

Crystal Structure and Conformation of 3-Deaza-4-deoxyuridine

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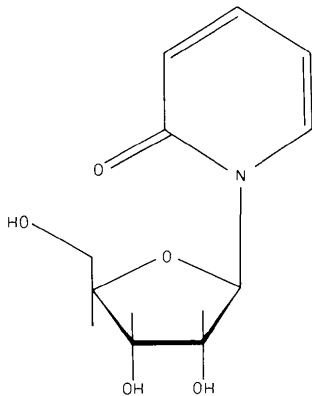
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$C_{10}H_{13}O_5N$ is orthorhombic, space group $P2_12_12_1$, with $a = 25.18$, $b = 7.127$, $c = 5.715$ Å, $Z = 4$. The structure was refined to $R = 0.049$ for 749 counter reflexions. Features of the nucleoside include an orientation of the base at the glycosidic bond N(1)–C(1') in the *anti* range (53.5°), a ribosyl moiety in the C(2')-*endo* conformation and a *gauche-gauche* arrangement of C(4')–C(5'). The packing is characterized by a staggered arrangement of the bases and a clear separation of hydrophobic and hydrophilic regions. Comparison with other pyrimidine nucleosides suggests an interrelationship between the puckering of the ribose and the orientation of the base, which has its structural basis in the formation of the intramolecular interaction C(6)–H...O(5').

The secondary and tertiary structures of nucleic acids are mainly determined by the stereochemistry of the monomeric building blocks. The influence of modifications in the base moiety on the stereochemistry of nucleic acids has not yet been clarified. Therefore, as part of our studies on the structures of pyrimidine nucleosides, some of which occur in tRNA, we have solved the crystal structure of 3-deaza-4-deoxyuridine (1- β -D-ribofuranosyl-2-pyridone), which is the least polar nucleoside of this series. This nucleoside, furthermore, represents a model compound, which shows the space filling of a pyrimidine nucleoside, but has no ability to form Watson–Crick-type hydrogen bonds with adenosine.



Experimental

1- β -D-Ribofuranosyl-2-pyridone was synthesized by a

Table 1. *Crystal data*

Molecular formula $C_{10}H_{13}O_5N$	
$M_r = 227$	
Space group $P2_12_12_1$	
$a = 25.18$ (1) Å	$Z = 4$
$b = 7.127$ (3)	$\rho_o = 1.46$ g cm $^{-3}$ (floatation)
$c = 5.715$ (5)	$\rho_c = 1.470$
$V = 1025.7$ Å 3	$\mu = 9.1$ cm $^{-1}$

known procedure (Vorbrüggen & Krolkiewicz, 1975). Crystals were grown as light-brown orthorhombic blocks from methanol and were identical with those obtained from water. The systematic absences $h00$, $0k0$ and $00l$ for odd indices determine the space group as $P2_12_12_1$. Crystal data are summarized in Table 1. Intensities were collected on a Stoe two-circle diffractometer (Cu $K\alpha$ radiation) equipped with a graphite monochromator; the crystal was orientated along c . In this way 906 symmetry-independent reflexions ($hk0-4$) with $\theta \leq 60^\circ$ were measured in the $\theta-2\theta$ scan mode. The data were corrected for background and for Lorentz and polarization factors, but not for absorption. 749 reflexions had $|E| > 3\sigma_E$.

Structure determination and refinement

The structure was solved with *SHELX-76* (Sheldrick, 1976) which uses scattering factors from *International Tables for X-ray Crystallography* (1974).

Isotropic refinement with unit weights reduced R to 0.138, which dropped to 0.091 with anisotropic

whereas C(2) is planar trigonal; the same feature is found in 2-pyridone. Of all substituents, C(1') shows the greatest deviation from the base plane (0.109 Å) and is situated on the opposite side of the ring from O(2).

Structure of the ribose

The ribose has a C(2')-*endo* conformation (Fig. 2) with C(1'), C(3'), C(4') and O(1') in the plane ($\sigma = 0.018$ Å) while C(2') deviates by 0.52 Å (Table 3). C(1')-O(1') is 0.032 Å shorter than C(4')-O(1'), as is nearly always found in nucleoside structures. The orientation at N(1)-C(1') is *anti* with a dihedral angle C(6)-N(1)-C(1')-O(1') of 53.5°. The base is held in this conformation by the characteristic intramolecular interaction H(C6)⋯O(5') (Table 4). C(5')-O(5') is *gauche* to C(3')-C(4') and to O(1')-C(4') with dihedral angles of 50.7 and -68.7° (Figs. 1 and 2).

