

Structure of 2',3'-*O*-Isopropylidene-5'-*O*-tosyluridine, C₁₉H₂₂N₂O₈S

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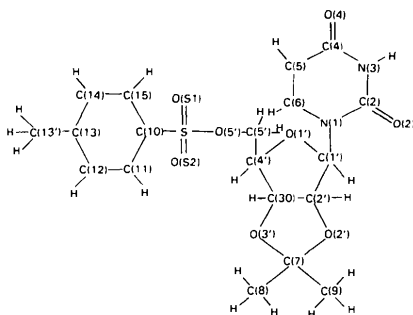
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Abstract. $M_r = 438.45$, trigonal, $P3_2$, $a = b = 13.385$ (4), $c = 9.900$ (5) Å, $V = 1536.0$ Å³, $Z = 3$, $D_x = 1.42$, $D_m = 1.42$ Mg m⁻³, $\lambda(\text{Cu } K\alpha) = 1.5418$ Å, $\mu(\text{Cu } K\alpha) = 1.800$ mm⁻¹, $T = 290$ K, $F(000) = 690$, $R = 6.0\%$ for 1222 unique reflections with $F_o \geq 2\sigma(F_o)$. This is the first 2',3'-*O*-isopropylidene pyrimidine nucleoside with the base in a *syn* orientation with respect to the ribose [$\chi_{\text{CN}} = 116.0$ (7)°]. The ribose has a C(3')-*endo* conformation with the phase angle of pseudorotation $P = 16.36$ (2)°. The dioxolane ring assumes an envelope conformation with O(2') displaced from the best four-atom plane by 0.50 (1) Å. The crystal structure is possibly stabilized by a bifurcated hydrogen bond between N(3) and the O(2) and O(4) atoms of screw-related molecules.

Introduction. We report here the structure of the title compound (I). The analysis was undertaken as part of our X-ray studies of nucleosides modified by the attachment of an isopropylidene group at the 2',3' positions of the ribose (Katti, Seshadri & Viswamitra, 1981; Gautham, Ramakrishnan, Seshadri, Viswamitra, Salisbury & Brown, 1982).



(I)

Experimental. Crystals grown by diffusion of distilled water into a solution of the compound in acetone, crystal used 0.22 × 0.20 × 1.12 mm; initial photographic studies led to the assignment of a trigonal

system referred to hexagonal axes, space group $P3_1$ or its enantiomer $P3_2$; unit-cell parameters refined from accurately determined 2θ values for 25 high-angle reflections, CAD-4 diffractometer, 5119 intensities collected by ω - 2θ scans over the entire hemisphere up to $\sin \theta/\lambda = 0.562$ Å⁻¹; equivalent reflections [$hkl = k(-h-k)l = (-h-k)h\ l$] averaged for a final total of 1222 unique reflections with $F_o \geq 2\sigma(F_o)$ after correction for Lorentz and polarization effects; structure solved by direct methods using *MULTAN* (Germain, Main & Woolfson, 1971); an *E* map computed with the best set of phases (combined figure of merit = 2.73) revealed 25 of the 30 atoms in the asymmetric unit; a difference map with these 25 atoms as input revealed the rest of the structure; H atoms were positioned from their expected geometry, as difference Fourier maps did not reveal their positions, and refined with isotropic temperature factors; non-hydrogen atoms refined anisotropically; final $R = 0.060$, $R_w = 0.071$; function minimized during refinement was $\sum w(|F_o| - |F_c|)^2$, $w = 1/\sigma^2(F_o)$; scattering factors from *International Tables for X-ray Crystallography* (1974).

Discussion. The final positional parameters are given in Table 1.* Table 2 lists the bond lengths and angles involving the non-hydrogen atoms.

Uracil base. The base is essentially planar, with the exocyclic O(4) showing the maximum deviation from the mean plane [0.114 (8) Å].*

The glycosidic torsion angle about the C(1')-N(1) bond is 116.0 (7)° which falls in the range associated with the *syn* conformation for nucleosides (Sundaralingam, 1969). This is the first 2',3'-*O*-isopropylidene pyrimidine nucleoside which assumes this orientation in

* Lists of structure factors, anisotropic thermal parameters, selected torsion angles, the results of mean-plane calculations, and a figure illustrating a possible bifurcated hydrogen bond have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38242 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

the crystal structure. Although not very common in pyrimidine nucleosides, the *syn* orientation has been observed in 4-thiouridine (-87.1°) (Saenger & Sheit, 1970) and 2'-acetyluridine-3',5'-cyclophosphate benzyl triester (-108.6°) (Depmeier, Engels & Klaska, 1977).

