PAULING, L. (1960). *The Nature of the Chemical Bond*, 3rd ed. Ithica: Cornell Univ. Press.
PHILIPS, D. C. (1956). *Acta Cryst.* **9**, 819.
STEWART, J. M. (1967). *XRAY67, Program System for X-ray Crystallography*. Technical Report 67-58. Computer Science Center, Univ. of Maryland.
SVETICH, G. W. & VOGE, A. A. (1971). *Chem. Commun.* p. 676.
WRIGHT, D. A. & WILLIAMS, D. A. (1968). *Acta Cryst.* B**24**, 1107.
YOSHINO, A., SHUTO, Y. & IITAKA, Y. (1970). *Acta Cryst.* B**26**, 744.

Acta Cryst. (1972). B**28**, 1767

The Crystal Structure of 6-Histaminopurine Dihydrate

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(*Received* 8 *November* 1971)

Crystals of the dihydrate of 6-histaminopurine are monoclinic, space group $P2_1/c$, with $a=5{\cdot}507$ (5), $b=31{\cdot}839$ (9), $c=7{\cdot}336$ (4) Å, and $\beta=105{\cdot}58$ (4)°. Using X-ray diffractometer data, the structure was solved by symbolic addition and was refined by least-squares methods to $R_1(\sum||F_o|-|F_c||/\sum|F_o|)=0{\cdot}136$ and $R_2(\sum|F_o^2-F_c^2|/\sum F_o^2)=0{\cdot}112$. The adenine moiety is in the N(7)–H tautomer form. The structure features hydrogen bonding between purine bases, resulting in ribbons parallel to **a** and stacking of adenine moieties along **c**. The stacked base planes are approximately parallel and are separated by an interplanar spacing of about 3·4 Å. There are no interactions between histamine imidazole rings or between imidazole and adenine rings.

Introduction

Many studies have demonstrated that base stacking is an important type of interaction among purine and pyrimidine derivatives in aqueous solution (Chan, Schweizer, Ts'o & Helmkamp, 1964; Broom, Schweizer & Ts'o, 1967; Solie & Schellman, 1968; Ts'o, 1968) and in the solid state (Bugg, Thewalt & Marsh, 1968; Bugg & Thewalt, 1969; Thewalt, Bugg & Marsh, 1970; Bugg & Thewalt, 1970; Bugg, Thomas, Sundaralingam & Rao, 1971; Bugg, 1971). However, in spite of the extensive evidence supporting the importance of base stacking, little is known about the forces involved, or about the geometrical arrangements that result from stacking interactions. We are currently examining base stacking patterns in crystals of purine derivatives to obtain information about the types of interactions responsible for stacking. In this paper we describe the crystal structure and base stacking pattern of 6-histaminopurine (Fig. 1). This and other 6-purinyl derivatives related to the plant-growth hormone, kinetin, have morphological effects on cells in tissue cultures (Lettré, 1960); among these purine derivatives, 6-histaminopurine is outstanding because of its cytotoxic activity against tumor cells (Lettré, 1960; Lettré & Werner, 1968).

Experimental

Crystals of 6-histaminopurine dihydrate were obtained as clear plates by slowly cooling a hot, saturated aqueous solution. The crystals are stable when stored in a high humidity atmosphere, but rapidly decompose when exposed to room atmosphere, apparently by loss of water of crystallization. Weissenberg and oscillation photographs showed that the crystals are monoclinic; the space group is $P2_1/c$, as indicated by the systematic absence of reflections $0k0$ with k odd and $h0l$ with l odd. A plate, approximately $0{\cdot}3\times0{\cdot}1\times0{\cdot}1$ mm, was cut from a larger crystal and was immediately coated with a heavy layer of epoxy in order to retard the rate of decomposition. The crystal was then mounted in an arbitrary orientation on a Picker FACS-1 diffractometer. Approximate cell parameters for use in collecting intensity data were obtained by measuring the angular settings of three high-angle (Cu $K\alpha_1$, $\lambda=1{\cdot}54051$ Å) reflections.

Intensity data were collected with the diffractometer, using a scintillation counter, nickel-filtered copper radiation, and a θ–2θ scanning technique. The scanning speed was $2°.\text{min}^{-1}$, and a 10 sec background measurement was performed at each terminus of the scans. Measurements were made for the 2075 independent

reflections in the range $4° \leq 2\theta \leq 128°$. Three suitable reflections were chosen as standards and monitored periodically during the data collection process. Despite the protective epoxy coating on the crystal, the intensities of the standard reflections decreased about 10% during data collection, indicating crystal decomposition. Crystal decomposition was also evidenced by increased mosaic spread in Weissenberg photographs taken after data collection was completed.

