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Non-Planarity of Hydroxamic Acids. Structures of 3-Hydroxyxanthine Dihydrate by X-ray Diffraction and Hydroxyurea by Neutron Diffraction*

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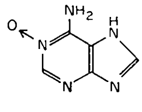
The crystal structures of 3-hydroxyxanthine dihydrate and hydroxyurea both display pyramidality at the N atom to which the hydroxyl group is attached. The effect is measured by a 0·19 Å displacement of the hydroxyl O atom from the best plane of the aromatic ring in 3-hydroxyxanthine, and by a 0·23 Å displacement of the H atom bound to hydroxylated N from the best plane through the heavy atoms in hydroxyurea. The effect appears to be characteristic of hydroxamic acids. An explanation in terms of molecular bonding is proposed. Crystal data based on $\lambda(\mathrm{Cu}\ K\alpha_1) = 1{\cdot}54051$ Å and some particulars of the structure determination follow. 3-Hydroxyxanthine dihydrate: triclinic, $P\bar{1}$, $Z = 2$, cell parameters changed with X-ray exposure; stable values and precision measures after ~100 h exposure are $a = 7{\cdot}8383\ (1)$, $b = 8{\cdot}4054\ (2)$, $c = 7{\cdot}4408\ (1)$ Å, $\cos\alpha = -0{\cdot}41039\ (2)$, $\cos\beta = -0{\cdot}32227\ (3)$, $\cos\gamma = 0{\cdot}40919\ (3)$, $\alpha = 114{\cdot}229\ (1)$, $\beta = 108{\cdot}800\ (2)$, $\gamma = 65{\cdot}846\ (2)°$, $t = 23 \pm 2\,°\mathrm{C}$. Solution by reiterative application of Sayre's equation, least-squares refinement, 2138 observations, $R(F) = 0{\cdot}038$. Hydroxyurea: monoclinic, $P2_1/c$, $a = 8{\cdot}3962\ (2)$, $b = 4{\cdot}9026\ (2)$, $c = 8{\cdot}8060\ (2)$ Å, $\cos\beta = -0{\cdot}51820\ (2)$, $\beta = 121{\cdot}212\ (1)°$, $t = 24\,°\mathrm{C}$. The H atoms of the hydroxyurea structure [Berman & Kim (1967), *Acta Cryst.* **23**, 180–181] were precisely located by neutron diffraction; least-squares refinement, 1955 observations, $R(F) = 0{\cdot}042$.

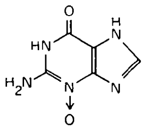
Introduction

Many low molecular weight compounds which share the property of inducing tumor formation, although having widely disparate structures, have been grouped together under the general heading of chemical carcinogens, or, more properly, following Stöhrer & Brown (1970), chemical oncogens. Several of the most potent of these are, or are transformed *in vivo* into, aromatic nitrogen compounds capable of electrophilic attack on cell components, thereby initiating the process of oncogenesis according to Miller & Miller (1969). Examples are 2-*N*-hydroxyacetylaminofluorene (Miller, Miller & Hartmann, 1961; Miller, Enomato & Miller, 1962) and 4-hydroxyaminoquinoline *N*-oxide (Shirasu, 1965).

It has been found by Brown and co-workers (Sugiura, Teller, Parham & Brown, 1970) that certain *N*-oxygenated purines, characterized as adenine 1-oxide (Stevens & Brown, 1958) (I), guanine 3-oxide (II), and 3-hydroxyxanthine (Wölcke & Brown, 1969) (III) (see Fig. 2 for the numbering system), have oncogenic properties. Compounds (II) and (III) undergo facile rearrangement to 8-hydroxy derivatives in the course of acetylation and other reactions (Wölcke, Pfleiderer, Delia & Brown, 1969) and consequently were initially erroneously identified as 7-*N*-oxides (Delia & Brown, 1966). The molecule of compound (III) contains a hydroxamic acid group and, as no detailed study of the molecular geometry of this functional group had been made, 3-hydroxyxanthine was chosen for this initial investigation by X-ray diffraction. Samples of all three compounds were kindly provided by Dr G. B. Brown of the Sloan–Kettering Institute for Cancer Research.



(I)



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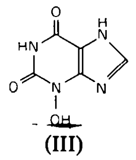

(III)

When this study revealed the pyramidal configuration of the N atom of the hydroxamic acid group, it was deemed desirable to examine another, preferably simpler, hydroxamic acid. Hydroxyurea is such a molecule; reliable positions of the non-hydrogen atoms as well as rough positions for H atoms were known from earlier X-ray diffraction studies (Larsen & Jerslev, 1966; Berman & Kim, 1967) but as one of the ligands of the hydroxylated N atom is an H atom whose position had not been accurately determined, a study by neutron diffraction was made.

