Aravamudan, 1982) (II), 3,3'-dithiopropionic acid [2·033 (1); 1·819 (31) Å] (Appa Rao, Seshasayee, Aravamudan, Nageswara Rao & Venkatasubramanian, 1982) (III), L-cystine dihydrochloride [2·044; 1·865 Å] (Steinrauf, Peterson & Jensen, 1958) (IV) and N,N'-diglycyl-L-cystine dihydrate [2·040 (5); 1·87 (2) Å] (Yakel & Hughes, 1954) (V). The observed carbonyl C—O distances of 1·212 (7) and 1·198 (7) Å are normal. The benzene rings are planar with a maximum deviation of 0·02 (1) Å. The average C—H bond distance is 0·98 (4) Å and the average C—C—H angle is 119 (1)°. The C—S—S—C dihedral angle in DBDS is 80·8 (3)° and can be compared with those reported in (I) (96·4°), (II) (99°), (III) (78·6°), (IV) (101°) and (V) (101°). The dihedral angles C(2)—C(1)—S(1)—S(2) and S(1)—S(2)—C(8)—C(9) are −173·1 (4) and 173·8 (4)°, respectively, indicating the near planarity of the CCSS group in both thiobenzoate fragments. The dihedral angles O(1)—C(1)—S(1)—S(2) and O(2)—C(8)—S(2)—S(1) are 7·8 (5) and −9·2 (5)°, indicating again small deviation from planarity of the OCSS groups. There are two intramolecular contacts, S(1)—O(2) [2·958 (6) Å] and S(2)—O(1) [3·008 (5) Å], probably as a result of the above mentioned dihedral angles. Intermolecular contacts greater than 3·5 Å

are S(1)—O(2')* [3·531 (5) Å] and S(2)—O(2') [3·851 (5) Å].

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* The prime denotes the symmetry equivalent $(-x, -y, -z)$.

References

APPA RAO, G. V. N., SESHASAYEE, M., ARAVAMUDAN, G., NAGESWARA RAO, T. & VENKATASUBRAMANIAN, P. N. (1982). *Acta Cryst.* B **38**, 2852–2855.
ARAVAMUDAN, G., SUBRAHMANYAN, T., SESHASAYEE, M. & APPA RAO, G. V. N. (1983). In preparation.
CROMER, D. T. & LIBERMAN, D. (1970). *J. Chem. Phys.* **53**, 1891–1898.
CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A**24**, 321–324.
JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.
KARLE, I. L., ESTLIN, J. A. & BRITTS, K. (1967). *Acta Cryst.* **22**, 273–280.
ROUT, G. C., SESHASAYEE, M. & ARAVAMUDAN, G. (1982). *Cryst. Struct. Commun.* **11**, 1389–1393.
SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.
STEINRAUF, L. K., PETERSON, J. & JENSEN, L. H. (1958). *J. Am. Chem. Soc.* **80**, 3835–3838.
STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
SUBRAHMANYAN, T., ARAVAMUDAN, G., ROUT, G. C. & SESHASAYEE, M. (1983). In preparation.
YAKEL, H. L. & HUGHES, E. W. (1954). *Acta Cryst.* **7**, 291–297.

Structure of 5'-Deoxy-5',6-epithio-5,6-dihydro-2',3'-*O*-isopropylideneuridine, $C_{12}H_{16}N_2O_5S$

BY N. GAUTHAM, T. P. SESHADRI AND M. A. VISWAMITRA

Department of Physics, ICMR Centre on Genetics and Cell Biology, Indian Institute of Science, Bangalore 560 012, India

AND S. A. SALISBURY AND D. M. BROWN

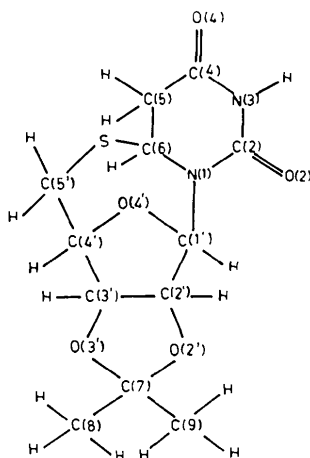*University Chemical Laboratory, Cambridge, England*

