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5-Ethyl-2′-deoxy-4′-thiouridine (*R*)-*S*-oxide monohydrate

Ming Sun,† Alasdair C. Macculloch, Thomas A. Hamor* and Richard T. Walker‡

School of Chemistry, University of Birmingham, Birmingham B15 2TT, England
Correspondence e-mail: tom_hamor@hotmail.com

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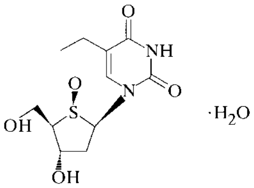
The pyrimidine ring of the title compound, $C_{11}H_{16}N_2O_5S\cdot H_2O$, is planar to within 0.026 (1) Å and makes an angle of 77.73 (8)° with the mean plane of the thiosugar ring. In terms of standard nucleoside nomenclature, this ring has a C1′-*exo*,C2′-*endo* conformation. The O5′—C5′—C4′—C3′ torsion angle is −167.4 (2)° and the glycosidic S4′—C1′—N1—C2 torsion angle is −101.8 (2)° (*anti*).

Comment

5-Substituted 2′-deoxy-4′-thiouridines possess significant antiviral activity (Dyson *et al.*, 1991; Rahim *et al.*, 1996). In order to provide data for structure–activity relationships, the crystal structure of the title compound, (I), synthesized by Macculloch (1998), is presented here.



(I)

Bond lengths in (I) (Fig. 1) are normal. The C1′—S4′ and C4′—S4′ bonds are 1.847 (2) and 1.837 (2) Å, respectively, slightly longer than the mean length of 1.818 Å measured in a 6-aza-2′-deoxy-4′-thiouridine (Basnak *et al.*, 1998), but in good agreement with the values found in 4′-thiothymidine (Koole *et al.*, 1992; Uenischi *et al.*, 1993) and 5-(2-bromovinyl)-2′-deoxy-4′-thiouridine (Koole *et al.*, 1992) which were in the range 1.83–1.85 Å. The thiosugar has a C1′-*exo*,C2′-*endo* ($_1T^2$) conformation (south), a pseudo-rotation phase angle (*P*) of 135.7° and a degree of pucker of 49.9°; these two atoms are displaced by 0.648 (5) and 0.134 (6) Å, respectively, on opposite sides of the C3′/C4′/S4′ plane. This appears to be an unusual conformation for sugar rings of this type. The conformation about C4′—C5′ is *trans* [O5′—C5′—C4′—C3′ −167.4 (2)°]. The glycosidic torsion angle, defined as S4′—C1′—N1—C2 (IUPAC–IUB Joint Commission on Biochemical Nomenclature, 1983) is −101.8 (2)°, similar to that found in the crystal structure of the sulfone of 4′-thiothymidine (−99.8°; Hancox *et al.*, 1994) and in some 6-aza-2′-deoxyuridines (Basnak *et al.*, 1998), but different from the angles between −121 and −146° found in other thiouridines (Bobek *et al.*, 1975; Koole *et al.*, 1992; Uenische *et al.*, 1993). The steeper inclination of the pyrimidine ring with respect to the sugar ring in both the sulfoxide and the sulfone is presumably due to steric interactions between these O atoms and the pyrimidine ring, specifically C6 and H6; O4″···C6 is 3.142 (3) Å and O4″···H6 is 2.77 Å in the title compound. In the 6-aza-nucleosides, repulsion between the N atom in the 6-position of the pyrimidine ring and the 4′-O or 4′-S atom of the sugar may affect the glycosidic torsion angle in a similar manner.

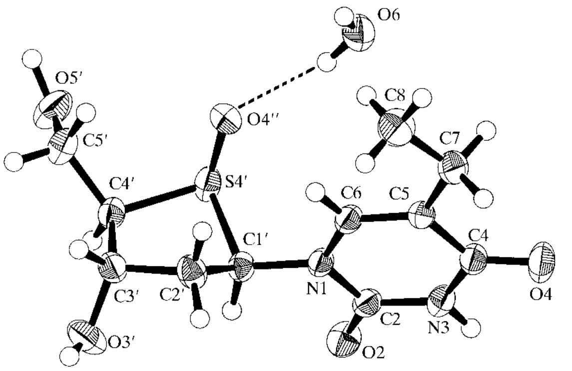


Figure 1
The molecular structure of (I) showing 50% probability displacement ellipsoids (*ORTEP*II; Johnson, 1976).

In the crystal, nucleoside and water molecules are linked through a three-dimensional network of hydrogen bonds. Atoms N3, O3′ and O5′ each donate a proton, forming bonds with, respectively, the water molecule, the O5′ atom and the O2 atom of neighbouring nucleoside molecules. The water molecule, in turn, forms hydrogen bonds with O5′ and the sulfone O atom of two different molecules (Table 2). All H atoms attached to electronegative atoms take part in hydrogen bonding consistent with the principle of maximum hydrogen bonding (Robertson, 1953).

