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## Structure of a Thionucleoside: 5'-Deoxy-5',6-epithio-5,6-dihydro-2',3'-O-isopropylidene-3-methyluridine

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**Abstract.** C<sub>13</sub>H<sub>18</sub>N<sub>2</sub>O<sub>5</sub>S,  $M_r = 314.35$ , orthorhombic,  $P2_12_12_1$  with  $a = 39.526$  (4),  $b = 6.607$  (2),  $c = 5.661$  (2) Å,  $Z = 4$ ,  $V = 1478.36$  Å<sup>3</sup>,  $D_c = 1.412$  Mg m<sup>-3</sup>, Cu  $K\alpha$  radiation. Final  $R = 0.073$  for 1154 observed counter reflections. The sulphur atom is in a pseudo-equatorial position with respect to the dihydrouracil ring. The sugar pucker is predominantly O(1')-*exo* unlike the C(3')-*exo*, C(4')-*endo* observed for 2',3'-O-isopropylideneuridine (ISPU). The five-membered dioxolane ring has C(7) displaced by 0.497 (7) Å from the best plane through atoms O(2'), C(2'), C(3'), O(3'), in contrast to ISPU where O(3') shows the maximum deviation.

**Introduction.** We report here the structure of the thiocyclonucleoside 5'-deoxy-5',6-epithio-5,6-dihydro-2',3'-O-isopropylidene-3-methyluridine. The investigation was taken up to assess the conformational change in the molecule because of the S atom covalently linking the uracil base and the ribose moiety. We have earlier reported the structure of 2',3'-O-isopropylideneuridine (ISPU) (Katti, Seshadri & Viswamitra, 1981), which does not have this linkage.

Crystals were grown by slow evaporation from solutions of the compound in 50/50 water/acetone mixtures. No suitable liquid was available for the experimental determination of the density.

The unit-cell parameters were determined from the  $2\theta$  values of 25 high-angle reflections on a CAD-4 diffractometer. 1213 unique reflections were collected with Cu  $K\alpha$  radiation in the  $\omega$ - $2\theta$  scan mode ( $\theta$  range 0–60°). Of these, 1154 having  $F \geq 3\sigma(F)$  were considered observed.

The structure was solved by direct methods using *MULTAN* (Germain, Main & Woolfson, 1971). The entire nucleoside molecule could be identified unambiguously from an *E* map using the set of phases with the best combined figure of merit (2.0). Block-diagonal isotropic least-squares refinement reduced  $R$  to 14%. The reliability index with anisotropic thermal parameters was 9.0%. At this stage the H atoms, except for those of the methyl groups, were fixed from their expected geometry. Further refinement with the Cruickshank (1961) weighting scheme converged at  $R = 0.073$ . The function minimized is of the form  $w(F_o - F_c)^2$  with  $w = 1/(a + bF_o + cF_o^2)$ , where  $a = 4.35$ ,  $b = -0.684$  and  $c = 3.34$ .

The positional parameters of the atoms are given in Table 1,\* bond distances and angles in Table 2. The

\* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36936 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Positional parameters ( $\times 10^5$  for S,  $\times 10^4$  for rest of non-H atoms and  $\times 10^3$  for H atoms) and isotropic temperature factors ( $\text{\AA}^2$ )