Abstract. $M_r = 300·33$, triclinic, $P1$, $a = 5·635$ (2), $b = 11·077$ (2), $c = 11·582$ (2) Å, $\alpha = 70·48$ (1), $\beta = 88·16$ (3), $\gamma = 80·56$ (3)°, $V = 670·325$ Å³, $Z = 2$, $D_x = 1·49$ Mg m⁻³, Cu $K\alpha$, $\lambda = 1·54184$ Å, $\mu = 2·308$ mm⁻¹, $F(000) = 316$, $T = 301$ K, $R = 0·054$, $R_w = 0·093$ for 1944 observed counter reflections. The sulphur position with respect to the dihydrouracil ring, which is of possible relevance to the action of thymidylate synthetase, is axial in molecule A and equatorial in B. Both molecules show the *anti* conformation about the glycosidic bond [torsion angle C(6)—N(1)—C(1')—O(4'), $\chi_{CN} = 21·6$ (9) and 29·4 (10)°] and have the C(4')-*endo*, O(4')-*exo* (^4_0T) sugar conformation. The dioxolane-ring conformation is O(2')-*endo* in A and C(7)-*endo* in B. The dihydrouracil rings show self base pairing with hydrogen bonds N(3A)···O(2B) and N(3B)···O(2A).

Introduction. As part of our systematic studies on modified nucleosides (Gautham, Ramakrishnan, Seshadri, Viswamitra, Salisbury & Brown, 1982), we report here the structure of the title compound (I). A main interest of this study has been to ascertain whether the S atom is equatorial or axial with respect to the

dihydrouracil ring. Our earlier study of the N(3)-methylated analogue of this compound, hereafter EDIMU, has shown a pseudoequatorial geometry for S (Gautham *et al.*, 1982). In the present structure, the two independent molecules in the crystal have different sulphur configurations – one axial and the other pseudoequatorial. The position of S in these compounds is of possible relevance to certain stereochemical aspects of the action of the enzyme thymidylate synthetase (Salisbury & Brown, unpublished results).

Experimental. Crystals grown from 50/50 water/acetone mixtures; space group *P*1, unlike the orthorhombic form reported earlier for the same compound (Satyanarayana, Viswamitra & Ramakrishnan, 1978), unit-cell parameters refined from 2θ values of 25 high-angle reflections, Enraf–Nonius CAD-4 diffractometer, crystal $1.08 \times 0.08 \times 0.11$ mm, ω–2θ scans, $\theta \le 60°$, background counts measured for one sixth of scan angle on either side of the Bragg peak, 011 and 110 reflections monitored for instrument and crystal stability, intensity variation < 5%, 1944 out of 2422 reflections $[|F_o| \ge 2\sigma(|F_o|)]$ considered observed, after corrections for Lorentz and polarization factors (h 0–6, k –13–13, l –13–13); structure solved with *MULTAN* (Germain, Main & Woolfson, 1971), but only when molecular scattering factors were incorporated in the calculation of the $|E|$ values using the coordinates of EDIMU; the two independent molecules in the unit cell, except for the isopropylidene groups, identified from an E map computed with the best set of phases (combined figure of merit = 2·11), difference Fourier revealed remaining atoms; least-squares (Shiono, 1968) refinement of non-hydrogen atoms, anisotropic, $R = 0.054$, H atoms fixed from expected geometry, maximum shift/error in final cycle = 0·22, $\sum w(F_o - F_c)^2$ minimized, $w = 1/\sigma^2(F_o)$, $R_w = 0.093$, atomic scattering factors for non-hydrogen atoms from Cromer & Waber (1965), for H from Stewart, Davidson & Simpson (1965),

residual electron density in final difference map −0·54–0·38 e Å^{-3}.*

Discussion. Table 1 lists the final positional parameters. Bond lengths and angles are given in Figs. 1 and 2.

