(iii) $l,l'(l \neq l')$ [both obtained from row (k)]
cf. equation (9),

for any given combination jk. The process is repeated systematically for all bonds (jk) specified in the lower triangular half of array (**B**); this avoids duplication since $\omega\{_{ijkl}\}$ is equivalent to $\omega\{_{lkji}\}$ in both magnitude and sign. The sines and cosines of $<\mathbf{r}_1\mathbf{r}_2$, $<\mathbf{r}_2\mathbf{r}_3$, required by equation (10), can be obtained from the previously stored valence angles. Cos $(<\mathbf{r}_1\mathbf{r}_3)$ can be obtained using:

$$\cos(<\mathbf{r}_1\mathbf{r}_3) = \cos(<\mathbf{r}_{ij}\mathbf{r}_{kl}) = \mathbf{r}_{ij} \cdot \mathbf{r}_{kl}/|\mathbf{r}_{ij}|\,|\mathbf{r}_{kl}| \,. \quad (11)$$

The sign of the rotation is given by the sign of the determinant V:

$$V = \begin{vmatrix} l_{ij} & m_{ij} & n_{ij} \\ l_{jk} & m_{jk} & n_{jk} \\ l_{kl} & m_{kl} & n_{kl} \end{vmatrix} \quad (12)$$

which is proportional to the volume of the parallelepipedon defined by the vectors $\mathbf{r}_1, \mathbf{r}_2, \mathbf{r}_3$.

The method was tested at the University of London Institute of Computer Science using the I.C.T. Atlas machine; the co-operation of the Staff is gratefully acknowledged. One of us (F.H.A.) thanks the Science Research Council for a Research Studentship.

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The Crystal and Molecular Structure of 6-Mercaptopurine Monohydrate

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The crystal structure of 6-mercaptopurine monohydrate, $C_5H_6N_4OS$, has been determined by X-ray diffraction methods. 2186 independent reflections were measured on a diffractometer with Mo $K\alpha$ radiation. The structure was refined to an $R = 0{\cdot}038$ by full-matrix least squares. Standard deviations in the bond lengths involving only non-hydrogen atoms are approximately 0·002 Å and for those involving hydrogen atoms, 0·02 Å. The corresponding standard deviations in angles are 0·1° and 1° respectively. The molecule is not strictly planar; the maximum deviation of 0·029 Å is displayed by N(1). The sulfur atom is attached in thion form to the C(6) atom, the C–S bond length being 1·676 Å and the angle N(1)–C(6)–C(5), 110·4°. In the imidazole ring the hydrogen atom is bonded to N(7) rather than to N(9). The water molecule participates in four hydrogen bonds in a nearly tetrahedral arrangement.

Introduction

A number of sulfur derivatives of nucleic acid components have been shown to possess anticarcinogenic properties. The effect of the drug 6-thioguanine may be a result of the incorporation of this molecule in the nucleic acid as an antagonist to a natural purine base (LePage, 1960), while the powerful drug 6-mercaptopurine is thought to enter the synthesis of nucleic acid at an early stage, probably as a competitor to hypoxanthine in the conversion of inosinic acid to nucleic acid (Skipper, 1954). The activity of the sulfur derivatives of nucleic acid components is very sensitive to minor structural modification; *e.g.* the purine molecule substituted by sulfur in the 2-position displays no anticarcinogenic effect (Robins, 1964). An accurate structure determination of 6-mercaptopurine monohydrate was undertaken to investigate the packing mode of this type of molecule and to determine to what extent the sulfur substituent alters the geometry of the purine skeleton.

Experimental

Crystals satisfactory for X-ray work were selected directly from a sample of 6-mercaptopurine obtained from the Sigma Chemical Company, St. Louis, Missouri. The crystals are faintly yellow, with a slightly distorted bipyramidal shape. Preliminary cell dimensions and space-group determination were carried out

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by precession and Weissenberg methods. From the systematic extinctions, hkl absent for $h+k=2n+1$, $h0l$ absent for $l=2n+1$, the space group is either Cc or $C2/c$. A Howells, Phillips & Rogers (1950) plot based on the $h0l$ reflections strongly indicated a centrosymmetric cell, thus $C2/c$ was chosen.

Final unit-cell parameters were determined by measuring the 2θ settings for 17 reflections on the diffractometer, with Mo $K\alpha$ radiation ($\lambda=0{\cdot}71069$ Å). From the least-squares treatment, the mean deviation from the computed value, $1/17\,\Sigma\,|2\theta_{\rm obs}-2\theta_c|$, was 0·003°. The following cell dimensions were obtained:

$$a=15{\cdot}294\pm0{\cdot}002,\ b=\ 7{\cdot}732\pm0{\cdot}001$$
$$c=12{\cdot}379\pm0{\cdot}001\text{Å},\ \beta=101{\cdot}64\pm0{\cdot}01^\circ\,.$$

The measured density of 1·57 g.cm^{-3} agrees well with the value 1·58 g.cm^{-3} calculated for 8 molecules in the unit cell.

