References

ACHESON, R. M. (1960). *An Introduction to the Chemistry of Heterocyclic Compounds.* New York: Interscience Publishers.

ALEXANDER, L. E. & PITMAN, D. T. (1956). *Acta Cryst.* **9**, 501.

BAEYER, A. (1863). *Liebigs Ann.* **127**, 1, 199.

BOLTON, W. (1963). *Acta Cryst.* **16**, 166.

BOLTON, W. (1964). *Acta Cryst.* **17**, 147.

BRUGNATELLI, G. (1818). *Ann. Chim. Phys.* **8**, 201.

BUSING, W. R. & LEVY, H. A. (1957). *Acta Cryst.* **10**, 180.

BUSING, W. R., MARTIN, K. O. & LEVY, H. A. (1962). ORFLS, Oak Ridge National Laboratory, Oak Ridge Tennessee, U.S.A.

CALDER, R. S. (1960). Ph. D. Thesis, Univ. of Cambridge.

CHATAR SINGH (1960). *Acta Cryst.* **13**, 1036.

CHATAR SINGH (1961). Ph. D. Thesis, Univ. of Cambridge.

CHATAR SINGH (1965). *Acta Cryst.* In the press.

CHU, S. C., JEFFREY, G. A. & SAKURAI, T. (1962). *Acta Cryst.* **15**, 661.

CLEWS, C. J. B. & COCHRAN, W. (1948). *Acta Cryst.* **1**, 4.

COCHRAN, W., SRINIVASAN, R. & TOLLIN, P. (1963). *Crystallography and Crystal Perfection.* London: Academic Press.

CRUICKSHANK, D. W. J. (1956*a*). *Acta Cryst.* **9**, 757.

CRUICKSHANK, D. W. J. (1956*b*). *Acta Cryst.* **9**, 915.

CRUICKSHANK, D. W. J. (1957). *Acta Cryst.* **10**, 470.

DUNN, J. S., SHEEHEN, H. L. & MCLETCHIE, N. G. B. (1943). *Lancet,* **244**, 484.

FULLER, W. (1959). *J. Phys. Chem.* **63**, 1705.

HAHN, T. (1957). *Z. Kristallogr.* **109**, 438.

JEFFREY, G. A., GHOSE, S. & WARWICKER, J. O. (1961). *Acta Cryst.* **14**, 881.

KATRITZKY, A. R. & LAGOWSKI, J. M. (1960). *Heterocyclic Chemistry.* London: Methuen.

LONSDALE, K. (1947). *Phil. Trans.* A**240**, 219.

MILLS, O. S. & ROLLETT, J. S. (1961). *Computing Methods and the Phase Problem in X-ray Crystal Analysis.* London: Pergamon Press.

PAULING, L. (1960). *The Nature of the Chemical Bond.* Ithaca: Cornell Univ. Press.

PIMENTEL, G. C. & MCCLELLAN, A. L. (1960). *The Hydrogen Bond.* London: Freeman.

VAUGHAN, P. & DONOHUE, J. (1952). *Acta Cryst.* **5**, 530.

WEISZ, O., COCHRAN, W. & COLE, W. F. (1948). *Acta Cryst.* **1**, 83.

WHEATLEY, P. J. (1957). *Acta Cryst.* **10**, 182.

WHEATLEY, P. J. (1960). *Acta Cryst.* **13**, 80.

WILSON, A. J. C. (1949). *Acta Cryst.* **2**, 318.

WÖHLER, F. & LIEBIG, J. (1838). *Liebigs Ann.* **26**, 241, 292.

Acta Cryst. (1965). **19**, 767

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

BY CHATAR SINGH*

Crystallographic Laboratory, Cavendish Laboratory, Cambridge, England

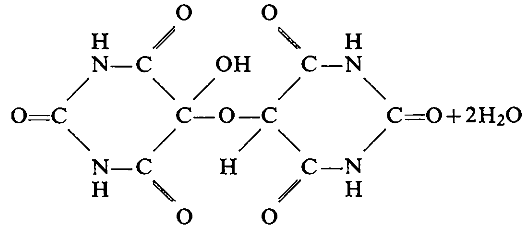
(*Received* 4 *November* 1964 *and in revised form* 15 *March* 1965)

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*).

