Acta Cryst. (1976). B**32**, 1099

The Crystal and Molecular Structure of 5,6-Dihydro-2-thiouracil, $C_4H_6N_2OS$

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(*Received* 1 *October* 1975; *accepted* 3 *October* 1975)

5,6-Dihydro-2-thiouracil crystallizes in space group $P2_1/n$ with $a=4{\cdot}738$, $b=20{\cdot}339$, $c=6{\cdot}016$ Å, $\beta=92{\cdot}41°$, $Z=4$. The structure was solved by direct methods and refined to an R of 0·051. The saturated heterocycle exhibits a half-chair conformation with C(5) and C(6) displaced by 0·226 and −0·238 Å on either side of the base plane. The molecule exists in the diketo form; the C(2)–S and C(4)–O lengths are 1·676 (3) and 1·216 (4) Å, respectively. The molecules are connected by N(3)–H···O(4) hydrogen bonds of 2·975 (4) Å forming infinite zigzag ribbons running parallel to [101]. These ribbons are joined by N(1)–H···S(2) [3·492 (3) Å] hydrogen bonds along [010].

Introduction

In connexion with studies on the chemical reactivities and transformation of thio-analogues of 5,6-dihydrouracil and the methyl derivatives (Škarić & Gašpert, 1968, 1969) the crystal and molecular structures of some have been studied. 5,6-Dihydro-2-thiouracil for the present structure determination was synthesized by Dr V. Škarić.

A pharmaceutical effect of some S containing pyrimidines and purines was established and it was observed that biological activity varied with the substitution position of the S atom.

In heterocyclic compounds the S atom can also act as a hydrogen-bond acceptor. Therefore their molecular and crystal structures are of interest, providing useful information on conformation, intramolecular dimensions and hydrogen bonds.

Experimental

Table 1. *Crystal data.*

5,6-Dihydro-2-thiouracil	$C_4H_6N_2OS$
F. W.	130·17
Space group	$P2_1/n$
a	4·738 (1) Å*
b	20·339 (10)
c	6·016 (1)
β	92·41 (2)°
U	579·2 Å^3
D_c	1·493 g cm^{-3}
Z	4
μ(Cu $K\alpha$)	10·40 cm^{-1}
Crystal size	0·30 × 0·14 × 0·07 mm
Crystal shape	plate

* Numbers in parentheses here and throughout this paper are the estimated standard deviations in the least significant digit.

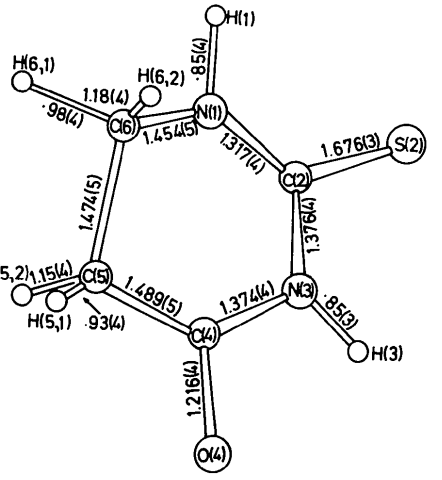

Fig. 1. The structural formula and intramolecular distances.

The space group was determined from Weissenberg photographs recorded by Cu $K\alpha$ radiation. The diffraction symmetry and extinctions determined $P2_1/n$ uniquely.

The intensities were collected on a Philips PW 1100 computer-controlled four-circle diffractometer by the ω-scan mode (scan width = 1·2°θ, scan speed = 0·05°θ s^{-1}) with graphite-monochromated Cu $K\alpha$ radiation. 1008 independent observed reflexions in the range $2<\theta<50°$ were recorded and only these were used in the calculations. 3 standard reflexions were measured after every 2 hours to provide a check on crystal and instrumental stability, and showed only the variations expected from counting statistics.

The data were corrected for background, Lorentz and polarization effects, but absorption was neglected.