Dihydrouracil base. As can be expected, the dihydrouracil residue is non-planar in both the independent molecules, *A* and *B*. C(5) shows the maximum deviation from the best four-atom plane, 0·345 (11) and 0·496 (10) Å in *A* and *B*, respectively; C(6) deviates in the opposite direction by 0·231 (9) and 0·179 (10) Å. Similar base puckering has been observed in EDIMU and other dihydrouracils (Rohrer & Sundaralingam, 1970; Suck, Saenger & Zechmeister, 1972; Konnert, Karle & Karle, 1970).

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* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates, torsion angles and mean-plane calculations have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38632 (24 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Fractional coordinates* ($\times 10^4$) *for non-hydrogen atoms and equivalent isotropic temperature factors* (Å^2)

$$B_{eq} = \tfrac{4}{3}\textstyle\sum_i\sum_j \beta_{ij}\mathbf{a}_i\cdot\mathbf{a}_j.$$

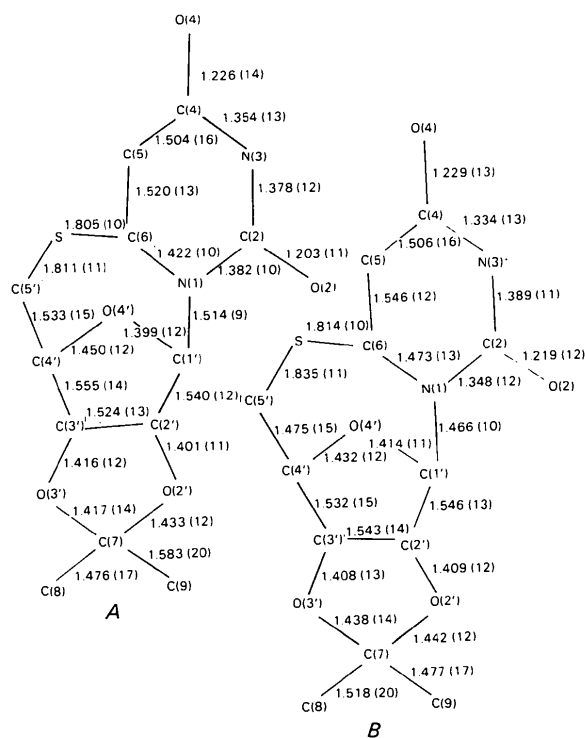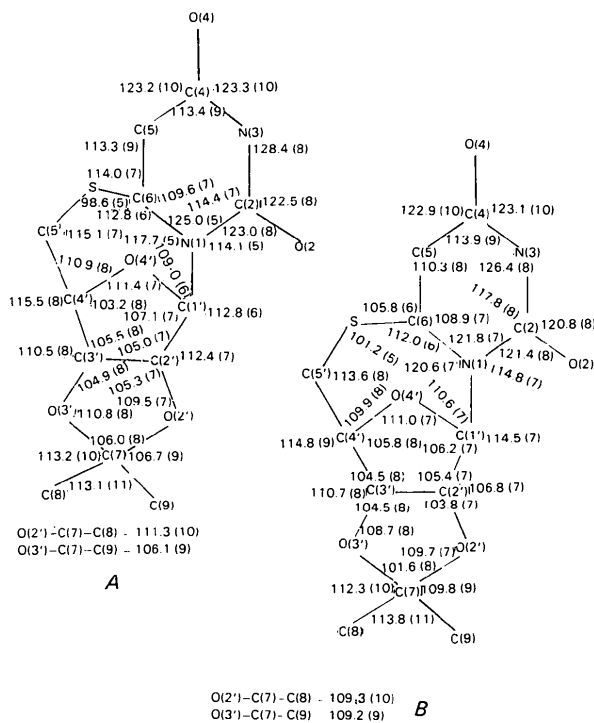|	x	y	z	B_{eq}
Molecule *A*				
N(1)	6432	6318	3992	2·85 (18)
C(2)	4252 (17)	7142 (8)	3694 (8)	3·19 (24)
O(2)	3590 (12)	7963 (5)	4153 (5)	3·54 (18)
N(3)	2941 (14)	6987 (7)	2784 (6)	3·19 (20)
C(4)	3549 (20)	6165 (10)	2142 (8)	3·99 (29)
O(4)	2125 (16)	5959 (8)	1479 (8)	5·78 (28)
C(5)	6162 (21)	5559 (11)	2291 (9)	4·41 (31)
C(6)	7175 (16)	5246 (9)	3577 (8)	3·33 (25)
S	6538 (6)	3733 (2)	4650 (3)	4·08 (7)