Ribose. The phase angle of pseudorotation P (Altona & Sundaralingam, 1972) is $16.36(2)^\circ$ indicating the 3E envelope or $C(3')$ -*endo* conformation. Though commonly observed in nucleosides and nucleotides, this is a geometry not previously seen in isopropylidene nucleoside derivatives. In 2',3'-O-isopropylideneadenosine (Sprang, Rohrer & Sundaralingam, 1978), the ribose has a $C(3')$ -*exo*, $C(4')$ -*endo* twist conformation. It is

Table 1. Final positional parameters ($\times 10^4$) and equivalent isotropic temperature factors for non-hydrogen atoms and positional parameters ($\times 10^3$) and isotropic temperature factors for hydrogen atoms

The temperature factor is of the form $\exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$ with $B_{eq} = \frac{1}{3} \sum_i \sum_j \beta_{ij} a_i \cdot a_j$.

	x	y	z	$B_{eq}/B(\text{\AA}^2)$
N(1)	6741 (5)	6091 (5)	2711 (5)	3.3 (2)
C(2)	6699 (6)	5047 (5)	2617 (6)	3.3 (2)
O(2)	6728 (4)	4626 (4)	1540 (4)	4.2 (2)
N(3)	6604 (5)	4503 (5)	3824 (5)	4.3 (2)
C(4)	6563 (7)	4923 (6)	5113 (6)	4.1 (2)
O(4)	6415 (6)	4318 (6)	6115 (5)	6.5 (2)
C(5)	6694 (7)	6053 (7)	5116 (7)	5.1 (3)
C(6)	6745 (6)	6558 (6)	3927 (7)	3.9 (2)
C(1')	6868 (5)	6753 (5)	1452 (6)	3.0 (2)
O(1')	5855 (4)	6158 (4)	670 (4)	4.0 (1)
C(2')	7881 (5)	6968 (6)	563 (6)	3.3 (2)
O(2')	8332 (4)	8096 (4)	35 (4)	3.9 (2)
C(3')	7380 (6)	6217 (6)	-682 (6)	3.0 (2)
O(3')	8020 (4)	6950 (4)	-1777 (4)	3.9 (2)
C(4')	6129 (5)	5953 (6)	-687 (6)	3.2 (2)
C(5')	5259 (6)	4736 (7)	-1059 (7)	4.2 (2)
O(5')	4142 (4)	4679 (6)	-1228 (5)	5.0 (2)
S	3051 (1)	3695 (2)	-473 (2)	4.3 (1)
O(S1)	2130 (5)	3790 (8)	-1037 (5)	8.4 (3)
O(S2)	3054 (6)	2633 (5)	-535 (7)	5.7 (2)
C(7)	8781 (6)	8091 (6)	-1271 (7)	4.1 (2)
C(8)	9987 (7)	8324 (8)	-1190 (10)	5.8 (3)
C(9)	8679 (9)	8956 (9)	-2146 (8)	6.5 (3)
C(10)	3225 (5)	4115 (6)	1228 (6)	3.4 (2)
C(11)	2899 (7)	4886 (7)	1642 (8)	4.8 (3)
C(12)	3019 (7)	5204 (7)	2994 (8)	5.0 (3)
C(13)	3462 (7)	4735 (8)	3929 (9)	5.0 (3)
C(14)	3770 (7)	3967 (8)	3484 (7)	5.3 (3)
C(15)	3658 (7)	3644 (7)	2142 (8)	4.7 (3)
C(13')	3573 (10)	5088 (12)	5432 (9)	8.9 (5)
H(3)	656 (6)	377 (6)	323 (6)	3.1 (12)
H(5)	681 (5)	657 (5)	589 (6)	2.4 (12)
H(6)	662 (5)	709 (5)	385 (6)	2.2 (12)
H(1')	692 (5)	763 (5)	174 (5)	1.0 (9)
H(2')	858 (5)	687 (5)	93 (5)	0.9 (10)
H(3')	767 (5)	562 (5)	-61 (5)	1.3 (10)
H(4')	600 (4)	641 (4)	-127 (5)	3.2 (13)
H(15')	567 (5)	459 (5)	-212 (6)	3.2 (13)
H(25')	515 (5)	411 (5)	-55 (6)	1.1 (10)
H(18)	1005 (5)	804 (5)	-106 (5)	1.3 (11)
H(28)	1042 (6)	912 (5)	-80 (6)	3.4 (12)
H(38)	1043 (5)	820 (5)	-213 (5)	1.5 (11)
H(19)	878 (5)	901 (5)	-296 (5)	2.2 (12)
H(29)	896 (5)	962 (5)	-176 (5)	1.9 (11)
H(39)	782 (5)	883 (5)	-205 (6)	2.3 (11)
H(11)	259 (5)	524 (5)	104 (4)	1.3 (11)
H(12)	280 (4)	574 (5)	338 (5)	1.7 (11)
H(14)	405 (5)	362 (5)	426 (6)	2.5 (12)
H(15)	395 (5)	292 (6)	185 (6)	3.3 (13)
H(113)	782 (5)	883 (5)	-205 (6)	2.3 (11)
H(213)	398 (5)	484 (5)	607 (5)	2.6 (12)
H(313)	438 (5)	605 (5)	569 (5)	2.0 (11)

