Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

5-Methyl-2′-deoxy-4′-thio-α-uridine (*R*)-*S*-oxide

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: tahamor@hotmail.com

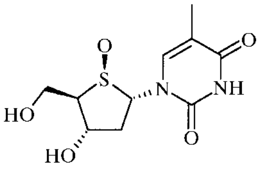
Received 20 June 2000
Accepted 18 September 2000

The pyrimidine ring of the title compound, $C_{10}H_{14}N_2O_5S$, is planar to within 0.024 (1) Å and makes an angle of 75.46 (10)° with the mean plane of the thiosugar ring. In terms of standard nucleoside nomenclature, this ring has the C3′-*endo* conformation. The O5′—C5′—C4′—C3′ torsion angle is 166.5 (3)° and the glycosidic torsion angle S4′—C1′—N1—C2 is −52.1 (2)° (*syn*).

Comment

5-Substituted 2′-deoxy-4′-thio-β-uridines possess significant antiviral activity (Rahim *et al.*, 1996). The α-anomers, however, are inactive. In order to provide data for structure–activity relationships in both anomeric series, the crystal structure of the title compound, (I), synthesized by Macculloch (1998), is presented here. Bond lengths in (I) (Fig. 1) are normal (Table 1). The C1′—S4′ and C4′—S4′ bonds are 1.870 (2) and 1.819 (3) Å, respectively, averaging a little larger than the values found in the crystal structures of 4′-thiothymidine (Koole *et al.*, 1992; Uenischi *et al.*, 1993), 5-(2-bromovinyl)-2′-deoxy-4′-thiouridine (Koole *et al.*, 1992), the sulfone of 4′-thiothymidine (Hancox *et al.*, 1994), α-5-adamantyl-4′-thio-2′-deoxyuridine (Sun *et al.*, 1996), 5-(2-thienyl)-6-aza-4′-thio-2′-deoxyuridine (Basnak *et al.*, 1998) and 5-ethyl-2′-deoxy-4′-thiouridine (*R*)-*S*-oxide (Sun *et al.*, 2000) at 1.80–1.85 Å. Interestingly, in the sulfoxide and the sulfone, C1′—S4′ > C4′—S4′ (mean lengths, excluding present work, 1.842 and 1.819 Å, respectively), whereas in the unoxygenated thionucleosides, C1′—S4′ tends to be slightly shorter than C4′—S4′ (mean lengths 1.828 and 1.833 Å, respectively).

The thiosugar has the C3′-*endo* (^3E) conformation, with C3′ displaced by 0.645 (3) Å from the accurately planar C1′/C2′/C4′/S4′ moiety (r.m.s. deviation 0.002 Å). The pseudo-rotation phase angle (*P*) is 17.9° and the degree of pucker is 48.9°. The conformation about C4′—C5′ is *trans* [O5′—C5′—C4—C3′ 166.5 (3)°]. The glycosidic torsion angle, defined as S4′—C1′—N1—C2 (IUPAC–IUB Joint Commission on Biochemical Nomenclature, 1983), is −52.1 (2)° (*syn*), differing by some 145° from this angle in α-5-adamantyl-4′-thio-2′-deoxyuridine (Sun *et al.*, 1996) and α-5-acetyl-2′-deoxyuridine (Hamor *et al.*, 1977). Thus, as in these other α-nucleosides, the pyrimidine ring is steeply inclined with respect to the sugar, but is essentially flipped over.



(I)

The structure discussed above accounts for 60.4 (6)% of the molecules in the crystal. The remaining molecules differ in the orientation about the C4′—C5′ bond, resulting in an alternative position for O5′ (denoted O5′*B*), the torsion angle O5′*B*—C5′—C4′—C3′ being 32.6 (6)° (*gauche*).

In the crystal, nucleoside molecules are linked through a network of hydrogen bonds. Atoms N3, O3′ and O5′ each donate an H atom, forming bonds with, respectively, the sulfoxide O4″ atom and the ketonic O4 and O2 atoms of neighbouring molecules (Table 2). In the minor conformer, O5′*B* appears to form a hydrogen bond with O2 of a different molecule. The H atom associated with O5′*B* could not be located and was not included in the calculations. A short contact of 2.373 (7) Å apparently occurs between O5′ of the major conformer and O5′*B* of the minor conformer related by the twofold screw axis parallel to **c** (Table 2). We consider that this contact is not real, and that molecules related in this way are either all major conformer or all minor conformer, so avoiding the occurrence of this short contact.

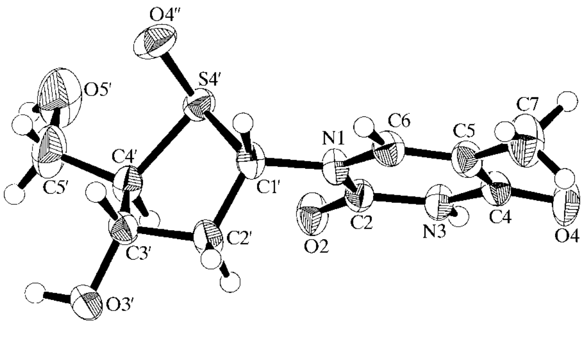


Figure 1
The molecular structure of the major conformer of (I) showing 50% probability displacement ellipsoids (*ORTEP*II; Johnson, 1976).

---

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

Experimental

Recrystallization was from methanol.