Structure determination and refinement

The structure was solved with *MULTAN* (Declercq, Germain, Main & Woolfson, 1973). An overall temperature factor ($B=2{\cdot}81$ Å^2) and a scale factor were determined (Wilson, 1942) and used to compute normalized structure factors by routine *NORMAL* included in *MULTAN*. The solution was based on 250 reflexions with $|E|>1{\cdot}2$. The E map corresponding to the solution with the best 'figure of merit' revealed the positions of seven non-hydrogen atoms. The remaining atom C(6) was located from the resulting Fourier synthesis. A full-matrix least-squares procedure minimizing $\sum w||F_o|-|F_c||^2$ with $w=1/\sigma^2_{F_o}$ was used for refinement.

Heavy-atom coordinates, isotropic thermal parameters and a scale factor were refined to an R of 0·20. Anisotropic refinement ($R=0·07$) and a subsequent difference synthesis located the H atoms. In the final cycles one scale factor, the atomic coordinates for all atoms, and anisotropic thermal parameters for the heavy atoms (91 parameters in all) were varied. For H atoms the isotropic thermal parameters are those of the bonded atom. Corrections for extinction were not applied. The final agreement indices were: $R=\sum||F_o|-|F_c||/\sum|F_o|=0·051$ and $R_w=[\sum w(|F_o|-|F_c|)^2/\sum wF_o^2]^{1/2}=0·066$.

Scattering factors given by Cromer & Mann (1968) and (for H) by Stewart, Davidson & Simpson (1965) were used. An anomalous dispersion correction was included for S (Cromer & Liberman, 1970).

The calculations were carried out on the UNIVAC 1110 computer at the University Computing Center in Zagreb with the X-RAY 72 system (Stewart, Kruger, Ammon, Dickinson & Hall, 1972).

Positional and thermal parameters are listed in Tables 2 and 3.*

Description and discussion of the structure

The numbering of the atoms and dimensions of the molecule are given in Figs. 1 and 2. The projection of the structure down **a** shows the packing of the molecules and hydrogen bonds (Fig. 4). Displacements of the atoms from the best least-squares plane are given in Table 4 and Fig. 3. Dihedral angles defining the conformation of the base are represented in Table 5.

5,6-Dihydro-2-thiouracil is not planar due to the saturation of C(5)–C(6). The puckering of the base is illustrated in Fig. 3 and can be numerically described by the dihedral angles N(3)–C(4)–C(5)–C(6) of 27·4°

Table 3. *Positional parameters* (× 10³) *and isotropic thermal parameters* (× 10²) *of hydrogen atoms*

	x	y	z	U (Å²)
H(1)	774 (6)	29 (2)	−125 (5)	3·3
H(3)	731 (6)	191 (1)	170 (5)	2·9
H(5,1)	280 (8)	169 (2)	−375 (6)	4·6
H(5,2)	641 (7)	171 (2)	−407 (6)	4·6
H(6,1)	512 (7)	62 (2)	−422 (6)	4·7
H(6,2)	272 (7)	60 (2)	−213 (6)	4·7

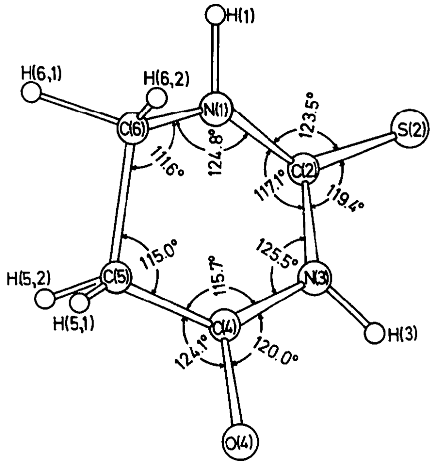

Fig. 2. Intramolecular angles.

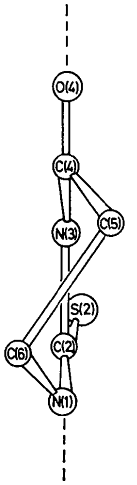

Fig. 3. Schematic view of the base parallel to the plane defined by N(1), C(2), N(3), C(4) illustrating the displacements of C(5) and C(6).