Packing of the molecules

Views down *c* (Fig. 3) and *b* (Fig. 4) illustrate the crystal structure, which is determined by the three

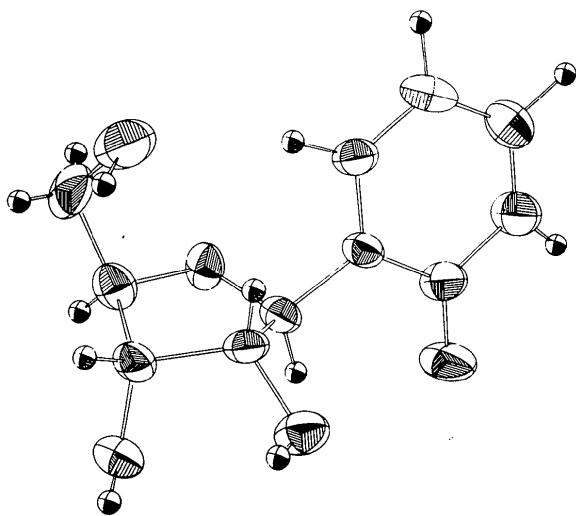


Fig. 2. The structural representation of 3-deaza-4-deoxyuridine with the thermal ellipsoids of the heavy atoms.

Table 4. List of intermolecular hydrogen bonds, including the characteristic intramolecular C(6)-H⋯O(5') interaction

X-H⋯Y	H⋯Y (Å)	X⋯Y (Å)	∠X-H⋯Y (°)
O(2')-H⋯O(3')	2.315	2.783	122.2
O(3')-H⋯O(2)	1.892	2.701	145.7
O(5')-H⋯O(1')	2.329	2.985	123.1
C(6)-H⋯O(5')	2.353	3.297	165.8

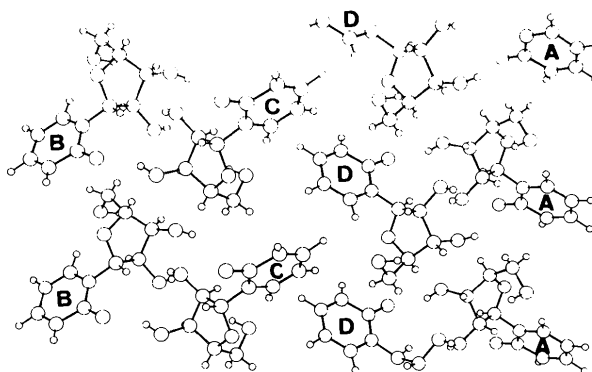


Fig. 3. A view down *c* with *a* horizontal and *b* vertical. The individual base stacks are designated with letters. They are related by the following symmetry operations: A ↔ B: screw axis parallel to *b*; A ↔ C: screw axis parallel to *a*; A ↔ D: screw axis parallel to *c*.

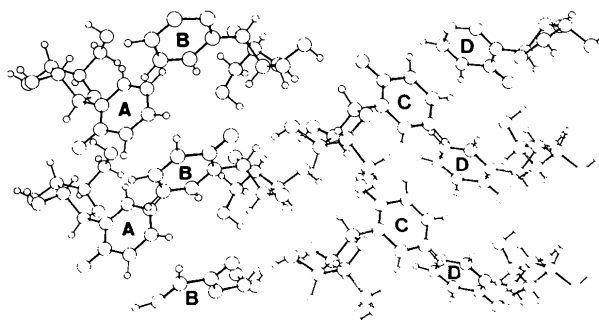


Fig. 4. A view down *b* with *a* horizontal and *c* vertical (for the definition of the letters A, B, C and D see Fig. 3).