Table 2. Bond lengths (\AA) and bond angles ($^\circ$)

N(1)-C(2)	1.373 (9)	C(4')-C(5')	1.499 (11)
N(1)-C(6)	1.356 (8)	C(3')-C(4')	1.528 (12)
N(1)-C(1')	1.489 (8)	C(5')-O(5')	1.468 (11)
C(2)-O(2)	1.215 (8)	O(5')-S	1.581 (7)
C(2)-N(3)	1.372 (8)	S-O(S1)	1.416 (8)
N(3)-C(4)	1.407 (8)	S-O(S2)	1.427 (7)
C(4)-O(4)	1.232 (9)	S-C(10)	1.754 (6)
C(4)-C(5)	1.433 (11)	C(7)-C(8)	1.485 (14)
C(5)-C(6)	1.342 (10)	C(7)-C(9)	1.507 (13)
C(1')-O(1')	1.412 (9)	C(10)-C(11)	1.368 (12)
C(1')-C(2')	1.518 (10)	C(10)-C(15)	1.385 (11)
C(2')-O(2')	1.416 (8)	C(11)-C(12)	1.390 (11)
C(2')-C(3')	1.519 (9)	C(12)-C(13)	1.406 (14)
O(2')-C(7)	1.426 (9)	C(13)-C(14)	1.357 (14)
C(3')-O(3')	1.426 (8)	C(13)-C(13')	1.546 (13)
O(3')-C(7)	1.437 (9)	C(14)-C(15)	1.382 (11)
C(4')-O(1')	1.454 (8)		
C(2)-N(1)-C(6)	121.2 (6)	O(1')-C(4')-C(5')	107.4 (6)
C(2)-N(1)-C(1')	118.9 (6)	C(4')-C(5')-O(5')	107.6 (6)
C(6)-N(1)-C(1')	119.7 (6)	C(5')-O(5')-S	118.8 (5)
N(1)-C(2)-O(2)	122.5 (6)	O(5')-S-O(S1)	102.8 (4)
N(1)-C(2)-N(3)	115.2 (6)	O(5')-S-O(S2)	110.4 (4)
O(2)-C(2)-N(3)	122.3 (7)	O(S1)-S-O(S2)	120.7 (5)
C(2)-N(3)-C(4)	126.2 (6)	O(5')-S-C(10)	105.5 (3)
N(3)-C(4)-O(4)	119.6 (7)	O(S1)-S-C(10)	109.3 (5)
N(3)-C(4)-C(5)	114.5 (7)	O(S2)-S-C(10)	107.2 (4)
O(4)-C(4)-C(5)	125.9 (8)	S-C(10)-C(11)	119.2 (6)
C(4)-C(5)-C(6)	118.6 (7)	S-C(10)-C(15)	119.9 (6)
C(5)-C(6)-N(1)	124.0 (7)	C(11)-C(10)-C(15)	120.8 (7)
N(1)-C(1')-O(1')	109.3 (5)	C(10)-C(11)-C(12)	119.2 (8)
N(1)-C(1')-C(2')	115.1 (5)	C(11)-C(12)-C(13)	120.4 (8)
O(1')-C(1')-C(2')	107.7 (5)	C(12)-C(13)-C(14)	118.7 (9)
C(1')-C(2')-O(2')	106.3 (5)	C(12)-C(13)-C(13')	119.6 (9)
C(1')-C(2')-C(3')	106.8 (5)	C(14)-C(13)-C(13')	121.6 (9)
O(2')-C(2')-C(3')	102.6 (5)	C(13)-C(14)-C(15)	121.5 (9)
C(2')-O(2')-C(7)	106.6 (5)	C(14)-C(15)-C(10)	119.3 (8)
C(2')-C(3')-O(3')	104.3 (5)	O(2')-C(7)-C(8)	111.5 (7)
C(2')-C(3')-C(4')	103.0 (5)	O(2')-C(7)-C(9)	108.5 (7)
O(3')-C(3')-C(4')	111.6 (6)	O(3')-C(7)-C(8)	111.2 (7)
C(3')-O(3')-C(7)	109.2 (5)	O(3')-C(7)-C(9)	109.1 (7)
C(3')-C(4')-O(1')	107.7 (5)	O(2')-C(7)-O(3')	104.2 (6)
C(3')-C(4')-C(5')	114.7 (6)		

$C(4')$ -*endo*, $O(1')$ -*exo* in 5'-deoxy-5',6-epithio-2',3'-O-isopropylidene-3-methyluridine (Gautham *et al.*, 1982). In 2',3'-O-isopropylideneuridine (Katti *et al.*, 1981) it is $C(3')$ -*exo*, $C(4')$ -*endo*.