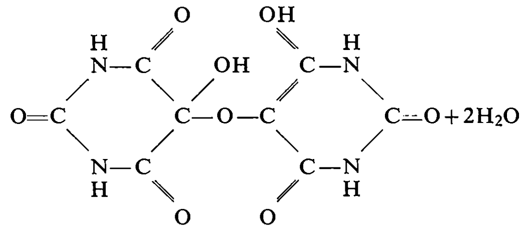
(I)



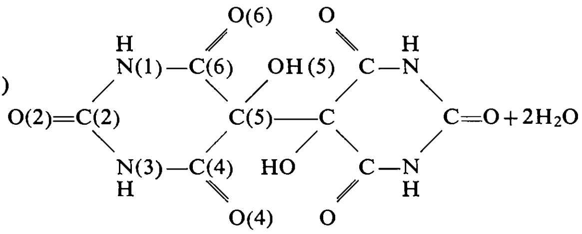
---

* Present address: Physics Department, University of Malaya, Kuala Lumpur, Malaysia.

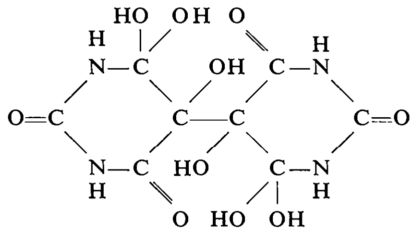
(II)



(III)



(IV)



Experimental

Commercially obtained alloxantin was dissolved in boiling water and recrystallized by slow cooling in a Dewar flask. Colourless crystals, elongated along the *c* axis and of uniform cross-section, were obtained. Unit-cell dimensions determined with a scintillation-counter diffractometer gave:

$a = 6{\cdot}703 \pm 0{\cdot}007$ Å $\quad \alpha = 67°\ 5' \pm 4'$
$b = 6{\cdot}879 \pm 0{\cdot}007$ $\quad \beta = 83\ 51\ \pm 5$
$c = 7{\cdot}311 \pm 0{\cdot}007$ $\quad \gamma = 71\ 0\ \pm 4$

Volume of the unit cell = 293 Å^3; $F(000) = 166$; $\mu = 17{\cdot}2$ cm^{-1} for Cu $K\alpha$. The density, measured was 1·87 g.cm^{-3} and calculated for $Z = 1$ was 1·83 g.cm^{-3}. The zero moment test of Howells, Phillips & Rogers (1950) applied to the three axial projections gave close agreement with the theoretical curve for centrosymmetry. Hence the crystal belongs to space group $P\bar{1}$, which requires the molecule to be centrosymmetric.

Intensity data

In the preliminary analysis 0*kl*, *h*0*l* and *hk*0 layer lines were recorded on Weissenberg photographs with Cu $K\alpha$ radiation, using the multiple-film technique. Later, the zero-layer intensities corresponding to the (**b**–**c**)-face-diagonal were also collected. The intensities, estimated visually, were reduced to relative observed structure amplitudes.

Structure determination

The structure of alloxantin was solved in the *b*-axis projection with the use of direct sign determination methods already outlined (Chatar Singh, 1965*a*). Using the twenty-three largest unitary structure factors, twenty-four sign-sets were produced by EDSAC II. At this stage the *T*-test (Cochran, Srinivasan & Tollin, 1963) was not available to obtain the correct sign-set. The electron density maps of the first eight sign-sets, each containing only twenty-three terms, were evaluated and it proved possible to fit the molecule into two of these maps; those obtained from sign-sets Nos. 6 and 7 [Fig. 1(*a*) and (*b*)]. The approximate coordinates were determined from Fig. 1(*b*). The oxygen atom of the water molecule, O(7), which could be at *A* or *B*, was located by not including its contribution in the calculation of the first electron density map. The agreement residual, with O(7) at *B*, was 24%, suggesting that the structure was essentially correct. When the *T*-test facility became available, the *T* values of the first twelve sign-sets were calculated. They ranged from 0·45 to 0·64; T_6 and T_7 had values of 0·57 and 0·45 respectively. Hence, the *T*-test criterion would have rejected set No. 6. It should be noted that set No. 8 also gave a *T* value of 0·45 but an inspection of its electron density map would have led to its rejection on physical grounds.

To obtain the *y* coordinates, the sharpened Patterson map of the *c*-axis projection was used to locate the centre of the pyrimidine ring (McDonald & Beevers, 1952). A model of the molecule was then orientated to fit the preliminary *x* and *z* coordinates. The approximate coordinates for the *c*-axis projection gave an *R* index of 29%.

