

that Ba_2TiO_4 undergoes at least one phase change above room temperature.

Midgley (1952) has suggested that the structures of the high-temperature modifications of Ca_2SiO_4 may be derived from the β -phase by rotating the SiO_4 tetrahedra. This may not happen with Ba_2TiO_4 for it is not possible to predict the effect of a temperature change on the Ti-O bond. If it ceases to be stronger than the other bonds then it is more likely that there will be a reconstructive change to a more close packed arrangement such as the Sr_2TiO_4 structure.

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References

BREDIG, M. A. (1950). *Jour. Amer. Ceram. Soc.* **33**, 188.
DOUGLAS, A. M. B. (1952). *Miner. Mag.* **29**, 875.

DOUGLASS, R. M. (1958). *Amer. Min.* **43**, 517.
FRAZER, B. C., DANNER, H. R. & PEPINSKY, R. (1955). *Phys. Rev.* **100**, 745.
GRÄNICHER, H. (1956). *Helv. Phys. Acta*, **29**, 211.
HARRISON, F. W. (1956a). *Acta Cryst.* **9**, 495.
HARRISON, F. W. (1956b). *Acta Cryst.* **9**, 198.
Internationale Tabellen zur Bestimmung von Kristallstrukturen (1935). Berlin: Borntraeger.
JONKER, G. H. & KWESTROO, W. (1958). *Jour. Amer. Ceram. Soc.* **41**, 390.
LIPSON, H. & COCHRAN, W. (1953). *The Crystalline State*, vol. III. London: Bell.
MEGAW, H. D. (1957). *Ferroelectricity in Crystals*. London: Methuen.
MIDGLEY, C. M. (1952). *Acta Cryst.* **5**, 307.
MURRAY, J. F. (1958). *Ceram. Bull.* **37**, 476.
O'DANIEL, H. & TSCHUISCHWILI, L. (1942). *Z. Kristallogr.* **104**, 348.
PAULING, L. (1940). *The Nature of the Chemical Bond*. Oxford: University Press.
RASE, D. E. & ROY, R. (1955). *J. Amer. Ceram. Soc.* **38**, 102.
ROOKSBY, H. P. (1947). *Nature, Lond.* **159**, 609.
RUDDLESDEN, S. N. & POPPER, P. (1957). *Acta Cryst.* **10**, 538.
SMITH, J. V. (1953). *Acta Cryst.* **6**, 613-620.
TODD, S. S. & LORENSON, R. E. (1952). *J. Amer. Chem. Soc.* **74**, 3764.

Acta Cryst. (1961). **14**, 881

The Crystal Structure of Barbituric Acid Dihydrate

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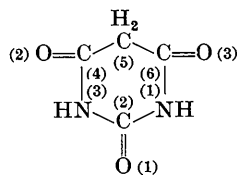
Barbituric acid dihydrate, $\text{C}_4\text{H}_4\text{N}_2\text{O}_3 \cdot 2\text{H}_2\text{O}$, forms crystals which have a hydrogen-bonded layer structure in which the barbituric acid and water molecules lie on the mirror planes of the space group Pnma . The barbituric acid is in the tri-keto form and, within the accuracy of the analysis, has mm symmetry. The water molecules are hydrogen-bonded in pairs and their hydrogen-bond coordination is unusual in that it is planar and approximately trigonal. The structure analysis was refined by isotropic and anisotropic least squares methods.

Introduction

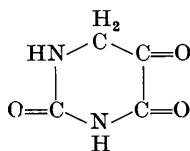
Barbituric acid, $\text{C}_4\text{H}_4\text{N}_2\text{O}_3$, is the parent compound for a wide variety of derivatives famous for their drug action. A recent compilation (Blicke & Cox, 1959) listed several hundred such compounds, under the general classification as 'barbiturates', which had been synthesized and examined with respect to their pharmacological activity.

