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The Structure of the Pyrimidines and Purines. VIII. The Crystal Structure of Alloxan, $C_4H_4N_2O_5$

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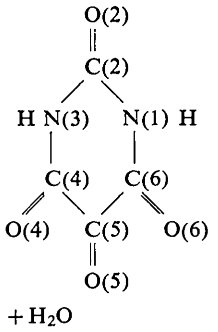
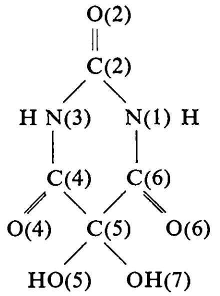
The crystal structure of alloxan, $C_4H_4N_2O_5$, has been determined by a direct sign determination method and refined by difference-Fourier and least-squares methods with anisotropic temperature parameters. The unit cell is triclinic, space group $P\bar{1}$, with $a=5{\cdot}770$, $b=6{\cdot}812$, $c=8{\cdot}206$ Å, $\alpha=74°\ 24'$, $\beta=81°\ 52'$, $\gamma=66°\ 29'$. The four hydrogen atoms in the structure were located directly from the difference density projections. The molecule is in the 2,4,6-triketo-5,5-dihydroxypyrimidine configuration and not the 2,4,5,6-tetraketo form with a water molecule. The molecules are joined by a hydrogen-bonded system involving all the electronegative atoms. Bond lengths and angles of alloxan are nearly the same as those in barbituric acid dihydrate and anhydrous alloxan, with the exception of bonds C(5)–C(4) and C(5)–C(6). These latter bonds have a mean value of 1·539 Å, which is significantly larger than any pyrimidine C–C distance reported in the literature. The molecule of alloxan is significantly distorted from planarity and this may be attributed to intermolecular approach distances which are significantly shorter than the normal van der Waals contacts and to the comparatively high crystal density (1·88 g.cm^{-3}).

Introduction

Alloxan, $C_4H_4N_2O_5$, was the first member of the pyrimidine series to be identified (Brugnatelli, 1818). It was assigned the configurational formula (I) by Wöhler & Liebig (1838) and formula (II) by Baeyer (1863).



(I)



(II)

Both formulae appear in text-books of chemistry (Katritzky & Lagowski, 1960; Acheson, 1960). In addition, tautomerism may occur in the pyrimidine ring through the migration of the hydrogen atoms. Also crystalline hydroxypyrimidines form hydrogen bonds involving the nitrogen and oxygen atoms. An accurate X-ray analysis of alloxan, undertaken with the aim of locating the hydrogen atoms directly, will elucidate its structural formula and provide information on the nature of hydrogen bonds. The ability of alloxan to cause diabetes (Dunn, Sheehen & McLetchie, 1943) has resulted in its being extensively studied.

Experimental

Alloxan was dissolved in warm water and recrystallized by gradual cooling. Colourless crystals were obtained which were almost equidimensional polyhedra. Those used for counter diffractometer work varied from 0·1 to 0·4 mm in cross-section.

Unit-cell dimensions, initially obtained from rotation and Weissenberg photographs (Chatar Singh, 1960), were redetermined using the counter diffractometer and the θ-method of Weisz, Cochran & Cole (1948).

$a=5{\cdot}770\pm0{\cdot}006$ Å	$\alpha=74°\ 24'\pm4'$
$b=6{\cdot}812\pm0{\cdot}007$	$\beta=81\ \ 52\ \pm5$
$c=8{\cdot}206\pm0{\cdot}008$	$\gamma=66\ \ 29\ \pm4$

Volume of the unit cell $=281{\cdot}5$ Å^3; $F(000)=164$; $\mu=18{\cdot}2$ cm^{-1} for Cu $K\alpha$ and $2{\cdot}16$ cm^{-1} for Mo $K\alpha$. The density, measured was 1·877 g.cm^{-3} and calculated for $Z=2$ was 1·880 g.cm^{-3}. Application of Wilson's (1949) ratio test to the *a*-, *b*- and *c*-axis data indicated centrosymmetry. Thus the crystal belongs to space group $P\bar{1}$.

Intensity data

Intensity data were collected in three stages. In the preliminary analysis only the 0*kl*, *h*0*l* and *hk*0 layer lines were recorded.

After solving the structure, all *hkl* reflexions in the copper sphere were recorded by the equi-inclination method and the multiple-film technique. Photographs were taken up to the fourth and fifth layers along the *a* and *b* axis respectively. The data were placed on the same relative scale by a cross-correlation procedure (Chatar Singh, 1961). In all 1183 independent reflexions were obtained, ten of which were not measurable.

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To permit direct location of the hydrogen atoms, the data for the 0*kl* and *hk*0 layers were collected with a scintillation-counter diffractometer (Calder, 1960). The stationary-counter and moving-crystal technique with pulse-height discrimination and Mo $K\alpha$ radiation were used. The crystal and counter were set manually. To detect and minimize errors, equivalent reflexions on either side of the primary beam were measured and further measurements only made if the agreement within each set of four reflexions was better than 2%. The integrated intensity of the reflexion peak, minus the mean value of the two integrated background measurements made on either side of the peak, was taken as a measure of the integrated intensity of the reflexion. Throughout the measurements a standard reflexion was integrated periodically.

For each crystal, the strong and weak reflexions were measured separately and the measurements repeated four to five times for internal consistency. The weak reflexions were placed on the same scale as the strong ones using the standard reflexion. For each projection, measurements were made on four or five different crystals of varying sizes to check on possible systematic error and extinction effects. Extinction effects were reduced to a minimum by using a very small crystal (0·1 mm cross-section) to measure the strong reflexions. Loss counts corrections were applied to reflexions exceeding 6000 counts per minute. The resolving time of the measuring instruments was five microseconds. The intensities were corrected for absorption by Busing & Levy's (1957) method and finally reduced to relative observed structure amplitudes. An estimate of the accuracy of the counter data was obtained by calculating the residual factor of the several sets of intensity values from the two layers. This factor never exceeded 2·2%. Hence the probable random error in the observed structure amplitudes is not more than 2%. A total of 306 0*kl* and 185 *hk*0 reflexions were measured. The twelve common 0*k*0 reflexions gave an agreement index of 1·3%.