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Experimental*

The sample of 3-hydroxyxanthine dihydrate as received included crystals suitable for study. Precession photographs showed no systematic absences and only Friedel symmetry. An arbitrary triclinic cell was chosen and reduced to the conventional cell by a simple application of the program *ORTEP*-II in which the lengths of all vectors from one lattice point to all others within 20 Å and the angles between them were computed. The absence of special angle values (60, 90, or 120°) confirmed the triclinic symmetry; reduced cell dimensions and angles were then assigned according to standard conventions (Donnay & Ondik, 1972) from the lists of vectors and angles.

The unit-cell parameters of 3-hydroxyxanthine dihydrate were determined four times during the course of data collection by a unit-weight least-squares adjustment in which the observations were the three diffractometer coordinates 2θ, ω, and φ in the parallel setting (χ fixed at 90°) for the Cu $K\alpha_1$ diffraction maxima of 12 high-angle Bragg reflections ($136° < 2\theta < 159°$). The standard error of an observation estimated from the sum of squares of the residuals was 0·010°. The calculated density for $Z = 2$ formula units of the dihydrate is 1·69 g cm^{-3}, to be compared with 1·67 g cm^{-3} observed by flotation in a mixture of chlorinated hydrocarbons. It was found that the unit-cell parameters changed during the course of data collection, presumably as a result of X-ray exposure; all three cell edges increased in length, the largest increase, about 0·05% (27σ), being along **a**. As is shown in Table 1, the values are substantially stable after about 65 h of exposure; the final measurements (about 100 h exposure) are those listed in the abstract.

Cell parameters for hydroxyurea were determined by X-ray diffraction on a small specimen at 21·1 and at 24·0°C, based on $\lambda(\text{Cu } K\alpha_1) = 1{\cdot}54051$ Å, using 15 reflections with $145° < 2\theta < 158°$. The following values were obtained:

t (°C)	a (Å)	b (Å)	c (Å)
21·8	8·3946 (2)	4·9023 (2)	8·8055 (2)
24·0	8·3962 (2)	4·9026 (2)	8·8060 (2)

	$\cos\beta$	β (°)
21·8	−0·51824 (3)	121·214 (2)
24·0	−0·51820 (2)	121·212 (1).

These values are within the standard error ranges of the previous studies.

X-ray data and analysis

Intensity data for 3-hydroxyxanthine dihydrate were recorded by means of the Oak Ridge computer-controlled X-ray diffractometer with Cu $K\alpha$ radiation for $2\theta < 160°$ (Ni-filtered for $2\theta < 130°$, unfiltered for $2\theta > 130°$) and with Cu $K\beta$ radiation (unfiltered) for $129{\cdot}5° < 2\theta < 160°$. Integration was done by the θ–2θ scan (moving counter, moving crystal) method for $2\theta > 40°$ and by the ω-scan (stationary counter, moving crystal) method for $2\theta < 65°$; in the overlapped region, intensities after normalization were in good agreement. Reference reflections were measured periodically during the data collection and used to normalize the data by linear interpolation between consecutive reference measurements. After normalization, structure factors from replicate (non-reference) measurements with different X-ray exposures were in good agreement, indicating that no substantial structural change accompanied the increase in cell parameters. For calculation of the absorption correction ($\mu = 1{\cdot}342$ mm^{-1} for Cu $K\alpha$, 0·998 mm^{-1} for Cu $K\beta$), the specimen dimensions (approximately 0·4 × 0·25 × 0·2 mm) and its orientation were directly measured by means of a travelling bifilar eyepiece on a microscope attached to the goniostat; the procedure consists of finding the χ and φ angle values at which each face (or approximate plane surface) is perpendicular to the diffraction-vector direction when $\omega = 0$, and the distance of the face from the instrument center. After reduction to structure-factor squares, data obtained at the different wavelengths were normalized by means of common structure factors (program *DATALIB*) and replicate and symmetry-equivalent values were averaged

Table 1. *Unit-cell parameters of* 3-*hydroxyxanthine dihydrate as a function of exposure to X-rays*

	Hours of X-ray exposure			
	<5	~21	~64	~100
a (Å)	7·83447 (13)	7·83611 (14)	7·83862 (18)	7·83834 (13)
b (Å)	8·40467 (19)	8·40483 (22)	8·40561 (28)	8·40536 (18)
c (Å)	7·44005 (12)	7·44023 (12)	7·44050 (15)	7·44083 (11)
$\cos\alpha$	−0·41017 (2)	−0·41026 (2)	−0·41038 (3)	−0·41039 (2)
$\cos\beta$	−0·32222 (3)	−0·32223 (4)	−0·32225 (5)	−0·32227 (3)
$\cos\gamma$	0·40901 (3)	0·40906 (3)	0·40922 (4)	0·40919 (3)