The crystal used for collecting data had dimensions 0·30 × 0·27 × 0·11 mm approximately, along **a**, **b** and **c** directions and was mounted along the b axis. Integrated intensities were measured by the moving-crystal moving-counter technique with a scan rate of 2°.min^{-1}. The scan ranges were calculated according to the relation $\Delta 2\theta=A+B\tan\theta$ (Alexander & Smith, 1964). A value of 1·8° was determined for the constant A by measuring the scan range sufficient for a fairly strong, low order reflection. B was taken as 1·0, a value which has been found to be satisfactory for Mo radiation.

The Mo tube was operated at a constant potential of 50 kV and a current of 14 mA. Radiation was filtered through a 0·001″ Nb foil and detected by a NaI(Tl) scintillation counter. The pulse height analyzer in the detecting circuit was set to pass approximately 95% of the Mo $K\alpha$ pulses. The take-off angle was 3° and the receiving aperture of the counter was fixed at 1 × 1°.

A background count was made at each end of the scan range for half the time of the total scan, and the net count deduced by subtracting the two backgrounds from the peak scan. For some low order reflections ($2\theta<12°$) it was difficult to decide where to start the peak scan because of the closeness of the Nb K absorption edge to the Mo $K\alpha$ peak. For these reflections both backgrounds were taken equal to that on the high 2θ side.

Within the sphere of reflection, limited at $\sin\theta/\lambda=$ 0·7, 2186 unique reflections were measured. Of these, 348 were less than the threshold value of $2\sigma_c$ where $\sigma_c=(N_{B1}+N_{Pk}+N_{B2})^{1/2}$. N_{Pk} is the number of counts in the scan and N_{B1} and N_{B2} are the background counts.

During the data collection three standard reflections were measured every four hours to check the stability of the crystal and the electronics. No deterioration of the crystal was observed, and fluctuation of the intensities of the standards indicated that the X-ray source and detecting circuitry were stable to within 1%. Thus the total error assigned to the net intensity of each reflection is

$$\sigma_I=[\sigma_c^2+(0{\cdot}01\sigma_c^2)^2]^{1/2}\,. \qquad (1)$$

The linear absorption coefficient of the crystal is 3·85 cm^{-1}. There is an 11% attenuation in the most extended direction of the crystal and 4% in the least extended. Although this spread is larger than the random error in I_o, the average difference in absorption is much less and, therefore, no correction was applied.

The data were corrected for Lorentz and polarization effects according to normal beam geometry, and the standard deviation in the structure factors was taken as

$$\sigma_F=[F^2+\sigma_I(\mathrm{Lp})^{-1}]^{1/2}-F\,. \qquad (2)$$

In order to correct the intensities for coincidence loss, the scan counts of 20 reflections in the range 2000–204,000 deka-counts were measured with and without a 0·001″ brass filter.

A plot of the observed filter factor *versus* counting rate is essentially linear, and can thus be expressed as:

$$N_{\rm obs}^{\rm direct}/N_{\rm obs}^{\rm trans}=aN_{\rm obs}^{\rm direct}+b\,. \qquad (3)$$

In the equation, $N_{\rm obs}^{\rm direct}$ is the scan counts measured without filter and $N_{\rm obs}^{\rm trans}$ the counts measured with filter. The constants a and b can be expressed in terms of the apparent deadtime of the counting system, τ, and the true filter factor $k_t=N_{\rm true}^{\rm direct}/N_{\rm true}^{\rm trans}$.

The relationship between the observed and the true counting rates is given by:

$$N_{\rm obs}=N_{\rm true}-\tau N_{\rm obs}\,.\,N_{\rm true}\,. \qquad (4)$$

Equation (4) can be rearranged and substituted into the expression for the observed filter factor, giving:

$$\begin{aligned}k_{\rm obs}&=N_{\rm obs}^{\rm direct}/N_{\rm obs}^{\rm trans}\\&=N_{\rm true}^{\rm direct}(1+\tau N_{\rm true}^{\rm trans})/N_{\rm true}^{\rm trans}(1+\tau N_{\rm true}^{\rm direct})\\&=k_t(1+\tau N_{\rm true}^{\rm trans})\,(1-\tau N_{\rm obs}^{\rm direct})\\&=(1-k_t)\tau N_{\rm obs}^{\rm direct}+k_t\,.\end{aligned}$$

The slope of the line equals $d(N_{\rm obs}^{\rm direct}/N_{\rm obs}^{\rm trans})/d(N_{\rm obs}^{\rm direct})=(1-k_t)\tau$. This derivation is strictly true if one assumes that all the peaks have the same form.