Structure determination

The structure of alloxan was solved in the *b*-axis projection by direct sign determination methods. The program written by Dr W. Cochran based on Sayre's relationship, $Y(\mathbf{h}, \mathbf{h}') = S(\mathbf{h})\ S(\mathbf{h}')\ S(\mathbf{h}+\mathbf{h}') \approx +1$, generates a number of sign sets using large unitary structure factors. The quantity $G(\mathbf{h})$, proportional to the unitary structure factor of the squared electron density distribution, was calculated from the expression $G(\mathbf{h}) = \Sigma_{\mathbf{h}}\, U(\mathbf{h}')\ U(\mathbf{h}+\mathbf{h}')$. $G(\mathbf{h})$ was used in the expression

$$T = \Sigma_{\mathbf{h}} \frac{\left||U(\mathbf{h})| - \alpha |G(\mathbf{h})|\right|}{|U(\mathbf{h})|}$$

to evaluate T for each sign set (Cochran, Srinivasan & Tollin, 1963). For the correct sign set T should be a minimum. Using 28 unitary structure factors, 23 sign sets were produced, one of which gave $T = 0{\cdot}38$ (others ranged from 0·46 to 0·58). This set was chosen to evaluate the electron density map (see Fig. 2 of Cochran *et al.*, 1963) from which the structure was recognized. The first set of structure factors gave an R index of 21%. To obtain the y coordinates, the sharpened Patterson map of the *a*-axis projection was used to locate the centre of the pyrimidine ring; a model of the molecule was then oriented to fit the preliminary x and z coordinates.

The refinement

As the main aim of this investigation was the direct location of the hydrogen atoms, the counter data were utilized. The refinement was conducted in two stages; in the first stage, only reflexions with $(\sin\theta/\lambda) > 0{\cdot}36$ were used. This approach helps to minimize errors due to the unknown hydrogens and extinction, if present.

The reliability index for the high-angle terms of the 0*kl* data, using isotropic temperature factors, was 22·1%. The difference synthesis [Fig. 1(*a*)] indicated marked anisotropic thermal vibrations of a number of atoms. Accordingly, anisotropic temperature factors

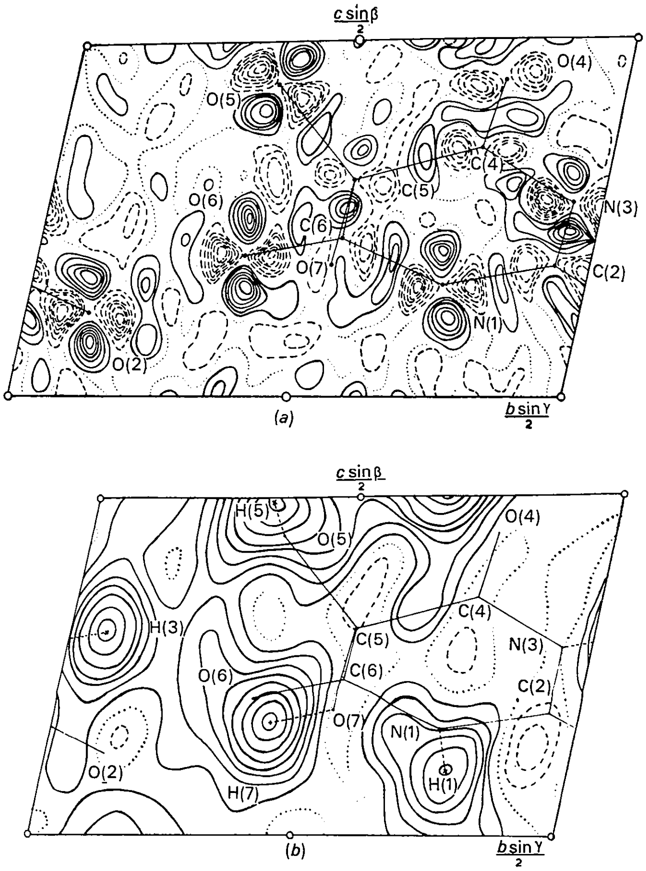

Fig. 1. Difference syntheses on (100): (*a*) of high-angle reflexions, $(\sin\theta/\lambda) \geq 0{\cdot}36$, showing marked anisotropic thermal vibrations; (*b*) of low-angle reflexions, $(\sin\theta/\lambda) < 0{\cdot}36$, with the contribution of the hydrogen atoms excluded. Contours in (*a*) are at equal but arbitrary levels and in (*b*) are at 0·1 e.Å^{-2} intervals. Zero levels are dotted and negative levels dashed.

were introduced. In the last three refinement cycles, seventeen very weak reflexions with $|F_o|/|F_c|>3$ were excluded from the computation. At $R=4{\cdot}7\%$, the remaining features of the difference synthesis could not be related to incorrect refinement of the atomic positions or thermal parameters. A difference synthesis calculated with the low-angle reflexions [Fig. 1(*b*)], but omitting the contribution of the four hydrogen atoms, revealed the hydrogen atom positions. Their coordinates were obtained from the maxima in this map. With the hydrogen atom contribution included, the structure factors gave an agreement index of 3·9% for all reflexions.

The *c*-axis counter data were refined independently by the same procedure. When the R index for the high-angle terms dropped to 4·5%, a difference synthesis of all terms, excluding the hydrogen contribution, clearly revealed the hydrogen atom positions. Their inclusion in the structure factor calculations gave an R value of 4·0%. The final atomic coordinates (Table 1) were taken to be the mean of the values determined from the two independently refined projections. The maximum difference in the common y coordinates was 0·004 Å giving a r.m.s. value of 0·002 Å. The final structure factors (2-D) are listed in Table 2.

Least-squares refinement

The hydrogen atoms having been located, an anisotropic least-squares refinement of the three-dimensional data was attempted. The refinement was carried out on the Manchester University Mercury Computer. The program (Mills & Rollett, 1961) used a weighting factor of the form

$$W=\frac{1}{(1+|F_o|^2/8\,|F_{\min}|^2)}\,.$$

Though the contribution of the hydrogen atoms was included in the structure factor calculations, their positional and thermal parameters were not refined. In four cycles, R decreased from 14·7% to 10·2%. At this stage fifteen very strong reflexions, with calculated structure factors about 27% larger than the observed, were omitted and the refinement continued on the Massachusetts Institute of Technology IBM 7094 Computer with Busing, Martin & Levy's (1962) program. All reflexions were given unit weight. The temperature factors of the hydrogen atoms were made equal to those of the atoms to which they are directly bonded and their positional parameters refined together with those of the 'heavy atoms'. After three cycles R decreased to 7·7%, which on the inclusion of the fifteen omitted reflexions becomes 8·7%. The final atomic coordinates are listed in Table 1 and the thermal parameters in Table 3. The final structure factors (3-D) are available from the author.