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* Computer programs used in this study were: *DATALIB* and *DATASORT*, for data reduction, by H. A. Levy and R. D. Ellison; *ORESTES*, for the calculation of normalized structure factors and their statistics, by W. E. Thiessen and H. A. Levy; *FORDAP*, for Fourier calculations, by A. Zalkin; *ORXFLS* for least-squares refinement (based on *ORFLS*, Busing, Martin & Levy, 1962); *ORFFE*, for function and error calculations (Busing & Levy, 1964); *ORTEP*-II, for stereo drawings (Johnson, 1976); *REL*, for direct phasing, by R. E. Long; and *ORSBA*, for rigid-body-motion analysis and distance corrections, by C. K. Johnson.

(program *DATASORT*). The raw set of 3204 measurements was thus reduced to 2138 symmetry-independent values and their standard errors,* which were used as input for the generation of normalized structure factor magnitudes, E (program *ORESTES*), and later as input for least-squares refinement (program *ORXFLS*). Statistical tests for the magnitude distribution of E indicated that the structure is centrosymmetric, space group $P\bar{1}$.

Structure solution using Long's (1965) computer program for iterative application of Sayre's (1952) equation was straightforward and led to an E map which shows the expected 14 C, N and O atoms as the 14 highest peaks. Full-matrix least-squares refinement minimized the function $\sum w(F_o^2 - yS^2F_c^2)^2$ with $w = [\sigma_o^2 + (0{\cdot}03F_o^2)^2]^{-1/2}$. The parameters adjusted were the position parameters of all atoms, isotropic thermal parameters for H atoms, anisotropic thermal parameters for other atoms, four scale factors, and an isotropic extinction parameter from which the extinction correction factor y was evaluated according to the procedure of Coppens & Hamilton (1970).

The final measures of disagreement were as follows:†

	R_1	R_2	wR_2	σ_1
All 2138 reflections	0·038	0·049	0·110	2·69
2046 reflections, $F^2 > \sigma(F^2)$	0·036	0·049	0·109	2·74.

In the final difference map of residual electron density (Fig. 1, see caption), 10 of the 11 highest maxima occur near the midpoints of chemical bonds of the aromatic rings, indicating that the present model, which does not provide for bonding electron density, is incomplete. Table 2 lists the final atomic coordinates for the structure from least-squares refinement using all data. Atomic scattering amplitudes for C, N, and O were those from Hanson, Herman, Lea & Skillman (1964) and those for H from Stewart, Davidson & Simpson (1965).

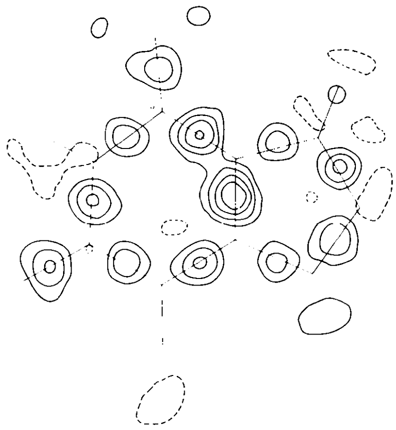

Fig. 1. An oblique section through the final difference electron density map in the plane of the aromatic ring. The contour interval is 0·1 e Å^{-3}. The subtracted structure factors were based on parameters from three cycles of a special least-squares refinement in which only the 1033 structure factors for which $\sin^2\theta/\lambda^2$ exceeded 0·3 were used.

Table 2. *Fractional coordinates* (× 10^4 *for non-hydrogen atoms;* × 10^3 *for hydrogen atoms*) *for 3-hydroxyxanthine dihydrate*

	x	y	z
N(1)	4305 (1)	3034 (1)	1795 (1)
C(2)	3309 (1)	4186 (1)	3323 (1)
N(3)	1944 (1)	5751 (1)	3013 (1)
C(4)	1597 (1)	6103 (1)	1258 (1)
C(5)	2622 (1)	4891 (1)	−230 (1)
C(6)	4079 (1)	3226 (1)	−51 (1)
N(7)	1904 (1)	5687 (1)	−1725 (1)
C(8)	543 (2)	7268 (2)	−1071 (2)
N(9)	291 (1)	7589 (1)	759 (1)
O(10)	3637 (1)	3824 (1)	4871 (1)
O(11)	729 (1)	6842 (1)	4363 (1)
O(12)	5071 (1)	2063 (1)	−1270 (1)
O(*W*1)	2209 (1)	9426 (1)	6754 (1)
O(*W*2)	2720 (1)	10518 (1)	4075 (1)
H(1)	522 (3)	210 (3)	210 (3)
H(7)	230 (2)	521 (2)	−289 (3)
H(8)	−21 (2)	804 (2)	−190 (2)
H(11)	118 (3)	772 (3)	519 (3)
H(*W*1)	150 (3)	1025 (3)	755 (3)
H(*W*2)	246 (3)	986 (3)	584 (4)
H(*W*3)	323 (3)	1142 (3)	466 (4)
H(*W*4)	344 (3)	963 (3)	313 (3)

