Acta Cryst. (1956). **9**, 501

The Crystal Structure of Dialuric Acid Monohydrate

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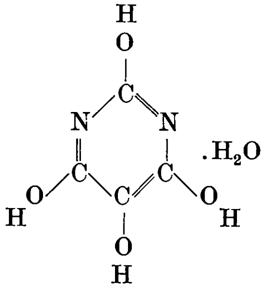
(*Received* 27 *November* 1955)

Dialuric acid monohydrate crystallizes in the monoclinic space group C_{2h}^5–$P2_1/n$. Four molecules are contained in the unit cell of dimensions $a = 12{\cdot}76_5$, $b = 3{\cdot}67_6$, $c = 13{\cdot}06_4$ Å, $\beta = 95{\cdot}4°$. The approximate structure was determined by the Patterson vector-superposition method, and the parameters were refined by Fourier difference syntheses and least-squares procedures. The intramolecular bond lengths show the molecule to be in the 2,4-diketo 5,6-dihydroxy tautomeric form with contributions from several resonance structures involving single charge separations. Three of the oxygen atoms are definitely not coplanar with the pyrimidine ring nucleus, their displacements from the ring plane being 0·13, 0·13, and 0·20 Å. The ring plane satisfies the equation $0{\cdot}045x + 1{\cdot}260y + 1{\cdot}719z = 1$, which represents an inclination of 21·6° to the (010) planes. The structure is bound firmly together by a complex three-dimensional network of hydrogen bonds, which accounts for its high melting point. Each water molecule is surrounded irregularly by eight oxygen atoms attached to six dialuric acid molecules.

Introduction

Dialuric acid (2,4,5,6-tetrahydroxypyrimidine or 5-hydroxybarbituric acid) is of immediate interest in biochemistry because of its diabetogenic properties (Tipson & Cretcher, 1951), while possibly more general interest attaches to its close structural relationship to the nucleic acids. In the latter connection its structure may be profitably compared with those of a number of pyrimidine and purine derivatives which have been solved in recent years (Pitt, 1948; Clews & Cochran, 1948, 1949; Cochran, 1951; Broomhead, 1951; Parry, 1954).

The formal structural formula of dialuric acid monohydrate is



It was felt that the crystal structure of this substance would prove of special interest to structural chemists as a consequence of its extraordinary hydrogen-bond-forming potential. If an intricate network of hydrogen bonds does, in fact, exist in the structure it might be expected to influence the internal state of the molecule, especially the tautomeric form assumed and the electronic resonance states predominating.

Experimental

The preparation of dialuric acid by reduction of alloxan with hydrogen sulfide in aqueous solution has been described in detail (Tipson & Cretcher, 1951). Crystals of suitable size for X-ray analysis were obtained by very slow cooling of a saturated aqueous solution under an atmosphere of hydrogen sulfide. The crystals were colorless, prismatic or needle-like in habit, and cleaved readily in a direction parallel to the long axis. The X-ray specimens were about 0·20×0·05 mm. in rectangular cross section and 0·6–1·0 mm. in length. The crystals displayed extinction parallel to the needle axis when viewed under crossed nicols with plane-polarized light. A striking physical property of dialuric acid monohydrate is its high melting point. Tipson & Cretcher observed no true melting or gas evolution when the crystals were heated to 300° C.

Zero- and first-level precession photographs taken about the needle axis showed the symmetry C_2, and zero- and first-level photographs about an axis normal to the needle axis showed the respective symmetries C_{2l} and C_l, indicating the most probable centrosymmetrical class to be C_{2h} (Buerger, 1942). The observed extinctions, $(h0l)$ with $h+l = 2n+1$ and $(0k0)$ with $k = 2n+1$, uniquely characterized the space group as C_{2h}^5–$P2_1/n$. Calibration of Mo $K\alpha$ precession photographs with a small quartz crystal showed the monoclinic unit cell dimensions to be:

$$a=12{\cdot}76_5\pm0{\cdot}020,\ b=3{\cdot}67_6\pm0{\cdot}007,\ c=13{\cdot}06_4\pm0{\cdot}020\ \text{Å},\quad \beta = 95{\cdot}4\pm0{\cdot}1°\ .$$

On the basis of a measured density* of 1·812 g.cm.$^{-3}$, the unit cell was found to contain 4 molecules (calculated 4·14 molecules).

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Intensity data of the types ($h0l$), ($hk0$), and ($0kl$) were obtained from Weissenberg photographs using Cu $K\alpha$ radiation in conjunction with the multiple-film technique. The intensities were determined by visual comparison with a graded density scale. No attempt was made to reduce the small prismatic crystals to cylindrical or spherical shapes in order to minimize absorption errors. Because of the very small cross-sectional dimensions of the crystals employed the ($h0l$) intensities were not significantly affected by absorption. The larger b dimension would be expected to introduce somewhat greater errors into the ($hk0$) and ($0kl$) intensities derived from Weissenberg photographs, but it was not felt that the accuracy inherent in the two-dimensional photographic procedures followed in this investigation warranted serious efforts to equalize the dimensions.

Solution and refinement of the structure

Because of the shortness of the b unit-cell dimension it was anticipated that the pyrimidine ring and its attached groups, which must be at least approximately planar, would not be inclined very steeply with respect to the (010) planes. Hence, it was foreseen that the ac projection of the structure would be well-resolved, a cogent reason for attacking the x and z parameters first. The great power of the reflections (012), (024), and (036) suggested that the molecular planes are oriented approximately parallel to these crystallographic planes, which would prescribe an inclination angle to the (010) plane of about 20°. With the help of this information it seemed hopeful that trial-and-error attempts to ascertain the x and z atomic coordinates would bear fruit. Accordingly planar models of the dialuric acid molecule were constructed with dimensions deduced from related pyrimidine structures together with accepted bond lengths. It was considered a sufficiently good approximation at this stage to regard the projection of the moderately tilted molecules on the ac plane as undistorted. Repeated attempts were made to fit four molecules of dialuric acid and four water molecules into an ac scaled outline of the unit cell, but it soon became apparent that no progress was being made. A Patterson $P(x, z)$ projection was next prepared and the vector superposition (Buerger, 1950) approach was tried with quick results. After a few alternative orientations of the molecule were tried, one was found that gave approximate agreement between calculated and observed ($h0l$) structure factors.