Refinement

b-Axis projection

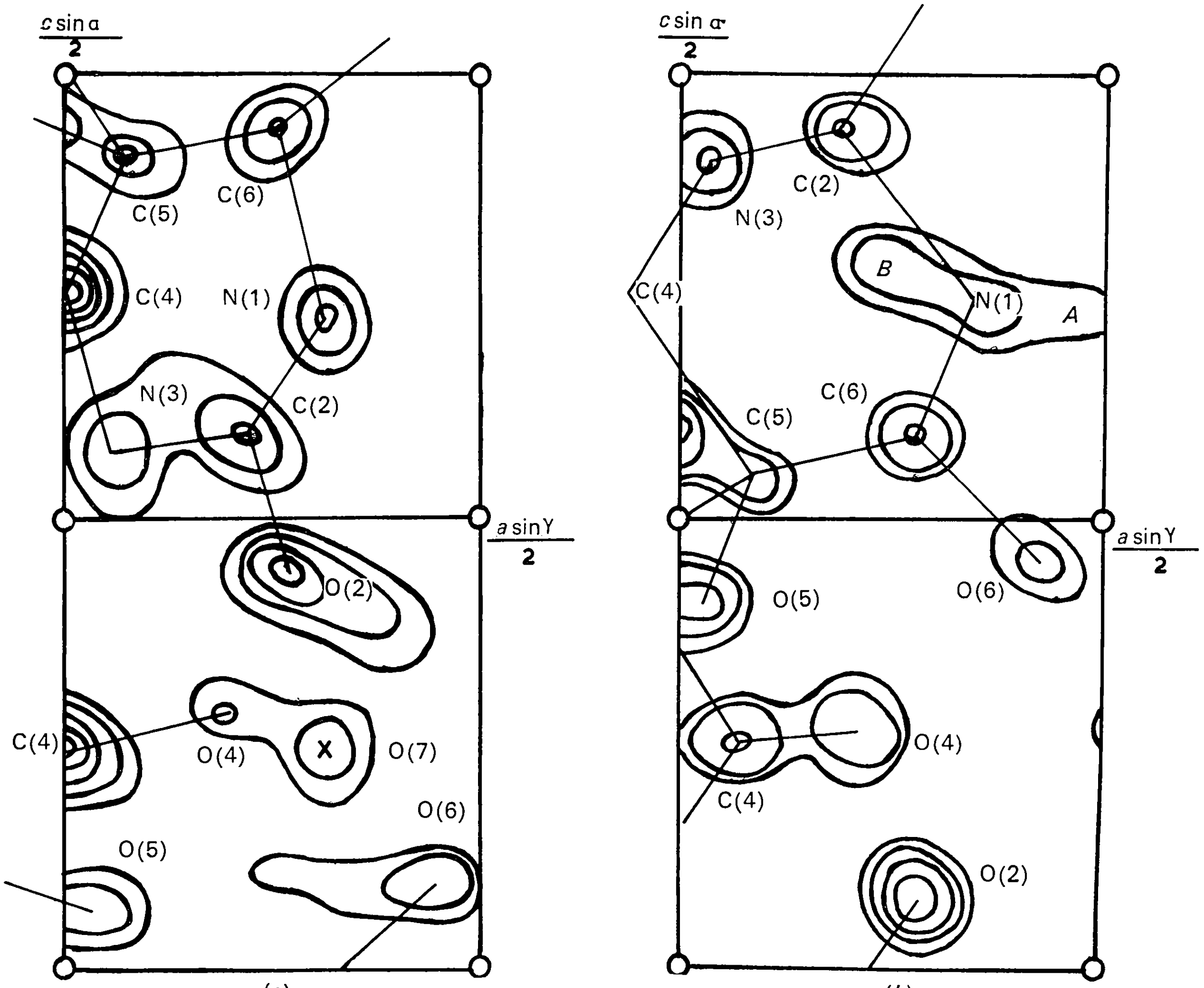
Starting with the approximate coordinates, the structure was refined by conventional difference-Fourier syntheses, with isotropic temperature factors. The *R* value for all reflexions (108) dropped to 12·3% after five cycles. The difference map showed large positive peaks near the oxygen atoms which may be associated with the unknown hydrogen atoms in the structure. It was therefore decided to leave out of the refinement all terms with $(\sin\theta/\lambda) < 0{\cdot}35$. This then gave eighty-five measurable high-angle independent reflexions for the refinement of thirty-four parameters. As the ratio is small, a continuous check was kept on the refinement process.

The first difference map of the high-angle terms did not show the large positive peaks. Instead it indicated that a number of atoms were being shifted in the wrong direction. The *R* value for the high-angle terms dropped gradually from 13·9% to 4·7%, while that for all reflexions at the latter stage was 6·8%.

