., Tokyo.

GUNJI KOYAMA
HIKARU NAKAMURA
SHOJI OMOTO
TOMOHISA TAKITA
KENJI MAEDA
Institute of Microbial Chemistry
Shinagawa-ku, Tokyo, Japan

YOICHI IITAKA
Faculty of Pharmaceutical Sciences,
University of Tokyo,
Bunkyo-ku, Tokyo, Japan

(Received November 21, 1968)

References

1) RALEIGH, J. A.: Dissertation (Supervisor, G. BÜCHI), Massachusetts Institute of Technology, Oct. 1966.
2) BYCROFT, B. W.; D. CAMERON, L. R. CROFT, A. W. JOHNSON, T. WEBB & P. COGGON: Viomycin, further degradation studies. Tetrahedron Letters 1968-25 : 2925~2930, 1968.
3) FLOYD, J. C.; J. A. BERTRAND & J. R. DYER: The crystal structure of viomycidine. Chem. Comm. 16 : 998~999, 1968.