The differences in the atomic coordinates derived from the three-dimensional photographic and two-dimensional counter data give an indication of the accuracy of the final parameters since the data were collected and refined by different techniques. The root mean square values of standard deviations from the two sets of data are 0·0049, 0·0047 and 0·0049 Å for carbon, nitrogen and oxygen atoms, respectively. Twenty-three parameters differed by less than 1 standard deviation, nine between 1 and 2 standard deviations, and one greater than 2 but less than 2½ standard deviations. The latter was of an atom only partially resolved in projection. Since there are no apparent systematic trends in these differences, it is concluded that there is no significant difference between the results derived from three-dimensional photographic data and two-dimensional counter data from well-resolved projections.

The standard deviations of the coordinates from 3-D data, assumed to be isotropic, are $\sigma(\Delta x_i)=0{\cdot}0034$, 0·0030, 0·0027 and 0·05 Å for carbon, nitrogen, oxygen and hydrogen atoms, respectively.

Extinction

The R index of the high-angle $0kl$ reflexions, measured from films, did not decrease below 12·3%. The

Table 1. *Atomic coordinates for alloxan*

	x/a		y/b		z/c	
Atom	Counter	3–D	Counter	3–D	Counter	3–D
C(2)	−0·2371	−0·2369	0·4453	0·4447	0·1784	0·1783
C(4)	0·1380	0·1393	0·2671	0·2660	0·3482	0·3472
C(5)	0·1926	0·1932	0·0464	0·0469	0·3015	0·3016
C(6)	−0·0267	−0·0283	0·0438	0·0436	0·2204	0·2196
N(1)	−0·2129	−0·2120	0·2452	0·2452	0·1544	0·1555
N(3)	−0·0562	−0·0559	0·4465	0·4468	0·2695	0·2689
O(2)	−0·4128	−0·4128	0·6135	0·6129	0·1193	0·1199
O(4)	0·2700	0·2700	0·2805	0·2802	0·4425	0·4425
O(5)	0·2528	0·2528	−0·1271	−0·1271	0·4435	0·4434
O(6)	−0·0297	−0·0296	−0·1242	−0·1247	0·1977	0·1985
O(7)	0·3930	0·3923	0·0317	0·0317	0·1827	0·1818
H(1)	−0·3203	−0·3430	0·2734	0·2500	0·0859	0·0959
H(3)	−0·0703	−0·0722	0·5687	0·5926	0·2891	0·2768
H(5)	0·3906	0·4016	−0·1750	−0·1609	0·4891	0·4752
H(7)	0·4531	0·4646	−0·0859	−0·1155	0·1594	0·1741

Table 2. *Observed and calculated structure factors* (×80) *from counter-data*

A minus sign before an 'observed' figure indicates that the reflexion was omitted from the difference synthesis

OBS.	CALC.	L	K
38	-37	-15	0
13	16	-14	
36	-31	-13	
41	-41	-12	
132	127	-11	
25	-40	-10	
92	90	-9	
346	-341	-8	
235	225	-7	
251	239	-6	
315	307	-5	
132	-145	-4	
1624	-1618	-3	
1507	-1517	-2	
134	-100	-1	
-29	4	-15	1
44	43	-14	
85	88	-13	
84	-82	-12	
139	-143	-11	
37	26	-10	
182	180	-9	
205	-211	-8	
-33	-2	-7	
143	146	-6	
212	236	-5	
327	322	-4	
452	-437	-3	
705	-700	-2	
323	369	-1	
805	774	0	
1104	-1116	1	
49	42	2	
426	-433	3	
313	316	4	
736	718	5	
180	178	6	
361	-345	7	
393	-404	8	
50	44	9	
164	166	10	
36	45	11	
67	-73	12	
68	67	13	
32	25	14	
75	-77	15	
35	-31	-14	2
13	9	-13	
130	-142	-12	
115	117	-11	
269	270	-10	
85	-82	-9	
109	-109	-8	
219	-225	-7	
78	-64	-6	
273	-259	-5	
973	945	-4	
170	-160	-3	
488	-516	-2	
274	282	-1	
431	449	0	
975	993	1	
1873	-1886	2	
183	-156	3	
160	-159	4	
539	531	5	
70	78	6	
191	193	7	
103	-119	8	
168	-173	9	
142	150	10	
83	-84	11	
66	66	12	
0	1	13	
58	-60	14	
37	-34	15	
56	54	16	
25	16	-14	3
54	55	-13	
59	-59	-12	
25	20	-11	
34	-24	-10	
100	-98	-9	
142	145	-8	
77	-79	-7	
231	238	-6	
42	40	-5	
115	104	-4	
758	-740	-3	
111	-114	-2	
20	35	-1	
176	201	0	
371	307	1	
50	-71	2	
1102	1132	3	
624	-629	4	
201	-230	5	
190	-189	6	
15	-6	7	
136	-157	8	
289	287	9	
191	197	10	
189	-186	11	
-20	0	12	
0	-27	13	
21	4	14	
-8	0	15	
-30	19	16	

OBS.	CALC.	L	K
30	-31	-13	4
-15	5	-12	
46	36	-11	
84	81	-10	
159	-163	-9	
120	-114	-8	
12	7	-7	
192	203	-6	
52	49	-5	
72	-68	-4	
255	255	-3	
381	-380	-2	
196	186	-1	
136	142	0	
333	-339	1	
162	-151	2	
13	-15	3	
87	97	4	
60	50	5	
265	268	6	
110	-107	7	
124	124	8	
39	-37	9	
277	-278	10	
37	-42	11	
126	132	12	
105	107	13	
29	-22	14	
42	-44	15	
-38	-12	16	
51	46	-12	5
50	-50	-11	
34	41	-10	
108	-111	-9	
100	100	-8	
205	210	-7	
29	-29	-6	
118	-131	-5	
412	-411	-4	
166	-164	-3	
13	7	-2	
1379	1422	-1	
75	-84	0	
747	-761	1	
416	-394	2	
98	83	3	
351	346	4	
125	-116	5	
118	125	6	
276	-280	7	
116	123	8	
19	-14	9	
154	151	10	
34	-20	11	
79	-83	12	
34	33	13	
58	-55	14	
-25	-4	15	
24	22	-11	6
89	92	-10	
83	-85	-9	
57	-64	-8	
89	90	-7	
34	-25	-6	
142	155	-5	
87	-91	-4	
91	-95	-3	
119	123	-2	
116	108	-1	
383	-396	0	
196	-186	1	
63	81	2	
354	328	3	
408	409	4	
-15	3	5	
329	-339	6	
304	-303	7	
41	40	8	
208	209	9	
59	50	10	
128	-132	11	
71	84	12	
49	50	13	
83	-84	14	
-37	-6	15	
59	-46	-10	7
83	-74	-9	
78	-80	-8	
54	54	-7	
38	-35	-6	
212	209	-5	
96	-101	-4	
257	-222	-3	
118	123	-2	
252	240	-1	
324	321	0	
583	-583	1	
224	-219	2	
99	96	3	
230	228	4	
32	20	5	
0	0	6	
19	-29	7	
122	-117	8	
192	199	9	
66	-62	10	
0	-1	11	
19	-16	12	
67	-72	13	
-19	-1	14	
72	67	15	