The difference synthesis computed using all reflexions, and taking into account the contributions of carbon, nitrogen and oxygen atoms only [Fig. 2(*a*)], clearly indicated the positions of the five hydrogen atoms. With the inclusion of the hydrogen atoms at positions read off Fig. 2(*a*) and with an isotropic temperature factor of 1·5Å^2, as deduced from the peak heights (McDonald, 1956), the R value of all reflexions dropped to 4·3%. Introducing anisotropic temperature factors for the three ketonic oxygens reduced the residual to 3·4%.

Table 1. *Fractional atomic coordinates and temperature factors of alloxantin*

	b-Axis projection			b_n-Axis projection		
Atom	x	z	B(Å^2)	x_n'	z_n'	B(Å^2)
C(2)	0·2232	0·4243	1·80	0·2274	0·1905	2·75
C(4)	−0·0550	0·2365	2·22	−0·0538	−0·0010	2·58
C(5)	0·0541	0·0410	1·55	0·0495	−0·0864	2·48
C(6)	0·2880	0·0769	1·90	0·2860	−0·1083	2·45
N(1)	0·3509	0·2586	1·40	0·3498	0·0526	2·35
N(3)	0·0251	0·4036	1·42	0·0241	0·1690	2·92
O(2)	0·2911	0·5794	1·95	0·2905	0·3355	2·78
O(4)	−0·2096	0·2374	2·13	−0·2096	−0·0476	3·20
O(5)	0·0223	−0·0951	1·82	0·0190	−0·3080	2·35
O(6)	0·4111	−0·0540	1·58	0·4100	−0·2545	2·75
O(7)	0·2504	0·2845	2·61	0·2481	−0·3686	3·44
H(1)	0·5156	0·2813	1·5	0·5156	−0·0703	1·6
H(3)	−0·0703	0·4766	1·5	−0·0703	0·2813	4·5
H(5)	0·1016	−0·1719	1·5	0·1016	−0·4063	4·5
H(7*a*)	0·1875	0·2031	1·5	0·1875	−0·4375	4·5
H(7*b*)	0·3281	0·2109	1·5	0·3438	−0·4063	2·0



(*a*) (*b*)

Fig. 1. Electron density projection of alloxantin on (010), (*a*) for sign set No. 6 ($T_6=0·57$) and (*b*) for sign set No. 7 ($T_7=0·45$)

The final atomic and thermal parameters are listed in Table 1 and the structure factors in Table 2.

a- and c-Axis projections

Both the *a*- and *c*-axis projections had considerable atomic overlap and could not be refined satisfactorily.

(b–c)-Axis projection

It was possible to find a projection in which only atoms C(4) and C(5) were partially overlapped. Denoting the new cell parameters by suffix *n*, a cell was chosen such that:

$$\mathbf{a}_n=\mathbf{a}; \qquad h_n=h$$
$$\mathbf{b}_n=(\mathbf{b}-\mathbf{c}); \quad k_n=\tfrac{1}{2}(k-l)$$
$$\mathbf{c}_n=(\mathbf{b}+\mathbf{c}); \quad l_n=\tfrac{1}{2}(k+l)$$

The volume of the new unit cell was twice that of the old and it contained two alloxantin molecules. Zero layer Weissenberg photographs taken about the b_n axis showed all rows of reflexions with l_n odd to be systematically absent, indicating the halving of the c_n axis in projection. The unique area to be refined was one-quarter of the total area of projection, containing one half molecule. Its fractional coordinates were given by $x_n'=x$ and $z_n'=(y+z)$.

The approximate coordinates obtained from the *b*- and *c*-axis projections gave an *R* index of 19%, which dropped to 9·4% for all terms in six cycles. Further refinement was done with the use of the high-angle terms [$(\sin\theta/\lambda)>0{\cdot}35$] and the residual gradually dropped to 5·4%. That for all reflexions at this stage was 8·1%. The difference synthesis, computed with all terms but without the contribution of the hydrogen atoms [Fig. 2(*b*)], was used to obtain the approximate hydrogen atom positions. Inclusion of the contribution of the hydrogen atoms to the structure factor calculations reduced *R* to 6·1%, which decreased further to 4·6% after a few more cycles. The final coordinates and temperature parameters are listed in Table 1 and the structure factors in Table 2.