From the graph we found $k_t=3{\cdot}10$, and τ was calculated to be $4{\cdot}2\times10^{-6}$ sec/count. The data were corrected according to a formula obtained by rearranging equation (4):

$$N_{\rm obs}^{\rm direct}=N_{\rm obs}^{\rm direct}/(1-\tau N_{\rm obs}^{\rm direct})\,. \qquad (5)$$

Determination and refinement of the structure

Approximate sulfur coordinates were found from a three-dimensional sharpened, origin-removed Patterson synthesis which clearly showed sulfur–sulfur vectors between atoms related by the twofold axis, the c glide and the center of symmetry. Structure factor

Table 1. *Final coordinates and thermal parameters with the corresponding standard deviations, in parentheses*

Thermal parameters defined by the expression:

$$T_i = \exp\left[-\tfrac{1}{4}(B_{11}h^2a^{*2} + B_{22}k^2b^{*2} + B_{33}l^2c^{*2} + 2B_{12}hka^*b^* + 2B_{13}hla^*c^* + 2B_{23}klb^*c^*)\right].$$

	x	y	z	B_{11} or B	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
				Å^2	Å^2	Å^2	Å^2	Å^2	Å^2
S	0·44631 (2)	0·66283 (5)	0·35599 (3)	2·88 (2)	3·54 (2)	2·64 (2)	−0·28 (1)	1·43 (1)	0·23 (1)
C(2)	0·36715 (10)	0·66845 (19)	0·64196 (11)	2·79 (5)	2·77 (6)	2·07 (5)	0·16 (5)	0·19 (4)	−0·08 (5)
C(4)	0·26274 (8)	0·51621 (17)	0·53010 (10)	2·16 (5)	2·18 (5)	2·01 (5)	0·35 (4)	0·71 (4)	0·30 (4)
C(5)	0·30638 (8)	0·53755 (17)	0·44215 (10)	2·34 (5)	2·20 (5)	1·87 (5)	0·15 (4)	0·48 (4)	0·05 (4)
C(6)	0·38593 (9)	0·63062 (17)	0·45313 (10)	2·41 (5)	2·28 (5)	2·23 (5)	0·38 (4)	0·67 (4)	0·36 (4)
C(8)	0·18434 (10)	0·38970 (20)	0·39111 (12)	2·65 (6)	2·86 (6)	2·69 (6)	−0·07 (5)	0·36 (5)	−0·16 (5)
N(1)	0·41108 (8)	0·69514 (16)	0·55917 (9)	2·15 (5)	2·39 (5)	2·38 (4)	−0·29 (4)	0·19 (4)	0·03 (4)
N(3)	0·29290 (7)	0·58103 (16)	0·63336 (9)	2·46 (5)	2·83 (5)	1·95 (4)	0·03 (4)	0·56 (4)	0·07 (4)
N(7)	0·25422 (8)	0·45569 (16)	0·35395 (9)	2·86 (5)	2·74 (5)	1·81 (4)	0·02 (4)	0·41 (4)	−0·24 (4)
N(9)	0·18647 (7)	0·42292 (16)	0·49672 (9)	2·28 (5)	2·72 (5)	2·49 (5)	−0·03 (4)	0·66 (4)	0·00 (4)
O	0·44132 (8)	0·09815 (18)	0·36961 (10)	3·02 (5)	3·70 (6)	3·29 (5)	−0·75 (4)	1·16 (4)	0·10 (4)
H(1)	0·4576 (10)	0·7585 (21)	0·5757 (12)	2·5 (3)					
H(2)	0·3939 (10)	0·7227 (19)	0·7089 (12)	2·5 (3)					
H(7)	0·2653 (12)	0·4514 (24)	0·2884 (15)	4·2 (4)					
H(8)	0·1389 (12)	0·3229 (22)	0·3446 (14)	3·5 (4)					
H(10)	0·4070 (14)	0·1036 (28)	0·4101 (17)	5·3 (5)					
H(11)	0·4561 (17)	−0·0051 (35)	0·3728 (20)	7·5 (7)					

calculations based only on sulfur positions gave $R=0{\cdot}55$ and the following three-dimensional F_o syntheses revealed all the remaining atoms other than hydrogen.

Refinement proceeded by three-dimensional full-matrix least-squares. The function minimized was $\Sigma\, w(|F_o|-|(1/k)F_c|)^2$ with $w=1/\sigma_F^2$. The atomic scattering factors used for sulfur were those given by Dawson (1960); for carbon, nitrogen and oxygen those given by Berghuis, Haanappel, Potters, Loopstra, MacGillavry & Veenendaal (1955); and for hydrogen those of Stewart, Davidson & Simpson (1965). The calculations were carried out on an IBM 7094 computer with programs from *X-ray* 63 (Stewart *et al.*, 1964).

Three cycles of isotropic refinement, including only the nonhydrogen atoms, decreased R to 11·7%. At this stage a three-dimensional difference synthesis was calculated, and the four hydrogen atoms attached to the purine moiety were located. A least-squares cycle with anisotropic temperature factors assigned to all the nonhydrogen atoms and the four ring hydrogen atoms included but not refined, was calculated. A new difference synthesis revealed the remaining two hydrogen atoms in the water molecule. Parameters for all atoms, anisotropic temperature factors for nonhydrogen atoms and isotropic temperature factors for the hydrogen atoms were refined by full-matrix least squares. Convergence was rapid; two cycles refining all atoms and an intermediate cycle refining only hydrogen parameters reduced all shifts to less than the standard deviations of the parameters. A final cycle was calculated and average shift in parameters was $0{\cdot}03\sigma$ with a maximum shift of $0{\cdot}16\sigma$.