Neutron data and analysis

A 20·8 mg crystal of hydroxyurea was grown by slow evaporation from aqueous solution. Neutron intensity measurements were made on the Oak Ridge computer-controlled neutron diffractometer at the High Flux Isotope Reactor at a temperature of 24 ± 2 °C on 1995 reflections comprising two symmetry-related sets with $2\theta < 130°$ for $\lambda = 1{\cdot}248$ Å. Integrations employed the θ–2θ scan technique, with counts made at intervals of 0·05° over a span of 4·0° for $2\theta \le 70°$ and $4{\cdot}0° + 0{\cdot}01(2\theta - 70{\cdot}0°)$ for $2\theta > 70°$. Backgrounds were measured at the end points of each scan. The neutron beam was monochromatized by reflection from Be(103) at a scattering angle of 75°.

The measurements were reduced to 1000 symmetry-independent structure factors, which were assigned phases calculated from the C, N, and O positions given by Berman & Kim (1967). Full-matrix least-squares refinement, which minimized the same function as for 3-hydroxyxanthine dihydrate, included in the final

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* Lists of structure factors and anisotropic temperature parameters for both compounds have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33460 (28 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

† $R_k = \sum |F_o|^k - |F_c|^k/\sum |F_o|^k$, $k = 1, 2$; for $k = 1$, $F_o = 0$ when $F_o^2 < 0$; $wR_2 = [\sum w(F_o^2 - F_c^2)^2]^{1/2}/\sum wF_o^2$, $\sigma_1 = [\sum w(F_o^2 - F_c^2)^2/(n - p)]^{1/2}$; n = number of observations, p = number of adjusted parameters.

stages an anisotropic extinction correction* of type 1 (Coppens & Hamilton, 1970). It became clear as refinement proceeded that this correction was inadequate for the strongest reflections; consequently, 40 reflections for which the extinction correction factor on F^2 exceeded 2·5 were ultimately omitted.

The final measures of disagreement were:

	R_1	R_2	wR_2	σ_1
1955 retained reflections	0·042	0·054	0·066	1·73
1785 retained reflections with $F^2 > \sigma(F^2)$	0·036	0·054	0·066	1·79.

Table 3 lists the final coordinates.

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* The use of anisotropic extinction requires that symmetry-related structure factors be entered as separate observations in the least-squares refinement.

Table 3. *Fractional coordinates* (× 10^4) *for hydroxyurea*

	x	y	z
C(1)	2745 (1)	262 (1)	271 (1)
N(2)	3558 (1)	2433 (1)	62 (1)
N(3)	1594 (1)	−1231 (1)	−1176 (1)
O(4)	3019 (1)	−485 (2)	1751 (1)
O(5)	1252 (1)	−385 (2)	−2825 (1)
H(6)	4538 (3)	3395 (4)	1160 (2)
H(7)	3263 (3)	3001 (3)	−1153 (2)
H(8)	697 (3)	−2579 (4)	−1195 (2)
H(9)	1900 (2)	−1793 (3)	−3122 (2)

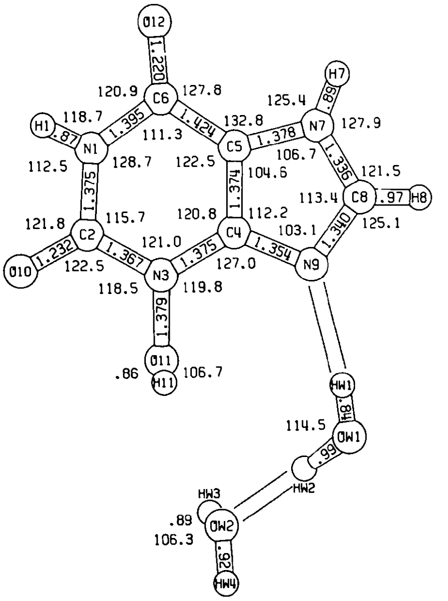


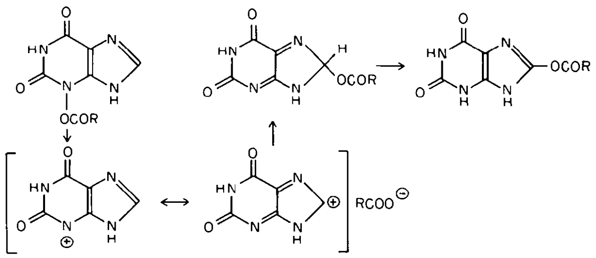
Fig. 2. The numbering system, bond lengths (Å) and valence angles (°) in the 3-hydroxyxanthine and associated water molecules. Estimated standard deviations: 0·001 Å for distances between non-hydrogen atoms, 0·02 Å for those involving H atoms; 0·1° for angles not involving H, 1·2° for those involving one H, and 2° for those involving two H atoms.

