

THE X-RAY STRUCTURE  
DETERMINATION OF OXETANOCIN

Sir:

In the previous paper<sup>1)</sup>, the production, isolation, and chemical and biological properties of oxetanocin have been reported. The crude material of oxetanocin was purified by a Diaion HP-20 column chromatography and crystallization from water as colorless needles.

X-Ray study was first carried out for this free oxetanocin crystal. The diffraction measurement was made on a Philips PW 1100 diffractometer. The crystal data and the course of structure determination are summarized in Table 1(a). Of the 1400 theoretically possible reflections within the  $2\theta$  range of  $6^\circ$  through  $156^\circ$ , 1230 reflections were measured as above the  $2\sigma$  (I) level. Intensities were corrected for

Lorentz and polarization factors but not for absorption. Hydrogen atoms were located on a difference electron-density map. After completing the structure elucidation of the free base of oxetanocin, the absolute configuration was determined by the anomalous dispersion method using its hydrobromide.

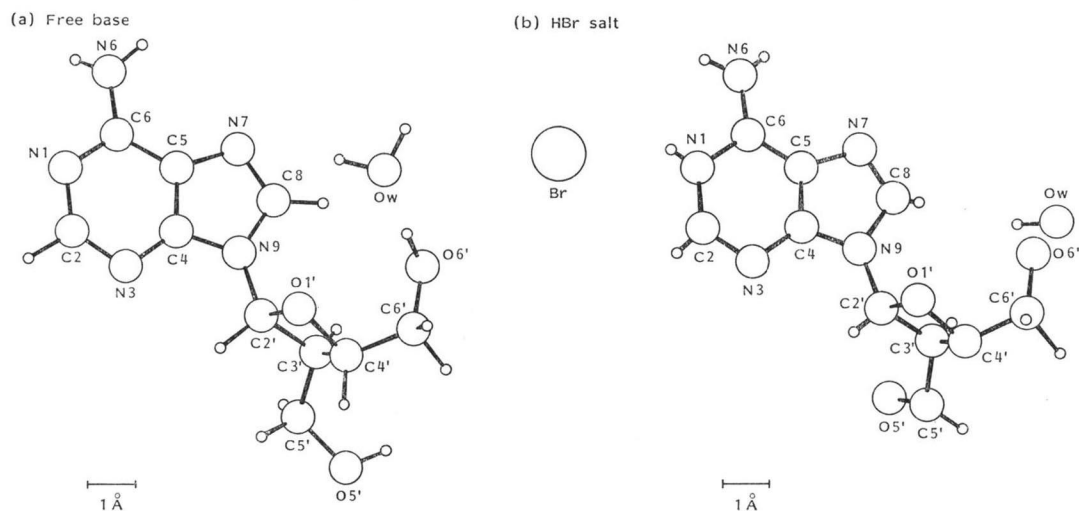
The hydrobromide was prepared by dissolving 15.7 mg of oxetanocin in 0.62 ml of 1 M HBr. Crystallization in the 10% (w/v) solution in isopropyl alcohol - water mixed solution gave well developed plate crystals.

The X-ray diffraction work has been carried out in an analogous way as for the free base and the process is summarized in Table 1(b). For the hydrobromide crystal, 329 Friedel pairs (hkl and  $\bar{h}\bar{k}l$  reflections) in the  $2\theta$  range  $6^\circ \sim 80^\circ$  were measured prior to extending the measurement to  $80^\circ \sim 140^\circ$ . Of these, 171 pairs having

Table 1. Crystal data and the course of structure determination.

