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Structure of 6,3′ : 6,5′-Dianhydro-5,5-dibromo-5,6-dihydro-6,6-dihydroxy-1-(β-D-xylofuranosyl)uracil

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The title compound, $C_9H_8Br_2N_2O_6$, crystallizes as hemihydrate in space group $P6_2$ with $a=12.612(1)$, $c=13.431(1)$ Å, and $Z=6$. The structure was solved by a combination of the direct and the heavy atom methods and refined to an R value of 0.051. The novel structure having two oxygen bridges between the base and the sugar was confirmed by the analysis. The base is oriented *anti* with respect to the sugar with torsional angles C(6)–N(1)–C(1′)–O(1′) = 57.2° and C(6)–N(1)–C(1′)–C(2′) = −55.6°, and the sugar ring is in a half-chair form, C(1′)-*endo*–C(2′)-*exo*. The oxygen atom of the water molecule lies on the two-fold axis and three independent hydrogen bonds connect the molecules of nucleoside and water in the crystals.

Keywords——uracil derivative; cyclonucleoside; X-ray analysis; molecular conformation; crystal structure

Some halogenopyrimidine nucleosides have potent medicinal properties; 5-iododeoxyuridine[1] and 1-(tetrahydro-2-furanyl)-5-fluorouracil[2] have been used clinically as antiviral and antitumor agents, respectively. As a part of our studies on the halogenation of pyrimidine nucleosides, we treated 6,3′-anhydro-1-(β-D-xylofuranosyl)-6-hydroxyuracil[3] with bromine water to afford the 5-bromo derivative, together with a dibromo compound ($C_9H_8Br_2N_2O_6$). The dibromonucleoside was assigned the 6,3′ : 6,5′-dianhydro-5,5-dibromo-5,6-dihydro-6,6-dihydroxy-1-(β-D-xylofuranosyl)uracil structure (I) on the basis of proton nuclear magnetic resonance (^{1}H-NMR) data.[4] This was the first example of formation of a cyclonucleoside with two oxygen bridges between the base and the sugar, starting from the mono-*O*-cyclonucleoside.[5] The present paper describes the structure determination, molecular conformation and crystal structure of the dibromo compound shown in the Chart.

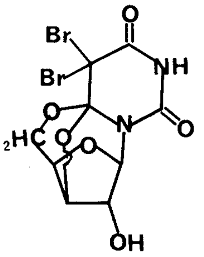
Experimental

The dibromo compound crystallizes in colorless elongated prisms of hemihydrate from an aqueous solution. A crystal of dimensions 0.2 × 0.2 × 0.5 mm was used for the measurements of crystal and intensity data on a Rigaku AFC-5 diffractometer with graphite-monochromated Mo$K\alpha$ radiation ($\lambda=0.71069$ Å). Cell dimensions were determined from 25 reflections ($29° < 2\theta < 31°$). The intensities of 1291 unique reflections were measured up to a maximum 2θ of 50°. The intensities of three standard reflections were checked every 60 reflections, and there was no significant change during the period of data collection. Lorentz and polarization corrections were applied, but no corrections were made for absorption. In all, 967 structure factors satisfied the condition $F_o \geqq 3\sigma(F_o)$ and were treated as observed. Crystal data are listed in Table I.

All non-hydrogen atoms including that of the water molecule were located by a combination of the direct (MULTAN 78[7]) and the heavy atom methods. The structure was refined anisotropically using the block-diagonal least-squares method (XRAY76[8]) to $R=0.067$, and the refinement, including the anomalous scattering for Br, gave a final R value of 0.051. Hydrogen atoms were not located even on the final difference map.

TABLE I. Crystal Data

Formula	$C_9H_8Br_2N_2O_6 \cdot 1/2H_2O$
M_r	409.0
Space group	$P6_2$
Cell dimensions	
a, Å	12.612 (1)
c, Å	13.431 (2)
Volume Å^3	1850.2 (2)
Z	6
D_x Mg·m^{-3}	2.20



Chart

TABLE II. Fractional Coordinates (× 10^4) of Nonhydrogen Atoms with Standard Deviations in Parentheses