The residual $R=\Sigma\,(|F_o|-|F_c|)/\,\Sigma\,|F_o|$ omitting reflections with $I_{\rm rel}<2\sigma_c$ is 0·038 and the weighted residual error $R_w=[\,\Sigma\,(w|F_o|-|F_c|)^2/\,\Sigma\, w|F_o|^2]^{1/2}$ is 0·037.

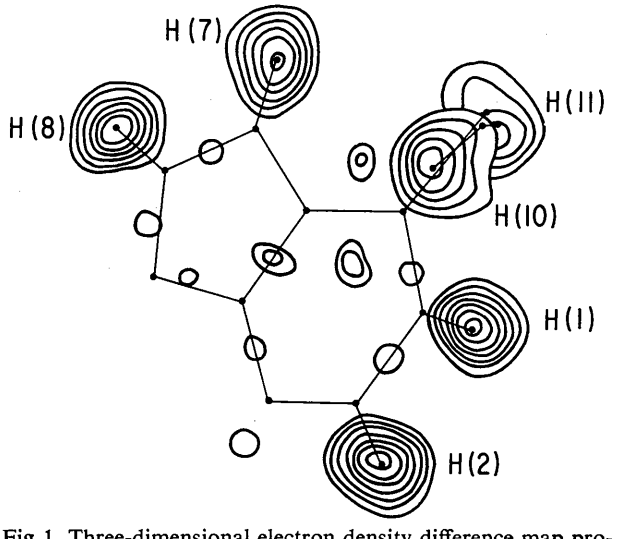


Fig. 1. Three-dimensional electron density difference map projected along [010]. Contours at intervals of 0·1 e.Å^{-3}, beginning at 0·2 e.Å^{-3}. Only one asymmetric unit is shown.

Table 2. *Observed and calculated structure factors multiplied by* 10

The reflections with observed intensity less than the threshold value of $2\sigma_c$ are marked with < signs.

The standard deviation of an observation of unit weight $[\Sigma w(|F_o|-|F_c|)^2/(m-n)]^{1/2}$ is 2·01. Final coordinates and temperature factors are listed in Table 1, and a list of observed and calculated structure factors is given in Table 2.

A three-dimensional difference synthesis was calculated, based only on the contribution of the heavy atoms. Sections of the ΔF synthesis through the hydrogen atoms are shown in Fig. 1 as viewed along [010]. The maximum electron densities for the hydrogen atoms attached to the purine skeleton range from 0·72 to 0·85 e.Å^{-3}, while those on the water molecule have densities of 0·54 and 0·66 e.Å^{-3}.

A residual difference synthesis based on all the atoms showed peaks of electron densities (0·1 to 0·3 e.Å^{-3}) approximately in the middle of the bonds. This can, in part, be interpreted as bonding electrons and, in part, as errors in the ellipsoidal approximation to the thermal motion. A peak of 0·23 e.Å^{-3} appeared almost exactly in the expected position of a hydrogen atom attached to N(3). In addition, there are peaks on each side of the C(5)–C(6) bond (0·33 and 0·32 e.Å^{-3}) which are evidently a result of errors in the data.

Comparison of observed and calculated structure factors (Table 2) indicates no appreciable extinction in the data. This is an indication of the relatively less severe extinction effects to be expected with Mo $K\alpha$ radiation. Furthermore, the data have been approximately corrected for coincidence loss, thus removing an effect which is qualitatively similar to secondary extinction.

Intramolecular bond lengths and angles are listed in Table 3 together with the corresponding standard deviations.

Table 3. *Intramolecular bond distances and valence bond angles with the corresponding standard deviations in parentheses*

Bond	
N(1)–C(2)	1·350 (0·0020) Å
C(2)–N(3)	1·307 (0·0020)
N(3)–C(4)	1·364 (0·0016)
C(4)–C(5)	1·397 (0·0020)
C(5)–C(6)	1·396 (0·0020)
C(6)–N(1)	1·384 (0·0017)
C(6)–S	1·676 (0·0016)
C(5)–N(7)	1·370 (0·0017)
N(7)–C(8)	1·346 (0·0021)
C(8)–N(9)	1·326 (0·0019)
N(9)–C(4)	1·363 (0·0018)
N(1)–H(1)	0·85 (0·016)
C(2)–H(2)	0·95 (0·014)
N(7)–H(7)	0·86 (0·019)
C(8)–H(8)	0·96 (0·016)
O–H(10)	0·80 (0·023)
O–H(11)	0·83 (0·023)
Angles	
C(6)—N(1)–C(2)	125·40 (0·12)°
N(1)—C(2)–N(3)	125·05 (0·12)
C(2)—N(3)–C(4)	112·98 (0·12)
N(3)—C(4)–C(5)	124·24 (0·12)
C(4)—C(5)–C(6)	121·92 (0·11)
C(5)—C(6)–N(1)	110·38 (0·13)
C(5)—C(6)–S	127·01 (0·10)
N(1)—C(6)–S	122·61 (0·10)
C(6)—C(5)–N(7)	132·18 (0·13)
C(4)—C(5)–N(7)	105·88 (0·12)
C(5)—N(7)–C(8)	106·11 (0·12)
N(7)—C(8)–N(9)	113·59 (0·12)
C(8)—N(9)–C(4)	104·52 (0·12)
N(9)—C(4)–C(5)	109·90 (0·11)
N(9)—C(4)–N(3)	125·85 (0·12)
C(6)—N(1)–H(1)	119·5 (1·1)
H(1)—N(1)–C(2)	115·1 (1·1)
N(1)—C(2)–H(2)	113·8 (1·0)
H(2)—C(2)–N(3)	121·1 (1·0)
C(5)—N(7)–H(7)	125·0 (1·2)
H(7)—N(7)–C(8)	128·9 (1·2)
N(7)—C(8)–H(8)	121·9 (1·1)
H(8)—C(8)–N(9)	124·5 (1·1)
H(10)–O–H(11)	103·4 (2·2)