	(a)	(b)
Compound name	Oxetanocin monohydrate	Oxetanocin hydrobromide monohydrate
Chemical formula	$C_{10}H_{13}N_5O_3 \cdot H_2O$	$C_{10}H_{13}N_5O_3 \cdot HBr \cdot H_2O$
Formula weight	269.3	350.2
Crystal		
Habit	Plate	Plate
X-Ray specimen size (mm)	$0.06 \times 0.06 \times 0.45$	$0.1 \times 0.2 \times 0.3$
Radiation	Graphite monochromated CuK $\alpha$	Graphite monochromated CuK $\alpha$
Crystal system	Monoclinic	Monoclinic
Space group	P2 <sub>1</sub>	C2
Lattice constants		
<i>a</i> (Å)	13.765 (7)	13.405 (8)
<i>b</i> (Å)	6.615 (4)	7.035 (5)
<i>c</i> (Å)	6.820 (5)	14.456 (10)
$\beta$ (°)	102.37 (5)	96.75 (5)
<i>V</i> (Å <sup>3</sup> )	606.6	1353.8
No. of formula unit in a cell	2	4
Calculated density (gcm <sup>-3</sup> )	1.475	1.719
$\mu$ for CuK $\alpha$ (cm <sup>-1</sup> )	9.41	43.83
$2\theta$ range (°)	$6 \sim 156$	$6 \sim 140$
No. of possible reflections	1400	1425
No. of independent   <i>F</i> <sub>obsd</sub>	1230	1258
No. of observed Friedel pairs	—	329
Method of structure determination	Direct	Heavy atom
Method of structure refinement	Block-diagonal-matrix least-squares	Block-diagonal-matrix least-squares
No. of refined atoms		
Heavier atoms (anisotropic)	19	20
Hydrogen atoms (isotropic)	15 (all H)	11 (out of 16 in all)
Final R value	0.064	0.078

Fig. 1. Molecular structure of oxetanocin.

Table 2. Selected torsional angles ( $^{\circ}$ ).

	Free base	HBr salt	
C8-N9-C2'-O1' ( $\chi$ )	67.0 (4)	68.9 (13)	mid-anti
C4-N9-C2'-O1'	-108.3 (3)	-105.4 (10)	
O1'-C4'-C6'-O6' ( $\psi_{oo}$ )	-58.2 (5)	-59.5 (15)	} $g^-g$
C3'-C4'-C6'-O6' ( $\psi_{oo}$ )	45.9 (5)	43.5 (17)	
C4'-C3'-C5'-O5'	-48.7 (5)	171.9 (7)	} $g^-t$
C2'-C3'-C5'-O5'	-146.4 (2)	71.6 (14)	

the difference of the observed structure factors between  $hkl$  and  $\bar{h}\bar{k}l$  greater than  $2\sigma(F_o)$  were selected and their  $r_{\text{obsd}} = |F_{\text{obsd}}(hkl)|/|F_{\text{obsd}}(\bar{h}\bar{k}l)|$  values were compared with  $r_{\text{calcd}} = |F_{\text{calcd}}(hkl)|/|F_{\text{calcd}}(\bar{h}\bar{k}l)|$ . Of the 69 pairs showing  $r_{\text{calcd}}$  values differ more than 5% from the unity 63 pairs clearly indicated the absolute configuration as shown in Fig. 1. Final atomic parameters for both compounds were sent to the Cambridge Crystallographic Data Centre.

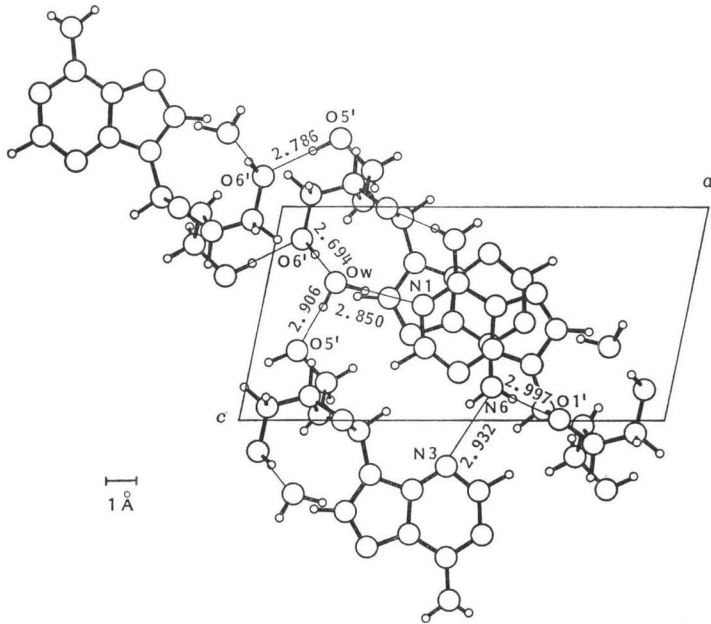
The molecular structures of oxetanocin free base and hydrobromide salt are drawn by the PLUTO program<sup>†</sup> and illustrated in Figs. 1(a) and (b). It is of note that the absolute configuration at C2' is *R* and the C4'-C6' bond is oriented  $\beta$  with respect to C2'-N9 and these configurations are identical with natural nucleosides having a  $\beta$ -D-ribose moiety.