The maximum amplitude of pucker, $\tau_{m, \max}$, is $20.5(7)^\circ$ [$C(3')$ is displaced by $0.322(7) \text{\AA}$ from the plane of the other four atoms], indicating a somewhat flattened ribose compared to unconstrained rings (Altona & Sundaralingam, 1972).

The dioxolane ring. The five-membered dioxolane ring shows considerable deviation from planarity with $O(2')$ displaced by $0.502(6) \text{\AA}$ in an *exo* conformation. The relevant torsion angle $C(2')-C(3')-O(3')-C(7)$ is only $4.8(7)^\circ$. Crystal structures have shown considerable flexibility in the dioxolane-ring conformation. For example, in 2',3'-O-isopropylideneuridine (Katti *et al.*, 1981) the dioxolane ring has an envelope conformation with $O(3')$ out of the ring plane by 0.457\AA . In 2',3'-O-isopropylideneadenosine (Sprang *et al.*, 1978), it assumes a $C(3')$ -*endo*, $O(3')$ -*exo* twist conformation.

The tosyl moiety. The conformation about the $C(4')-C(5')$ bond is *gauche-trans*, unlike the *gauche-gauche* conformation usually observed in 5'-nucleotide structures. Instead of the phosphate group, the present structure has a sulphonyl group with a bulky phenyl ring attached in the 5'-position.

The torsion angle about C(5')-O(5') is 129.9 (6)°, making C(4')-C(5') *trans* to the O(5')-S bond. The torsion angle C(5')-O(5')-S-C(10) is 74.7 (6)°. Thus S-C(10) is *cis* with respect to the C(5')-O(5') bond. These conformational parameters result in the molecule taking a folded shape as shown in Fig. 1. The torsion angles O(5')-S-C(10)-C(11) and O(5')-S-C(10)-C(15) are 82.7 (7) and -99.1 (7)° respectively. The O(5')-S bond thus takes up an axial geometry with respect to the phenyl ring.

Crystal packing. The crystal structure appears to be stabilized by a possible bifurcated hydrogen bond between N(3) and the O(2) and O(4) atoms of two screw-related molecules.*

There are no inter- or intramolecular stacking interactions. Fig. 2 shows the crystal structure down the the 3_2 screw axis.

Haschmeyer & Rich (1967) have shown from energy calculations that for pyrimidine nucleosides with a

* A figure illustrating this has been deposited. See deposition footnote.

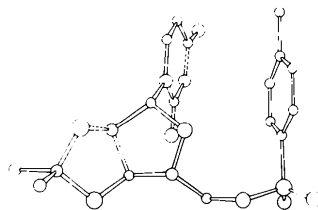


Fig. 1. A view of the folded molecule.

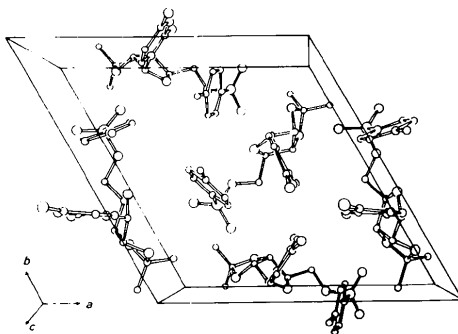


Fig. 2. The crystal packing viewed down the 3_2 screw axis.

C(3')-*endo* ribose the glycosidic torsion angles prefer the *anti* region. The present structure, where the *syn* conformation co-exists with a C(3')-*endo* sugar, is thus an interesting deviation. 4-Thiouridine also shows a *syn* conformation with a C(3')-*endo* sugar when crystallized with two water molecules per asymmetric unit (Saenger & Sheit, 1970), but takes up the more usual *anti* orientation when crystallized without the water molecules (Saenger, 1979). In this respect the present structure differs from 4-thiouridine as it has no water molecules in the crystal structure. The observed value of 116.0° for the glycosidic torsion angle seems to provide the optimum position for O(2) to be in close van der Waals contact with all the atoms of the ribose ring [O(2)-C(1') = 2.759 (8), O(2)-C(2') = 2.882 (8), O(2)-C(3') = 2.877 (8), O(2)-C(4') = 3.175 (8), O(2)-O(1') = 2.950 (8), O(2)-C(5') = 3.286 (9) Å]. The *gauche-trans* conformation about C(4')-C(5') relieves the unacceptable short contacts that would occur if the conformation were *gauche-gauche* when the orientation of the heterocycle is *syn*. Van der Waals packing forces thus appear to play the major role in stabilizing the observed conformation.

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