Table 2. *Final positional* (× 10⁴) *and thermal* (× 10³) *parameters for non-hydrogen atoms*

$$T=\exp\,[-2\pi^2(h^2a^{*2}U_{11}+k^2b^{*2}U_{22}+\cdots+2U_{23}klb^*c^*)]\,.$$

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(2)	7880 (6)	1040 (1)	514 (5)	35 (1)	28 (1)	33 (1)	0 (1)	−5 (1)	−2 (1)
C(4)	4992 (6)	1948 (1)	−967 (5)	44 (2)	29 (1)	37 (2)	−1 (1)	−9 (1)	3 (1)
C(5)	4512 (9)	1563 (2)	−3055 (6)	73 (2)	40 (2)	43 (2)	3 (2)	−29 (2)	−1 (1)
C(6)	4784 (8)	845 (2)	−2801 (6)	57 (2)	44 (2)	45 (2)	10 (14)	−24 (2)	−11 (2)
N(1)	7041 (5)	672 (1)	−1193 (4)	42 (1)	30 (1)	39 (1)	7 (1)	−14 (1)	−7 (1)
N(3)	6753 (5)	1662 (1)	628 (4)	47 (1)	27 (1)	30 (1)	2 (1)	−12 (1)	−3 (1)
O(4)	4093 (6)	2500 (1)	−685 (4)	75 (2)	32 (1)	53 (1)	14 (1)	−22 (1)	−3 (1)
S(2)	10210 (2)	787 (0)	2506 (1)	70 (1)	42 (1)	46 (1)	18 (0)	−31 (0)	−10 (0)

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* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31420 (12 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

and C(5)–C(6)–N(1)–C(2) of 28·6°. The displacements of C(5) and C(6) from the best least-squares plane defined by N(1), C(2), N(3), C(4) are 0·226 Å and −0·238 Å. Thus the base exhibits a half-chair conformation. O(4) and S(2) are displaced from the least-squares plane by −0·043 Å and 0·105 Å, respectively. The heterocycle exists in the diketo form: C(2)–S(2) of 1·676 (3) Å and C(4)–O(4) of 1·216 (4) Å have double-bond character.

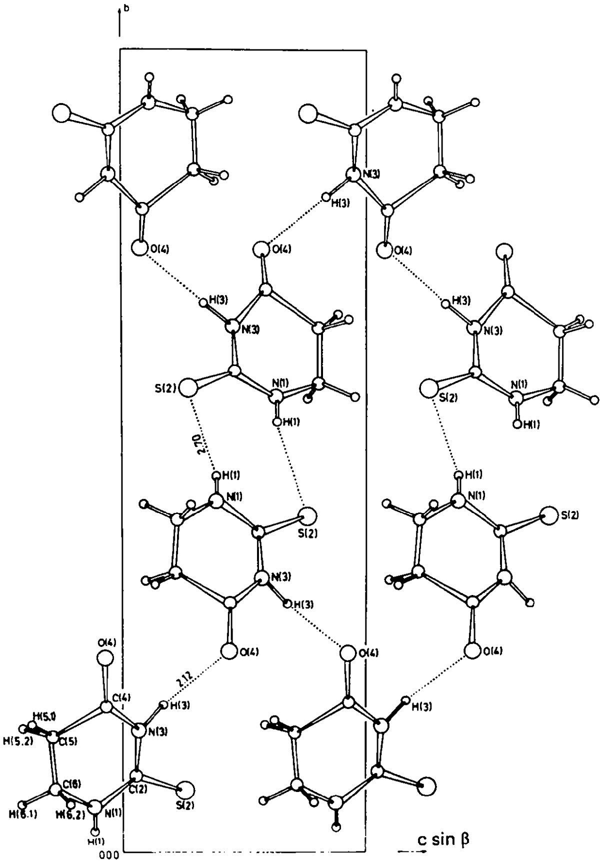

Fig. 4. A view of the crystal structure along **a** showing the packing arrangement and hydrogen bonds.

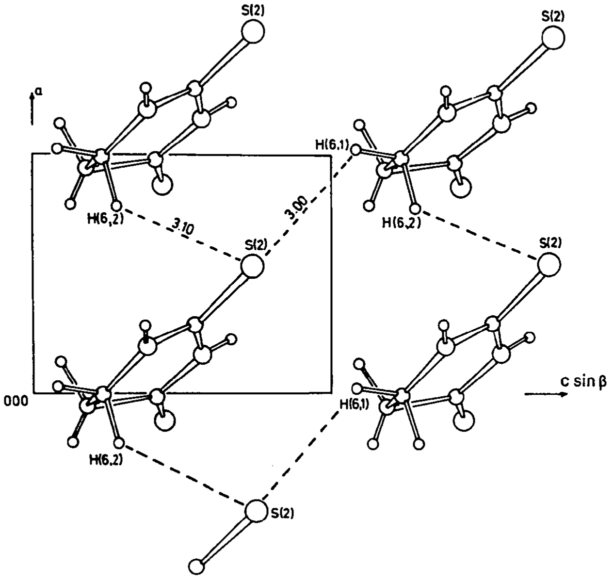

Fig. 5. The molecular packing viewed down **b**.