Final coordinates and accuracy

The final coordinates derived from the *b*- and b_n-axis projections are listed in Table 3. The average differ-

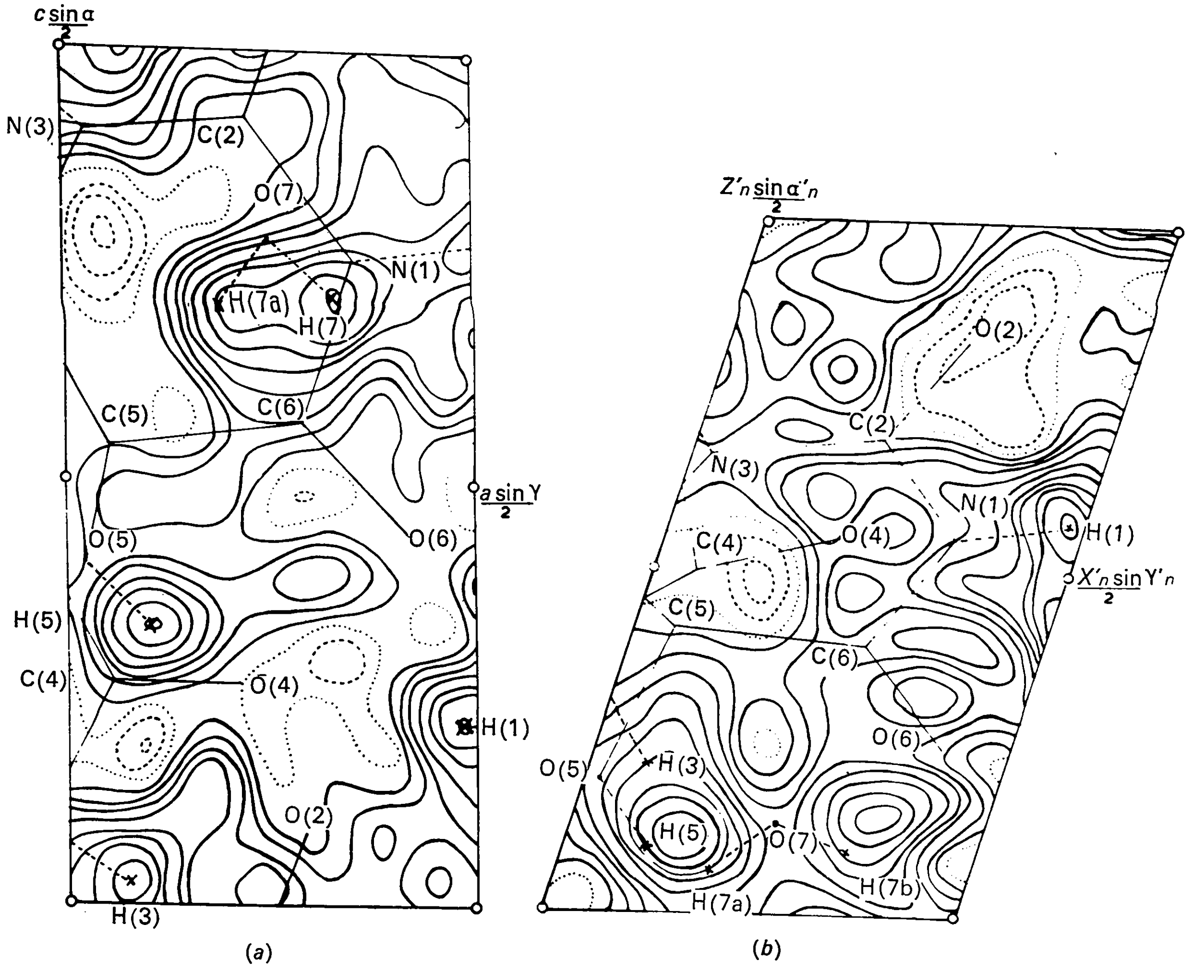


Fig. 2. (*a*) Difference synthesis of all reflexions on (010) with the contribution of the hydrogen atoms excluded. (*b*) Difference synthesis of all reflexions on the b_n axis with the contribution of the hydrogen atoms excluded. Both maps are contoured at 0·1e.Å^{-2} intervals with zero level dotted and negative levels dashed.

Table 2. *Observed and calculated structure factors* (× 50)

O in the OBS column indicates an unobserved reflexion

OBS.	CALC.	L	H
50	-60	-8	0
27	22	-7	
631	-630	-6	
45	43	-5	
215	233	-4	
235	235	-3	
66	-76	-2	
257	274	-1	
112	113	-8	1
18	-13	-7	
217	-225	-6	
92	80	-5	
108	105	-4	
219	-224	-3	
41	-45	-2	
223	224	-1	
665	690	0	
203	-219	1	
137	131	2	
2	0	3	
393	-393	4	
70	59	5	
23	30	6	
21	-18	7	
153	157	-8	2
26	20	-7	
178	191	-6	
12	-8	-5	
178	-176	-4	
657	647	-3	
314	300	-2	
210	211	-1	
296	-277	0	
934	906	1	
606	602	2	
559	-554	3	
204	-200	4	
22	-17	5	
24	-11	6	
279	-287	7	
62	-61	8	
41	46	-8	3
26	-30	-7	
175	-170	-6	
134	-122	-5	
396	-394	-4	
19	-14	-3	
51	-44	-2	
79	-85	-1	
738	721	0	
299	298	1	
446	439	2	
133	144	3	
147	147	4	
26	38	5	
274	-280	6	
20	15	7	