C(1')	7645 (17)	6314 (8)	5141 (8)	3·23 (25)
O(4')	9865 (12)	5490 (6)	5323 (6)	3·61 (19)
C(2')	6179 (15)	5812 (8)	6298 (7)	2·81 (22)
O(2')	5993 (12)	6613 (7)	7022 (6)	4·12 (19)
C(3')	7679 (20)	4534 (9)	7065 (8)	3·69 (25)
O(3')	8650 (17)	4811 (7)	8044 (6)	5·67 (26)
C(4')	9713 (18)	4227 (9)	6216 (9)	3·72 (27)
C(5')	9271 (19)	3267 (9)	5583 (10)	4·29 (29)
C(7)	7841 (19)	6119 (10)	7960 (9)	4·18 (29)
C(8)	6944 (30)	6259 (15)	9128 (12)	7·16 (50)
C(9)	10021 (28)	6868 (15)	7453 (14)	7·01 (52)
Molecule *B*				
N(1)	−3970 (13)	10582 (7)	2095 (6)	3·01 (19)
C(2)	−2123 (17)	9640 (8)	2641 (7)	3·11 (24)
O(2)	−1207 (14)	8858 (6)	2160 (6)	4·11 (19)
N(3)	−1341 (14)	9561 (7)	3793 (7)	3·38 (20)
C(4)	−2396 (21)	10238 (9)	4484 (9)	4·20 (29)
O(4)	−1447 (17)	10258 (8)	5417 (6)	4·48 (25)
C(5)	−4927 (19)	10899 (8)	4068 (8)	3·38 (25)
C(6)	−5067 (17)	11545 (9)	2660 (8)	3·28 (24)
S	−8243 (5)	12082 (3)	2261 (2)	3·66 (6)
C(1')	4281 (15)	10839 (8)	778 (7)	2·81 (21)
O(4')	4563 (11)	12186 (6)	128 (6)	3·58 (18)
C(2')	−6496 (17)	10365 (8)	427 (8)	3·26 (24)
O(2')	−5736 (13)	9767 (6)	451 (6)	4·12 (20)
C(3')	−8205 (16)	11607 (10)	308 (10)	3·88 (29)
O(3')	8109 (14)	11601 (7)	−1521 (6)	5·01 (24)
C(4')	7040 (19)	12718 (9)	190 (8)	3·74 (26)
C(5')	8121 (21)	13284 (9)	729 (10)	4·59 (30)
C(7)	−7363 (17)	10288 (10)	1500 (9)	4·03 (30)
C(8)	9442 (28)	9530 (18)	1281 (18)	8·38 (7)
C(9)	−6035 (26)	10302 (15)	2623 (11)	6·84 (48)

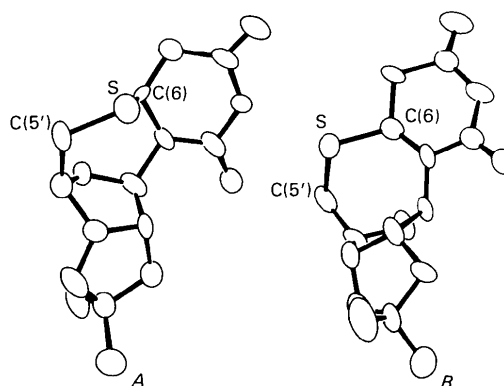Fig. 1. Bond lengths (Å).