The structural interest in the molecule of barbituric acid itself, I, lies in its behaviour as a carboxylic acid comparable in strength with formic and benzoic acids. This acidity ($K_a = 1.0 \times 10^{-4}$) is apparently associated with the particular combination of the active methylene group of the malonyl system with the potential imino carboxylic configuration of urea, since comparable acidity is not shown either by the malonyl esters or urea derivatives separately or by related cyclic compounds such as isobarbituric acid, II, ($K_a = 2.5 \times 10^{-9}$), alloxan, III, ($K_a = 2.3 \times 10^{-7}$), and diketopiperazine, IV.

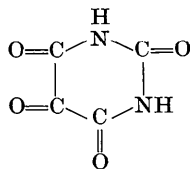
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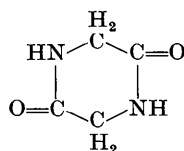
I



II

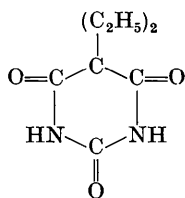


III

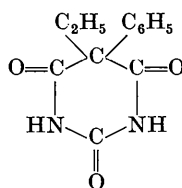


IV

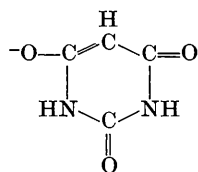
The value for K_a quoted above corresponds to the first dissociation constant of barbituric acid, the second and third are much smaller. Since the substitution of both hydrogens of the methylene group, as in veronal, V, or phenobarbital, VI, results in a large reduction in acid strength, the aromatic resonance energy of the barbiturate ions VII, VIII, and XI, must be the significant factors in the acid behaviour.



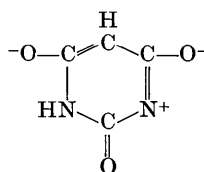
V



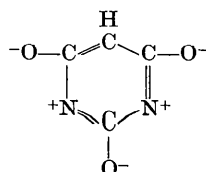
VI



VII



VIII



IX

Barbituric acid crystallizes from aqueous solution with two water molecules, with which it would be expected to be associated by hydrogen bonding. The purpose of this investigation is to study the structure of this association and of the barbituric acid molecule therein.

The crystal data

Barbituric acid dissolves readily in water and on crystallization forms a dihydrate. The two crystalline modifications originally reported by Baeyer (1863) were found to be identical except for a difference in habit. By slow evaporation of aqueous solution, prisms with a tendency to elongate about the b axis were obtained, while evaporation of an aqueous solution saturated with iodine deposited crystals acicular about the c axis.

The crystals are orthorhombic, class mmm , with the normal form showing $\{110\}$, $\{101\}$, $\{100\}$ and $\{010\}$ as reported by Groth (1919). The cell dimensions are

$$(\lambda_{K\alpha_1} = 1.540, \lambda_{K\alpha_2} = 1.544 \text{ \AA})$$

$$a = 12.74, b = 6.24, c = 8.89 \text{ \AA},$$

giving axial ratios 2.04:1:1.42 compared with Groth's optical value of 2.0232:1:1.4343. There are four molecules in the cell with $D_M = 1.561$, $D_X = 1.552$ g.cm.⁻³. From the systematic extinctions ($0kl$ for $k+l$ odd, hkl for h odd) the space group is $Pn2_1a$ or $Pnma$. The morphology, absence of piezoelectric effect and subsequent complete structure analysis established the higher symmetry. The refractive indices are $\alpha = 1.40$ parallel to b , $\beta = 1.645$ parallel to a , $\gamma = 1.65$ parallel to c . There is marked cleavage parallel to (010). The crystals slowly decompose in air, presumably losing water, to become opaque and eventually form powder pseudomorphs. The powder patterns of this material are different from those of the hydrate and of the original anhydrous compound.

Experimental

The intensities were eye-estimated from multiple-film Weissenberg photographs using a small crystal of almost uniform cross-section, somewhat elongated about the b axis. Intensity photographs were taken with $\text{Cu } K\alpha$ radiation of the three principle zones, of the first to fourth layers about the b axis, and of the first to fourth layers about the c axis. A duplicate set of intensities were also estimated from films on which the zero and first to zero and fourth layers of the b axis were recorded by the double-slit technique of Stadler (1950) in order to reduce the interlayer correlation errors. No corrections were made for absorption. There were 556 observed reflections recorded for the determination of the 22 positional parameters and 44 anisotropic thermal parameters, excluding the hydrogen atoms.