Crystal data

$C_{10}H_{14}N_2O_5S$
$M_r = 274.29$
Orthorhombic, $P2_12_12_1$
$a = 8.018\ (8)$ Å
$b = 20.134\ (13)$ Å
$c = 7.389\ (8)$ Å
$V = 1192.8\ (19)$ Å^3
$Z = 4$
$D_x = 1.527$ Mg m^{-3}

Mo $K\alpha$ radiation
Cell parameters from 6670 reflections (post-refined using complete data set)
$\theta = 3.42$–$25.20°$
$\mu = 0.288$ mm^{-1}
$T = 293\ (2)$ K
Rod, colourless
0.50 × 0.30 × 0.25 mm

Data collection

Rigaku R-AXIS II area-detector diffractometer
Image-plate scans
6670 measured reflections
1034 independent reflections (plus 912 Friedel-related reflections)

1941 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.021$
$\theta_{\rm max} = 25.2°$
$h = -9 \rightarrow 9$
$k = -23 \rightarrow 23$
$l = -8 \rightarrow 7$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.030$
$wR(F^2) = 0.082$
$S = 1.094$
1946 reflections
173 parameters
H-atom parameters not refined

$w = 1/[\sigma^2(F_o^2) + (0.0458P)^2 + 0.4010P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} = -0.001$
$\Delta\rho_{\rm max} = 0.27$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.15$ e Å^{-3}
Absolute structure: Flack (1983)
Flack parameter = −0.02 (9)

Table 1
Selected geometric parameters (Å, °).

S4′—O4′′	1.513 (2)	O5′*B*—C5′	1.287 (7)
S4′—C4′	1.819 (3)	N1—C2	1.376 (3)
S4′—C1′	1.870 (2)	N1—C6	1.384 (3)
O2—C2	1.218 (3)	N1—C1′	1.465 (3)
O3′—C3′	1.420 (3)	N3—C2	1.368 (3)
O4—C4	1.236 (3)	N3—C4	1.388 (3)
O5′—C5′	1.399 (4)		
O4′′—S4′—C4′	105.35 (12)	N1—C1′—C2′	114.5 (2)
O4′′—S4′—C1′	103.61 (10)	N1—C1′—S4′	112.34 (13)
C4′—S4′—C1′	91.79 (10)	C2′—C1′—S4′	107.98 (15)
C2—N1—C6	121.7 (2)	O5′*B*—C5′—C4′	118.3 (3)
C2—N1—C1′	118.2 (2)	O5′—C5′—C4′	112.3 (3)
C6—N1—C1′	120.0 (2)		
C2—N1—C1′—S4′	−52.1 (2)	C1′—S4′—C4′—C3′	26.2 (2)
C6—N1—C1′—S4′	131.1 (2)	C3′—C4′—C5′—O5′*B*	32.6 (6)
C4′—S4′—C1′—C2′	−0.3 (2)	S4′—C4′—C5′—O5′*B*	−86.7 (5)
S4′—C1′—C2′—C3′	−26.2 (2)	C3′—C4′—C5′—O5′	166.5 (3)
C1′—C2′—C3′—C4′	46.5 (2)	S4′—C4′—C5′—O5′	47.2 (4)
C2′—C3′—C4′—S4′	−46.0 (2)		

H atoms were located from difference maps but their parameters were not refined; the range of C—H distances is 0.94–1.09 Å. The H atoms bonded to C5′ were placed in calculated positions.

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N3—H3···O4′′$^{\rm i}$	0.96	1.81	2.747 (3)	164
O3′—HO3′···O4$^{\rm ii}$	0.91	1.90	2.769 (3)	157
O5′—HO5′···O2$^{\rm iii}$	1.00	1.99	2.963 (4)	163
O5′*B*···O2$^{\rm iv}$			2.907 (6)	
O5′*B*···O5′$^{\rm iii}$			2.373 (7)	

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

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.

We thank the EPSRC and the University of Birmingham for funds to purchase the X-ray diffractometer and the British Council (Sino–British Friendship Scholarship to MS).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GS1102). Services for accessing these data are described at the back of the journal.

References

Basnak, I., Sun, M., Hamor, T. A., Focher, F., Verri, A., Spadari, S., Wroblowski, P., Herdewijn, P. & Walker, R. T. (1998). *Nucleosides Nucleotides*, **17**, 187–206.

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.

Hamor, T. A., O'Leary, M. K. & Walker, R. T. (1977). *Acta Cryst.* B**33**, 1218–1223.

Hancox, E. L., Hamor, T. A. & Walker, R. T. (1994). *Tetrahedron Lett.* **35**, 1291–1294.

IUPAC-IUB Joint Commission on Biochemical Nomenclature (1983). *Eur. J. Biochem.* **131**, 9–15.

Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

Koole, L. H., Plavec, J. P., Liu, H., Vincent, B. R., Dyson, M. R., Coe, P. L., Walker, R. T., Hardy, G. W., Rahim, S. G. & Chattopadhayaya, J. (1992). *J. Am. Chem. Soc.* **114**, 9936–9943.

Macculloch, A. C. (1998). PhD thesis, University of Birmingham, England.

Molecular Structure Corporation (1993). *TEXSAN*. Version 1.6. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.

Rahim, S. G., Trivedi, N., Bogunovic Batchelor, M. V., Hardy, G. W., Mills, G., Selway, J. W. T., Snowden, W., Littler, E., Coe, P. L., Basnak, I., Whale, R. F. & Walker, R. T. (1996). *J. Med. Chem.* **39**, 789–795.

Rigaku Corporation (1994). *R-AXIS* II *Software*. Rigaku, Tokyo, Japan.

Sheldrick, G. M. (1993). *SHELXL*93. University of Göttingen, Germany.

Sun, M., Basnak, I., Hamor, T. A. & Walker, R. T. (1996). *Acta Cryst.* C**52**, 2556–2558.

Sun, M., Macculloch, A. C., Hamor, T. A. & Walker, R. T. (2000). *Acta Cryst.* C**56**, 116–117.

Uenischi, J., Takahashi, K., Motoyama, M. & Akashi, H. (1993). *Chem. Lett.* pp. 255–256.