OBS.	CALC.	L	K
48	50	-9	8
54	-51	-8	
71	78	-7	
71	74	-6	
24	29	-5	
162	-152	-4	
167	-180	-3	
66	57	-2	
129	125	-1	
107	118	0	
122	-118	1	
284	273	2	
127	-128	3	
156	-152	4	
0	28	5	
0	-3	6	
151	-153	7	
151	127	8	
179	184	9	
120	-116	10	
0	-22	11	
21	-15	12	
31	23	13	
-24	-5	14	
29	-15	-8	9
62	55	-7	
29	23	-6	
0	-20	-5	
96	92	-4	
169	-170	-3	
44	37	-2	
149	149	-1	
23	-21	0	
112	-112	1	
117	-128	2	
30	-37	3	
117	95	4	
246	251	5	
-7	1	6	
25	-28	7	
85	-85	8	
203	-201	9	
41	29	10	
115	123	11	
80	87	12	
35	-45	13	
48	-44	-6	10
70	-72	-5	
13	-7	-4	
28	-26	-3	
315	307	-2	
-47	16	-1	
264	-259	0	
24	-31	1	
81	74	2	
91	93	3	
105	-101	4	
-7	24	5	
61	-54	6	
0	17	7	
0	-19	8	
86	98	9	
50	36	10	
67	-68	11	
18	13	12	
29	25	-3	11
41	-40	-2	
131	-136	-1	
58	-54	0	
115	126	1	
127	121	2	
80	84	3	
65	-71	4	
115	-113	5	
57	-63	6	
29	25	7	
83	91	8	
-8	-1	9	
88	-99	10	
166	-151	0	12
78	-80	1	
80	93	2	
43	47	3	
53	-62	4	
19	-21	5	
46	45	6	
-25	3	7	

r= 3.9

OBS.	CALC.	K	H
172	-178	-12	0
57	-54	-11	
254	-261	-10	
23	-37	-9	
107	111	-8	
322	310	-7	
370	-393	-6	
77	-80	-5	
131	164	-4	
175	202	-3	
428	445	-2	
812	780	-1	
76	75	-11	1
259	-258	-10	
65	62	-9	
159	164	-8	
170	169	-7	
151	149	-6	
177	-188	-5	
667	669	-4	
592	-627	-3	
259	-260	-2	
362	349	-1	
885	898	0	
105	127	1	
467	473	2	
405	-385	3	
627	-629	4	
457	-465	5	
467	-470	6	
78	66	7	
337	-342	8	
117	115	9	
61	-55	10	
120	-111	11	
59	-60	12	
35	-40	-9	2
39	-41	-8	
124	-120	-7	
36	-32	-6	
42	39	-5	
172	-176	-4	
298	-278	-3	
1067	1048	-2	
154	-117	-1	
462	-442	0	
276	256	1	
349	368	2	
482	496	3	
559	-543	4	
445	434	5	
379	386	6	
-34	4	7	
28	-26	8	
37	32	9	
94	102	10	
0	8	11	
53	-57	12	
71	72	-10	3
135	152	-9	
8	-4	-8	
152	-158	-7	
100	94	-6	
125	-123	-5	
303	-312	-4	
214	210	-3	
435	415	-2	
624	628	-1	
285	284	0	
331	-325	1	
143	123	2	
506	-522	3	
157	-158	4	
93	103	5	
150	165	6	
380	387	7	
46	-52	8	
97	-96	9	
63	-55	10	
97	-90	11	
98	-93	12	
81	77	-9	4
117	-115	-8	
53	-53	-7	
217	-225	-6	
284	-290	-5	
134	-135	-4	
556	-589	-3	
69	80	-2	
130	124	-1	
445	439	0	
44	51	1	
251	-275	2	
74	76	3	
115	-98	4	
54	-55	5	
202	203	6	
413	427	7	
139	145	8	
189	189	9	
127	-119	10	
53	-48	11	
67	-67	12	

OBS.	CALC.	K	H
136	-133	-7	5
16	7	-6	
96	-89	-5	
75	70	-4	
-49	1	-3	
188	104	-2	
103	101	-1	
492	501	0	
453	445	1	
387	381	2	
403	389	3	
43	-45	4	
549	563	5	
112	-118	6	
69	59	7	
52	52	8	
67	67	9	
89	-84	10	
213	-221	11	
105	108	-6	6
187	-184	-5	
131	139	-4	
202	197	-3	
115	119	-2	
14	1	-1	
259	-255	0	
320	315	1	
281	-271	2	
190	-183	3	
34	-34	4	
222	222	5	
85	-94	6	
169	-178	7	
60	-60	8	
104	-95	9	
77	-83	10	
159	-153	11	
54	59	12	
72	-69	-6	7
87	-88	-5	
89	-99	-4	
114	107	-3	
0	32	-2	
35	26	-1	
10	6	0	
25	24	1	
244	-244	2	
38	11	3	
42	35	4	
114	115	5	
220	224	6	
145	146	7	
127	170	8	
93	-99	9	
69	-58	-3	8
93	-85	-2	
142	159	-1	
68	64	0	
105	-99	1	
23	-11	2	
53	45	3	
0	10	4	
91	-94	5	
80	85	6	
196	201	7	
63	57	8	
40	-33	9	
157	-154	-3	9
75	-71	-2	
31	-22	-1	
48	-49	0	
45	-34	1	
40	-30	2	
137	133	3	
37	36	4	
45	43	5	
63	67	6	
90	84	7	
69	73	8	
72	69	1	10
44	37	2	
92	93	3	
90	100	4	
149	161	5	
90	94	6	

r= 4.0

difference synthesis indicated that the positional and isotropic thermal parameters were correctly refined. Using low-order terms, a difference synthesis was computed which revealed that most of the atoms were situated in regions of negative electron density. This was tentatively ascribed to extinction, since the calculated structure factors of the five strongest reflexions were 28% larger than the observed values, as shown in the following table:

$0kl$	F_c	sF_o (film)	sF_o (counter)
002	1532	1135	1564
003	1584	1233	1594
011	1131	890	1070
021	972	864	962
022	1826	1365	1822

Replacing these with counter data values gave a difference synthesis which showed no minima around the atoms. The reliability index for the low-angle terms improved from 17·2% to 7·4%. This emphasizes the importance of refining high-order reflexions in determining the atomic positions, thermal and scale parameters. If all reflexions had been refined simultaneously, the extinction effect would have been masked by erroneous temperature and scale factors.