Accurate values for the cell parameters were obtained immediately after data collection. Using measurements of 2θ values for 10 high-angle (Cu $K\alpha_1$) and 7 low-angle (Cu $K\beta$, $\lambda = 1{\cdot}3922$ Å) reflections, the unit-cell parameters were obtained from a least-squares analysis. Crystal data are listed in Table 1. These cell parameters are not significantly different from the approximate parameters obtained prior to collecting intensity data.

Table 1. *Crystal data*

Stoichiometry	$C_{10}H_{11}N_7.2H_2O$
Z	4
Space group	$P2_1/c$
a	5·507 (5) Å
b	31·839 (9)
c	7·336 (4)
β	105·58 (4)°
Cell volume	1239·0 Å^3
ϱ(calculated)	1·422 g.cm^{-3}
ϱ(observed)	1·42
μ	8·92 cm^{-1}

(The unit-cell parameters were measured at 25±2°C. The reported standard deviations are five times those obtained from the least-squares analysis.)

The intensity values were scaled by a least-squares procedure that utilized the intensities of the standard reflections to calculate scale factors as a function of exposure time. The intensities were assigned variances, $\sigma^2(I)$, according to the statistics of the scan and background counts plus an additional term $(0{\cdot}03S)^2$, where S is the scan count. The intensities and their estimated standard deviations were corrected for Lorentz and polarization factors, but no correction for absorption effects was applied. Structure factors were placed on an approximately absolute scale by means of a K curve (Karle & Hauptman, 1953), and normalized structure factor magnitudes ($|E|$) were derived. The statistical distribution of the $|E|$ values, along with the theoretical values for centrosymmetric space groups given in parentheses, are $\langle|E|\rangle = 0{\cdot}81$ (0·798), $\langle|E^2|\rangle = 1{\cdot}00$ (1·000), $\langle|E^2-1|\rangle = 0{\cdot}96$ (0·968).

A suitable trial structure was obtained by the symbolic addition procedure (Zachariasen, 1952; Karle & Karle, 1963). The starting set of reflections consisted of three origin-defining reflections (1,1,−2, 2,1,−4, 3,18,1) and three reflections assigned symbols (1,29,0, 5 6 0, 2 4 5). Beginning with this set and using a computer program (Thewalt, 1971), we assigned phases or symbols to additional reflections with $|E| > 1{\cdot}4$ by iterative application of the $\sum_2$ formula. During the final iteration cycles one symbol was eliminated, leaving two with a total of four possible phase combinations. E maps were calculated with each of these four phase combinations, and the correct structure was readily recognized in one of the maps. Coordinates for all of the nonhydrogen atoms were obtained from the correct E map.

The trial structure was refined by block-diagonal least-squares methods. The quantity minimized was $\sum w(F_o - 1/k|F_c|)^2$, where k is a scale factor and the weight w is equal to $[2F_o/\sigma(F_o^2)]^2$. Atomic scattering factors for the heavy atoms were obtained from *International Tables for X-ray Crystallography* (1962), and those for hydrogen from Stewart, Davidson & Simpson (1965). Initially, both the heavy-atom positional and anisotropic temperature parameters were refined to an R index $(= \sum||F_o| - |F_c||/\sum|F_o|)$ of 0·16. At this stage, a difference Fourier map clearly revealed the positions of all hydrogen atoms except those bonded to the water molecules. Further refinement of the positional parameters, anisotropic temperature factors for the heavy atoms, and isotropic temperature factors for the hydrogen atoms reduced the R index to 0·15. The general agreement between observed and calculated structure factors was consistent with the estimated errors in the values of $|F_o|$, but 27 reflections showed discrepancies which greatly exceeded the estimated errors. Most of these reflections had very small values of F_o, and it is likely that the measured intensities were affected by decomposition, as well as by the excessive background scattering from the epoxy coating. The 27 reflections were given zero weights, and the refinement was continued to $R = 0{\cdot}14$. A difference Fourier map now revealed the positions of the water hydrogen atoms; coordinates of these hydrogen atoms, along with isotropic temperature parameters, were added to the other parameters in the last cycles of refinement. In the latter stages of refinement, the agreement between observed and calculated structure factors improved considerably for several of the 27 reflections that had

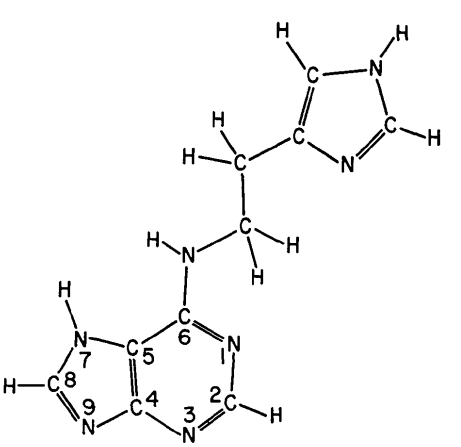

Fig. 1. Structural formula of 6-histaminopurine.