By means of four successive electron-density syntheses most of the signs of the structure amplitudes were determined and the x and z atomic coordinates were improved sufficiently to reduce the reliability index to 0·20 for the 145 observed reflections. Two difference syntheses coupled with a least-squares evaluation of the scale factor and isotropic temperature coefficients reduced R to 0·182. At this stage the thermal vibration coefficients used in calculating the structure factors were $B = 2{\cdot}07$ Å^2 for the carbon and nitrogen atoms and $B = 2{\cdot}70$ Å^2 for the oxygen atoms. Improved agreement between values of F_c and F_o could not be achieved by introducing anisotropic vibrational components.

The electron-density projection $\varrho(x, z)$ is shown in Fig. 1. All atoms in the dialuric acid molecule as well as the water oxygen atom are clearly resolved. Although the degree of tilt with respect to the (010) planes is not sufficient to cause conspicuous fore-

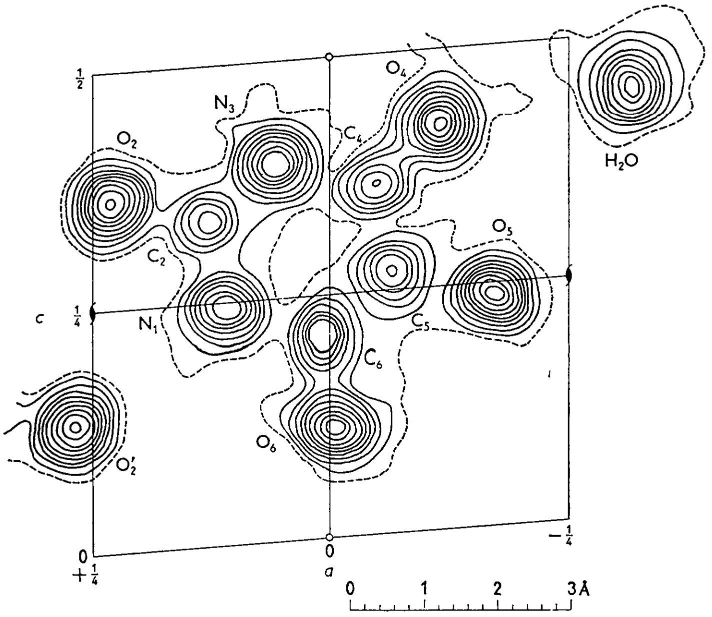


Fig. 1. The electron density projected on (010). Contours at intervals of 1 e.Å^{-2} with the 1-electron contour broken.

shortening in the projection of the molecule, closer observation reveals enough foreshortening in approximately the c direction to suggest a tilt of the order of 20° or 25°, which agrees with the earlier prediction that the molecular planes would be found to be approximately parallel to (012).

It should be pointed out that the ac projection of the structure is not affected by interchanging the sites of the screw axes and symmetry centers, which is to say that a twofold ambiguity existed at this stage as to whether or not the origin should be shifted by an increment of $\frac{1}{4}$ in both x and z. Hence, it remained for the solution of the y parameters to be accomplished before the correct choice of origin could be made. The $(h0l)$ structure factors are not affected by this change in origin, whereas the $(hk0)$ and $(0kl)$ structure factors calculated for the two orientations are different, so that the right choice of the x and z coordinates should permit refinement of the y coordinates whereas the wrong choice should not.

The elucidation of the y parameters proved to be very difficult, mainly because of the many near superpositions among the atomic sites in both the ab and bc projections. In spite of the clues afforded by the foreshortening of the (010) molecular projection and by the unusual strength of the (012), (024), and (036) reflections, determined efforts to arrive at useful preliminary values of the y parameters were in the main unsuccessful. Confidence could be placed in the signs of only about one half the structure amplitudes, and this yielded Fourier projections that served only to confirm the approximate tilt of the molecule as already proposed. In the hope that a better resolved projection would be obtained were more of the phase signs correctly known, X-RAC was employed to determine most of the remaining doubtful signs by means of the minimum negativity criterion. The resulting Fourier projection $\varrho(y, z)$, shown in Fig. 2, although doubtless more accurate than those previously obtained, still did not permit more accurate parameters to be deduced except possibly for the resolved water oxygen atom O_7. Throughout these experiments the value of the reliability index for the 65 observed $(hk0)$ and $(0kl)$ reflections hovered between 0·30 and 0·35.

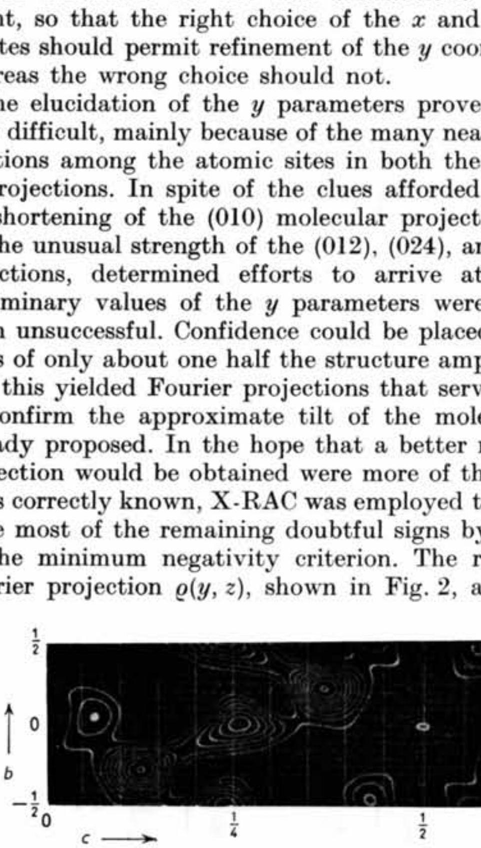


Fig. 2. X-RAC projection of the electron density on (100).