OBS.	CALC.	L	H
118	115	-7	4
15	-8	-6	
151	165	-5	
132	130	-4	
25	-28	-3	
180	192	-2	
23	-29	-1	
535	526	0	
266	-269	1	
140	-150	2	
42	51	3	
362	-360	4	
111	-103	5	
302	-296	6	
74	-78	-6	5
26	-26	-5	
48	40	-4	
191	176	-3	
171	-178	-2	
22	22	-1	
237	236	0	
167	174	1	
109	112	2	
150	-145	3	
21	0	4	
58	46	5	
74	-73	6	
15	-16	-6	6
6	1	-5	
212	-206	-4	
81	75	-3	
310	-306	-2	
117	-111	-1	
90	-91	0	
24	-17	1	
199	203	2	
199	-207	3	
49	60	4	
18	-18	5	
162	-155	-4	7
118	110	-3	
197	191	-2	
17	-10	-1	
35	-32	0	
99	91	1	
177	193	2	
65	-62	3	
165	-177	4	
100	-89	-1	8
47	-41	0	
12	-17	1	

r= 3.4

OBS.	CALC.	H	L
72	-68	-6	0
212	202	-5	
514	517	-4	
719	718	-3	
279	-265	-2	
662	700	-1	
85	-85	-7	1
0	9	-6	
0	-27	-5	
0	23	-4	
185	-199	-3	
240	219	-2	
314	307	-1	
846	922	0	
323	326	1	
0	31	2	
516	499	3	
58	-75	4	
198	203	5	
57	54	6	
194	-178	7	
130	-130	-7	2
176	185	-6	
60	-62	-5	
237	-245	-4	
127	-130	-3	
86	-60	-2	
327	338	-1	
163	-147	0	
220	-225	1	
386	-399	2	
105	-110	3	
112	96	4	
179	-191	5	
185	-187	6	
165	-156	7	
98	-106	-5	3
85	-78	-4	
277	274	-3	
263	-263	-2	
0	80	-1	
527	527	0	
0	12	1	
97	95	2	
0	-48	3	
298	306	4	
127	118	5	
84	-86	6	

OBS.	CALC.	H	L
50	-39	-5	4
153	-154	-4	
124	-136	-3	
0	33	-2	
0	35	-1	
74	-56	0	
190	-188	1	
439	437	2	
58	58	3	
129	-142	4	
383	383	5	
82	86	6	
156	-162	-3	5
0	-22	-2	
56	47	-1	
0	-52	0	
66	-59	1	
118	-112	2	
0	12	3	
0	29	4	
124	120	5	
117	-107	6	
99	-90	7	
179	207	-1	6
62	47	0	
0	6	1	
0	29	2	
74	63	3	
110	112	4	
41	-44	0	7
104	-117	1	
158	172	2	
68	58	3	
37	-28	4	
27	-31	5	

r= 4.6

Table 3. *Final atomic coordinates of alloxantin*

Atom	x/a	y/b	z/c
C(2)	0·2254	−0·2338	0·4243
C(4)	−0·0544	−0·2375	0·2365
C(5)	0·0518	−0·1274	0·0410
C(6)	0·2870	−0·1852	0·0769
N(1)	0·3504	−0·2060	0·2586
N(3)	0·0246	−0·2346	0·4036
O(2)	0·2908	−0·2439	0·5794
O(4)	−0·2096	−0·2850	0·2374
O(5)	0·0207	−0·2129	−0·0951
O(6)	0·4106	−0·2005	−0·0540
O(7)	0·2493	0·3469	0·2845
H(1)	0·5156	−0·3516	0·2813
H(3)	−0·0703	−0·1953	0·4766
H(5)	0·1016	−0·2344	−0·1719
H(7*a*)	0·1875	0·3594	0·2031
H(7*b*)	0·3360	0·3828	0·2109

ence between the common x coordinates was 0·014 Å, with a maximum difference of 0·03 Å. The standard deviations of electron density and atomic coordinates are

$\sigma(\varrho)_b = 0\cdot18$ e.Å^{-2}; $\sigma(\varrho)_{bn} = 0\cdot19$ e.Å^{-2}

	$\sigma(x)$ (Å)	$\sigma(y)$ (Å)	$\sigma(z)$ (Å)
Carbon	0·009	0·014	0·010
Nitrogen	0·007	0·013	0·009
Oxygen	0·006	0·011	0·008
Hydrogen	assumed to be 0·1 Å.		