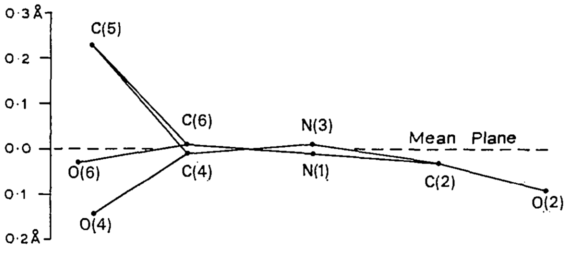

Fig. 2. Puckering of the alloxan molecule.

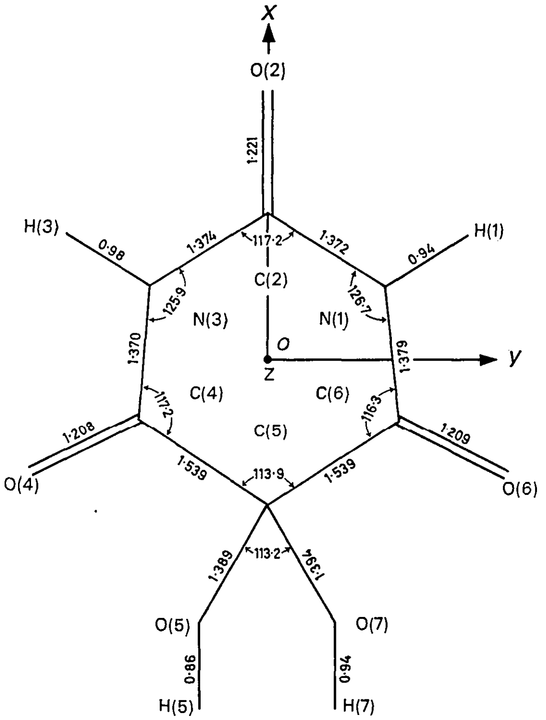

Fig. 3. Bond lengths and angles of alloxan.

Discussion of the structure

Planarity of the molecule

The least-squares plane through the six pyrimidine ring atoms revealed that the deviations were highly significant; Δ/σ ranged from 1·7 to 30. The molecule is therefore not planar; which is to be expected of a *gem*-dihydroxypyrimidine. The puckering of the pyrimidine ring is illustrated (Fig. 2) by calculating the deviations from the mean plane through atoms N(1), N(3), C(4) and C(6). The mean plane through atoms O(2), C(2), C(5), O(5) and O(7) makes an angle of 86½° with that through the pyrimidine ring.

Molecular vibration analysis

Using the anisotropic thermal parameters (Table 3) and the molecular axes as in Fig. 3, the observed U_{ij} values were obtained (Table 4); they are similar to those of pyrazine (Wheatley, 1957). The symmetric tensors **T** and **ω** (Table 5), in terms of which the rigid-body vibrations of the molecule are expressed, were used to calculate U_{ij}. The good agreement between the two sets of U_{ij}'s gives a measure of the rigid-body as-

Table 3. *Anisotropic thermal parameters of alloxan from three-dimensional data analysis*

b_{ij} are coefficients in the expression $\exp\{-(b_{11}h^2+b_{22}k^2+b_{33}l^2+2b_{12}hk+2b_{13}hl+2b_{23}kl)\}$

Atom	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
C(2)	0·0199	0·0086	0·0090	−0·0034	−0·0033	−0·0025
C(4)	0·0177	0·0106	0·0094	−0·0046	−0·0036	−0·0022
C(5)	0·0156	0·0084	0·0076	−0·0029	−0·0028	−0·0008
C(6)	0·0171	0·0086	0·0089	−0·0034	−0·0027	−0·0021
N(1)	0·0198	0·0071	0·0116	−0·0015	−0·0061	−0·0028
N(3)	0·0199	0·0079	0·0116	−0·0027	−0·0064	−0·0021
O(2)	0·0256	0·0084	0·0145	0·0009	−0·0100	−0·0028
O(4)	0·0231	0·0173	0·0157	−0·0034	−0·0089	−0·0073
O(5)	0·0197	0·0101	0·0105	−0·0045	−0·0051	0·0030
O(6)	0·0273	0·0085	0·0166	−0·0063	−0·0056	−0·0041
O(7)	0·0201	0·0119	0·0118	−0·0070	0·0012	−0·0034

sumption. The root mean square translation oscillations along the molecular axes OX, OY and OZ are 0·14, 0·12 and 0·16 Å, respectively. The corresponding r.m.s. angular oscillations are 3·3°, 2·6°, and 2·5°. Within experimental error, the principal axes of **T** coincide with the molecular axes. The largest translational vibrations are along the long axis of the molecule, OX, and along the plane normal, OZ. The T and ω tensors are similar to those of anthracene (Cruickshank, 1957).