It was now decided to try to improve the y atomic coordinates with the aid of a least-squares treatment of those structure amplitudes $F(hk0)$ and $F(0kl)$ the signs of which seemed established. The x and z coordinates, already known with considerable accuracy, were regarded as constants and the dialuric acid molecule was initially assumed to be planar with parameters A, B, and C:

$$Ax+By+Cz = 1 .$$

The y coordinate of the water oxygen, O_7, constituted a fourth parameter D. The partial derivatives $\partial F_i/\partial A$, $\partial F_i/\partial B$, and $\partial F_i/\partial C$ were expressed in terms of $\partial F_i/\partial y$ of each of the dialuric acid atoms, and normal equations were composed in the usual way to be solved for values of the increments δA, δB, δC, and δD which would minimize the quantity $\sum_i w_i(\Delta F_i)^2$ summed over all the reflections employed. A sequence of four least-squares solutions of this kind reduced R to about 0·26, but again the results tended to converge without further improvement.

It seemed probable that the cause of the meager improvement achieved through the least-squares calculations lay in the stringency of the arbitrary planarity condition imposed, which required not only the pyrimidine ring, but the appended oxygen atoms as well, to occupy a common plane. The more precise investigations of pyrimidine and purine structures published previously (references cited earlier) had failed to disclose significant deviations from planarity of the ring atoms, although in some structures, notably those possessing intermolecular hydrogen bridges, substituent groups often deviated considerably. The extensive network of hydrogen bonds to be expected in dialuric acid monohydrate would appear to be conducive to bending of the carbon–oxygen bonds out of the ring plane.

As a result of these considerations the least-squares procedure was revised so as to relax the planarity requirement by exempting the four substituent oxygen atoms, thus increasing the parameters to eight. Without high-speed computing equipment the numerical evaluation of the coefficients of the eight normal equations and their solution are laborious operations, especially since both the diagonal and non-diagonal terms must be calculated. The solution process was shortened considerably by applying Crout's method (Crout, 1941). Two least-squares refinements of this kind improved the y parameters sufficiently to reduce the reliability index of the observed reflections to 0·201 on the basis of the isotropic thermal coefficients $B = 2{\cdot}07$ Å^2 for ring atoms and $2{\cdot}70$ Å^2 for extra-ring atoms.

The refinement of atomic parameters was now halted, and the intramolecular bond lengths were computed, revealing several anomalous values, as given in the second column of Table 1. These bond lengths were improved, as indicated in the last column, by judicious small movements of atoms N_1, N_3, C_2, and C_5, which reduced R for the 145 observed $(h0l)$ reflections from 0·182 to 0·160. An analysis of F_c/F_o ratios at small and large values of $(\sin \theta)/\lambda$ revealed a need for

Table 1. *Anomalous bond lengths observed in partially refined structure*

Bond	Observed length (Å)	Expected length (Å)	Improved length (Å)
N_1–C_2	1·27	1·31	1·32
N_3–C_2	1·26	1·31	1·32
C_5–C_6	1·22	1·38	1·33
C_5–O_5	1·54	1·22–1·43	1·43

another change in scale factor and a further increase in the thermal vibration coefficient of the oxygen atoms, B_2. The final values of the coefficients arrived at were $B_1 = 2{\cdot}07$ Å^2 (C and N atoms) and $B_2 = 3{\cdot}50$ Å^2 (O atoms). The atomic coordinates are given in Table 2. These coordinates preserve the planarity of the pyrimidine ring nucleus, which satisfies the equation

$$0{\cdot}045x+1{\cdot}260y+1{\cdot}719z = 1\ .$$

No attempt was made to evaluate the accuracy of the atomic coordinates and bond lengths by standard statistical methods. However, an appraisal of the sensitivity of the reliability index to parameter changes, together with a consideration of other comparable structure determinations, leads to the conclusion that the probable error in x and z is approximately 0·0015 and in y about 0·006. These variances are equivalent to about 0·02 Å.

Table 2. *Atomic coordinates*

Atom	x	y	z
C_2	0·135	0·321	0·334
C_4	−0·047	0·283	0·366
C_5	−0·072	0·422	0·267
C_6	0·004	0·502	0·208
O_2	0·230	0·254	0·366
O_4	−0·112	0·162	0·423
O_5	−0·177	0·542	0·234
O_6	−0·003	0·676	0·117
$O_7(H_2O)$	−0·314	0·502	0·446
N_1	0·111	0·452	0·241
N_3	0·063	0·236	0·396