Discussion of the molecular and crystalline structure

The molecular dimensions are shown in Fig. 2 and listed in Table 3. The molecule is not exactly planar; deviations from the least-squares plane are listed in Table 4 and the puckering of the molecule is shown in Fig. 3. The maximum deviation, displayed by N(1) and H(1), is apparently a result of the strong hydrogen bond N(1)–H(1)···O, where the oxygen is situated 0·17 Å above the least-squares plane. The appreciable deviation of N(7) and H(7), however, cannot be accounted for in this way because the position of N(3) to which N(7) is hydrogen bonded, should indicate a slight deviation in the opposite direction. Other struc-

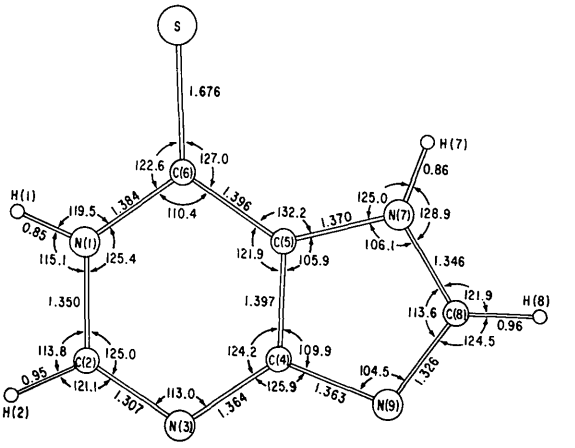


Fig. 2. Bond distances and angles.

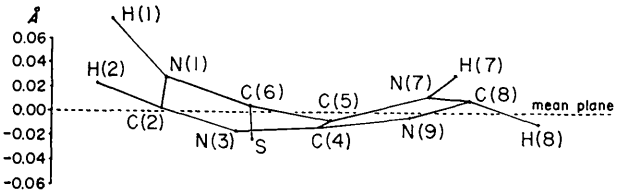
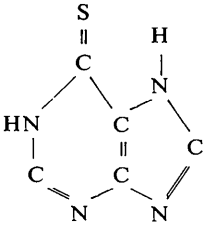


Fig. 3. The puckering of the molecule.

ture determinations of purine derivatives show that very often the purine moiety is nonplanar. As in the present case, this cannot always be explained by strong hydrogen bonding between an atom in the ring and another atom not lying in the plane of the ring (Macintyre, 1964).

The unsubstituted purine molecule contains a total of ten π-electrons and thus both the pyrimidine and the imidazole rings can be considered as parts of an aromatic system. This is consistent with the bond lengths found in X-ray analyses of purine (Watson, Sweet & Marsh, 1965) as far as the six-membered ring is concerned, although the five-membered ring seems to be pseudoaromatic.

In 6-mercaptopurine monohydrate the sulfur atom, substituted at C(6), is bonded in the thion rather than in the thiol form. In solution, however, a tautomeric equilibrium between the two forms may exist. The attachment of a hydrogen atom to N(1) increases the number of π-electrons in the pyrimidine ring while the engagement of C(6) in a partial double bond with sulfur leads to a decrease. The overall effects of these changes, as reflected by the molecular dimensions, are difficult to interpret in terms of simple valence bond theory, although it would appear that the following canonical form



is dominant. In the MO–LCAO calculations carried out on the molecule (Pullman & Pullman, 1963) the hydrogen atom is assumed to be bonded to N(9) of the imidazole ring. This can explain in part the poor agreement between the bond lengths found experimentally and those deduced from the calculations.

The introduction of a sulfur atom and the attachment of a hydrogen atom to N(1) have partly destroyed the aromaticity of the six-membered ring, while virtually no significant alteration can be observed in the imidazole ring when compared with purine.

The small internal angle at C(6) (110·4°) is not specific for molecules with sulfur substituents in this position, for example in guanine hydrochloride dihydrate (Iball & Wilson, 1965) with oxygen attached to C(6), the corresponding angle is 110·8°.