Fig. 2. Bond angles (°).

Fig. 3. Molecule A; S axial. Molecule B; S pseudoequatorial.

Sulphur geometry. The location of sulphur with respect to dihydrouracil is axial in A and pseudo-equatorial in B. This is evident from its displacements [1·958 (3) Å in A, 0·654 (3) Å in B] from the best four-atom plane. Fig. 3 illustrates these differences in sulphur disposition.

The sulphur geometry in B closely resembles that found in EDIMU.

Our interest in the present structure arose because of its possible relevance to the mode of action of the enzyme thymidylate synthetase. There is much evidence to show that a nucleophilic group (probably an —SH) in the apoenzyme adds to C(6) of 2'-deoxyuridine 5'-phosphate and this activates the C(5) atom for electrophilic attack by the methylene group of the co-factor methylene tetrahydrofolate (Bruice, Garrett, Wataya & Santi, 1980). There is also much evidence that, in this and other addition reactions to the 5,6 double bond of uracil and cytosine derivatives, the process involves largely *trans* diaxial geometry (Blackburn, Solan, Brown & Coe, 1976). There might in the enzymic reaction be a need for conformational inversion about the C(5)—C(6) bond. The present structure shows that, at least energetically, the two conformations are equally possible.

The C(6)—S—C(5') bond angles of 98·6 (5) and 101·2 (5)° for A and B, respectively, fall within the range observed for C—S—C angles when sulphur is part of a closed ring (McDowell, 1975).

Glycosidic bond. Both A and B are in the *anti* conformation with the glycosidic torsion angle C(6)—N(1)—C(1')—O(4') being 21·6 (9) and 29·4 (10)° respectively. In EDIMU, $\chi_{CN} = 32·5°$.

Ribose. The pseudorotation phase angle P as calculated from the ribose torsion angles (Altona & Sundaralingam, 1972) is 249·38 (7)° in A and 254·55 (6)° in B. The furanose rings have thus a twist conformation (^4_0T). The maximum amplitude of pucker, $\tau_{m,max}$ is 28·7 (7)° in A and 27·4 (7)° in B. These are much smaller than the average value (*ca* 38°) found for

$C_{12}H_{16}N_2O_5S$

unconstrained ribose rings (Altona & Sundaralingam, 1972).

With respect to the three-atom plane, the conformation can be described as C(4')-*endo*, O(1')-*exo* for both molecules. The results of the planes' calculations have been deposited.*

Dioxolane ring. The two molecules have very different dioxolane conformations. In molecule *A*, O(2') is displaced by 0·264 (7) Å with respect to the best plane through C(2'), C(3'), O(3') and C(7). The phase angle of pseudorotation is 230·17 (2)° [O(2')-*endo*] and $\lambda_{m,max}$, the maximum amplitude of pucker is 19·2 (7)°.

In molecule *B*, O(3'), C(3'), C(2') and O(2') form the best plane. C(7) is displaced by 0·480 (10) Å and the pseudorotation parameters are $P = 94·91$ (2)° [C(7)-*endo*] and $\lambda_{m,max} = 35·1$ (7)°. This conformation is similar to that found in 2',3'-*O*-isopropylideneuridine (Katti, Seshadri & Viswamitra, 1981).

Both molecules are *gauche–gauche* about the C(4')–C(5') bond, the only possible conformation because of the base–sugar cyclization.