Table 3. *Observed and calculated structure factors**

hkl	F_o	F_c
200	33	35
400	< 2	0
600	10	10
800	5	5
1000	7	12
1200	6	7
1400	< 4	1
1600	10	11
002	51	$\overline{55}$
004	24	$\overline{26}$
006	51	$\overline{52}$
008	29	$\overline{26}$
0010	14	$\overline{13}$
0012	< 4	$\overline{3}$
0014	< 4	0
0016	4	3
101	18	$\overline{23}$
301	12	16
501	43	40
701	55	50
901	13	$\overline{16}$
1101	14	15
1301	5	6
1501	< 3	$\overline{2}$
$10\bar{1}$	20	$\overline{18}$
$30\bar{1}$	5	2
$50\bar{1}$	60	57
$70\bar{1}$	12	$\overline{13}$
$90\bar{1}$	15	15
$110\bar{1}$	25	26
$130\bar{1}$	< 4	$\overline{4}$
$150\bar{1}$	7	5
202	3	1
402	25	$\overline{25}$
602	19	19
802	4	$\overline{7}$
1002	< 4	$\overline{3}$
1202	17	$\overline{15}$
1402	< 3	$\overline{1}$
$20\bar{2}$	35	$\overline{34}$
$40\bar{2}$	39	$\overline{42}$
$60\bar{2}$	30	$\overline{27}$
$80\bar{2}$	4	$\overline{4}$
$100\bar{2}$	< 4	2
$120\bar{2}$	6	3
$140\bar{2}$	6	$\overline{4}$
$160\bar{2}$	4	$\overline{5}$
103	13	14
303	9	$\overline{8}$
503	32	$\overline{32}$
703	42	$\overline{37}$
903	7	$\overline{4}$
1103	5	5
1303	< 4	3
1503	5	$\overline{5}$
$10\bar{3}$	5	6
$30\bar{3}$	54	$\overline{56}$
$50\bar{3}$	19	17
$70\bar{3}$	4	$\overline{8}$
$90\bar{3}$	18	$\overline{18}$
$110\bar{3}$	44	$\overline{41}$
$130\bar{3}$	5	$\overline{7}$
$150\bar{3}$	< 3	5
204	28	$\overline{26}$
404	34	$\overline{33}$
604	37	35
804	9	$\overline{9}$
1004	< 4	$\overline{2}$
1204	8	6
1404	6	$\overline{5}$
$20\bar{4}$	16	$\overline{13}$
$40\bar{4}$	52	$\overline{44}$
$60\bar{4}$	18	$\overline{17}$
$80\bar{4}$	20	$\overline{17}$
$100\bar{4}$	19	23
$120\bar{4}$	5	4
$140\bar{4}$	5	$\overline{5}$
$160\bar{4}$	3	$\overline{3}$
105	77	78
305	29	$\overline{27}$
505	15	$\overline{18}$
705	< 3	5
905	6	$\overline{8}$
1105	12	$\overline{8}$
1305	< 3	$\overline{2}$
$10\bar{5}$	31	$\overline{33}$
$30\bar{5}$	3	6
$50\bar{5}$	5	3
$70\bar{5}$	15	$\overline{20}$
$90\bar{5}$	< 4	3
$110\bar{5}$	5	4
$130\bar{5}$	< 4	$\overline{2}$
$150\bar{5}$	7	$\overline{5}$
206	15	$\overline{15}$
406	< 3	$\overline{3}$
606	6	7
806	19	20
1006	20	$\overline{20}$
1206	< 4	2
$20\bar{6}$	11	$\overline{10}$
$40\bar{6}$	46	43
$60\bar{6}$	8	$\overline{2}$
$80\bar{6}$	8	$\overline{6}$
$100\bar{6}$	< 4	$\overline{3}$
$120\bar{6}$	11	$\overline{12}$
$140\bar{6}$	12	10
107	10	$\overline{3}$
307	9	11
507	17	$\overline{16}$
707	3	$\overline{5}$
907	< 4	$\overline{3}$
1107	7	4
1307	< 3	1
$10\bar{7}$	13	$\overline{12}$
$30\bar{7}$	14	17
$50\bar{7}$	36	$\overline{37}$
$70\bar{7}$	8	8
$90\bar{7}$	9	8
$110\bar{7}$	< 4	1
$130\bar{7}$	< 3	1
$150\bar{7}$	8	5
208	25	22
408	13	12
608	18	$\overline{20}$
808	10	$\overline{9}$
1008	< 4	4
1208	< 3	3
1408	< 3	2
$20\bar{8}$	< 3	$\overline{1}$
$40\bar{8}$	17	18
$60\bar{8}$	6	3
$80\bar{8}$	6	$\overline{3}$
$100\bar{8}$	15	$\overline{15}$
$120\bar{8}$	< 4	1
$140\bar{8}$	< 3	0
109	< 3	0
309	< 4	2
509	8	9
709	40	41
909	8	10
1109	< 3	$\overline{4}$
1309	< 2	$\overline{1}$
$10\bar{9}$	22	17
$30\bar{9}$	< 3	$\overline{3}$
$50\bar{9}$	5	$\overline{2}$
$70\bar{9}$	< 4	3
$90\bar{9}$	15	20
$110\bar{9}$	17	12
$130\bar{9}$	< 3	3
2010	18	17
4010	< 4	1
6010	< 4	3
8010	< 4	$\overline{1}$
10010	3	2
12010	3	6
$20\overline{10}$	15	20
$40\overline{10}$	19	22
$60\overline{10}$	< 4	1
$80\overline{10}$	8	10
$100\overline{10}$	< 4	0
$120\overline{10}$	< 3	2
1011	10	$\overline{13}$
3011	7	10
5011	7	$\overline{6}$
7011	14	$\overline{13}$
9011	< 3	4
11011	4	$\overline{3}$
$10\overline{11}$	< 4	$\overline{4}$
$30\overline{11}$	14	13
$50\overline{11}$	10	4
$70\overline{11}$	6	$\overline{4}$
$90\overline{11}$	9	$\overline{9}$
$110\overline{11}$	10	$\overline{11}$
2012	< 4	3
4012	< 4	$\overline{2}$
6012	7	$\overline{6}$
8012	< 3	0
$20\overline{12}$	12	$\overline{14}$
$40\overline{12}$	38	$\overline{43}$
$60\overline{12}$	6	$\overline{5}$
$80\overline{12}$	< 4	$\overline{4}$
$100\overline{12}$	< 3	$\overline{1}$
1013	9	$\overline{11}$
3013	12	$\overline{14}$
5013	< 3	2
7013	7	$\overline{6}$
9013	5	$\overline{4}$
$10\overline{13}$	< 4	$\overline{2}$
$30\overline{13}$	< 4	7
$50\overline{13}$	< 4	$\overline{2}$
$70\overline{13}$	< 3	$\overline{1}$
$90\overline{13}$	8	$\overline{6}$
2014	4	$\overline{3}$
4014	< 3	3
6014	< 2	1
$20\overline{14}$	< 4	0
$40\overline{14}$	8	5
$60\overline{14}$	< 3	0
$80\overline{14}$	6	$\overline{3}$
1015	< 3	3
3015	12	8
$10\overline{15}$	< 3	2
$30\overline{15}$	< 3	$\overline{1}$
$50\overline{15}$	< 3	$\overline{2}$
$70\overline{15}$	5	6
$20\overline{16}$	6	4
$40\overline{16}$	4	0
110	28	$\overline{20}$
210	37	38
310	33	28
410	8	- $\overline{5}$
510	3	$\overline{4}$
610	25	16
710	42	$\overline{32}$
810	12	14
910	4	$\overline{2}$
120	40	43
220	15	$\overline{16}$
320	3	$\overline{4}$
420	< 3	$\overline{3}$
520	12	12
620	< 4	3
720	21	$\overline{13}$
820	< 4	$\overline{3}$
920	< 3	$\overline{2}$
1020	4	$\overline{2}$
130	6	$\overline{6}$
230	5	3
330	5	2
430	7	6
530	10	10
630	9	$\overline{11}$
730	8	7
830	7	$\overline{2}$
020	10	$\overline{4}$
040	12	14
011	8	2
012	98	104
013	31	22
014	13	8
015	3	$\overline{4}$
016	37	$\overline{35}$
017	16	13
018	< 3	$\overline{8}$
019	23	$\overline{23}$
0110	14	10
0111	< 4	$\overline{1}$
0112	< 4	$\overline{2}$
021	< 3	1
022	28	$\overline{23}$
023	29	$\overline{24}$
024	60	61
025	9	$\overline{4}$
026	23	$\overline{17}$
027	12	7
028	11	$\overline{11}$
029	13	$\overline{9}$
0210	< 4	$\overline{8}$
0211	11	$\overline{6}$
0212	6	2
031	12	11
032	16	$\overline{16}$
033	5	13
034	4	$\overline{3}$
035	22	$\overline{18}$
036	17	16
037	< 4	$\overline{3}$
038	5	$\overline{3}$
039	< 4	$\overline{3}$
0310	4	$\overline{2}$
0311	5	3