In a review of the internal valence angle at nitrogen atoms in six-membered rings, Singh (1965) has pointed out that this angle is significantly larger than 120° when the nitrogen is carrying an extra-annular hydrogen, and less than 120° when the nitrogen has no attachment. This empirical rule is also valid for the 6-mercaptopurine. In addition, a similar trend is observed for the internal valence angles of the nitrogen atoms in the five-membered ring. Thus the angles at N(7) and N(9) are 106·1° and 104·5° respectively. The same feature is observed in purine (Watson *et al.*, 1965) 106·5° and 103·8°, theophylline (Sutor, 1958) 106·7° and 102·0°, and adenine hydrochloride (Cochran, 1951) 105° and 102°; while in guanine hydrochloride dihydrate (Iball & Wilson, 1965) and uric acid (Ringertz, 1966) where hydrogen atoms are attached to both nitrogen atoms in the five-membered ring, the angles are not significantly different.

Table 4. *Deviations of the atoms from the least-squares plane through the ten nonhydrogen atoms of the ring system*

$7{\cdot}1809x - 6{\cdot}5136y + 2{\cdot}0322z = -0{\cdot}41052$ Å, x,y,z are fractions of unit-cell edges.

	Deviation
S	−0·022 Å
N(1)	0·029
C(2)	0·003
N(3)	−0·016
C(4)	−0·012
C(5)	−0·007
C(6)	0·005
N(7)	0·013
C(8)	0·010
N(9)	−0·004
H(1)	0·077
H(2)	0·023
H(7)	0·030
H(8)	−0·009

The bond lengths where hydrogen atoms are involved are all shorter than the expected internuclear distances. This may in part be a result of the displacement of the electron cloud toward the atom to which hydrogen is bonded. For the two C–H distances the displacement is $0{\cdot}12 \pm 0{\cdot}01$ Å if one assumes 1·075 Å as the true internuclear distance. An A–H covalent bond involved in an A–H$\cdots B$ hydrogen bond is expected to increase with increasing strength of the hydrogen bond. Empirical curves of $r(A\text{–H})$ *versus* $R(A\cdots B)$ have been plotted for different hydrogen bonds (Pimentel & McClellan, 1960). These curves are expected to give true internuclear A–H distances to within $\pm 0{\cdot}03$ Å for a given hydrogen bond length. In Table 5 the N–H and O–H bond lengths found in 6-mercaptopurine are compared with the internuclear distances deduced from the curves.

Table 5. *Comparison between observed and expected A–H bond lengths*

Hydrogen bond	$R(A\cdots B)_{obs}$	$r(A\text{–}H)_{obs}$	$r(A\text{–H})_{calc}$	Displacement
N(7)–H(7)····N(3)	2·92 Å	0·86 Å	1·04 Å	0·18 Å
N(1)–H(1)····O	2·76	0·85	1·06	0·21
O——H(10)···N(9)	2·81	0·80	1·01	0·21

Molecular packing and hydrogen bonding

The introduction of a sulfur atom in purine has not changed the tendency of this type of molecule to pack one on top of the other. Molecules related by centers of symmetry are stacked in infinite columns parallel to the *b* axis, the interplanar spacings between planes of molecules are 3·18 and 3·33 Å. In Fig. 4 are shown the two molecules lying 3·33 Å apart as viewed along the normal to the molecular plane. It will be seen that there is a carbon atom situated approximately above the center of each ring. Molecules lying 3·18 Å apart do not overlap to any appreciable extent. The shortest atom-to-atom distances between the molecules are listed in Table 6.

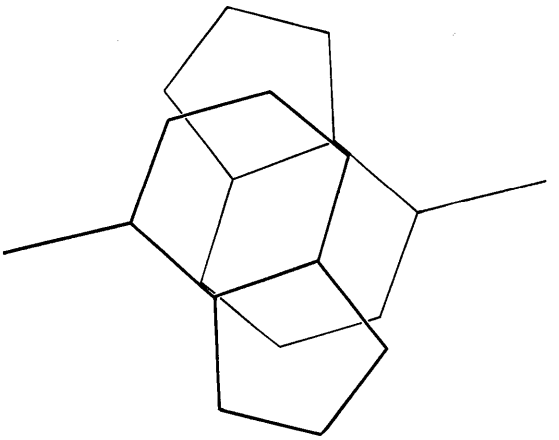


Fig. 4. The diagram shows two molecules lying 3·33 Å apart projected along the normal to the mean plane of the molecule

The columns of stacked molecules are chained together through N(7)–H(7)···N(3) hydrogen bonds, of length 2·92 Å, forming layers running parallel to (100)

Table 6. *Intermolecular distances*

The second figure in parentheses indicates the symmetry operation.