The structure analysis and refinement

The refractive indices, cleavage, and observation that (020) and (040) were very intense reflections with strong diffuse thermal streaks suggested that this was a layer structure in which the planar barbituric acid molecules lay in the mirror plane of the higher sym-

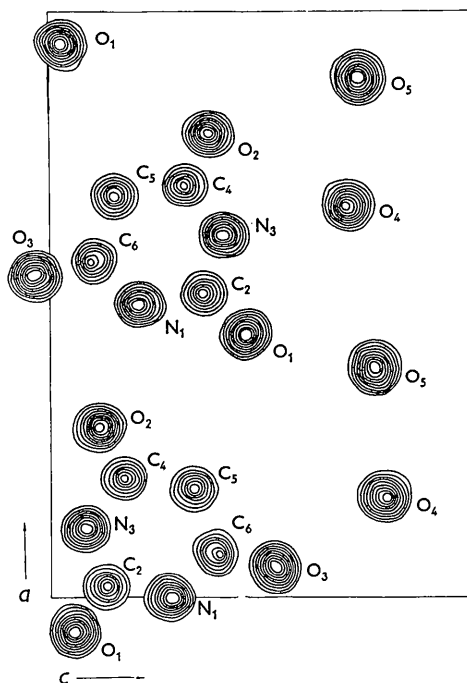


Fig. 1. Barbituric acid dihydrate. Electron density distribution on section at $y=0.25$. Contour intervals $1 \text{ e.}\text{\AA}^{-3}$, zero omitted.

metry space group. The close correspondence in relative intensities of the even and odd orders respectively of the b axis layer-lines suggested that the oxygen atoms of the water molecules occupied two independent special positions, also on the mirror planes.

From these premises, trial and error calculations led to a structure which, on successive Fourier refinement of the section at $y=0.25$, gave the electron density distribution shown in Fig. 1. Further refinement was carried out by least-squares using individual isotropic temperature factors. Since, with the exception of the $(0k0)s$, the range of structure factor values was small, a modified Hughes weighting scheme was used with $\omega = \frac{1}{2}|F_{\text{min.}}|$ for structure factors below $2|F|$ minimum and $1/|F|$ for the remainder. The unobserved reflections were given zero weight. After five cycles, the parameter shifts were negligible in comparison with the standard deviations. Hydrogen atom positions consistent with these parameters were then selected assuming linear $\text{O}\cdots\text{H}-\text{O}$ and $\text{O}\cdots\text{H}-\text{N}$ bonds with $\text{H}-\text{O}$, $\text{H}-\text{N}$ and $\text{C}-\text{H}$ all equal to 1.0 \AA , and with the two methylene $\text{C}-\text{H}$ bonds tetrahedrally disposed above and below the mirror plane. With these coordinates as fixed parameters and temperature factors equal to that of the atom to which the hydrogen was attached, two more cycles of isotropic least-squares

Table 1. Fractional atomic coordinates and thermal parameters in \AA^2
(With standard deviations in parentheses)