Table 2. *The final heavy-atom parameters and their e.s.d.s*

The β_{22} values have been multiplied by 10^5; all other values have been multiplied by 10^4. The temperature factors are in the form: $T=\exp(-\beta_{11}h^2-\beta_{22}k^2-\beta_{33}l^2-\beta_{12}hk-\beta_{13}hl-\beta_{23}kl)$.

	x	y	z	β_{11}	β_{12}	β_{13}	β_{22}	β_{23}	β_{33}
N(1)	4868(7)	3407(1)	3030(6)	0236(14)	0015(4)	0042(18)	00045(3)	0002(3)	0161(9)
C(2)	2640(9)	3254(1)	1971(8)	0200(17)	0010(5)	0034(24)	00074(5)	0002(4)	0214(12)
N(3)	2007(7)	2857(1)	1614(6)	0178(13)	-0013(4)	-0047(19)	00057(4)	-0008(3)	0168(9)
C(4)	3875(8)	2586(1)	2499(6)	0162(14)	0017(4)	0030(18)	00059(4)	-0001(3)	0105(9)
C(5)	6189(7)	2708(1)	3579(6)	0115(13)	-0002(4)	-0030(19)	00043(4)	0001(3)	0128(9)
C(6)	6707(8)	3133(1)	3882(6)	0186(14)	-0009(4)	0076(19)	00035(4)	-0008(3)	0118(9)
N(6)	8872(7)	3298(1)	4974(6)	0235(14)	0008(4)	0011(19)	00033(3)	0008(3)	0180(9)
N(7)	7465(7)	2340(1)	4144(5)	0163(12)	-0007(4)	-0049(17)	00042(3)	0013(3)	0150(8)
C(8)	5853(9)	2030(1)	3387(7)	0223(17)	-0008(5)	-0011(24)	00045(4)	-0004(4)	0189(11)
N(9)	3640(7)	2157(1)	2312(6)	0202(14)	-0004(4)	0011(19)	00047(3)	-0002(3)	0140(9)
C(10)	9259(9)	3753(1)	5205(7)	0216(17)	0007(4)	-0045(24)	00041(4)	0003(4)	0194(11)
C(11)	11773(9)	3852(1)	6581(6)	0264(17)	-0005(5)	0063(20)	00064(4)	-0004(3)	0100(9)
C(12)	12015(9)	4320(1)	6951(6)	0238(16)	-0002(4)	0061(20)	00039(4)	-0012(3)	0140(10)
C(13)	13719(9)	4589(1)	6623(7)	0278(17)	-0004(5)	0109(24)	00043(4)	0005(4)	0212(12)
N(14)	13124(8)	4974(1)	7201(6)	0380(18)	-0040(4)	0065(23)	00042(3)	-0014(3)	0223(11)
C(15)	11130(11)	4920(2)	7846(9)	0449(23)	0001(6)	0356(30)	00079(6)	-0025(5)	0344(16)
N(16)	10353(9)	4525(1)	7725(8)	0405(18)	-0018(5)	0447(24)	00061(4)	-0029(4)	0437(14)
O(17)	4290(7)	4248(1)	1959(6)	0417(16)	-0008(4)	-0038(22)	00046(3)	0014(3)	0289(10)
O(18)	8318(8)	4013(1)	0027(6)	0548(18)	0083(5)	0350(22)	00165(5)	0040(4)	0289(11)

been assigned zero weights, but we did not include these reflections in the final cycles of refinement. During the final cycle of refinement, no parameter shift exceeded $\frac{1}{5}$ of the e.s.d.