<sup>†</sup> PLUTO: Cambridge Crystallographic Database, Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England, 1983.

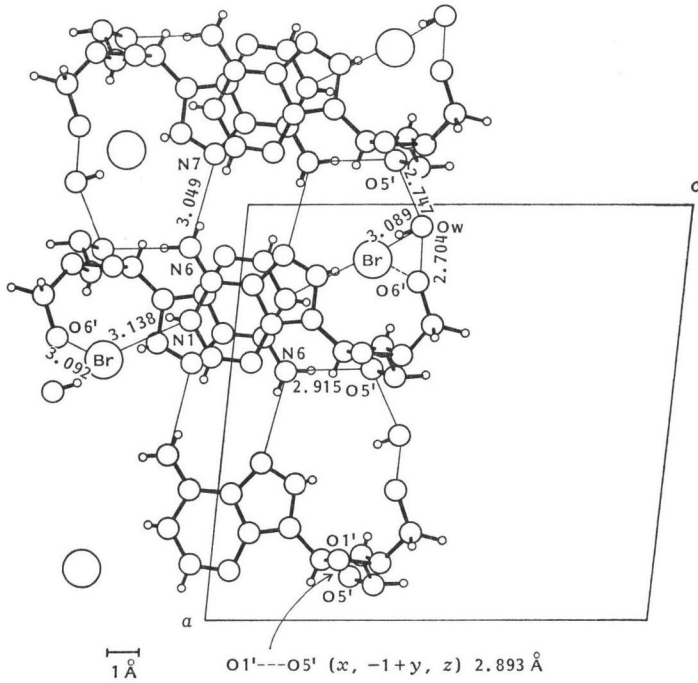
The conformation of the molecule may be described by taking the same well-known parameters defined for nucleosides. The values are listed in Table 2 comparing the two compounds. Thus the  $\chi$  angles, which denote the torsion angle about the glycosyl bond are both anti and the orientations of the C6'-O6' bonds are  $gg$  in both compounds while the C5'-O5' bonds take different conformation; in the free base it is nearly  $gt$  but in the hydrobromide it is  $tg$ . This difference reflects the differences in intermolecular hydrogen bonds which can be seen in Figs. 2(a) and (b). As is usually seen in four-membered rings, the oxetane ring is puckered along the line through O1' and C3'. The adenine rings are oriented almost perpendicularly to  $b$  as is seen in Figs. 2(a) and (b) and they are stacked each other along the diad screw axis parallel to  $b$ . Thus the distances between the stacked base planes are approximately one half of the axial length of  $b$ .

Fig. 2. Crystal structure projected along *b*.

(a) Free base



(b) HBr salt



HIKARU NAKAMURA<sup>†</sup>  
SHIGERU HASEGAWA  
NOBUYOSHI SHIMADA  
AKIO FUJII  
TOMOHISA TAKITA  
YOICHI IITAKA<sup>†</sup>

Research Laboratories,  
Pharmaceutical Group,  
Nippon Kayaku Co., Ltd.,  
3-31-12 Shimo, Kita-ku,  
Tokyo 115, Japan

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#### References

<sup>†</sup>Faculty of Pharmaceutical Sciences,  
University of Tokyo,  
Hongo, Bunkyo-ku,  
Tokyo 113, Japan

- 1) SHIMADA, N.; S. HASEGAWA, T. HARADA, T. TOMISAWA, A. FUJII & T. TAKITA: Oxetanocin, a novel nucleoside from bacteria. *J. Antibiotics* 39: 1623~1625, 1986