Atom	Isotropic		Anisotropic					
	x	z	x	z	B_{11}	B_{22}	B_{33}	B_{13}
O ₁	-0.0572 (0.0005)	0.0413 (0.0008)	-0.0575 (0.0005)	0.0412 (0.0008)	1.60 (0.26)	4.59 (0.41)	1.99 (0.29)	-0.67 (0.23)
O ₂	0.2900 (0.0005)	0.1119 (0.0009)	0.2899 (0.0005)	0.1124 (0.0008)	1.05 (0.24)	7.10 (0.48)	2.28 (0.30)	0.20 (0.23)
O ₃	0.0512 (0.0005)	0.5224 (0.0008)	0.0511 (0.0005)	0.5221 (0.0007)	2.52 (0.30)	4.96 (0.42)	1.00 (0.24)	0.44 (0.23)
O ₄	0.1712 (0.0006)	0.7830 (0.0008)	0.1710 (0.0006)	0.7833 (0.0008)	2.41 (0.30)	6.59 (0.48)	1.56 (0.27)	0.00 (0.16)
O ₅	0.3866 (0.0006)	0.7619 (0.0008)	0.3867 (0.0006)	0.7615 (0.0008)	1.93 (0.29)	4.87 (0.40)	2.16 (0.28)	-0.12 (0.24)
N ₁	-0.0012 (0.0006)	0.2804 (0.0008)	-0.0012 (0.0005)	0.2810 (0.0008)	0.91 (0.26)	3.04 (0.38)	0.93 (0.34)	0.10 (0.28)
C ₂	0.0165 (0.0006)	0.1277 (0.0011)	0.0165 (0.0006)	0.1274 (0.0011)	0.74 (0.28)	2.88 (0.44)	1.75 (0.34)	0.16 (0.25)
N ₃	0.1178 (0.0006)	0.0788 (0.0008)	0.1168 (0.0005)	0.0786 (0.0008)	1.10 (0.26)	2.96 (0.36)	1.03 (0.26)	0.37 (0.22)
C ₄	0.2050 (0.0007)	0.1722 (0.0010)	0.2044 (0.0006)	0.1707 (0.0010)	0.88 (0.28)	3.30 (0.47)	1.63 (0.32)	-0.44 (0.25)
C ₅	0.1871 (0.0007)	0.3377 (0.0010)	0.1870 (0.0006)	0.3386 (0.0010)	0.71 (0.28)	3.36 (0.47)	1.83 (0.34)	-0.08 (0.25)
C ₆	0.0756 (0.0006)	0.3889 (0.0009)	0.0752 (0.0006)	0.3888 (0.0009)	0.54 (0.26)	2.71 (0.40)	1.01 (0.30)	-0.15 (0.24)
H ₁	0.128	0.685	—	—	—	—	—	—
H ₂	0.249	0.782	—	—	—	—	—	—
H ₃	0.406	0.655	—	—	—	—	—	—
H ₄	0.440	0.836	—	—	—	—	—	—
H ₅	0.140	-0.027	—	—	—	—	—	—
H ₆	0.312	-0.067	—	—	—	—	—	—
H ₇	0.226	0.380	—	—	—	—	—	—

All atoms have the y coordinates 0.25, which were not varied. All the hydrogen parameters are assumed, and not varied.

Table 2 (cont.)

h	k	l	F _{obs}	F _{calc}	h	k	l	F _{obs}	F _{calc}	h	k	l	F _{obs}	F _{calc}	h	k	l	F _{obs}	F _{calc}
1	5	1	4.0	-6.9	6	5	0	13.7	-11.5	11	5	2	7.6	12.8	4	6	4	.0	1.4
1	5	2	7.7	-8.7	6	5	1	7.0	-11.5	11	5	3	7.3	8.2	5	6	1	.0	2.0
1	5	3	11.4	12.1	6	5	2	20.4	19.3	0	6	0	42.4	-73.8	5	6	2	.0	-1.2
1	5	4	20.9	-22.1	6	5	3	17.9	13.8	0	6	2	.0	5.9	5	6	3	7.3	5.4
2	5	0	25.2	-23.9	6	5	3	17.9	13.8	0	6	4	9.6	3.6	5	6	4	8.6	-10.0
2	5	1	-11.2	-11.2	6	5	4	.0	-4.3	1	6	1	.0	-2.9	6	6	0	.0	-5.0
2	5	2	5.5	-5.7	6	5	4	.0	-4.3	1	6	2	.0	3.1	6	6	1	5.3	.0
2	5	3	.0	.0	7	5	1	.0	13.3	1	6	3	.0	-3.2	6	6	2	12.1	15.4
2	5	4	20.5	16.0	7	5	2	11.4	-9.8	1	6	4	.0	5.3	6	6	3	4.4	-4.5
3	5	1	20.6	20.6	7	5	3	13.3	12.2	2	6	0	11.8	-15.9	7	6	1	6.7	-9.0
3	5	2	7.8	-8.9	7	5	4	7.8	-8.9	2	6	1	18.5	15.4	7	6	2	.0	-3.2
3	5	3	.0	4.1	8	5	0	.0	-7.2	2	6	2	.0	-7.9	7	6	3	.0	1.2
3	5	4	.0	-3.6	8	5	1	6.9	4.1	2	6	3	10.4	5.2	8	6	0	.0	5.5
4	5	0	.0	6.3	8	5	2	5.3	4.1	2	6	4	.0	-5.9	8	6	1	4.6	-7.3
4	5	1	28.2	-26.5	8	5	3	3.4	2.9	3	6	1	.0	.3	8	6	2	6.0	8.4
4	5	2	22.9	-20.8	9	5	1	10.8	-9.6	3	6	2	.0	-5.9	8	6	3	.0	2.4
4	5	3	28.3	22.9	9	5	2	11.7	-11.3	3	6	3	.0	1.7	9	6	1	7.4	-8.4
4	5	4	8.3	12.6	9	5	3	7.8	3	6	4	.0	2.4	9	6	2	7.2	11.6	
4	5	5	24.0	21.0	10	5	1	.0	-20.5	4	6	0	.0	-2.4	9	6	3	4.4	1.7
5	5	1	5.6	5.4	10	5	2	8.2	-12.7	4	6	1	.0	2.0	10	6	0	.0	-16.6
5	5	2	20.3	17.0	10	5	3	.0	-3.4	4	6	2	7.5	3.8	10	6	1	.0	3.8
5	5	3	.0	-7.7	10	5	4	24.3	-25.7	4	6	3	7.0	1.7	10	6	2	7.1	15.4
5	5	4	.0	.0	11	5	1	.0	.0	4	6	4	.0	.0	6	7	0	.0	4.6