Atom	x/a	y/b	z/c
N(1)	2832 (9)	4498 (9)	3101 (8)
C(2)	3388 (12)	4815 (12)	4050 (10)
N(3)	3540 (9)	3925 (10)	4519 (9)
C(4)	3254 (11)	2779 (11)	4181 (9)
C(5)	2759 (13)	2503 (10)	3105 (11)
C(6)	2053 (12)	3158 (11)	2874 (10)
O(2)	3737 (9)	5799 (9)	4409 (8)
O(4)	3424 (10)	2090 (10)	4667 (8)
Br	1761 (2)	785 (1)	2901 (2)
Br′	4214 (1)	3171 (1)	2272 (2)
C(1′)	2421 (11)	5293 (12)	2660 (11)
C(2′)	2315 (14)	5067 (13)	1523 (11)
C(3′)	1236 (12)	3780 (11)	1546 (12)
C(4′)	408 (12)	3824 (13)	2401 (11)
C(5′)	−29 (12)	2711 (14)	3071 (13)
O(1′)	1213 (8)	4937 (8)	2952 (7)
O(2′)	1965 (8)	5852 (9)	1036 (8)
O(3′)	1753 (8)	3020 (9)	1858 (7)
O(5′)	995 (8)	2644 (9)	3466 (7)
W	5000 (0)	0 (0)	2987 (11)

Results and Discussion

The final positional parameters are listed in Table II. Figures 1 and 2 show bond lengths and angles, respectively. All of the bond distances and the valency angles are consistent with the structure I. Thus, the novel structure having two oxygen bridges between the base and the sugar has been confirmed by the present analysis.

The conformation of the molecule is shown in Fig. 3 as a stereoscopic drawing. Table III lists some of the conformational parameters. The six-membered ring of the base is not planar, and C(6) is displaced by 0.63 Å from the least-squares plane through the other five atoms. N(1) and three atoms bonded to N(1) are not coplanar, the sum of the valency angles at N(1) being 351 °. Because of the nonplanar conformation of the base part, the definition of the glycosidic torsion angle (χ_{CN}) is unsuitable for quantitative treatment. Four torsion angles about the glycoside bond are accordingly listed in Table III. Atom C(6) is *gauche* to both O(1′) and C(2′) about the N(1)–C(1′) bond (57.2 and 55.6 °), which results in the positioning of C(6) almost over the center of the sugar ring. This arrangement is different from the

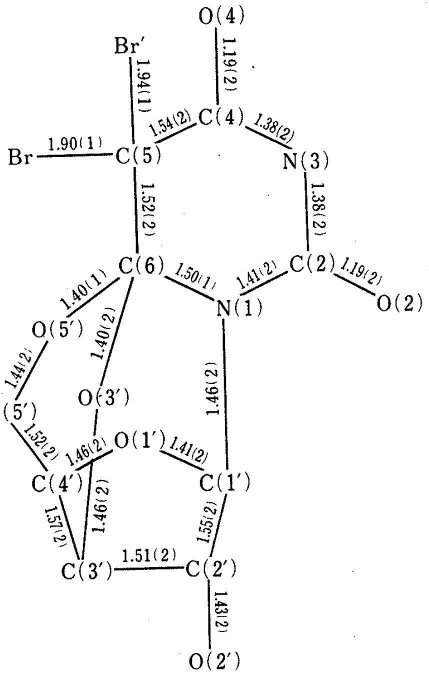
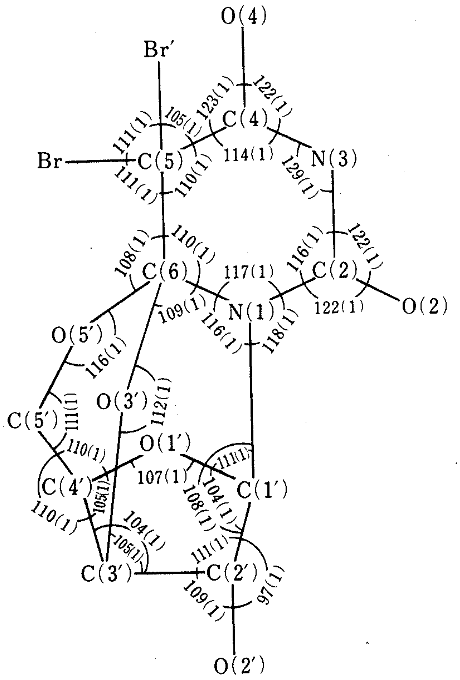


Fig. 1. Bond Lengths (Å) with Standard Deviations in Parentheses



∠O(5′)–C(6)–N(1)	110(1)
∠O(5′)–C(6)–O(3′)	111(1)
∠O(3′)–C(6)–C(5)	109(1)
∠C(4′)–C(3′)–O(3′)	110(1)
∠Br –C(5)–C(4)	111(1)
∠Br′ –C(5)–C(6)	109(1)

Fig. 2. Bond Angles (°) with Standard Deviations in Parentheses

Table III. Conformational Parameter (°)