$$B_{eq} = (4/3) \sum_i \sum_j \beta_{ij} a_i \cdot a_j$$

	x	y	z	$B_{eq}/B_{iso}$
N(1)	1010 (1)	9504 (8)	7021 (10)	3.7 (1)
C(2)	883 (1)	8096 (10)	8538 (12)	3.7 (2)
O(2)	1043 (1)	6640 (8)	9202 (10)	4.9 (1)
N(3)	551 (1)	8350 (10)	9364 (11)	4.4 (1)
C(3)	434 (2)	6899 (15)	11206 (16)	6.1 (3)
C(4)	332 (2)	9840 (12)	8560 (16)	5.0 (2)
O(4)	57 (1)	10118 (9)	9446 (14)	7.0 (2)
C(5)	452 (2)	10993 (12)	6464 (16)	5.0 (2)
C(6)	828 (2)	11380 (11)	6452 (13)	4.0 (2)
S	9326 (4)	122845 (29)	34984 (36)	4.35 (4)
C(1')	1378 (1)	9488 (10)	6722 (13)	3.6 (2)
O(1')	1516 (1)	11431 (7)	7198 (8)	4.1 (1)
C(2')	1518 (1)	8863 (10)	4331 (13)	3.6 (2)
O(2')	1784 (1)	7449 (7)	4702 (10)	4.6 (1)
C(3')	1692 (1)	10730 (11)	3361 (13)	4.0 (2)
O(3')	2041 (1)	10278 (8)	3502 (10)	5.2 (1)
C(4')	1605 (2)	12401 (13)	5005 (13)	4.3 (2)
C(5')	1311 (2)	13717 (11)	4167 (17)	5.1 (2)
C(7)	2070 (1)	8131 (11)	3403 (13)	4.3 (2)
C(8)	2388 (2)	7474 (17)	4699 (15)	5.9 (2)
C(9)	2065 (3)	7333 (21)	886 (16)	9.2 (4)
H'(5)	37 (2)	1237 (11)	648 (12)	5.1 (15)
H''(5)	40 (1)	1017 (10)	496 (12)	4.4 (14)
H(5')	123 (2)	1467 (15)	532 (20)	9.0 (28)
H'(5')	136 (2)	1450 (10)	238 (12)	3.4 (15)
H(4')	185 (2)	1325 (11)	517 (14)	5.3 (18)
H(1')	145 (1)	844 (7)	783 (8)	0.61 (9)
H(3')	167 (2)	1093 (17)	137 (19)	8.3 (27)
H(2')	134 (13)	834 (9)	385 (11)	2.8 (12)
H(6)	88 (1)	1250 (7)	767 (8)	3.8 (9)

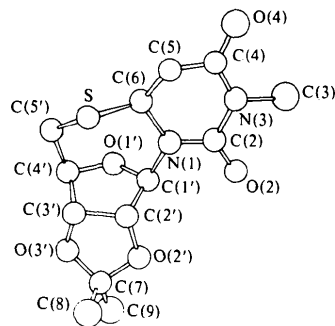


Fig. 1. Chemical structure and numbering.

chemical structure and the numbering of the atoms are shown in Fig. 1.

**Discussion.** The glycosidic torsion angle  $\chi_{CN}$  [ $32.5 (7)^\circ$ ] lies in the *anti* region of the conformational wheel. It is significantly different from those of ISPU ( $3.4^\circ$ ) and 2',3'-methoxymethylenuridine ( $56.6^\circ$ ) (MMU) (de Kok, Romers, de Leeuw, Altona & van Boom, 1977). The present conformation results from the constraint imposed by the covalently linked sulphur bridge between the base and the sugar.

The compound is formed by the spontaneous cyclization of 2',3'-isopropylidene-3-methyl-5'-thiouridine (Salisbury & Brown, unpublished results) and is therefore formally derived from 5,6-dihydrouracil. The heterocyclic ring formed cannot, therefore, be planar and this is borne out by the present structure determination. C(5) has the maximum deviation [ $0.286 (8) \text{\AA}$ ] (Table 3). The exocyclic O(2) and O(4)

Table 2. Bond distances ( $\text{\AA}$ ) and angles ( $^\circ$ )