* Unobserved reflections are assigned F_o values less than the minimum detectable levels for the corresponding regions of the diffraction patterns.

Final values of the reliability index are:

($h0l$) reflections, 145 of observable intensity,
$R = 0{\cdot}134$;
($hk0$) and ($0kl$) reflections, 65 of observable intensity,
$R = 0{\cdot}173$.

Observed and calculated structure factors are listed in Table 3. In regard to the considerably larger value of the reliability index for the ($hk0$) and ($0kl$) reflections compared with that for the ($h0l$) reflections, little further improvement in the former data could be hoped for regardless of the methods employed because, as mentioned earlier, the natural habit of the crystals used in the X-ray analysis was unfavorable for these reflections. A consideration of the crystal dimensions and absorption coefficient discloses the possibility of errors in F_o of as much as 12% in certain orientations.

In this investigation Hartree atomic scattering factors were used in computing the structure factors. The Fourier-series summations were performed by the Patterson–Tunell strip-and-stencil method (Patterson & Tunell, 1942).

Description of the structure

1. *Framework features*

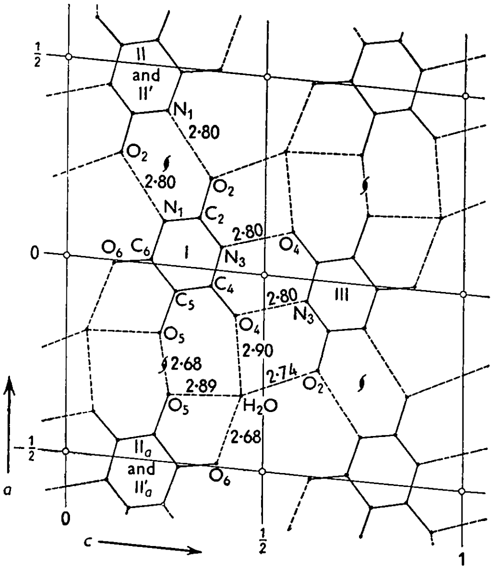


Fig. 3. Diagram of the structure as projected on (010). Broken lines indicate actual or possible hydrogen bonds.

Fig. 3 shows the structural arrangement projected on (010). As expected, it is found that the molecules of dialuric acid are tied together and to the water molecules by an intricate network of hydrogen bridges. The basic framework comprises both N–H · · · O and O–H · · · O bonds. Each I molecule of dialuric acid is linked to five adjoining molecules as follows:

(a) to a II molecule above it (larger y) and to a II′ molecule below it (smaller y) by a spiral sequence of hydrogen bonds of length 2·80 Å between N_1 of one molecule and O_2 of the other and situated about a screw axis,
(b) to a III molecule by a pair of hydrogen bonds of length 2·80 Å between N_3 and O_4 and situated about a symmetry center, and
(c) to a II_a molecule above it and to a II_a' molecule below it through a zigzag chain of hydrogen bonds, 2·68 Å long, between equivalent oxygen atoms, O_5, and which intersect a screw axis.

The water molecule does not play a dominant role in the framework structure. It fits into a cavity wherein it is surrounded irregularly by eight oxygen atoms belonging to six dialuric acid molecules. It is bound rather strongly to O_6 of molecule II_a and O_2 of III by hydrogen bonds of the respective lengths 2·68 and 2·74 Å. In addition, it makes two rather close approaches to other oxygen atoms, being 2·89 Å from O_5 of molecule II_a and 2·90 Å from O_4 of molecule I. The remaining oxygen atoms coordinate at distances of 3·07, 3·45, 3·57, and 3·80 Å. Inasmuch as the hydrogen positions are not directly revealed in the present investigation, it is not possible to determine which oxygen atom, other than O_2, is the receptor of a hydrogen atom donated by the water molecule. The y coordinates of the spiral and zigzag hydrogen bond sequences can be appreciated from an inspection of Fig. 4. This illustration also conveys some idea of the coordination of oxygen atoms about a water molecule. For clarity only one water coordination group, and one zigzag and one spiral hydrogen bond sequence are delineated.

The perpendicular distance between the planes of successive pyrimidine rings in the b direction is 3·56 Å. The coordinates of the axis of tilt (direction of steepest descent) of the ring plane are:

Elevation (with respect to the (010) planes)	21·6°;
Azimuth (with respect to the c axis)	6·9°.