were computed to give the atomic parameters in Table 1. Two cycles of anisotropic temperature factor refinement were then computed to give the final parameters, also given in Table 1, and to give a final agreement index of $R=0.14$. No corrections were made for extinction. The only reflections which appeared to be seriously affected by extinction were (011) and (013) and these were omitted from the final least-squares computations.

The observed and calculated structure factors are given in Table 2. The bond lengths, bond angles and shorter intermolecular distances are given in Tables 3 and 4. The standard deviation of the bond lengths and other interatomic distances is 0.010 Å with a variation of ± 0.001 Å, that of the bond angles is 0.7° , except for the angles between the hydrogen bonds on the water molecule, for which it is 0.3° . The greatest change in bond length in going from the isotropic analysis to the final stage of the anisotropic analysis was 0.021 Å, in C₄-C₅; this is about twice the final standard deviation for that bond length.

The trial and error calculations and the earlier Fourier syntheses were calculated on a hand machine using Beevers-Lipson strips, prior to the advent of the digital computer. Later the Fourier synthesis shown in Fig. 1 and subsequent differential Fourier syntheses and isotropic structure factor calculations were computed on an IBM 650 using Shiono's (1957)

Table 3. Bond lengths and valence angles

N ₁ -C ₂	1.378 Å	N ₁ -C ₂ -N ₃	118.0°
C ₂ -N ₃	1.356	C ₂ -N ₃ -C ₄	125.5
N ₃ -C ₄	1.388	N ₃ -C ₄ -C ₅	117.4
C ₄ -C ₅	1.503	C ₄ -C ₅ -C ₆	115.8
C ₅ -C ₆	1.501	C ₅ -C ₆ -N ₁	118.5
C ₆ -N ₁	1.367	C ₆ -N ₁ -C ₂	124.8
C ₂ -O ₁	1.217	O ₁ -C ₂ -N ₁	119.3
C ₄ -O ₂	1.211	O ₁ -C ₂ -N ₃	122.6
C ₅ -O ₃	1.219	O ₂ -C ₄ -N ₃	118.7
O ₄ -O ₅	2.772	O ₂ -C ₄ -C ₅	123.8
O ₄ -O ₃	2.773	O ₃ -C ₆ -C ₅	121.9
O ₅ -O ₁	2.771	O ₃ -C ₆ -N ₁	119.6
O ₅ -O ₃	2.845	O ₃ -O ₄ -O ₅	119.7
O ₄ -N ₃	2.705	N ₃ '-O ₄ -O ₅	108.8
O ₂ -N ₁	2.837	O ₃ -O ₄ -N ₃	131.4
		O ₁ '-O ₅ -O ₃	117.3
		O ₄ -O ₅ -O ₁	108.9
		O ₄ -O ₅ -O ₃	133.8