Table 4. *Least-squares plane*

Atoms included in the calculation of the least-squares plane are denoted by an asterisk.

	Displacement (Å)
N(1)*	−0·010
C(2)*	0·020
N(3)*	−0·021
C(4)*	0·010
C(5)	0·226
C(6)	−0·238
O(4)	−0·043
S(2)	0·105
H(1)	−0·008
H(3)	0·021
H(5,1)	−0·162
H(5,2)	1·385
H(6,1)	0·190
H(6,2)	−1·429

Table 5. *Dihedral angles describing the conformation of the base*

The positive sense of the rotation is clockwise while looking along the *BC* bond.

A B C D	
C(6)–N(1)–C(2)–N(3)	−7·4 (4)
N(1)–C(2)–N(3)–C(4)	−5·2 (4)
C(2)–N(3)–C(4)–C(5)	−5·6 (4)
N(3)–C(4)–C(5)–C(6)	27·4 (4)
C(4)–C(5)–C(6)–N(1)	−36·9 (4)
C(5)–C(6)–N(1)–C(2)	28·6 (4)
C(6)–N(1)–C(2)–S(2)	172·6 (2)
S(2)–C(2)–N(3)–C(4)	174·8 (2)
C(2)–N(3)–C(4)–O(4)	179·3 (3)
O(4)–C(4)–C(5)–C(6)	−157·7 (3)

Bond lengths and angles are compared (Table 6) with those of 5,6-dihydrouracil (Rohrer & Sundaralingam, 1970), 2,4-dithiouracil (Shefter & Mautner, 1967) and uracil (Stewart & Jensen, 1967). It is difficult to form any general conclusions about the differences in molecular dimensions because of several factors: the conjugation of the lone electron pair on N(1) with C(2)=O,S(2) or with C(5)–C(6), electron delocalization of different sorts, and hydrogen-bonding. But a remarkable shortening of N(1)–C(2) in saturated pyrimidines was observed in 5,6-dihydro-2-thiouracil (1·317 Å), 5,6-dihydrouracil (1·335 Å) (Rohrer & Sundaralingam, 1970), 5,6-dihydrouridine, molecules *A* and *B* (1·356 Å, 1·351 Å) (Suck, Saenger & Zechmeister, 1972) and 5,6-dihydro-2,4-dithiouridine (1·331 Å) (Kojić-Prodić, Kvick & Ružić-Toroš, 1976). The C(5)–C(6) distance of 1·474 (5) Å is significantly shorter than the sp^3 single bond value of 1·533 Å (Bartell, 1959).

The molecules are connected by hydrogen bonds N(3)–H···O(4) of 2·975 (4) Å forming infinite zigzag ribbons along [101] (Fig. 4 and Table 7). These ribbons are joined by N(1)–H···S(2) hydrogen bonds of

Table 6. *Bond lengths* (Å) *and angles* (°) *of* 5,6-*dihydro*-2-*thiouracil compared with those of* 5,6-*dihydrouracil*, 2,4-*dithiouracil and uracil*