Results and discussion

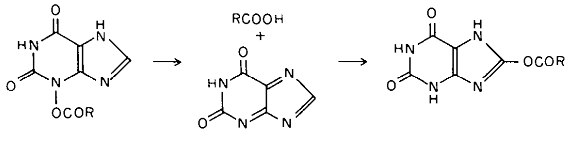
3-*Hydroxyxanthine dihydrate*

The structure analysis yielded the molecular structure shown with bond distances and bond angles in Fig. 2. Like purine (Watson, Sweet & Marsh, 1965) and 6-mercaptopurine (Brown, 1969), 3-hydroxyxanthine is revealed to exist as the N(7)–H tautomer. Although purine chemists seem to use N(7)–H and N(9)–H tautomers interchangeably when writing structural formulas, sometimes even in the same paper (Sugiura *et al.*, 1970), crystallographic results consistently indicate the N(7)–H tautomer to be the more stable.

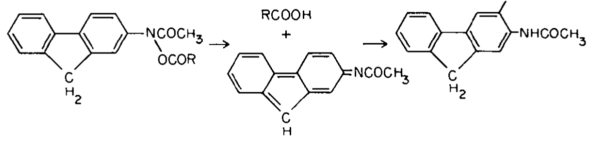
The proper tautomer assignment is pertinent in formulating pathways for reactions of 3-hydroxyxanthine and its analogues. For example, the pathway proposed for the rearrangement reaction from 3-oxy to 8-oxy species by Wölcke, Pfleiderer, Delia & Brown (1969) assumes the N(9)–H tautomer and is applicable to the N(7)–H structure only with the assumption that the reaction proceeds through N(9)–H intermediates.



An appealing alternative pathway assumes a neutral 'dehydro-xanthine' (IV) intermediate. It is interesting that the known rearrangement of 2-hydroxyaminofluorene esters can be formulated with an analogous intermediate (V) with a $4n$ π-electron configuration.



(IV)



(V)

For 3-hydroxyxanthine dihydrate the bond distances and angles shown in Fig. 2 (uncorrected for apparent shortening produced by thermal motion) are, by and large, normal, indicating the expected degree of delocalization of π electrons and suggesting that the molecule should be substantially planar. The most striking feature of the structure is that N(3) is distinctly pyramidal. The pyramidality, as displayed in Table 4, is manifested by the departure by 0·188 Å of O(11) from the best plane through all the atoms of the ring system except N(1). Deviations of N(1) and O(10) from this plane are also significant. A careful examination of the hydrogen bonding and other pertinent molecular contacts fails to suggest an explanation of these deviations from planarity in terms of packing (Fig. 3). In fact, as described below, the deviation results in an exceptionally short contact between adjacent molecules. Nevertheless, the lingering possibility that packing forces might somehow give rise to the observed distortion led us to examine a second case, that of hydroxyurea.

Hydroxyurea

The molecular structure resulting from the neutron-diffraction analysis, together with bond distances and bond angles (the cell parameters for 22 °C were used), is shown in Fig. 4. In contradistinction to 3-hydroxyxanthine, the hydroxamic acid O atom lies approximately in the plane of the remaining non-hydrogen atoms, as shown in Table 5. Nevertheless, the hydroxamic acid N(3) atom is pyramidal, as indicated by the departure of H(8) from the plane by 0·231 Å. The amino group H atoms H(6) and H(7) also have moderate deviations from the best plane.

As may be seen in Fig. 5, a packing diagram of the structure, the departures from the plane of H(6) and H(7) may be attributed to the influence of hydrogen bonding. The situation is further detailed in Fig. 6, from which it is clear that the N(2)–H(6)···O(4) and N(2)–H(7)···O(4) hydrogen bonds are shorter and straighter than they would be if H(6) and H(7) were closer to the molecular plane.

The larger deviation of H(8) cannot be explained in this way. Indeed, Fig. 6 shows that if H(8) were to move toward the molecular plane, an intermediate position would cause the N(3)–H(8)···O(5) hydrogen bond to be shorter and straighter. Thus the influence of hydrogen bonding is to tend to decrease the observed pyramidality of N(3).