Table 4. Non-bonding interatomic distances less than 4.0 Å between molecules

Within the layers					
O ₁ -O ₂ '	3.64 Å	O ₄ -C ₅	3.94 Å	O ₄ -O ₁ '	3.71 Å
O ₁ -C ₅ '	3.45	O ₄ -C ₄ '	3.46	O ₄ -O ₂ '	3.67
O ₁ -C ₄ '	3.98	O ₄ -C ₂ '	3.63	O ₅ -O ₂ '	3.35
O ₂ -O ₃ '	3.55	O ₄ -O ₂ '	3.29	O ₅ -C ₆ '	3.93
		O ₅ -C ₂ '	3.82		
Between the layers					
O ₁ -O ₄ '	3.78 Å	O ₃ -O ₂ '	3.81 Å	O ₅ -O ₃ '	3.96 Å
O ₁ -O ₁ '	3.53	O ₃ -O ₃ '	3.41	O ₅ -N ₃ '	3.51
O ₁ -N ₃ '	3.38	O ₃ -O ₅ '	3.96	O ₅ -N ₁ '	3.45
O ₁ -C ₂ '	3.50	O ₃ -N ₁ '	3.63	O ₅ -C ₂ '	3.56
O ₂ -O ₃ '	3.81	O ₃ -C ₆ '	3.60	O ₅ -C ₄ '	3.43
O ₂ -O ₄ '	3.50	O ₄ -N ₁ '	3.85	O ₅ -C ₅ '	3.33
O ₂ -C ₅ '	3.96	O ₄ -C ₄ '	3.64	O ₅ -C ₆ '	3.35
C ₂ -C ₂ '	3.87	O ₄ -C ₅ '	3.65		

To molecule, ' in adjacent cell,
 '' at $\frac{1}{2}+x, \frac{1}{2}, \frac{1}{2}-z$,
 ''' at $\bar{x}, \frac{1}{2}, z$,
 '''' at $\frac{1}{2}-x, \frac{1}{2}, \frac{1}{2}+z$.

programs. The isotropic and anisotropic least-squares computations were done on an IBM 704 using the Busing & Levy (1959) full matrix program.

The final temperature factors, shown in Table 1, clearly indicate the considerably greater thermal motion of the atoms normal to the mirror plane of the structure, which was anticipated from the distribution of the diffuse thermal spectra. Within the errors, shown by the standard deviations, the thermal parameters are self-consistent and there is no reason to suspect the choice of the higher symmetry space group. The oxygen atoms appear to have a systematically greater thermal motion normal to the layer plane than do the pyrimidine ring atoms. It is not possible to distinguish whether this is a purely thermal effect, e.g. out of the plane oscillation of the molecule about its center, or whether it is indicative of displacements of the oxygen atoms statistically above or below the mirror plane. These displacements could be of the same order of magnitude as the difference between the root mean square thermal displacements of the oxygens and the ring atoms in the b axis direction. In either case, this could result in some of the C-O and O-O

distances being observed shorter by about 0.01 Å than the real distances.

Discussion of the structure

The crystal structure consists of planar layers of barbituric acid and water molecules hydrogen-bonded into a compact arrangement, giving rise to a comparatively high density crystal, as is frequently found in structures in which carbonyl oxygens are attached to pyrimidine rings. The separation between layers is 3.12 Å; considerably less than the 3.65 Å separation in the uracil structure (Parry, 1954), which also has a planar hydrogen-bonded layer structure.