Glycosidic torsion angles	
C(4)–N(1)–C(1′)–O(1′)	−88.1
C(4)–N(1)–C(1′)–C(2′)	159.0
C(6)–N(1)–C(1′)–O(1′)	57.2
C(6)–N(1)–C(1′)–C(2′)	−55.6
Sugar ring torsion angles	
τ_0 C(4′)–O(1′)–C(1′)–C(2′)	42.5
τ_1 O(1′)–C(1′)–C(2′)–C(3′)	−50.6
τ_2 C(1′)–C(2′)–C(3′)–C(4′)	38.8
τ_3 C(2′)–C(3′)–C(4′)–O(1′)	−16.5
τ_4 C(3′)–C(4′)–O(1′)–C(1′)	−16.1
Conformation about C(4′)–C(5′)	
ψ_{oo} O(5′)–C(5′)–C(4′)–O(1′)	−58.0
ψ_{oc} O(5′)–C(5′)–C(4′)–C(3′)	56.6

structures reported for pyrimidine 5′-cyclonucleosides containing one oxygen or sulfur bridge,[9-11] where in place of C(6), the O(5′) or S atom is positioned over the center of the ring. The furanose ring is not in a usual envelope form but in a C(1′)-*endo*–C(2′)-*exo* half-chair form (pseudorotation phase angle[12] $P=322$ °). The displacements of C(1′) and C(2′) from the plane of the remaining three atoms (C(3′), C(4′) and O(1′)) are 0.38 and 0.42 A°, respectively. The conformation about the C(4′)–C(5′) bond is *gauche–gauche* with ψ_{oo} of

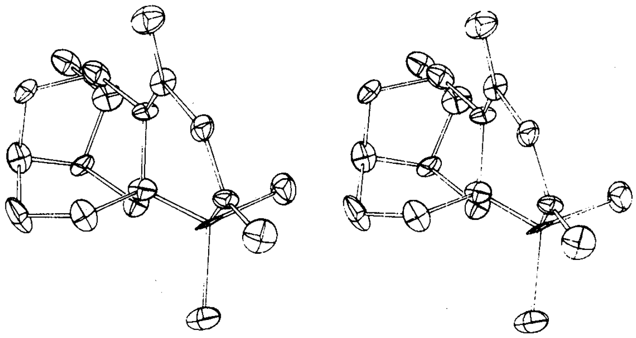


Fig. 3. Stereoscopic Drawing of the Molecule

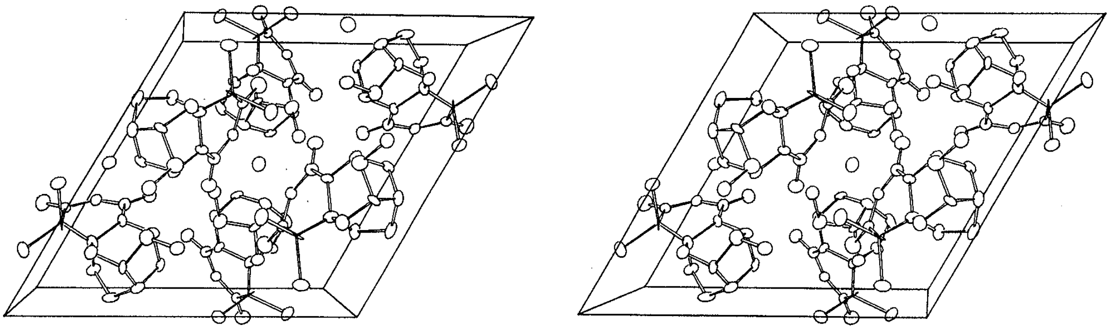


Fig. 4. Packing Diagram Viewed along the c Axis

$-58.0°$ and ψ_{oc} of $56.6°$. As for the newly formed three rings, one six-membered ring is puckered in a chair form (the ring C(6), N(1), C(1′), C(2′), C(3′) and O(3′)) and the other is in a twisted boat form (the ring C(6), O(3′), C(3′), C(4′), C(5′) and O(5′)), and the seven-membered ring is in a distorted chair form.

Figure 4 shows the molecular packing viewed along the c axis. The oxygen atom of the water lies on the two-fold axis. Though hydrogen atoms are not located, the interatomic distances of possible donor and acceptor atoms clearly indicate three independent intermolecular hydrogen bonds. The carbonyl oxygen O(2) accepts hydrogen from O(2′) of the adjacent molecule at $(y-x, 1-x, 1/3+z)$ with the donor–acceptor distance of 2.73 (1) Å. The hydroxyl oxygen O(2′) accepts hydrogen from the water molecule (O(2′)–W = 2.84 (1) Å). The other hydrogen bond is formed between the donor N(3) and the water molecule with the N–O distance of 2.93 (2) Å. No base stacking is apparent.

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