Table 4. *Distances* (Å) *of atoms from a least-squares plane fitted to all the ring atoms except* N(1) *in the* 3-*hydroxyxanthine molecule*

Atoms in the right-hand column were not used to determine the plane

C(2)	0·0000 (7)	C(6)	0·0003 (6)	N(1)	0·0148 (12)
N(3)	0·0025 (8)	N(7)	0·0009 (8)	O(10)	−0·0114 (13)
C(4)	−0·0014 (9)	C(8)	0·0025 (9)	O(11)	−0·1881 (13)
C(5)	−0·0023 (9)	N(9)	−0·0025 (7)	O(12)	0·0025 (15)

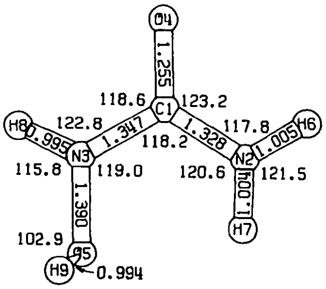


Fig. 4. The numbering system, bond lengths (Å) and valence angles (°) in the hydroxyurea molecule. Estimated standard deviations: 0·0008 Å for distances between non-hydrogen atoms, 0·0016 Å for those involving H atoms; 0·05° for angles not involving H, 0·1° for those involving one H, and 0·14° for that involving two H atoms.

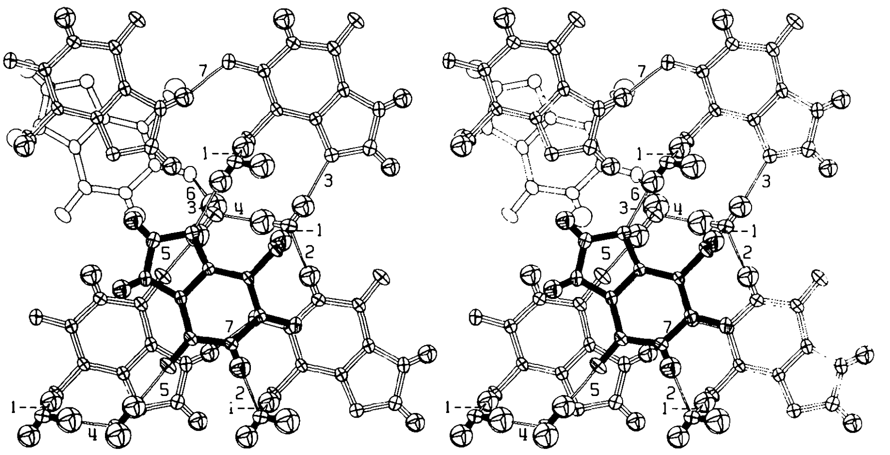


Fig. 3. A stereoscopic view of the crystal packing in 3-hydroxyxanthine dihydrate. The view direction is normal to the molecular plane. The horizontal translation left to right is **c** and the approximately vertical translation, bottom to top, is **b**–**a**. The translation from the bottom-layer molecule to the top-layer molecule is **b**. The numerals identify the hydrogen bonds whose characteristics are listed in Table 6.

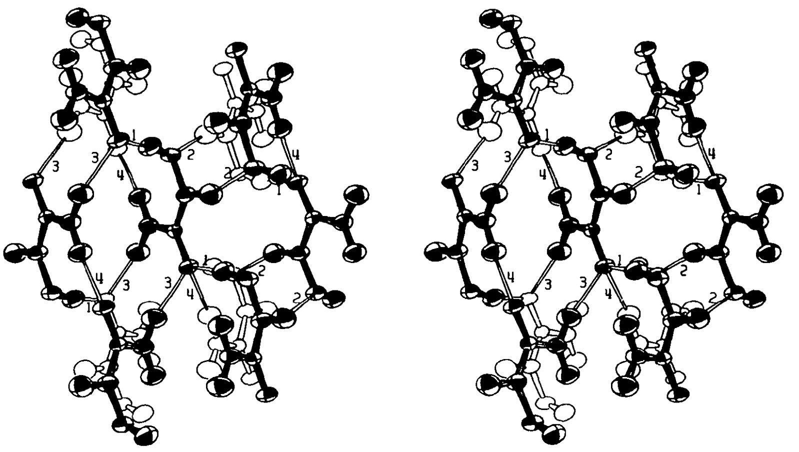


Fig. 5. A stereoscopic view of the crystal packing in hydroxyurea. The view direction is along −**b**. The horizontal translation right to left is **a**. The numerals identify hydrogen bonds whose characteristics are listed in Table 7.