	5,6-Dihydro-2-thiouracil	5,6-Dihydrouracil	2,4-Dithiouracil	Uracil
N(1)–C(2)	1·317 (4)	1·335 (5)	1·342 (8)	1·371 (2)
C(2)–N(3)	1·376 (4)	1·395 (5)	1·406 (7)	1·376 (2)
N(3)–C(4)	1·374 (4)	1·364 (5)	1·358 (7)	1·371 (2)
C(4)–C(5)	1·489 (5)	1·515 (6)	1·414 (8)	1·430 (2)
C(5)–C(6)	1·474 (5)	1·507 (6)	1·365 (9)	1·340 (2)
C(6)–N(1)	1·454 (5)	1·464 (5)	1·360 (8)	1·358 (2)
C(2)–O(2)	—	1·222 (4)	—	1·215 (2)
C(2)–S(2)	1·676 (3)	—	1·645 (6)	—
C(4)–O(4)	1·216 (4)	1·211 (5)	—	1·245 (1)
C(4)–S(4)	—	—	1·684 (6)	—
N(1)–H(1)	0·85 (4)	0·84 (5)	0·59	0·84 (2)
N(3)–H(3)	0·85 (3)	0·86 (6)	0·95	0·88 (2)
C(5)–H(5,1)	0·93 (4)	1·00 (7)	0·92	0·93 (2)
C(5)–H(5,2)	1·15 (4)	0·97 (6)	—	—
C(6)–H(6,1)	0·98 (4)	0·99 (5)	1·04	0·96 (2)
C(6)–H(6,2)	1·18 (4)	1·03 (6)	—	—
C(6)–N(1)–C(2)	124·8 (3)	122·1 (2)	126·6 (5)	122·7 (1)
N(1)–C(2)–N(3)	117·1 (3)	116·1 (2)	112·4 (5)	114·0 (1)
C(2)–N(3)–C(4)	125·5 (3)	126·7 (2)	125·5 (5)	126·7 (2)
N(3)–C(4)–C(5)	115·7 (3)	115·1 (3)	117·4 (5)	115·5 (1)
C(4)–C(5)–C(6)	115·0 (3)	112·6 (3)	118·9 (5)	118·9 (2)
C(5)–C(6)–N(1)	111·6 (3)	110·3 (3)	119·2 (5)	122·3 (2)
N(1)–C(2)–O(2)	—	124·4 (2)	—	123·7 (1)
N(1)–C(2)–S(2)	123·5 (2)	—	125·9 (5)	—
O(2)–C(2)–N(3)	—	119·5 (2)	—	122·3 (2)
S(2) –C(2)–N(3)	119·4 (2)	—	121·7 (4)	—
N(3)–C(4)–O(4)	120·0 (3)	120·9 (2)	—	119·2 (2)
N(3)–C(4)–S(4)	—	—	119·3 (4)	—
O(4)–C(4)–C(5)	124·1 (3)	123·9 (3)	—	125·3 (2)
S(4)–C(4)–C(5)	—	—	123·2 (4)	—

Table 7. *Hydrogen bonds and* C(6)···S(2) *contacts*

X–H···Y	X···Y	X–H	H···Y	∠X–H···Y	Symmetry operation
N(3)–H(3)·····O(4)	2·975 (4) Å	0·85 (3) Å	2·12 (3) Å	171 (3)°	$x,y,z;\ \frac{1}{2}+x,\frac{1}{2}-y,\frac{1}{2}+z$
N(1)–H(1)·····S(2)	3·492 (3)	0·85 (4)	2·70 (3)	164 (3)	$x,y,z;\ (1-x)+1,y,\bar{z}$
C(6)–H(6,1)···S(2)	3·488 (4)	0·98 (4)	3·00 (4)	112 (2)	$x,y,z;\ 1-(\frac{1}{2}+x),\frac{1}{2}-y,\frac{1}{2}+z$
C(6)–H(6,2)···S(2)	3·488 (4)	1·18 (4)	3·10 (4)	128 (2)	$x,y,z;\ (\frac{1}{2}+x)-1,\frac{1}{2}-y,(\frac{1}{2}+z)+1$

3·492 (3) Å along [010]. Interbase contact realized through N(1)–H···S(2) hydrogen bonds of 3·335 Å was observed in 2,4-dithiouracil (Shefter & Mautner, 1967).

Two intermolecular contacts H(6,1)···S(2) of 3·00 (4) and H(6,2)···S(2) of 3·10 (4) Å (Table 7) are nearly equal to the H···S van der Waals distance of 3·05 Å (Pauling, 1960). However, the C(6)–H–S(2) angles [112 (2)° and 128 (2)°] are unfavourable for hydrogen-bonding. The C(6)H_2···S zigzag ribbons perpendicular to **b** (Fig. 5) are well defined in the structure.

The intensities were collected at the Department of General and Inorganic Chemistry, Faculty of Science, University of Zagreb. The authors thank M. Sc. Milenko Bruvo for collecting the data. Good quality crystals were grown by Dr Janko Herak.

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