The final R index for all reflections is 0·136. The R index based on F^2 values, $(\sum|F_o^2-F_c^2|\sum F_o^2)$, is 0·112. The goodness-of-fit, $\{\sum[1/\sigma^2(F_o^2)](F_o^2-F_c^2/k^2)^2/(m-s)\}^{1/2}$ where m is the number of reflections used and s is the number of parameters refined, is 2·03. Excluding the hydrogen atom contributions to the calculated structure factors, the R index is 0·162 and the goodness-of-fit is 2·69. The average e.s.d.'s in the positional coordinates of the heavy atoms are 0·003–0·006 Å and those for the hydrogen atoms are 0·03–0·07 Å, corresponding to e.s.d.'s of about 0·008 Å for bond lengths between heavy atoms and 0·07 Å for bond lengths involving hydrogen atoms. The e.s.d.'s in bond angles are approximately 0·5° for angles involving only heavy atoms and 6° for angles involving hydrogen atoms. Since the block-diagonal approximation was used for the least-squares refinement, these e.s.d.'s are probably underestimates of the true values.

At the conclusion of the refinement, a three-dimensional electron density difference map was calculated with only the heavy-atom contributions included in the values for the calculated structure factors. This map showed peaks averaging 0·6 e.Å^{-3} at the hydrogen atom positions, with a range of 0·3 to 0·8 e.Å^{-3}; no other peaks or troughs exceeded 0·55 e.Å^{-3} in magnitude. A final difference Fourier map, calculated with all atoms in the calculated structure factors, showed no peaks or troughs exceeding 0·55 e.Å^{-3} in magnitude.

The final heavy-atom parameters and their e.s.d.'s are listed in Table 2; the hydrogen atom parameters and their standard deviations are listed in Table 3. Observed and calculated structure factors are given in Table 4.

Crystal packing, hydrogen bonding and base stacking

Fig. 2 shows the crystal structure projected down the **c** direction. The hydrogen bonding scheme is shown in Figs. 2 and 3, and the hydrogen bond distances and angles are listed in Table 5. All of the hydrogen atoms that are covalently bonded to nitrogen or oxygen atoms participate in hydrogen bonding. The hydrogen-bonded adenine bases form planar ribbons lying approximately parallel to the $(10\bar{2})$ plane. Within these ribbons, adjacent bases are joined by N(7)–H···N(3) and N(6)–H···N(9) hydrogen bonds. Histamine moieties and water molecules occupy the regions between the stacks of adenine ribbons. There are no contacts between histamine imidazole rings or between the histamine imidazole rings and adenine moieties. The water molecules are hydrogen-bonded together to form chains running parallel to the *a* axis, and are also hydrogen-bonded to atoms N(1), N(14) and N(16).

Table 3. *The final hydrogen atom parameters and their e.s.d.'s*

The positional parameters have been multiplied by 10^3.

	x	y	z	β(Å^2)
H(2)	137 (8)	348 (1)	115 (6)	3·7 (1·1)
H(6)	999 (7)	312 (1)	550 (5)	1·2 (0·8)
H(7)	902 (7)	229 (1)	502 (6)	2·1 (0·9)
H(8)	643 (7)	175 (1)	367 (5)	1·4 (0·8)
H(10)	771 (8)	388 (1)	549 (6)	3·3 (1·1)
H(10′)	919 (9)	388 (1)	392 (7)	4·1 (1·2)
H(11)	1324 (12)	373 (2)	604 (9)	8·8 (1·9)
H(11′)	1195 (7)	373 (1)	786 (5)	1·3 (0·8)
H(13)	1528 (8)	453 (1)	611 (6)	2·9 (1·0)
H(14)	1393 (12)	525 (2)	734 (9)	8·0 (1·9)
H(15)	1017 (10)	514 (2)	833 (8)	6·0 (1·5)
H(17)	457 (10)	400 (2)	248 (8)	6·9 (1·6)
H(17′)	268 (11)	427 (2)	140 (8)	7·1 (1·7)
H(18)	875 (11)	423 (2)	−78 (9)	8·5 (1·9)
H(18′)	707 (12)	405 (2)	42 (10)	10·0 (2·2)

The adenine moieties are stacked forming continuous columns which run parallel to the *c* axis. Within these columns adjacent base planes are approximately parallel (the dihedral angle between adjacent planes is 2°) and are separated by an average interplanar spacing of 3·3–3·6 Å. The base stacking pattern, as viewed perpendicular to the adenine ring, is depicted in Fig. 3. The bases are stacked in an alternating pattern, with the imidazole rings of adjacent bases pointing in opposite directions. This same general type of alternating pattern has been noted in numerous other crystal structures of adenine derivatives (Bugg *et al.*, 1971; Bugg, 1971). Fig. 3 shows that the stacking pattern entails a small amount of base overlap, with atoms N(9) and C(8) of one base positioned above the ring system of an adjacent adenine moiety. This type of stacking, with hetero-atoms of one base interacting with the ring of a parallel base, is present in most crystal structures of purine and pyrimidine derivatives (Bugg *et al.*, 1971).