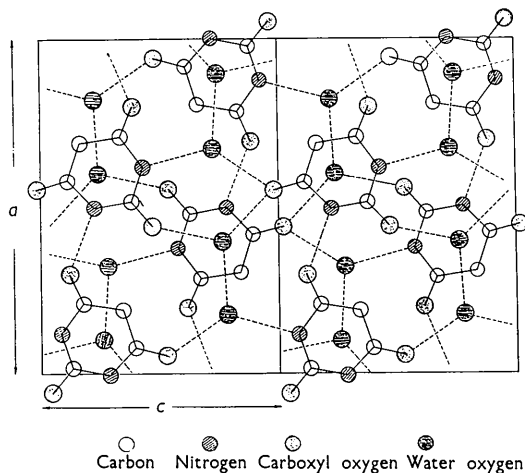


Fig. 2. Barbituric acid dihydrate crystal structure. Showing the superposition of adjacent hydrogen-bonded layers.

In this structure, however, the adjacent layers are displaced with respect to each other by the n and a glide symmetry perpendicular to the a and c axes respectively, as shown in Fig. 2; consequently the shortest distances between atoms in adjacent layers are 3.33 and 3.35 Å (water O_5 to carbon atoms C_5 and C_6). The shortest non-bonding distance within the layers is the water to carbonyl oxygen distances of 3.29 and 3.35 Å. These and other interatomic distances less than 4 Å are listed in Table 4.

The dimensions of the barbituric acid molecules are given in Table 3, and Fig. 3. The bond lengths show decisively that, in the hydrated crystals, the molecule is the tri-keto isomer, I. This is in contrast to the 5-hydroxy barbituric acid monohydrate, (dialuric acid), where Alexander & Pitman (1956) found the diketo tautomer, X, in the crystal. Although, in that analysis, the evidence for the tautomeric form is based on the coplanarity of the 5-hydroxyl oxygen with the pyrimidyl ring rather than the observed bond lengths, which were less decisive.

Within the accuracy of the analysis, the barbituric acid molecule has mm symmetry, as would be expected for the tri-keto tautomer. The three carbonyl

bond-lengths do not differ significantly from the mean of 1.216 Å. The mean value of N_1-C_2 and C_2-N_3 is 1.367 Å, that of N_1-C_6 and N_3-C_4 is 1.378 Å, and the difference is not significant. The mean C-C bond length is 1.50 Å, which corresponds with the value suggested for a single sp^3-sp^2 carbon link by Coulson (1948), (1951), and rediscovered by Somayaajulu (1959) from the sum of orbital radii corrected for electronegativity differences by the Stevenson & Schomaker rule.

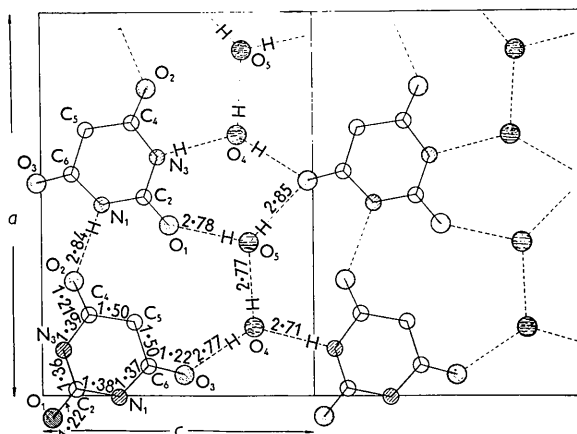


Fig. 3. Barbituric acid dihydrate crystal structure. Showing bond lengths in a single hydrogen-bonded layer.

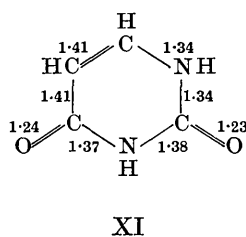
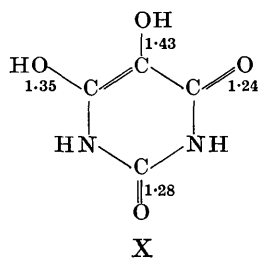
The angles of the pyrimidine ring also correspond with the mm symmetry, with the C-N-C angles (mean, 125.0°) significantly larger than those at the carbon atoms (mean, 117.5°). The $C_4-C_5-C_6$ is actually the smallest observed ring angle as would be expected at an sp^3 carbon, but the accuracy of the analysis is insufficient to establish this feature.