2. *Molecular structure*

The dimensions of the dialuric acid molecule are shown in Fig. 5. Bearing in mind that the probable error in the bond lengths is approximately 0·03 Å, we may conclude that the average C_2–N_1 and C_2–N_3 distance of 1·32 Å is significantly shorter than the average of the N_1–C_6 and N_3–C_4 distances, 1·42 Å. It is probable but not certain that the two C–C distances are unequal, C_5–C_6 being apparently shorter than C_5–C_4. The four oxygen atoms are attached to the ring by bonds of two lengths. O_2 and O_4 are 1·28 and 1·24 Å distant from their ring carbon atoms, which distances may be regarded as equal within the experimental error and characteristic of a bond possessing half single- and half double-bond character. Contrasting with this result, the C_6–O_6 and C_5–O_5 bonds are

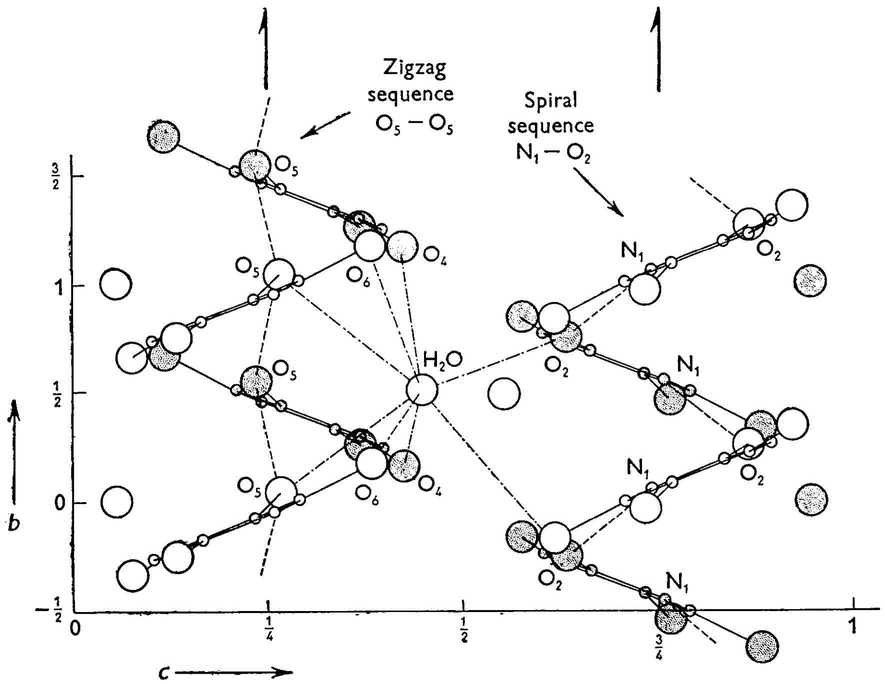


Fig. 4. Projection of the structure on (100). Broken lines indicate hydrogen bonds of the zigzag and spiral sequences. Dot-dash lines connect a water molecule with its eight coordinated oxygen atoms.

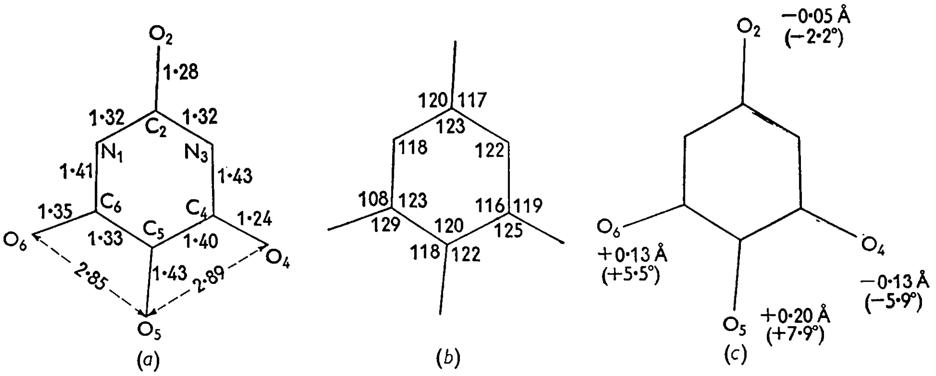


Fig. 5. Dimensional features of the dialuric acid molecule. (a) Interatomic distances (Å). (b) Bond angles (°). (c) Departures from plane of ring.

clearly much longer, their average length of 1·39 Å approaching the single-bond value, 1·43 Å. The apparent difference of 0·08 Å between these two distances is probably, but not certainly, a real one. If it is taken to be real, C_5–O_5 has purely single-bond character while C_6–O_6 has an appreciable double-bond component.

Fig. 5(c) gives the displacements of the oxygen atoms from the plane of the pyrimidine ring. Clearly the displacements of O_4, O_5, and O_6 are all greater than the experimental error and all involve angular displacements of the bonds from the ring plane of more than 5°. The displacement of O_2 is less than twice the probable error, and so is not definite. In order to demonstrate more conclusively the reality of these deviations from the ring plane, the y coordinate of each oxygen atom in turn was arbitrarily changed so as to place it in the plane $0{\cdot}045x+1{\cdot}260y+1{\cdot}719z=1$, after which the structure factors and reliability index

Table 4. *Effect on R of moving the oxygen atoms into the plane of the pyrimidine ring*

Atom moved	Non-planar y parameter	Planar y parameter	R
None	—	—	0·173
O_2	0·254	0·273	0·181
O_4	0·162	0·206	0·200
O_5	0·542	0·472	0·204
O_6	0·676	0·630	0·207
Entire molecule planarized	—	—	0·209

for the ($hk0$) and ($0kl$) reflections were recomputed. Table 4 shows that the increase in R is so great for O_4, O_5, and O_6 as to positively establish the reality of their departures from the plane of the pyrimidine ring. Placing O_2 in the plane increases R from 0·173 to 0·181, which is insufficient to prove the reality of its observed displacement of −0·05 Å. Finally all the atoms comprising the dialuric acid molecule were assigned y coordinates that placed them on the 'best' plane through all the atomic sites as deduced by least squares:

$$-0{\cdot}110x+1{\cdot}123y+2{\cdot}032z = 1\,.$$

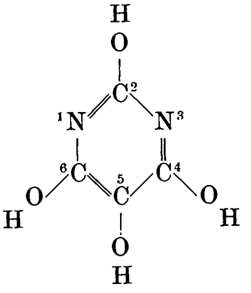
This resulted in an increase in R from 0·173 to 0·209, which clearly precludes the completely planar configuration.

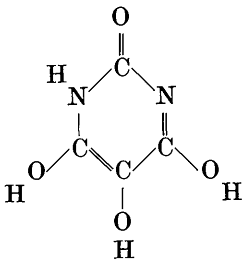
The probable error in the bond-angle determinations (see Fig. 5(b)) is estimated to be somewhat less than 2°. Therefore it may be said that all the internal angles of the pyrimidine nucleus are 120° within the error of measurement except for the angle $N_3C_4C_5$, which appears to be significantly smaller, namely, 116°. Likewise the exterior angles at the C_2 site approximate 120°. However, the exterior angles at the C_4 and C_6 sites are plainly unequal, the C_4–O_4 and C_6–O_6 bonds being considerably bent in directions that increase the 'normal' vector distances between the neighboring pairs of *ortho*-substituted oxygen atoms, O_4 and O_5, and O_5 and O_6. These vector distances are respectively 2·89 and 2·85 Å.