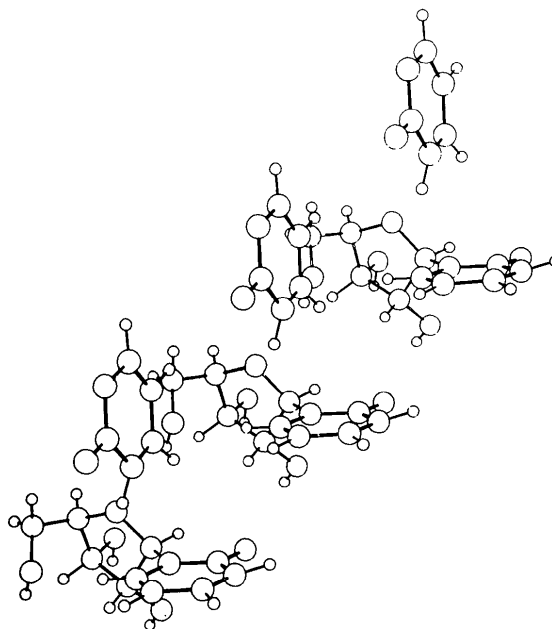


Fig. 5. A view parallel to the base stack B with the bases A perpendicular to it (see Fig. 4).

screw axes. The three-dimensional structure can be divided into layers parallel to the *bc* plane showing the sequence: base-ribose...ribose-base...base-ribose *etc.*, with adjacent ribose moieties connected by hydrogen bonds (Table 4). The bases are stacked along *c* at a distance of 3.51 Å. They are located not directly one upon another but show a staggered arrangement with only a small O(2)...H(C6) overlap. The stacked bases *A* (Fig. 4) are nearly perpendicular (94.6°) to the six-membered rings of the adjacent base stack *B*, and the same is true for the bases *C* and *D*. This feature is illustrated in Fig. 5 which shows a view parallel to the planes of the bases *B*. C(3) (3.58), H(C3) (2.74) and H(C4) (3.21 Å) of the bases *A* have the smallest distances from the best planes of *B*.

Discussion

The structure of 3-deaza-4-deoxyuridine is similar to that of comparable nucleosides. For example, 3-deazauridine (Schwalbe & Saenger, 1973), 5-chlorouridine (Hawkinson & Coulter, 1971) and 5-hydroxyuridine (Thewalt & Bugg, 1973) also exhibit the C(2')-*endo* conformation of the ribose with C(6)-N(1)-C(1')-O(1') dihedral angles of 52.3, 51.4 and 42.1°. 3-Deaza-4-deoxyuridine (53.5°) fits into this group. On the other hand, uridine (Green, Rosenstein, Shiono, Abraham, Trus & Marsh, 1975), 5-methyluridine (Hunt & Subramanian, 1969), 5-nitrouridine (Egert, Lindner, Hillen & Gassen, 1977) and 2-thiouridine (Hawkinson, 1977) exist in the C(3')-*endo* conformation with dihedral angles about the glycosidic bond of 18.3 (24.3), 29.4, 25.6 and 17°. From these values it is evident that there is a relation between the puckering of the ribose and the orientation of the base. This could be explained by the formation of the intramolecular interaction C(6)-H...O(5') (Saenger, 1973). This characteristic hydrogen bonding, which seems to stabilize the orientation of the glycosidic bond, occurs, for example, in 3-deaza-4-deoxyuridine, uridine, 3-deazauridine, 5-chlorouridine, 5-methyluridine and 5-nitrouridine. The formation of a C(6)-H...O(5') interaction requires a greater C(6)-N(1)-C(1')-O(1') dihedral angle in C(2')-*endo* than in C(3')-*endo* puckering.

The packing of the molecules is comparable with that of other nucleosides. The separation of hydrophobic and hydrophilic regions is a principle which is always realized. Alternating layers of bases and sugars as in 3-deaza-4-deoxyuridine are found, for example, in 2-thiouridine, 5-hydroxyuridine and 6-methyluridine (Suck & Saenger, 1972). Also, the interaction between the bases fits with the known structures of pyrimidine nucleosides because an extensive base stacking has never been found, but the bases only partially overlap as in uridine or 2-thiouridine. Hydrophilic interactions, for example hydrogen bonds, seem to mainly determine the crystal structure and are optimized at the expense of the base stacking. Indeed, it is questionable whether conclusions concerning the conformation of nucleic acids are valid from the crystalline structures of their building blocks.

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