Recently, the structure of 2',3'-*O*-isopropylidene-5'-deoxy-6(*R*),5'-cyclo-5,6-dihydrouridine has been solved by Yamagata, Fujii, Fujiwara, Tomita & Ueda (1981), in which the C(5') atom of the ribose is linked directly to C(6) of the dihydrouracil base. This structure is characterized by a high χ_{CN} value (60·4°) and a highly puckered sugar ring ($\tau_{m,max} = 47°$) unlike the flatter rings observed in the present structure.

Molecular packing. An interesting feature of the crystal structure (Fig. 4) is the base pairing observed between the dihydrouracils of *A* and *B*, utilizing the hydrogen bonds N(3*B*)–H⋯O(2*A*) [2·996 (11) Å] and N(3*A*)–H⋯O(2*B*) [2·804 (11) Å]. A similar base-pairing scheme has also been observed between symmetry-related molecules by Yamagata *et al.* (1981) in the structure mentioned above. This H-bonding pattern cannot occur in EDIMU as N(3) is blocked by methylation.
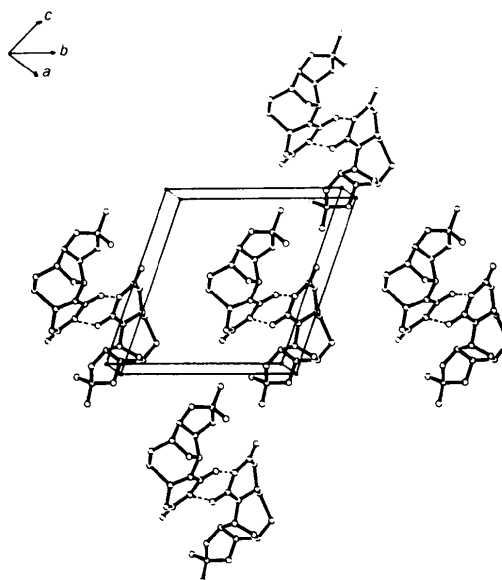
* See deposition footnote.

Fig. 4. Crystal packing.

References

ALTONA, C. & SUNDARALINGAM, M. (1972). *J. Am. Chem. Soc.* **94**, 8205–8212.

BLACKBURN, G. M., SOLAN, V. C., BROWN, D. M. & COE, P. F. (1976). *J. Chem. Soc. Chem. Commun.* pp. 724–726.

BRUICE, T. W., GARRETT, C., WATAYA, Y. & SANTI, D. V. (1980). *Methods Enzymol.* **64**, 125–135.

CROMER, D. T. & WABER, J. T. (1965). *Acta Cryst.* **18**, 104–109.

GAUTHAM, N., RAMAKRISHNAN, P., SESHADRI, T. P., VISWAMITRA, M. A., SALISBURY, S. A. & BROWN, D. M. (1982). *Acta Cryst.* **B38**, 2707–2709.

GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* **A27**, 368–376.

KATTI, S. K., SESHADRI, T. P. & VISWAMITRA, M. A. (1981). *Acta Cryst.* **B37**, 407–410.

KONNERT, J., KARLE, I. L. & KARLE, J. (1970). *Acta Cryst.* **B26**, 770–778.

MCDOWELL, J. J. H. (1975). *Acta Cryst.* **B31**, 2256–2264.

ROHRER, D. C. & SUNDARALINGAM, M. (1970). *Acta Cryst.* **B26**, 546–553.

SATYANARAYANA, M., VISWAMITRA, M. A. & RAMAKRISHNAN, P. (1976). *Curr. Sci.* **45**, 826–827.

SHIONO, R. (1968). *SFLS* program. Private circulation.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

SUCK, D., SAENGER, W. & ZECHMEISTER, K. (1972). *Acta Cryst.* **B28**, 596–605.

YAMAGATA, Y., FUJII, S., FUJIWARA, T., TOMITA, K.-I. & UEDA, T. (1981). *Biochim. Biophys. Acta*, **654**, 242–248.