Discussion of the structure

Planarity of the molecule

As in alloxan (Chatar Singh, 1965*a*), the least-squares plane through the six pyrimidine ring atoms revealed that the deviations were highly significant; Δ/σ ranged from 1·2 to 15·7. Hence it was concluded that the molecule was not planar. The puckering of the pyrimidine ring can be illustrated by calculating the deviations from the mean plane through atoms N(1), N(3), C(4) and C(6) (Fig. 3). The structural distortions are remarkably similar to those of alloxan (Chatar Singh, 1965*a*) though their magnitudes are significantly greater in alloxantin. The mean plane through atoms O(2), C(2), C(5), O(5) and C′(5) makes an angle of 91° with the mean plane through the pyrimidine ring.

Molecular dimensions

The intramolecular bond lengths and angles (Fig. 4) are listed in Table 4, together with their standard deviations.

The mean value of the four C–N bonds (1·382 Å) is not significantly different from the individual C–N distances. This is also true for the three C–C bonds at position 5 (1·540 Å), the three C=O bonds (1·208 Å) and the five N–H and O–H bonds (0·86 Å), with the possible exception of N(1)–H(1) $(\Delta/\sigma=3{\cdot}4)$.

In discussing the bond lengths and angles in alloxantin it is convenient to compare them with those in alloxan (Chatar Singh, 1965*a*), since the latter has already been compared with other pyrimidines. The mean values of the C–N bonds, the C=O bonds, the C–C bonds, the X–H bonds and the C–(OH) bond (1·400 Å) do not differ significantly from the corresponding ones in alloxan. The valence angles at the nitrogen atoms are consistent with the empirical observation made with regard to their dependence on extra-annular attachment (Chatar Singh, 1965*b*). Hence the significance tests indicate that the mean intramolecular distances in alloxan and alloxantin are very similar. Therefore, using the evidence already presented for alloxan, it follows that the alloxantin molecule is in the 2,4,6-triketo configuration with one hydroxyl group attached to atom C(5). The location of the five hydrogen atoms, together with their consistent hydrogen-bonded network, conforms with the pinacol configurational formula (III) with two water molecules as proposed by Retinger (1917).

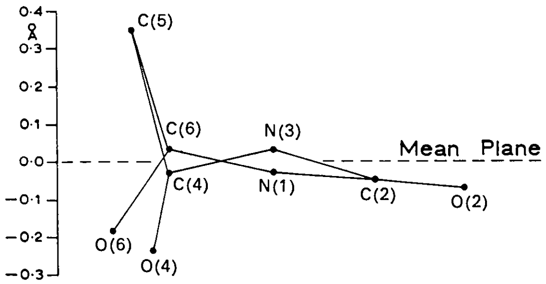


Fig. 3. Puckering of the alloxantin molecule.

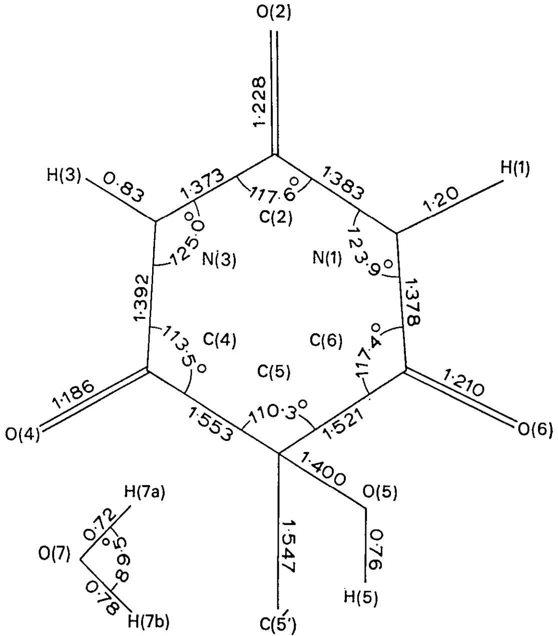


Fig. 4. Bond lengths and angles of alloxantin.