(i)	x,	y,	z
(ii)	$1-x$,	y,	$\frac{1}{2}-z$
(iii)	x,	$1-y$,	$z-\frac{1}{2}$
(iv)	$1-x$,	$1-y$,	$1-z$
(v)	$\frac{1}{2}-x$,	$\frac{1}{2}-y$,	$1-z$
(vi)	x,	$1-y$,	z
(vii)	$\frac{1}{2}-x$,	$\frac{3}{2}-y$,	$1-z$

	Distance
S(–) (i) —S(–) (ii)	3·365 Å
N(7) (i)—N(3) (iii)	2·922
H(7) (i)—N(3) (iii)	2·06
O(–) (i)—C(2) (iii)	3·346
O(–) (i)—H(2) (iii)	2·41
O(–) (i)—N(1) (iv)	2·761
O(–) (i)—H(1) (iv)	1·91
O(–) (i)—N(9) (v)	2·809
H(10) (i)–N(9) (v)	2·02
O(–) (i)—S(–) (vi)	3·373
H(11) (i)–S(–) (vi)	2·58
H(10) (i)–H(1) (iv)	2·32
C(4) (i)—C(8) (v)	3·337
N(9) (i)—C(8) (v)	3·251
N(9) (i)—N(9) (v)	3·297
N(3) (i)—C(5) (vii)	3·362
N(9) (i)—N(1) (vii)	3·318

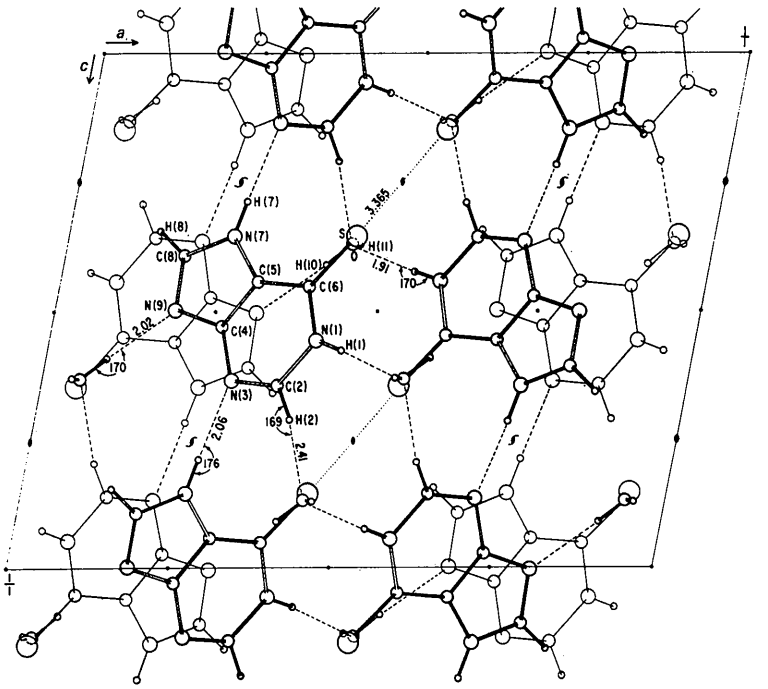


Fig. 5. Packing of molecules viewed along the *b* axis.

(Fig. 5). The water molecule forms a bridge N(1)–H(1)···O–H(10)···N(9) between the layers, completing the three-dimensional network.

The water molecule has a distorted tetrahedral coordination forming four hydrogen bonds to N(9), N(1), C(2) and S in different molecules (Fig. 6). The O···H(1)–N(1) bond and the O–H(10)···N(9) bond of lengths 2·76 and 2·81 Å respectively deviate only slightly from linearity.

Whether one should reckon the C(2)–H(2)···O contact as a true hydrogen bond may be questionable. In a review comparing short C–H···O distances found in X-ray analyses, Sutor (1963) points out the ability of an activated carbon atom to form hydrogen bonds to oxygen. The two nitrogen atoms in bonding to C(2) induce a net positive charge on the atom, thus increasing the possibility for hydrogen bonding. Both the short O···H(2) distance of 2·42 Å and the angle C(2)–H(2)···O of 169° favor the assumption of a hydrogen bond.

The ability of the sulfur atom to participate in hydrogen bonding has been discussed by several authors (Krachow, Lee & Mautner, 1965; Mautner & Shefter, 1967). In 6-mercaptopurine the S···O distance is 3·373 Å and the S···H(11) distance is 2·58 Å. The angle S···H(11)–O is 162°, which is not an unusual deviation from linearity for hydrogen bonds.

By reviewing a large number of structure investigations of sulfur-containing compounds, it was found that sulfur does not display a unique van der Waals radius. This is in accordance with Pauling's statement, '... the effective van der Waals radius of an atom in a crystal depends on the strength of the attractive forces holding the molecules together, and also on the orientation of the contact relative to the covalent bond or bonds formed by the atom ...' (Pauling, 1960). A value of 1·75 ± 0·1 Å seems to be a reasonable empirical value for the van der Waals radius of sulfur. Even if the lower limit of 1·65 Å is used, the S···H(11) distance is shorter by 0·27 Å than the sum of the van der Waals radii. The fact that the true internuclear O–H distance is probably 0·2 Å longer than the observed value, gives a total shortening of 0·47 Å, which is evidently the result of hydrogen bonding.