N(1)—C(2)	1.360 (9)	C(1')—O(1')	1.421 (8)
N(1)—C(6)	1.467 (9)	C(2')—C(3')	1.515 (10)
C(2)—N(3)	1.406 (8)	C(2')—O(2')	1.420 (8)
C(2)—O(2)	1.210 (8)	C(3')—O(3')	1.414 (8)
N(3)—C(4)	1.386 (10)	C(3')—C(4')	1.484 (11)
N(3)—C(3)	1.490 (11)	C(4')—O(1')	1.441 (9)
C(4)—O(4)	1.211 (9)	C(4')—C(5')	1.527 (11)
C(4)—C(5)	1.488 (12)	C(5')—S	1.811 (8)
C(5)—C(6)	1.509 (9)	O(3')—C(7)	1.424 (9)
C(6)—S	1.823 (8)	C(7)—C(8)	1.519 (10)
N(1)—C(1')	1.468 (8)	C(7)—C(9)	1.520 (12)
C(1')—C(2')	1.519 (10)		
N(1)—C(2)—N(3)	118.1 (6)	O(2')—C(2')—C(3')	104.8 (5)
N(1)—C(2)—O(2)	123.3 (6)	C(2')—C(3')—C(4')	105.8 (6)
O(2)—C(2)—N(3)	118.6 (6)	C(2')—C(3')—O(3')	104.5 (6)
C(2)—N(3)—C(4)	124.0 (6)	O(3')—C(3')—C(4')	110.4 (6)
C(2)—N(3)—C(3)	116.6 (6)	C(3')—C(4')—O(1')	105.4 (6)
N(3)—C(4)—C(5)	115.3 (7)	C(3')—C(4')—C(5')	113.9 (6)
C(3)—N(3)—C(4)	119.5 (6)	O(1')—C(4')—C(5')	109.6 (6)
O(4)—C(4)—C(5)	112.5 (7)	C(4')—C(5')—S	113.3 (6)
C(4)—C(5)—C(6)	113.9 (6)	C(5')—S—C(6)	99.6 (4)
C(5)—C(6)—S	106.4 (5)	C(2')—O(2')—C(7)	107.6 (5)
C(5)—C(6)—N(1)	109.7 (6)	C(3)—O(3')—C(7)	106.7 (5)
S—C(6)—N(1)	111.6 (5)	O(3')—C(7)—O(2')	103.3 (5)
C(6)—N(1)—C(1')	117.8 (5)	O(3')—C(7)—C(8)	109.4 (6)
C(2)—N(1)—C(1')	115.6 (5)	O(3')—C(7)—C(9)	112.4 (7)
N(1)—C(1')—O(1')	110.7 (5)	O(2')—C(7)—C(8)	108.6 (6)
N(1)—C(1')—C(2')	117.8 (5)	O(2')—C(7)—C(9)	111.3 (7)
C(1')—C(2')—C(3')	105.5 (5)	C(8)—C(7)—C(9)	111.5 (7)
C(1')—C(2')—O(2')	108.4 (5)		

Table 3. Least-squares planes and the deviations of the atoms ( $\text{\AA}$ )

Uracil base			
Equation of the plane			
$-10.023x - 3.835y - 4.381z = -7.787$			
N(1)	0.054 (6)	C(6)	-0.234 (7)
C(2)	0.056 (7)	O(2)*	0.164 (5)
N(3)	-0.070 (6)	C(3)*	-0.203 (10)
C(4)	-0.070 (9)	O(4)*	-0.289 (7)
C(5)	0.286 (8)	S*	0.608 (2)
Ribose			
Equation of the plane			
$-34.061x + 1.295y - 2.649z = -5.218$			
C(2')	0.040 (6)	C(1')	-0.028 (6)
C(3')	-0.052 (7)	O(1')*	-0.367 (4)
C(4')	0.035 (7)		
Dioxolane ring			
Equation of the plane			
$-2.200x - 2.170y - 5.338z = -4.534$			
O(3')	-0.015 (6)	O(2')	0.015 (6)
C(3')	0.039 (8)	C(7)*	0.497 (7)
C(2')	-0.036 (7)		

\* Atoms not included in the calculation of the planes.

atoms are displaced on opposite sides of the base by 0.164 (5) and 0.289 (7) Å. Fig. 2 shows a view of the molecule parallel to the mean plane of the base. The sulphur atom takes up a pseudo-equatorial position with respect to the dihydrouracil ring. Since there is much evidence that other related nucleophilic addition reactions of the 5,6 double bond of uracil and cytosine derivatives are *trans*-diaxial in character (Blackburn, Solan, Brown & Coe, 1976), a subsequent conformational inversion has occurred in the present case. This is discussed in more detail in a later paper.

The phase angle  $P$  of pseudorotation (Altona & Sundaralingam, 1972) calculated from the ribose torsion angles is 253.76 (2)°. The sugar conformation can be described as  ${}^0T_4$ . It is predominantly O(1')-*exo* with O(1') displaced by 0.367 (4) Å from the best four-atom plane. With respect to the three-atom plane, the sugar pucker can be described as O(1')-*exo*, C(4')-*endo*. It is different from the C(2')-*exo*, C(3')-*exo* conformation observed for 2,5'-anhydro-2',3'-*O*-isopropylideneuridine (Delbaere & James, 1973) and also from the C(3')-*exo*, C(4')-*endo* conformation observed for ISPU. The maximum amplitude of pucker,  $\tau_{m, \max} = 28.9$  (26)°, is slightly greater than 23.1 and 23.7° reported for MMU and ISPU but is significantly smaller than that (38°) normally found in S-type rings (Altona & Sundaralingam, 1972), indicating a flattening of the ribose moiety.