Molecular dimensions

The intramolecular bond lengths and angles (Fig. 3) are listed in Table 6 (together with their standard deviations). The bond lengths have been corrected for angular oscillations of the molecule, using the radial error relationship of Cruickshank (1956*a*), with the Gaussian peak-width parameter q^2 equal to 0·12 Å^2. The correction increased the C–N and C–C bonds by 0·0025 Å and C–O bonds by 0·0017 Å, leaving the angles vir-

Table 4. *Observed and calculated* U_{ij} (10^{-2} Å^2)

	U_{11}		U_{22}		U_{33}		U_{12}		U_{13}		U_{23}	
Atom	obs.	calc.	obs.	calc.	obs.	calc.	obs.	calc.	obs.	calc.	obs.	calc.
C(2)	2·19	2·09	1·46	1·68	2·86	2·85	0·62	0·63	0·17	0·01	−0·04	0·25
C(4)	2·38	2·39	1·31	1·43	2·76	3·11	0·23	0·46	0·26	0·34	0·36	0·07
C(5)	1·91	2·10	1·73	1·63	2·31	2·91	0·26	0·63	0·03	0·08	0·22	0·26
C(6)	2·09	2·40	1·40	1·43	2·67	3·09	0·45	0·79	0·24	0·35	0·18	0·43
N(1)	2·01	2·34	1·83	1·42	3·63	3·01	0·96	0·48	0·45	0·28	−0·05	0·09
N(3)	2·15	2·34	1·82	1·43	3·51	2·99	0·76	0·78	0·33	0·28	0·23	0·42
O(2)	2·29	2·09	3·31	2·52	4·85	3·89	1·36	0·62	0·41	0·05	−0·50	0·26
O(4)	3·41	3·12	1·51	1·69	4·86	4·68	0·53	0·03	1·22	1·09	−0·23	−0·44
O(5)	2·42	2·16	3·33	3·35	2·88	3·87	0·04	0·66	−0·44	−0·33	1·14	0·28
O(6)	2·98	3·14	1·22	1·64	4·71	4·63	1·30	1·19	0·71	1·15	0·72	0·88
O(7)	2·94	2·62	0·93	1·63	3·10	3·14	0·41	0·65	0·55	0·62	0·76	0·29

r.m.s. $(\Delta U_{ij}) = 0{\cdot}0038$ Å^2, $\sigma(U_{ij}) = 0{\cdot}0042$ Å^2.

Table 5. *Values of* T_{ij} (10^{-2} Å^2) *and* ω_{ij} (deg.^{2}) *and their standard deviations*

$$\mathbf{T}_{ij} = \begin{pmatrix} 2{\cdot}09 & 0{\cdot}62 & 0{\cdot}00 \\ & 1{\cdot}34 & 0{\cdot}25 \\ & & 2{\cdot}43 \end{pmatrix} ; \quad \omega_{ij} = \begin{pmatrix} 11{\cdot}18 & -0{\cdot}32 & -6{\cdot}69 \\ & 6{\cdot}97 & -0{\cdot}01 \\ & & 6{\cdot}10 \end{pmatrix}$$

$$\sigma(\mathbf{T}_{ij}) = \begin{pmatrix} 0{\cdot}14 & 0{\cdot}13 & 0{\cdot}14 \\ & 0{\cdot}16 & 0{\cdot}17 \\ & & 0{\cdot}23 \end{pmatrix} ; \quad \sigma(\omega_{ij}) = \begin{pmatrix} 1{\cdot}46 & 1{\cdot}20 & 1{\cdot}17 \\ & 1{\cdot}32 & 1{\cdot}22 \\ & & 1{\cdot}13 \end{pmatrix}$$

Table 6. *Intramolecular bond lengths and angles*

Bond	Length, l	Length, l (corrected)	$\sigma(l)$	Angle	
C(2)–N(1)	1·370 Å	1·372	±0·005 Å	C(6)–N(1)–C(2)	126·7±0·3°
C(2)–N(3)	1·372	1·374	±0·005	C(6)–N(1)–H(1)	118·5±3·2
C(4)–N(3)	1·368	1·370	±0·005	C(2)–N(1)–H(1)	114·6±3·2
C(6)–N(1)	1·376	1·379	±0·005	N(1)–C(2)–N(3)	117·2±0·3
C(5)–C(4)	1·537	1·539	±0·005	N(1)–C(2)–O(2)	121·1±0·3
C(5)–C(6)	1·537	1·539	±0·005	N(3)–C(2)–O(2)	121·7±0·3
C(2)–O(2)	1·219	1·221	±0·005	C(2)–N(3)–C(4)	125·9±0·3
C(4)–O(4)	1·206	1·208	±0·005	C(2)–N(3)–H(3)	115·4±3·2
C(6)–O(6)	1·208	1·209	±0·005	C(4)–N(3)–H(3)	118·7±3·2
C(5)–O(5)	1·387	1·389	±0·005	N(3)–C(4)–C(5)	117·2±0·3
C(5)–O(7)	1·392	1·394	±0·005	N(3)–C(4)–O(4)	121·3±0·3
N(1)–H(1)	0·94	—	±0·05	C(5)–C(4)–O(4)	121·5±0·3
N(3)–H(3)	0·98	—	±0·05	C(5)–C(6)–N(1)	116·3±0·3
O(5)–H(5)	0·86	—	±0·05	C(5)–C(6)–O(6)	121·8±0·3
O(7)–H(7)	0·94	—	±0·05	N(1)–C(6)–O(6)	121·6±0·3
				C(4)–C(5)–C(6)	113·9±0·3
				C(4)–C(5)–O(5)	111·3±0·3
				C(4)–C(5)–O(7)	103·1±0·3
				C(6)–C(5)–O(5)	107·2±0·3
				C(6)–C(5)–O(7)	108·2±0·3
				O(5)–C(5)–O(7)	113·2±0·3
				C(5)–O(5)–H(5)	111·4±3·2
				C(5)–O(7)–H(7)	106·4±3·2

tually unaltered. Their magnitudes are similar to those in anthracene (Cruickshank, 1956*b*).

The mean value of the four C–N bonds (1·374 Å) is not significantly different from the individual C–N distances. This is also true of the three C=O bonds (1·213 Å), the four N–H and O–H bonds (0·93 Å), the two C–C bonds (1·539 Å), and the two C–(OH) bonds (1·392 Å). The C=O value of 1·213 Å does not differ significantly from previous double-bond values (1·20 Å, Vaughan & Donohue, 1952; 1·205 Å, Hahn, 1957; 1·215 Å, Pauling, 1960). The C–C mean value of 1·539 Å does not differ from the standard single-bond value of 1·544 Å from diamond (Lonsdale, 1947). The C–(OH) mean value is equal to a pure single-bond distance (Hahn, 1957). The C–N value of 1·374 Å differs significantly from the single and double-bond values of 1·475 and 1·265 Å (Hahn, 1957) respectively. Hence, the bond lengths of alloxan show decisively that the molecule is in the 2,4,6-triketo configuration with a *gem*-dihydroxy group at C(5). The location of the four hydrogen atoms, together with the consistent hydrogen-bonded system, confirms the tautomeric form given in formula (II). Thus the controversy about the structural configuration is resolved. The correct description of alloxan is 2,4,6-triketo-5,5-dihydroxypyrimidine. The valence angles at the nitrogen atoms are significantly larger than those at the carbon atoms. The angle C(4)–C(5)–C(6) is the smallest in the ring, as expected of sp^3 hybridization.