Table 5. *Distances* (Å) *of atoms from a least-squares plane fitted to* C(1), N(2), N(3), *and* O(4) *in the hydroxyurea molecule*

C(1)	−0·0054 (5)	O(5)	−0·0353 (13)
N(2)	0·0018 (2)	H(6)	0·1162 (22)
N(3)	0·0017 (2)	H(7)	−0·0394 (21)
O(4)	0·0019 (2)	H(8)	−0·2310 (23)
		H(9)	0·8741 (20)

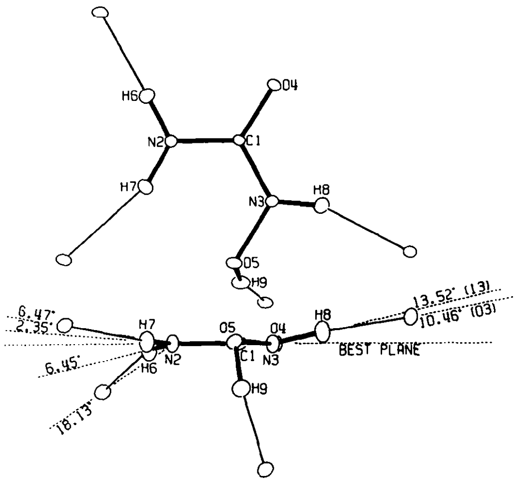


Fig. 6. Two views of the hydroxyurea molecule showing the geometry of the hydrogen bonds formed by each H atom in the molecule. The angles are the inclinations of the N—H and N···O vectors from the best plane.

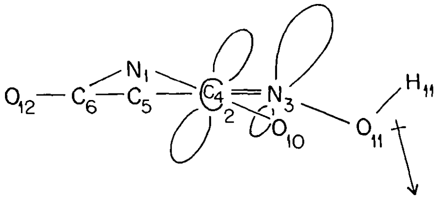


Fig. 7. Diagram illustrating the source of non-planarity in the 3-hydroxyxanthine molecule. The view is along the C(2) → C(4) vector. The 'π' orbitals of C(2) and N(3), as perturbed by the O(11) lone-pair dipole moment (arrow), are schematically indicated.

Explanation in terms of bonding

It follows from the octet rule that there can be no π-electron delocalization from the O atom of the hydroxamic acid group to the N atom to which it is attached. Thus, unlike the case of carboxylic acids (Donohue, 1968), the hydroxyl H atom, not being restricted to the plane of the remainder of the molecule, is free to assume any position favorable for hydrogen bonding. In both of the hydroxamic acids reported here, the dihedral angle of the N—O—H group with the 'molecular plane' is about 90°. As a consequence of this orientation of the O atom ligands, there is an electric dipole moment associated with the O atom lone pairs directed nearly perpendicular to the molecular plane. We may therefore expect a polarization of the π electrons of the neighboring N atom, with the π lobe adjacent to the H atom enriched and that opposite impoverished. In other words, *sp* hybridization occurs, and consequently the N atom becomes pyramidal. Fig. 7 illustrates these concepts for 3-hydroxyxanthine. In this case the argument has further consequences. The N(1)—C(2)—O(10) plane is seen to be slightly tipped with respect to the reference molecular plane; this effect is in the expected direction for maximizing π-orbital overlap between C(2) and N(3).

A similar, but smaller effect seems to be operative in the crystal structure of 1-ethoxy-2,4,6-trinitrobenzene (Gramaccioli, Destro & Simonetta, 1968) in which the

Table 6. *Hydrogen-bond characteristics and water molecule dimensions in* 3-*hydroxyxanthine dihydrate*

Label*	*D*–H···*A*	*D*–H	H···*A*	*D*···*A*	∠H–*D*–H
1	O(11)–H(11)···O(*W*1)	0·86 (2) Å	1·74 (2) Å	2·606 (1) Å	
2	N(1)–H(1)···O(*W*1)	0·87 (2)	2·03 (2)	2·866 (1)	
3	O(*W*1)–H(*W*1)···N(9)	0·84 (2)	2·01 (2)	2·839 (1)	114 (2)°
4	–H(*W*2)···O(*W*2)	0·99 (2)	1·72 (2)	2·701 (1)	
5	O(*W*2)–H(*W*4)···O(12)	0·92 (2)	1·84 (2)	2·756 (1)	106 (2)
6	–H(*W*3)···O(10)	0·89 (2)	2·11 (2)	2·933 (1)	
7	N(7)–H(7)···O(10)	0·89 (2)	1·94 (2)	2·816 (1)	

* So designated in Fig. 3.

ethoxy O atom is 0·112 Å out of the aromatic ring plane and the ethoxy plane is nearly perpendicular to it. This type of distortion is apparently to be expected in hydroxamic acids, and more generally wherever an O atom exocyclic to an aromatic ring or other planar system has its second substituent out of the plane.