The molecular structure

Bond distances and angles are given in Fig. 4. Table 6 lists deviations from the least-squares plane through the adenine ring. Table 7 shows deviations from the

least-squares plane through the histamine imidazole ring.

An outstanding feature of the structure is that the adenine moiety assumes the N(7)–H, rather than the N(9)–H, tautomer form. In addition to the evidence obtained from the location and refinement of hydrogen atoms, the presence of the N(7)–H tautomer form is obvious from the hydrogen bonding scheme: N(7) is hydrogen-bonded to N(3) (an acceptor site) and N(9) is hydrogen-bonded to N(6) (a donor site). The bond lengths and angles within the imidazole ring of the adenine moiety are as expected for the N(7)–H tautomer. In particular, the observation that the C(8)–N(7)–C(5) angle is 4·6° larger than the C(8)–N(9)–C(4) angle is consistent with earlier evidence that the internal bond angles at nitrogen atoms of heterocyclic rings are greater for those N atoms with an extra-annular substituent than for those possessing no substituent (Voet & Rich, 1970; Sundaralingam & Jensen, 1965; Singh, 1965). The finding that the

Table 4. *Observed and calculated structure factors*

From left to right, the columns contain values of k, $10F_o$, and $10F_c$. An asterisk signifies a reflection which was assigned zero weight during the latter stages of refinement (see text).

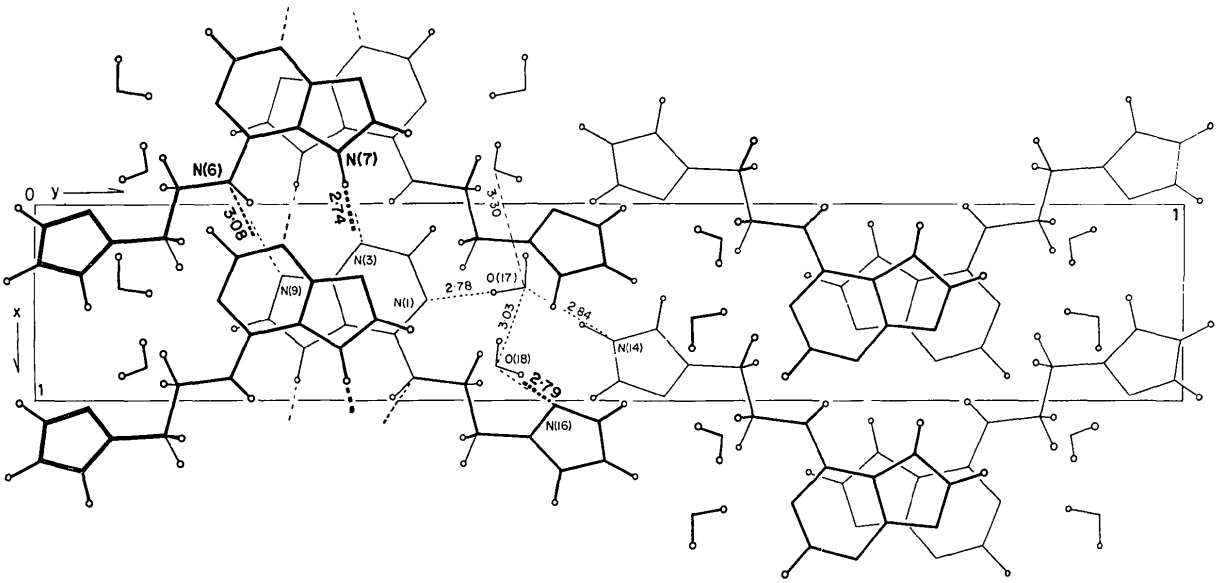

Fig. 2. The structure viewed down the *c* axis. Dashed lines represent hydrogen bonds.

Table 5. *Hydrogen bond distances and angles*

(The relative positions of the donor and acceptor atoms can be seen in Fig. 2.).