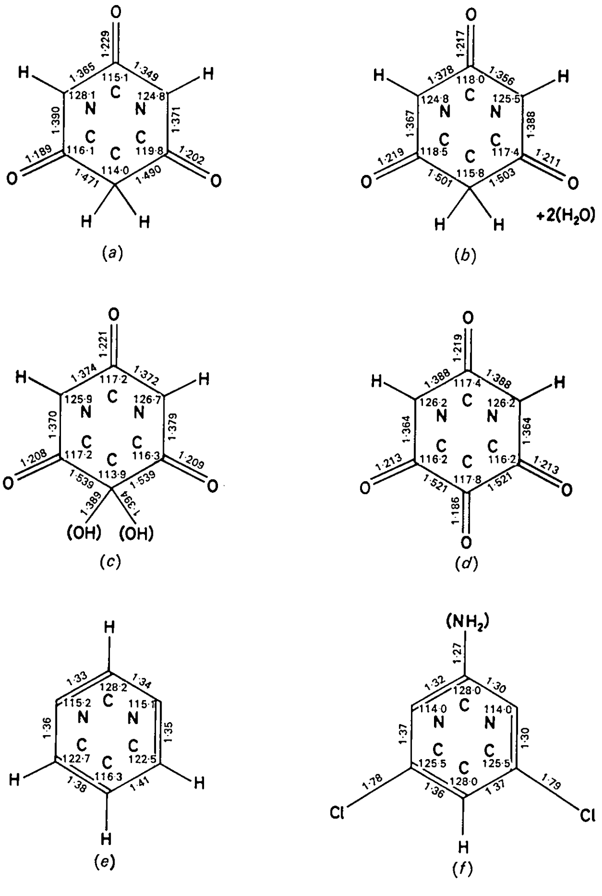

Fig. 4. Some related pyrimidines. (*a*) Anhydrous barbituric acid. (*b*) Barbituric acid dihydrate. (*c*) Alloxan. (*d*) Anhydrous alloxan. (*e*) Pyrimidine (Wheatley, 1960). (*f*) 2-Amino-4,6-dichloropyrimidine (Clews & Cochran, 1948).

Comparison of the C–C bond-lengths of alloxan with corresponding bonds in other pyrimidines (Fig. 4) shows that their mean value of 1·539 Å is the largest reported. It may be possible to explain why these bonds are greater than those in anhydrous barbituric acid (Bolton, 1963), barbituric acid dihydrate (Jeffery, Ghose & Warwicker, 1961) and anhydrous alloxan (Bolton, 1964) in terms of the electromeric effect. The drift of electrons out of the pyrimidine ring towards the substituents at C(5) increases with increasing electronegativity of the series 2(OH) > O > 2H. This results in a differential decrease in the π character of the C(5)–C(4) and C(5)–C(6) bonds, with consequent variation in their lengths; those associated with the most electronegative group, 2(OH), being the longest. The C=O and C–N distances of 1·213 and 1·374 Å are not significantly different from those in other pyrimidines. The *gem*-dihydroxy C–(OH) bond length of 1·392 ± 0·005 Å is not significantly different from the *vic*-dihydroxy C–(OH) values of 1·35 and 1·43 ± 0·03 Å in dialuric acid monohydrate (Alexander & Pitman, 1956). The N–H and O–H distances are shorter than the accepted values (N–H = 1·04 Å and O–H = 1·03 Å, Pimentel & McClellan, 1960) but agree with results obtained from X-ray analyses.

It is interesting to note that the valence angle at nitrogen atoms with an extra-annular hydrogen atom [Fig. 4(*a*), (*b*), (*c*), (*d*)] is significantly larger than that of nitrogen atoms without an attachment [Fig. 4(*e*) and (*f*)]. In the former case the angle is greater than 120° while in the latter it is less than 120°. This observation makes it possible to decide whether or not a nitrogen atom in a heterocyclic ring has an extra-annular hydrogen attached to it (Chatar Singh, 1965).

Hydrogen-bonding system

The N–H directions associated with the hydrogen atoms, H(1) and H(3) are symmetrically disposed with respect to adjacent covalent bonds (Table 6). The N(1)–H(1) · · · O(2′)(V) distance of 3·044 ± 0·005 Å (Fig. 5) corresponds to a rather weak bond. The average value for such a bond is 2·82 ± 0·07 Å (Fuller, 1959). This relative lengthening may be attributed to its significant deviation from linearity (angle N(1)–H(1)–O(2′) = 151·7°) and to the formation of two hydrogen bonds by the same carbonyl oxygen O(2′); namely N(1)–H(1) · · · O(2′) and O(7)–H(7) · · · O(2′). The latter situation occurs in urea (Vaughan & Donohue, 1952). The N(3)–H(3) · · · O(6) (I*a*) distance of 2·881 Å corresponds to a normal bond. The O(5)–H(5) · · · O(4) (IV*a*) and O(7)–H(7) · · · O(2) (II*b*) distances of 2·731 and 2·778 Å respectively correspond to typical hydrogen bonds (2·74 ± 0·03 Å; Fuller, 1959). Thus all the four hydrogen atoms participate in the formation of hydrogen bonds.

The N(3)–H(3) ··· O(6) hydrogen bonds link molecule I with I*a*, I*b*, *etc.*; II with II*a*, II*b*, *etc.*, forming endless chains in the *xy* plane extending along the *b* axis. The symmetry-related bonds link molecule III with III*a*, *etc.*, IV with IV*a*, *etc.*, to form another layer of parallel chains separated by $\frac{1}{2}c$. The O(7)–H(7) ··· O(2) (II*b*) hydrogen bond links adjacent chains in the *xy* plane, while the O(5)–H(5) ··· O(4) (IV*a*) bond links two such layers of chains separated by $\frac{1}{2}c$. The N(1)–H(1) ··· O(2′)(V) bond links molecule I to molecule V, belonging to a layer with negative *z* (Fig. 5, lower-half), thereby forming a three-dimensional hydrogen-bonded network.