No intermolecular distances not involving hydrogen bonds are shorter than the sum of the van der Waals radii. The distance between two sulfur atoms related by a twofold axis is 3·365 Å, which gives an effective van der Waals radius within the range indicated above.

Thermal motion

The temperature parameters found for all the atoms are quite normal for this type of molecule. There seems to be no predominant direction for thermal vibration. The isotropic temperature factors calculated for the hydrogen atoms are equal to, or larger than, the corresponding values of the atoms to which they are bonded. As expected, the water molecule displays a larger thermal motion than the atoms in the ring system.

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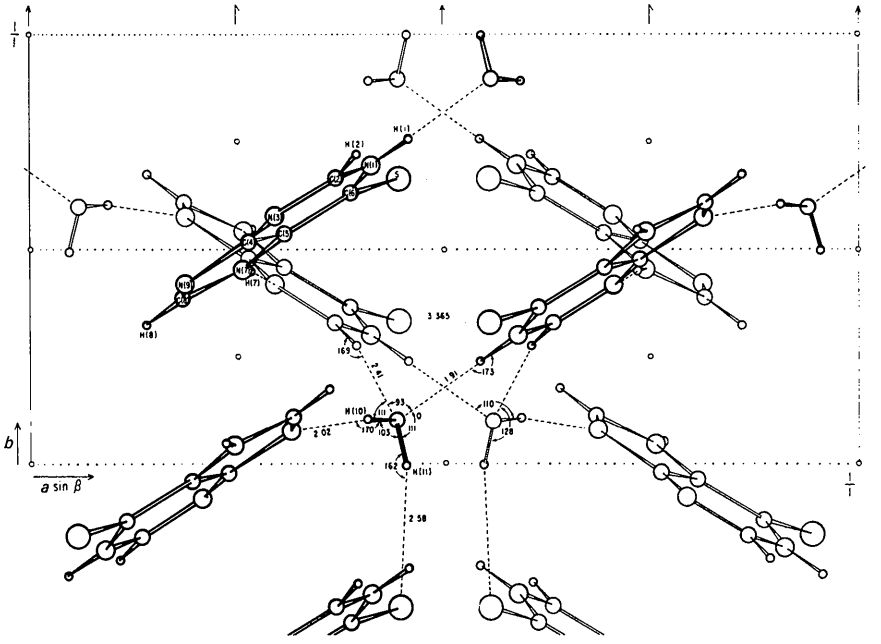

Fig. 6. Packing of molecules viewed along the *c* axis.

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The Crystal and Molecular Structure of 6-Mercaptopurine Monohydrate. A Second, Independent X-ray Diffraction Determination*

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The structure of 6-mercaptopurine monohydrate, $C_5H_4N_4S.H_2O$ was determined by the heavy-atom method. The space group is $C2/c$; $a=15{\cdot}3314(4)$, $b=7{\cdot}7255(1)$, $c=12{\cdot}3397(2)$ Å, $\beta=101{\cdot}526(2)°$, $Z=8$. These cell parameters differ significantly from those of Sletten, Sletten and Jensen (*Acta Cryst.* (1969) B**25**, 1330) Counter data were recorded for 3792 independent reflections (Mo radiation, $\sin\theta/\lambda \leq 0.86$) and corrected for absorption. The use of anisotropic thermal parameters for the hydrogen atoms results in no significant changes in other structure parameters. The most reliable parameters for the C, N and S atoms are taken to be those from refinement in which the low-angle data ($\sin\theta/\lambda \leq 0.55$ Å^{-1}) are excluded. The corresponding bond lengths (with standard errors from 0.0011 to 0.0016) show some small but significant differences from those of Sletten *et all.* On analysis by the Schomaker–Trueblood method the thermal parameters of the C, N and S atoms show an excellent fit to the rigid-body model. The apparent positions determined for the hydrogen atoms are remarkably close to those found by Sletten *et all.*

Introduction

The determination at Oak Ridge (OR) of the crystal structure of 6-mercaptopurine monohydrate was undertaken for essentially the same reasons that prompted the parallel study at the University of Washington (UW)–see the accompanying paper of Sletten, Sletten & Jensen (1969). The discovery of the duplication of effort was made when a summary of the preliminary OR results was published in abstract form (Brown, 1967) at just the time that the manuscript of Sletten *et al.* on the UW results was refereed for publication in this journal.

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On interchange of information it was found that the agreement between the two sets of cell parameters was rather poor, though each set had apparently been determined with moderately high precision. Furthermore, even when the same set of cell parameters was used in calculating bond lengths from the two sets of coordinates, there were maximum and mean absolute differences of 0·007 and 0·0034 Å for bonds not involving hydrogen atoms, showing a level of agreement somewhat disappointing in view of the apparent high precision of the two determinations. On the other hand, the agreement for the bonds C–H, N–H, and O–H (maximum and mean absolute differences of 0·030 and 0·015 Å) could hardly have been expected to be better.

The cell parameters have now been redetermined in both laboratories with nearly the same results as before,