Donor atom	Hydrogen atom	Acceptor atom	Donor–acceptor	Hydrogen–acceptor	Donor–hydrogen–acceptor angle
N(7)	H(7)	N(3) (*a*)	2·739 Å	1·80 Å	175°
N(6)	H(6)	N(9) (*a*)	3·083	2·27	160
N(14)	H(14)	O(17) (*b*)	2·840	1·89	170
O(17)	H(17)	N(1) (*c*)	2·784	1·94	166
O(17)	H(17′)	O(18) (*d*)	3·298	2·49	155
O(18)	H(18)	O(17) (*c*)	3·029	2·22	167
O(18)	H(18′)	N(16) (*e*)	2·789	1·84	163

(*a*) $x+1, -y+\frac{1}{2}, z+\frac{1}{2}$ (*d*) $x-1, y, z$
(*b*) $-x+2, -y+1, -z+1$ (*e*) $x, y, z-1$
(*c*) x, y, z

Table 6. *Deviations* (Å) *of atoms from the least-squares plane through the purine ring*

The equation of the least-squares plane, where the coefficients of *X*, *Y*, and *Z* are equal to direction cosines with respect to the axes *a*, *b*, and *c**, and *X*, *Y*, and *Z* are orthogonal coordinates (Å), is:

$$0{\cdot}5902\,X+0{\cdot}0211\,Y-0{\cdot}8070\,Z=-0{\cdot}271 \text{ Å}.$$

N(1)	0·002†	C(8)	−0·016†
C(2)	−0·006†	N(9)	0·012†
N(3)	0·007†	C(10)	−0·014
C(4)	−0·011†	H(2)	0·16
C(5)	0·007†	H(6)	−0·05
C(6)	−0·004†	H(7)	−0·09
N(6)	−0·039	H(8)	−0·05
N(7)	0·009†		

† Atoms included in the calculation of the plane.

Table 7. *Deviations* (Å) *of atoms from the least-squares plane through the imidazole ring*

The equation of the least-squares plane, where the coefficients of *X*, *Y*, and *Z* are equal to direction cosines with respect to the axes *a*, *b*, and *c**, and *X*, *Y*, *Z* are orthogonal coordinates (Å), is:

$$-0{\cdot}3626\,X+0{\cdot}1764\,Y-0{\cdot}9151\,Z=-3{\cdot}970 \text{ Å}.$$

C(12)†	0·000
C(13)†	−0·001
N(14)†	0·002
C(15)†	−0·002
N(16)†	0·001
C(11)	−0·003
H(13)	−0·05
H(14)	−0·09
H(15)	0·04

† Atoms included in the calculation of the plane.

N(7)–C(8) bond is longer than the C(8)–N(9) bond is also consistent with the presumed N(7)–H tautomer form. Since purine nucleosides and nucleotides have sugar residues bonded to the N(9) position, it is generally assumed that the free purine bases are in the N(9)–H tautomer form. However, there is no clear preference for the N(9)–H tautomer form in crystals of purines. Purine (Watson, Sweet & Marsh, 1965), thioguanine (Bugg & Thewalt, 1970), 6-mercaptopurine (Brown, 1969; Sletten, Sletten & Jensen, 1969), theophylline (Sutor, 1958), and 2-mercapto-6-methylpurine (Donohue, 1969) also crystallize as N(7)–H tautomers.

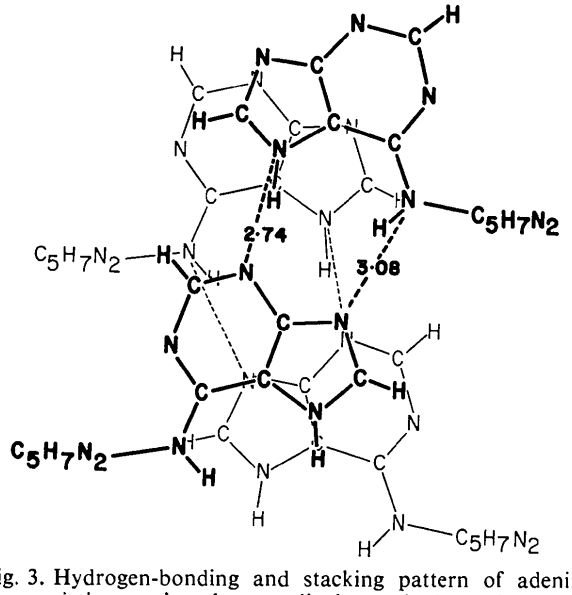

Fig. 3. Hydrogen-bonding and stacking pattern of adenine moieties, as viewed perpendicular to the base plane.