Description of the crystal structures

3-*Hydroxyxanthine dihydrate*

The molecular plane is inclined 5·72° from the (110) crystal plane, the inclination axis passing diagonally through the molecule, approximately parallel to the C(2)···C(5) vector. Fig. 3, in which the view direction is the normal to the molecular plane, shows that the structure contains hydrogen-bonded layers with 3-hydroxyxanthine molecules forming a roughly square net in which molecules separated by the **c** translation are joined by a hydrogen bond, N(7)–H···O(10). The two water molecules of the stoichiometric unit, which are hydrogen-bonded to each other, form a total of three hydrogen bonds to molecules within the layer and one hydrogen bond to a molecule in each adjacent layer. Characteristics of all the hydrogen bonds and dimensions of the water molecules are listed in Table 6.

Adjacent layers are related by inversion centers. Interlayer contacts of two types are here designated as 'front-side' if the hydroxamic acid H atoms are directed toward the adjacent layer and 'back-side' if directed away. In the back-side contact, pairs of molecules overlap with a shear displacement of about one-half the width of the molecule, as may be seen in the upper-left corner of Fig. 3. This contact is one typical of aromatic molecules, the interplanar separation being 3·32 Å. The hydroxamic acid atom O(11), as a result of its displacement out of the plane of the aromatic rings, is closer, 3·11 Å from the plane of the neighboring molecule; the shortest interatomic contact is with N(7) at 3·13 Å.

In front-side contact, each molecule makes peripheral approaches to two others, as illustrated in the lower middle of Fig. 3. In one approach, the C(6)–O(12) carbonyl group of one molecule approximately overlaps the N(7)–H pair of the other, with the N(7)···O(12) distance at 3·31 Å. The other approach is between equivalent C(2)–O(10) carbonyl groups with their opposed electric dipole moments directly superposed. The interatomic contact distance here is 3·11 Å; this interaction appears to be a significant one, along with interlayer hydrogen bonding, in stabilizing the layer structure.

Table 7. *Characteristics of the hydrogen bonds in hydroxyurea*

Label*	*D*–H···*A*	*D*···*A*	H···*A*
1	O(5)–H(9)···O(4)	2·648 (1) Å	1·669 (2) Å
2	N(3)–H(8)···O(5)	2·907 (1)	1·962 (2)
3	N(2)–H(6)···O(4)	2·969 (1)	1·995 (2)
4	N(2)–H(7)···O(4)	3·094 (1)	2·131 (2)

* So designated in Fig. 5.

Hydroxyurea

The general arrangement of molecules in the structure was described by Larsen & Jerslev (1966). The molecular plane (best plane through the C, N, and O atoms) makes an angle of 55·5° with the crystal *b* axis, so that neighboring molecules have their planes inclined 69° to each other. Parallel molecules are inclined to the (21$\bar{1}$) crystal planes by only 8·03°. Fig. 5, a view down the *b* axis, shows the hydrogen-bond network linking neighboring molecules.

The shortest hydrogen bonds, O(5)–H(9)···O(4) with H···O 1·669 Å, labeled '1' in Fig. 5 and Table 7, link molecules related by glide planes $(x,\frac{3}{4},z)$ into infinite strings. Adjacent strings are linked across screw axes $(0,y,\frac{3}{4})$ by N(3)–H(8)···O(5) hydrogen bonds '2' with H···O 1·962 Å to form infinite sheets parallel to (100), and these sheets are further linked across screw axes $(\frac{1}{2},y,\frac{1}{4})$ by N(2)–H(6)···O(4), H···O = 1·995 Å, hydrogen bonds '3' forming the three-dimensional net. Weaker N(2)–H(7)···O(4) hydrogen bonds '4', H···O = 2·131 Å, are accommodated between molecules related by the glide planes $(x,\frac{1}{4},z)$.

As pointed out by Larsen & Jerslev, the structure contains a set of open channels parallel to the *b* axis containing centers of symmetry (0,0,0) and (0,$\frac{1}{2}$,0). The minimum distances from the origin inversion center to neighboring atoms are 1·92 Å to H(8) and 2·16 Å to N(3).

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Kristall- und Molekülstruktur der 1,4:3,6-Dianhydro-α-D-glucopyranose (1,5:3,6-Dianhydro-β-D-glucofuranose)

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1,4:3,6-Dianhydro-α-D-glucopyranose, $C_6H_8O_4$, a pyrolysis product of D-glucose, crystallizes in space group $P2_12_12_1$ with $a = 6{\cdot}295$ (2), $b = 9{\cdot}002$ (4), $c = 10{\cdot}862$ (5) Å, $Z = 4$. The tricyclic structure of the title compound was solved by direct methods and refined to a final R_w value of 0·05 for 507 independent reflexions. The pyranose ring of the molecule adopts an almost ideal $B_{1,4}$(D) boat conformation and the furanose ring a distorted envelope conformation, E_O(D) (phase angle $P = 276{\cdot}8°$).