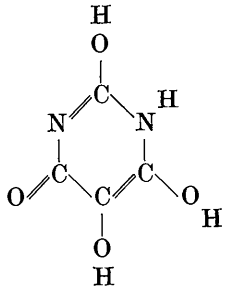
It should be noted that the internal angles of the pyrimidine ring in dialuric acid monohydrate are at variance with the corresponding angles found in halogen- and amino-substituted pyrimidines (Clews & Cochran, 1948, 1949) as well as with the internal angles proposed by Clews & Cochran (1949) for pyrimidine itself. On the other hand, the present angles agree well with Pitt's findings for 4,6-dimethyl-2-hydroxypyrimidine (Pitt, 1948). The most characteristic angular feature of the halogen- and amino-substituted pyrimidines is the large angle of about 130° at the C_2 site, whereas in dialuric acid monohydrate and 4,6-dimethyl-2-hydroxypyrimidine this angle is close to 120°. These latter two pyrimidines resemble each other in another respect, namely, the smaller lengths of the C_2–N_1 and C_2–N_3 bonds compared with the N_1–C_6 and N_3–C_4 bonds.

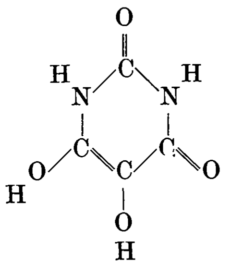
Discussion

The chemical reactions which dialuric acid undergoes show that in solution there is equilibrium between a tautomeric form possessing only enol oxygen atoms (I) and one or more tautomers possessing keto oxygen atoms and N–H groups (II, III, and IV for example).

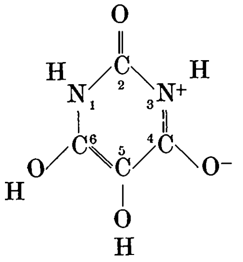

(I)

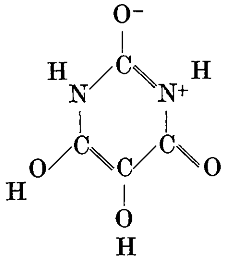

(II)
Mono-keto

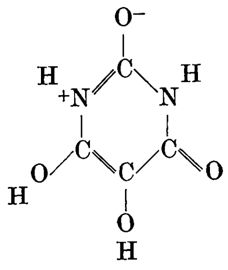

(III)
Mono-keto

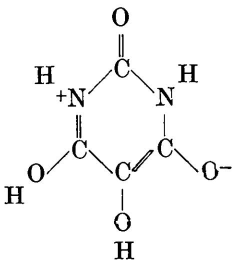

(IV)
Di-keto

That we are dealing with tautomer (IV) in the crystal structure of the monohydrate is demonstrated by the short C_2–O_2 and C_4–O_4 distances (refer to Fig. 5(a)) as well as by the normal, or near normal, single bonds C_5–O_5 and C_6–O_6. In all but one respect the observed dimensions of the molecule can be explained by contributions of the following four valence bond structures having a single pair of formal charges:


(A)

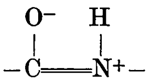

(B)


(C)


(D)

If the contributions of (*B*) and (*C*) are considered somewhat more important than those of (*A*) and (*D*), these dimensions can be understood: (*a*) the shorter C_2–N_1 and C_2–N_3 distances (1·32 Å) compared with the average length (1·42 Å) of C_6–N_1 and C_4–N_3, (*b*) the possibly smaller C_4–O_4 than C_2–O_2 bond, and (*c*) the smaller C_5–C_6 than C_4–C_5 distance. The only dimensional feature not explained by the above valence bond picture is the apparent difference in the observed lengths of the two formally single carbon–oxygen bonds C_5–O_5 (1·43 Å) and C_6–O_6 (1·35 Å). Since this difference is not actually outside the experimental error limits, serious efforts to explain it are hardly warranted. Suffice it to say that a significant shortening of the formally single bond C_6–O_6 would seem to entail contributions from a second tautomer possessing a double bond $C_6{=}O_6$, but this proposal is of questionable chemical validity and it poses difficulties in constructing a satisfactory model of the hydrogen bridge network.

The contributions of resonance forms of the types (*A*), (*B*), (*C*), and (*D*) require the pyrimidine ring to be planar, thus substantiating the planar assumption which has been implicit throughout the solution and refinement of the structure. An additional consequence of the contribution of the resonance form



$$-\overset{O^-}{\overset{|}{C}}=\overset{H}{\overset{|}{N^+}}-$$

has been emphasized by Donohue (1952). Since this resonance feature requires all four atoms, including hydrogen, to be coplanar, restrictions are imposed on the position of the acceptor atom which is hydrogen-bonded to the nitrogen atom. In the dialuric acid monohydrate structure the condition to be fulfilled is that the acceptor oxygen atom (O_2 or O_4) shall be coplanar with the pyrimidine ring containing the donating nitrogen atom. Fig. 6 shows to what extent this condition is met. The assumed linear hydrogen bonds N_1–H ··· O_2 and N_3–H ··· O_4 make angles of 14° and 9° respectively with the plane of the pyrimidine nucleus, which may be regarded as at least rough conformation to Donohue's restriction. The near equality of the exterior angles defining the direction of these hydrogen bonds is noteworthy. It should be observed that the length of the N–H ··· O hydrogen bridges, 2·80 Å, agrees well with those reported in similar compounds, the majority of which range between 2·77 and 2·89 Å (see Table 5).