The tautomer form of the imidazole ring of the histamine moiety is also noteworthy, since there are two feasible tautomer forms for this ring: the N(14)–H or the N(16)–H form. In this structure, the hydrogen atom is bonded to N(14). As expected for this tautomer, the C(13)–N(14)–C(15) angle is significantly larger than the C(12)–N(16)–C(15) angle. This tautomer form is also displayed by the imidazole ring in the crystal structure of *l*-histidine (Madden & McGandy, 1970; Madden, McGandy & Seeman, 1970). As in the crystal structure of histamine diphosphate monohydrate (Veidis, Palenik, Schaffrin & Trotter, 1969), the histamine moiety assumes the fully extended conformation, with atom N(6) lying *trans* to atom C(12).

Fig. 5 shows a view of the 6-histaminopurine molecule, including the ellipsoids of thermal vibration.

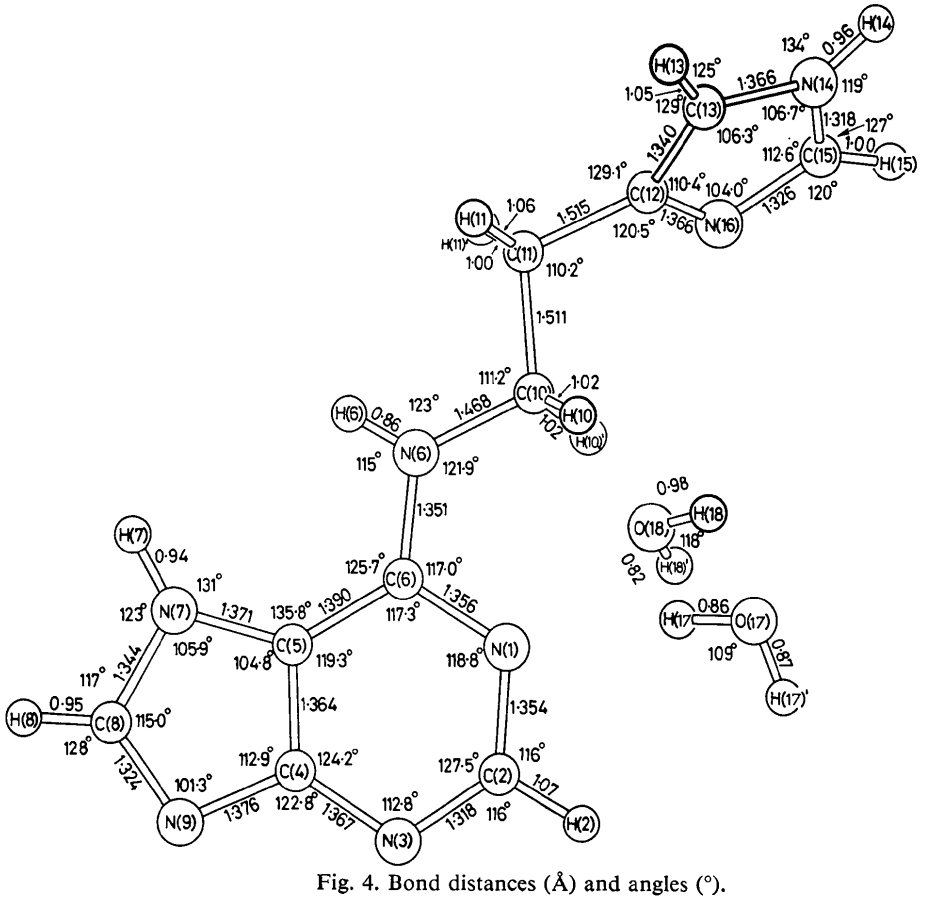

Fig. 4. Bond distances (Å) and angles (°).

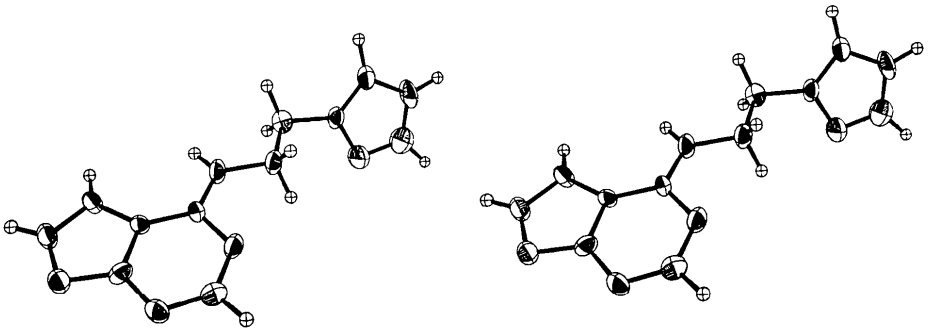

Fig. 5. Stereoscopic view of the 6-histaminopurine molecule. The heavy atoms are represented by ellipsoids, defined by the principal axes of thermal vibration and scaled to include 50% probability. The hydrogen atoms are represented by spheres of 0·1 Å radius. This drawing was prepared using the computer program *ORTEP* (Johnson, 1965).