Experimental

The title compound was recrystallized from MeOH–H_2O solution.

Crystal data

$C_{11}H_{16}N_2O_5S\cdot H_2O$
$M_r = 306.33$
Orthorhombic, $P2_12_12_1$
$a = 9.343\ (4)$ Å
$b = 21.922\ (8)$ Å
$c = 6.447\ (3)$ Å
$V = 1320.5\ (10)$ Å^3
$Z = 4$
$D_x = 1.541$ Mg m^{-3}
Mo *Kα* radiation
Cell parameters from 7338 reflections (post-refined using complete data set)
$\theta = 1.86$–25.18°
$\mu = 0.274$ mm^{-1}
$T = 293\ (2)$ K
Rod, colourless
0.40 × 0.25 × 0.25 mm

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† Current address: Department of Chemistry, Tianjin Normal University, Tianjin 300074, People's Republic of China.
‡ Deceased.

Data collection

Rigaku R-AXIS II area-detector diffractometer
Image-plate scans
7338 measured reflections
1122 independent reflections (plus 1062 Friedel-related reflections)
2169 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.040$
$\theta_{\rm max} = 25.18°$
$h = -10 \rightarrow 11$
$k = -26 \rightarrow 26$
$l = -7 \rightarrow 7$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.031$
$wR(F^2) = 0.077$
$S = 1.062$
2184 reflections
197 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0329P)^2 + 0.5503P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} = 0.001$
$\Delta\rho_{\rm max} = 0.19$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.16$ e Å^{-3}
Absolute structure: Flack (1983)
Flack parameter = 0.00 (8)

Table 1
Selected geometric parameters (Å, °).

S4′—O4″	1.498 (2)	O5′—C5′	1.423 (3)
S4′—C4′	1.837 (2)	N1—C2	1.379 (3)
S4′—C1′	1.847 (2)	N1—C6	1.383 (3)
O2—C2	1.234 (3)	N1—C1′	1.453 (2)
O3′—C3′	1.423 (3)	N3—C2	1.368 (3)
O4—C4	1.227 (3)	N3—C4	1.396 (3)
O4″—S4′—C4′	107.64 (10)	C2′—C1′—S4′	104.47 (14)
O4″—S4′—C1′	105.97 (9)	C1′—C2′—C3′	105.0 (2)
C4′—S4′—C1′	88.44 (9)	O3′—C3′—C2′	111.6 (2)
C2—N1—C6	121.5 (2)	O3′—C3′—C4′	106.5 (2)
C2—N1—C1′	117.6 (2)	C2′—C3′—C4′	108.6 (2)
C6—N1—C1′	120.9 (2)	C5′—C4′—C3′	113.7 (2)
N1—C1′—C2′	116.0 (2)	C5′—C4′—S4′	110.1 (2)
N1—C1′—S4′	111.53 (14)	C3′—C4′—S4′	109.59 (13)
C2—N1—C1′—C2′	138.8 (2)	C1′—C2′—C3′—C4′	−35.7 (2)
C6—N1—C1′—C2′	−41.0 (3)	C2′—C3′—C4′—S4′	5.3 (2)
C2—N1—C1′—S4′	−101.8 (2)	C1′—S4′—C4′—C3′	20.6 (2)
C6—N1—C1′—S4′	78.4 (2)	C3′—C4′—C5′—O5′	−167.4 (2)
C4′—S4′—C1′—C2′	−41.13 (15)	S4′—C4′—C5′—O5′	69.2 (2)
S4′—C1′—C2′—C3′	50.9 (2)		

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H3···O6$^{\rm i}$	0.86	2.07	2.898 (3)	161
O3′—HO3′···O5′$^{\rm ii}$	0.90 (2)	2.06 (2)	2.934 (2)	164 (2)
O5′—HO5′···O2$^{\rm iii}$	1.00 (2)	1.90 (3)	2.869 (2)	164 (3)
O6—H*W*1···O4″	0.87 (2)	2.08 (2)	2.855 (3)	148 (2)
O6—H*W*2···O5′$^{\rm iii}$	0.91 (3)	2.35 (2)	3.210 (3)	158 (2)

Symmetry code: (i) $-\frac{3}{2} - x, -y-, \frac{1}{2} + z$; (ii) $x, y, 1 + z$; (iii) $x - \frac{1}{2}, -y - \frac{1}{2}, -2 - z$.

H atoms were placed in calculated positions, except for those bonded to O3′ and O5′, and those of the water molecule, which were located from difference maps and refined with isotropic displacement parameters.

Data collection: *R-AXIS II Software* (Rigaku, 1994); cell refinement: *R-AXIS II Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1993); program(s) used to solve structure: *TEXSAN*; program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*93.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: HA1268). Services for accessing these data are described at the back of the journal.

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