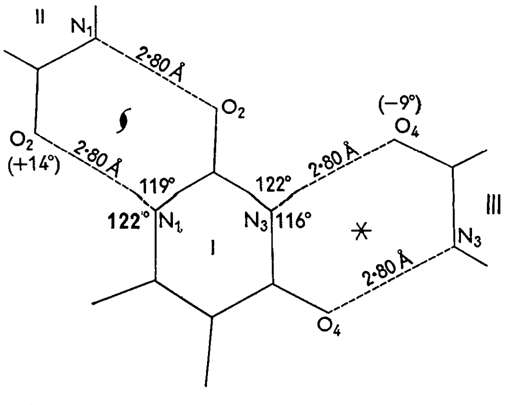


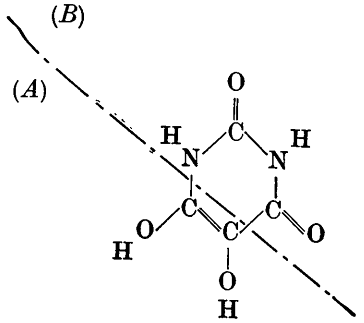
Fig. 6. Orientation of the N–H ··· O hydrogen bonds. The angles +14° and −9° denote the degree to which the bonds N_1–H ··· O_2 and N_3–H ··· O_4 are bent out of the plane of pyrimidine ring I.

Table 5. *Observed bond lengths in some heterocyclic compounds containing amide groups*

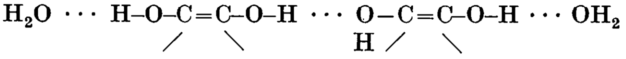
	Bond lengths (Å)			
Compound	C–O	C–N	N–H ··· O	Reference
Diketopiperazine	1·25	1·33	2·84	Corey, 1938
4,6-Dimethyl-2-hydroxy-pyrimidine	1·25	1·35	2·78 2·89	Pitt, 1948
Guanine hydrochloride	1·20	1·41	2·82 2·62	Broomhead, 1951
Cyanuric acid	1·21 1·215	1·345 1·355 1·365	2·83 2·88	Wiebenga, 1952
α-Pyridone	1·236	1·401	2·77	Penfold, 1953
Uracil	1·23	1·344 1·384	2·81 2·86	Parry, 1954
Parabanic acid	1·212	1·360 1·381	2·837 2·873	Davies & Blum, 1955
Dialuric acid monohydrate	1·28 1·24	1·32 1·32 1·43	2·80 2·80	This study

The present X-ray identification of the tautomeric form as the 2,4-di-keto configuration disagrees with infra-red results for the crystalline material published earlier (Tipson & Cretcher, 1951), which failed to show absorption bands characteristic of the –CO–NH–CO– group. However, when an attempt was made later to confirm the earlier infra-red findings, using a different lot of crystals, a changed spectrum was obtained which conclusively revealed the presence of this group. At a later date we hope to define more clearly by X-ray and infra-red studies the tautomeric forms obtainable in the solid state.

Additional light is shed on the dialuric acid monohydrate structure by dividing the molecule into two parts as follows:

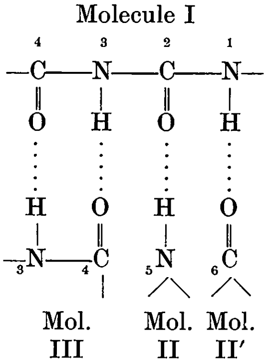


The component (*A*) is concerned only in hydrogen bonding with other oxygen atoms, namely, $O_6{-}H \cdots O_7$ and $O_5{-}H \cdots O_5'$. These hydrogen bridges are rather strong, as indicated by their 2·68 Å length, and the hydrogen-donating oxygen atoms are attached to the pyrimidine nucleus by essentially single bonds. Portion (*B*) is completely absorbed in N–H ··· O bonding between N atoms of one molecule and C=O groups of another, in this way providing the backbone of the intermolecular framework. The carbonyl oxygen atoms involved are bound to the pyrimidine nucleus by bonds having a heavy double-bond component. The intermolecular linkages set up by component (*A*) may be represented schematically



$$H_2O \cdots H{-}O{-}C{=}C{-}O{-}H \cdots O{-}C{=}C{-}O{-}H \cdots OH_2$$

and the framework network set up by component (*B*) may be represented



The exceptional resistance of dialuric acid monohydrate to melting is clearly due to the strong three-dimensional hydrogen bond network which permeates the structure. Fig. 3 shows that the structure may also be regarded as consisting of strongly knit layers of dialuric acid and water molecules parallel to $(10\bar{1})$. These layers are bound together only by a low-density pattern of spiral $N_1{-}H \cdots O_2$ hydrogen bonds, which probably accounts for the observed easy cleavage along planes parallel to the *b* axis since all other sections through the structure are crossed by much stronger bonding forces.

The bond lengths in the urea group of dialuric acid monohydrate agree closely with those in urea itself (Vaughan & Donohue, 1952):

	Dialuric acid monohydrate	Urea
C=O	1·28 Å	1·262 Å
C–N	1·32	1·335

In Table 5 the bond lengths C–O and C–N as observed in the amide groups contained in seven heterocyclic rings are listed and compared with the dimensions found in dialuric acid monohydrate. It may be noted that the somewhat short length, 1·35 Å, of the formally single bond $C_6{-}O_6$ agrees closely with the C–O distance of 1·36–1·37 Å in resorcinol (Robertson, 1936, 1938).

It is apparent that the internal structure of the dialuric acid molecule is closely related to its outer environment. Those oxygen atoms, O_5 and O_6, forming hydrogen bonds by donating hydrogen atoms to other oxygen atoms remain singly bonded to the pyrimidine nucleus, whereas atoms O_2 and O_4 transfer their hydrogens to the adjacent nitrogen atoms and enter into a resonance pattern with the ring atoms. This is a familiar form of resonance in molecules containing amide groups and, as illustrated in Table 5, the present bond lengths of C–O and C–N are fairly consistent with previously reported values.

The authors are indebted to Dr R. S. Tipson for suggesting the problem and supplying the specimens, to Dr Ray Pepinsky for the X-RAC projections, to Messrs E. C. Sommer, Lynn Thomas, and E. R. Michalek for much assistance with the calculations, to Dr Foil A. Miller for the infra-red information, and to Dr G. A. Jeffrey for helpful discussions concerning the interpretation of the structure. They are appreciative of Dr H. P. Klug's continued interest during the long duration of the investigation.

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