Intermolecular contacts

Apart from the hydrogen bonds, a number of intermolecular distances of less than 3·2 Å (Table 7) occur between the *gem*-dihydroxy oxygen atoms, O(5) and O(7), of molecule I and several atoms of neighbouring molecules. The three intermolecular C ··· O distances between molecules I and III*a* (Fig. 5) of 2·950, 3·044 and 2·982 Å, though short, are not significantly different from the sum of the van der Waals radii of carbon and oxygen (3·1 Å; Pauling, 1960). These contacts do not involve the C=O group oxygen as in anhydrous barbituric acid (Bolton, 1963) and chloranil (Chu, Jeffrey & Sakurai, 1962) but the C–OH group oxygen which is already hydrogen bonded. The O ··· O distances of 2·905 and 2·988 Å between oxygen atoms of two molecules are also equivalent to the sum of their van der Waals radii. These and other short van der Waals contacts of Table 7, together with the forces associated with the formation of hydrogen bonds, may be responsible for the puckering of the alloxan molecule.

Table 7. *Intermolecular distances less than* 3·2 Å

$\sigma(l) = \pm 0{\cdot}005$ Å

O(6)(I) ··· O(4)(III*a*) = 3·172
O(5)(I) ··· C(4)(III*a*) = 2·950*
O(5)(I) ··· C(5)(III*a*) = 3·044*
O(5)(I) ··· C(6)(III*a*) = 2·982*
O(5)(I) ··· N(1)(III*a*) = 3·169
O(5)(I) ··· N(3)(III*a*) = 3·171
O(5)(I) ··· O(5)(III*a*) = 2·905*
O(7)(I) ··· N(1)(II) = 3·117
O(7)(I) ··· O(6)(II) = 3·081
O(7)(I) ··· O(2)(VI) = 2·988*
O(7)(I) ··· O(7)(VII) = 3·138

The numbering of the molecules is as in Fig. 5.

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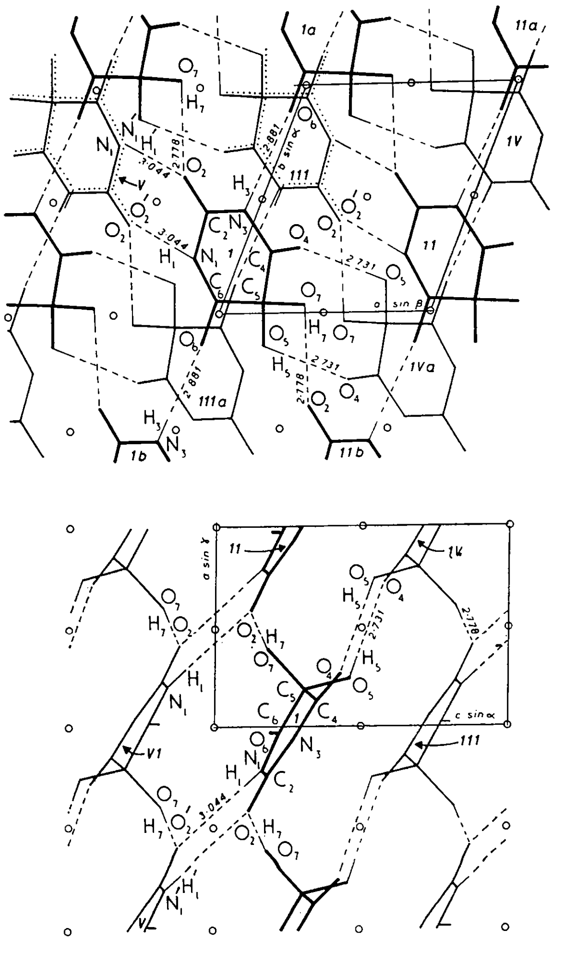

Fig. 5. Hydrogen-bonding in alloxan projected on (001) and (010).

I	(x, y, z)	I*a*	$(x, 1+y, z)$
II	$(1+x, y, z)$	II*a*	$(1+x, 1+y, z)$
III	$(-x, 1-y, 1-z)$	III*a*	$(-x, -y, 1-z)$
IV	$(1-x, 1-y, 1-z)$	IV*a*	$(1-x, -y, 1-z)$
V	$(-1-x, 1-y, -z)$	VI	$(-x, 1-y, -z)$
I*b*	$(x, -1+y, z)$		
II*b*	$(1+x, -1+y, z)$		
VII	$(1-x, -y, -z)$		

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The Structure of the Pyrimidines and Purines.
IX. The Crystal Structure of Alloxantin Dihydrate

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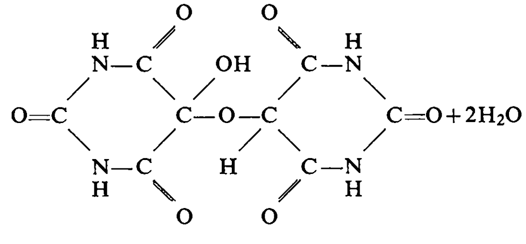
The crystal structure of alloxantin dihydrate, $C_8H_6O_8N_4 . 2H_2O$, has been determined by a direct sign determination method and refined by difference-Fourier methods. The unit cell is triclinic, space group $P\bar{1}$, with $a=6{\cdot}703$, $b=6{\cdot}879$, $c=7{\cdot}311$ Å, $\alpha=67°\ 5'$, $\beta=83°\ 51'$, $\gamma=71°\ 0'$. The crystal density is 1·83 g.cm^{-3}. The hydrogen atoms in the structure were located directly from the difference-density projections. The molecule is in the triketopinacol configuration with two molecules of water. Molecules are linked together by a hydrogen-bonded network involving all the electronegative atoms and the water molecules. Bond lengths and angles are not significantly different from those of alloxan. Alloxantin has a number of features in common with alloxan. Its molecule is significantly distorted from planarity and a number of intermolecular approach distances are shorter than the normal van der Waals contacts.

Introduction

Alloxantin dihydrate, $C_8H_6O_8N_4 . 2H_2O$, was first prepared by Wöhler & Liebig (1838). Slimmer & Stieglitz (1904) assigned to it the hemiacetal formula (I), while Piloty & Finckh (1904) suggested formula (II). Retinger (1917) introduced the pinacol formula (III) and Moubasher & Othman (1950) the formula (IV). In addition, tautomerism may occur in the pyrimidine rings through the migration of the hydrogen atoms. An X-ray analysis of alloxantin, undertaken with the aim of locating the hydrogen atoms directly, will elucidate its structural configuration. In its physiological action alloxantin resembles alloxan (Chatar Singh, 1965*a*).

(I)



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