With the tri-keto tautomer and two water molecules there are six hydrogens available for hydrogen-bond formation, and, as is the general rule, the maximum number of hydrogen bonds is formed. The water molecules are associated in pairs with a hydrogen bond of 2.77 Å between them. Other water to water oxygen distances are greater than 3.5 Å. One water molecule of the pair is bonded to two carbonyls on different adjacent molecules at 2.84 and 2.77 Å; the other is bonded to a carbonyl and an imino group on adjacent molecules at 2.77 and 2.71 Å, respectively. The sixth hydrogen bond of the system is formed between a carbonyl and the other imino group on adjacent molecules at 2.83 Å. These dimensions and those of the barbituric acid molecule are consistent with the configuration of hydrogen atoms shown in Fig. 3. Although we have no direct evidence for the hydrogen positions this arrangement seems unambiguous.

The approximately trigonal and planar arrangement of the hydrogen bonds about each of the two water oxygen atoms is a departure from the usual tetrahedral water coordination and we could find no comparable

example in the literature. However, if it is assumed that the hydrogen atoms do not deviate far from the line of centers of the oxygen atoms, then the water structure in this crystal corresponds approximately to the model used by Tsubomura (1954) in his quantum mechanical calculations. Another unusual feature is that the NH-OH₂ bond is the shortest of the six hydrogen bonds in the system. Despite the compact packing of the molecules, this hydrogen bonding arrangement does not appear to be a particularly stable one, since the transparent crystals decompose, presumably losing water, so that they become opaque in a few days under normal atmospheric conditions.

It is of interest to compare this structure with that of uracil, XI, (Parry, 1954), which also has a hydrogen-bonded layer structure. In uracil the layers superimpose without translation since the interlayer separation of 3.63 Å is the *c* axis. The crystals are anhydrous and were obtained by sublimation. There are, there-



fore, only two hydrogens available for hydrogen-bond formation. Consequently although one carbonyl oxygen is normally hydrogen-bonded to two imino groups at 2.81 and 2.86 Å, the other has as its nearest non-bonded neighbouring atoms the CH groups of adjacent molecules at a somewhat close approach of 3.19 and 3.28 Å. This may partially explain the difficulty in obtaining good untwinned uracil crystals from solu-

tion, although one wonders why uracil from aqueous solutions does not also form a hydrate, whereby the water molecules would make possible the formation of a more complete system of hydrogen bonds, as in the barbituric acid dihydrate. We found no evidence in the barbituric acid hydrate structure of the distinction between the two sets of C-N bond lengths in the pyrimidine ring which was reported in uracil. Taken in pairs, the observed lengths of the C₁-N₁, N₁-C₆ and C₂-N₃, N₃-C₄ bonds do, in fact, differ by 0.011 and 0.032 Å, but since the comparison involves a common atom these differences are not significant in terms of the standard deviations.

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References

- ALEXANDER, L. E. & PITMAN, D. T. (1956). *Acta Cryst.* **9**, 501.
 BAEYER, A. (1863). *Ann. Phys.* **127**, 199.
 BLICKE, F. F. & COX, R. H. (1959). *Medicinal Chemistry*, Vol. IV. New York: Wiley.
 BUSING, W. & LEVY, H. A. (1959). Oak Ridge National Laboratory, Central Files Number 59-4-37.
 COULSON, C. A. (1948). *V. Henri Memorial Volume*, p. 15. Liège: Desoer.
 COULSON, C. A. (1951). *J. Phys. Chem.* **56**, 311.
 GROTH, P. (1919). *Chemische Kristallographie*, Vol. III. Leipzig: Engelmann.
 PARRY, G. S. (1954). *Acta Cryst.* **7**, 313.
 SHIONO, R. (1957). Technical Report No. 2, University of Pittsburgh Computation and Data Processing Center. IBM 650 Library Program File No. 84001, 84002.
 SOMAYAJULU, G. R. (1959). *J. Chem. Phys.* **31**, 919.
 STADLER, H. P. (1950). *Acta Cryst.* **3**, 262.
 TSUBOMURA, H. (1954). *Bull. Chem. Soc. Japan*, **27**, 445.