The computer programs used in this study included the thermal-ellipsoid plotting program *ORTEP* (Johnson, 1965), and a block-diagonal least-squares program obtained from Dr James Trotter at the University of British Columbia. The other programs were written in our laboratories.

This work was supported, in part, by U.S.P.H.S. Research Grant DE-02670 from the National Institute of Dental Research and N.I.H. Research Grant RR-145. We thank Dr Johnson and Dr Trotter for furnishing copies of their programs, and Dr Werner and Mr Bieger for providing samples of the compound.

References

BROOM, A D., SCHWEIZER, M. P. & TS'O, P. O. P. (1967). *J. Amer. Chem. Soc.* **89**, 3612.

BROWN, G. M. (1969). *Acta Cryst.* B**25**, 1338.

BUGG, C. E. (1971). In the proceedings of *The Fourth Jerusalem Symposium on the Purines: Theory and Experiment*. New York: Academic Press.

BUGG, C. E. & THEWALT, U. (1969). *Biochem. Biophys. Res. Commun.* **37**, 623.

BUGG, C. E., THEWALT, U. (1970). *J. Amer. Chem. Soc.* **92**, 7441.

BUGG, C. E. & THEWALT, U. & MARSH, R. E. (1968). *Biochem. Biophys. Res. Commun.* **33**, 436.

BUGG, C. E., THOMAS, J. M., SUNDARALINGAM, M. & RAO, S. T. (1971). *Biopolymers*, **10**, 175.

CHAN, S. I., SCHWEIZER, M. P., TS'O, P. O. P. & HELMKAMP, G. K. (1964). *J. Amer. Chem. Soc.* **86**, 4182.

DONOHUE, J. (1969). *Acta Cryst.* B**25**, 2418.

International Tables for X-Ray Crystallography (1962). Vol. III, p. 202. Birmingham: Kynoch Press.

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Oak Ridge, Tennessee.

KARLE, J. & HAUPTMAN, H. (1953). *Acta Cryst.* **6**, 473.

KARLE, I. L. & KARLE, J. (1963). *Acta Cryst.* **16**, 969.

LETTRÉ, H. (1960). *Prog. Exp. Tumor Res.* **1**, 329.

LETTRÉ, H. & WERNER, D. (1968). *Naturwissenschaften* **55**, 43.

MADDEN, J. J. & MCGANDY, E. L. (1970). Abstracts, American Crystallographic Association Meeting, Columbia, South Carolina, Paper 05.

MADDEN, J. J., MCGANDY, E. L. & SEEMAN, N. C. (1970). Private communication.

SINGH, C. (1965). *Acta Cryst.* **19**, 861.

SLETTEN, E., SLETTEN, J. & JENSEN, L. H. (1969). *Acta Cryst.* B**25**, 1330.

SOLIE, T. N. & SCHELLMAN, J. A. (1968). *J. Mol. Biol.* **33**, 61.

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

SUNDARALINGAM, M. & JENSEN, L. H. (1965). *J. Mol. Biol.* **13**, 930.

SUTOR, D. J. (1958). *Acta Cryst.* **11**, 83.

THEWALT, U. (1970). *Z. Kristallogr.* **132**, 454.

THEWALT, U., BUGG, C. E. & MARSH, R. E. (1970). *Acta Cryst.* B**26**, 1089.

TS'O, P. O. P. (1968). *Molecular Associations in Biology*, pp. 39-76. Edited by B. PULLMAN. New York: Academic Press.

VEIDIS, M. V., PALENIK, G. J., SCHAFFRIN, R. & TROTTER, J. (1969). *J. Chem. Soc.* (*A*), p. 2659.

VOET, D. & RICH, A. (1970). *Progress in Nucleic Acid Research and Molecular Biology*. Vol. 10, pp. 183-265, Edited by J. N. DAVIDSON & W. E. COHN. New York: Academic Press.

WATSON, D. G., SWEET, R. M. & MARSH, R. E. (1965). *Acta Cryst.* **19**, 573.

ZACHARIASEN, W. H. (1952). *Acta Cryst.* **5**, 68.