The torsion angle O(2)–C(2')–C(3')–O(3') is –5.8 (7)° so that the C(2')–O(2') and C(3')–O(3') bonds are in an almost eclipsed configuration. C(7) shows the highest deviation [0.497 (7) Å] from the best

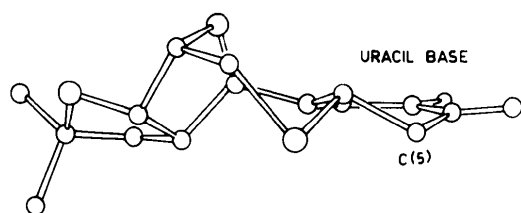


Fig. 2. The pucker of the base.

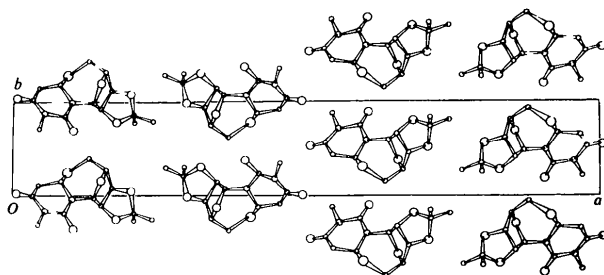


Fig. 3. Molecular packing.

Table 4. Torsion angles involving non-hydrogen atoms (°)

Dihydrouracil base		Ribose ring	
C(6)–N(1)–C(2)–O(2)	–172.6 (6)	O(1')–C(1')–C(2')–C(3')	–9.3 (7)
C(6)–N(1)–C(2)–N(3)	7.5 (9)	C(1')–C(2')–C(3')–C(4')	–8.1 (7)
N(1)–C(2)–N(3)–C(4)	6.3 (10)	C(2')–C(3')–C(4')–O(1')	22.4 (7)
O(2)–C(2)–N(3)–C(4)	–173.5 (7)	C(3')–C(4')–O(1')–C(1')	–29.7 (7)
N(1)–C(2)–N(3)–C(3)	–174.0 (6)	C(4')–O(1')–C(1')–C(2')	24.3 (7)
O(2)–C(2)–N(3)–C(3)	6.2 (9)	C(3')–C(4')–C(5')–S	54.4 (8)
C(2)–N(3)–C(4)–O(4)	–173.9 (7)	O(1')–C(4')–C(5')–S	–63.5 (7)
C(2)–N(3)–C(4)–C(5)	9.1 (10)		
C(3)–N(3)–C(4)–O(4)	6.4 (11)	Dioxolane ring	
C(3)–N(3)–C(4)–C(5)	–170.6 (7)	O(2')–C(7)–O(3')–C(3')	–36.8 (7)
N(3)–C(4)–C(5)–C(6)	–36.5 (9)	C(7)–O(3')–C(3')–C(2')	26.2 (7)
O(4)–C(4)–C(5)–C(6)	146.5 (8)	O(3')–C(3')–C(2')–O(2')	–5.8 (7)
C(4)–C(5)–C(6)–N(1)	46.9 (8)	C(3')–C(2')–O(2')–C(7)	–16.7 (7)
C(4)–C(5)–C(6)–S	167.7 (5)	C(2')–O(2')–C(7)–O(3')	32.9 (6)
C(5)–C(6)–N(1)–C(2)	–33.7 (8)		

plane of atoms O(3'), C(3'), C(2'), O(2'). This is in contrast to ISPU, where O(3') shows the maximum deviation (0.457 Å). The maximum amplitude of pucker  $\lambda_{m, \max}$  for the dioxolane ring (Sprang, Rohrer & Sundaralingam, 1978) is 37.0 (4)°. It is close to 33.9 and 32.3° observed for ISPU and MMU respectively. The phase angle of pseudorotation is 99.43 (1)°.

The conformation about C(4')–C(5') is *gauche-gauche*, as seen from the torsion angles about this bond (Table 4). The other two conformers possible in nucleosides, namely *gt* and *tg*, cannot occur in this structure since in these orientations the C(6)–S length would be 3–3.8 Å.

In the crystal the molecules pack only through van der Waals interactions, with the shortest distance [3.11 (1) Å] being between C(5') of one molecule and O(2') of another translated along *b*. Fig. 3 shows the molecular packing.

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