Table 4. *Intramolecular bond lengths and angles*

Bond length	σ(*l*)
C(2)–N(1) = 1·383	±0·013 Å
C(2)–N(3) = 1·373	±0·012
C(4)–N(3) = 1·392	±0·013
C(6)–N(1) = 1·378	±0·013
C(5)–C(4) = 1·553	±0·016
C(5)–C(6) = 1·521	±0·013
C(5)–C(5′) = 1·547	±0·039
C(2)–O(2) = 1·228	±0·013
C(4)–O(4) = 1·186	±0·013
C(6)–O(6) = 1·210	±0·012
C(5)–O(5) = 1·400	±0·014
N(1)–H(1) = 1·202	±0·1
N(3)–H(3) = 0·831	
O(5)–H(5) = 0·761	
O(7)–H(7*a*) = 0·723	
O(7)–H(7*b*) = 0·782	

Angle
C(6)–N(1)–C(2) = 123·9 ± 0·8°
C(6)–N(1)–H(1) = 99·8 ± 7·0
C(2)–N(1)–H(1) = 114·4 ± 7·0
N(1)–C(2)–N(3) = 117·6 ± 1·1
N(1)–C(2)–O(2) = 120·0 ± 0·9
N(3)–C(2)–O(2) = 122·3 ± 0·9
N(3)–C(4)–O(4) = 123·2 ± 0·8
C(2)–N(3)–C(4) = 120·5 ± 0·8
C(2)–N(3)–H(3) = 120·2 ± 7·0
C(4)–N(3)–H(3) = 112·5 ± 7·0
N(3)–C(4)–C(5) = 113·5 ± 0·8
C(5)–C(4)–O(4) = 122·3 ± 0·8
C(5)–C(6)–N(1) = 117·4 ± 0·8
C(5)–C(6)–O(6) = 120·5 ± 0·8
N(1)–C(6)–O(6) = 122·0 ± 0·8
C(4)–C(5)–C(6) = 110·3 ± 0·9
C(4)–C(5)–O(5) = 106·8 ± 1·0
C(4)–C(5)–C(5′) = 110·3 ± 1·0
C(6)–C(5)–O(5) = 109·5 ± 1·0
C(6)–C(5)–C(5′) = 110·1 ± 1·0
O(5)–C(5)–C(5′) = 109·7 ± 1·0
C(5)–O(5)–H(5) = 123·0 ± 6·9
H(7*a*)–O(7)–H(7*b*) = 89·5 ± 10·7

The C(5)–C′(5) single bond of length 1·547 ± 0·039 Å, linking the two halves of the alloxantin molecule through the centre of symmetry, though comparable to a similar type of bond between two pyridine rings (1·50 ± 0·025 Å) in 2,2′-bipyridine (Merritt & Schroeder, 1956) is, nevertheless, much longer than that between two benzene rings (1·48 Å) in biphenyl (Pauling, 1960, p. 291). The angle subtended by the hydrogen atoms of the water molecule, angle H(7*a*)–O(7)–H(7*b*), is 89·5 ± 10·5°; not significantly different from the average angle in hydrogen-bonded water (105 ± 13°; Fuller, 1959).

Hydrogen-bonded system

The N(1)–H(1) · · · O(4) and N(3)–H(3) · · · O′(7) (Fig. 5) distances of 2·82 and 2·80 Å respectively correspond to average N–H · · · O type hydrogen bonds found between a ring > NH and > C = O group (2·82 ± 0·07 Å; Fuller, 1959) and between > NH and a water molecule (2·81 ± 0·07 Å). The O(5)–H(5) · · · O(2) distance of 2·86(5) Å corresponds to a normal O–H · · · O hydrogen-bond found in alloxan (Chatar Singh, 1965*a*) and other related compounds (Fuller, 1959). The O(7)–H(7*a*) · · · O′(5) and O(7)–H(7*b*) · · · O′(6) distances of 2·94 Å and 2·84 Å are of normal length for a hydrogen bond between a water molecule and a ring hydroxyl, and a ring > C = O group (Fuller, 1959).

The basic hydrogen-bond framework consists of N–H · · · O and O–H · · · O type bonds, but each bond has a different hydrogen acceptor group. For example, in the two N–H · · · O type hydrogen-bonds, one oxygen belongs to a C = O group, but the other to a water molecule. There are, thus, five distinct types of hydrogen bond in alloxantin in contrast to only two types in alloxan. The water molecule fits into the gap between the half-alloxantin molecules with constant *y* and plays its part in linking them together into endless chains extending in the *xz* plane by hydrogen bonds of the type O(7)–H(7*a*) · · · O′(5), O(7)–H(7*b*) · · · O′(6) and O(7) · · · H(3)–N(3) (Fig. 5). There is a direct link between two alloxantin molecules at the same height through the bonds O(5)–H(5) · · · O(2) and N(1)–H(1) · · · O(4). The separation between the hydrogen-bonded planar layers is approximately $\frac{1}{2}b$.

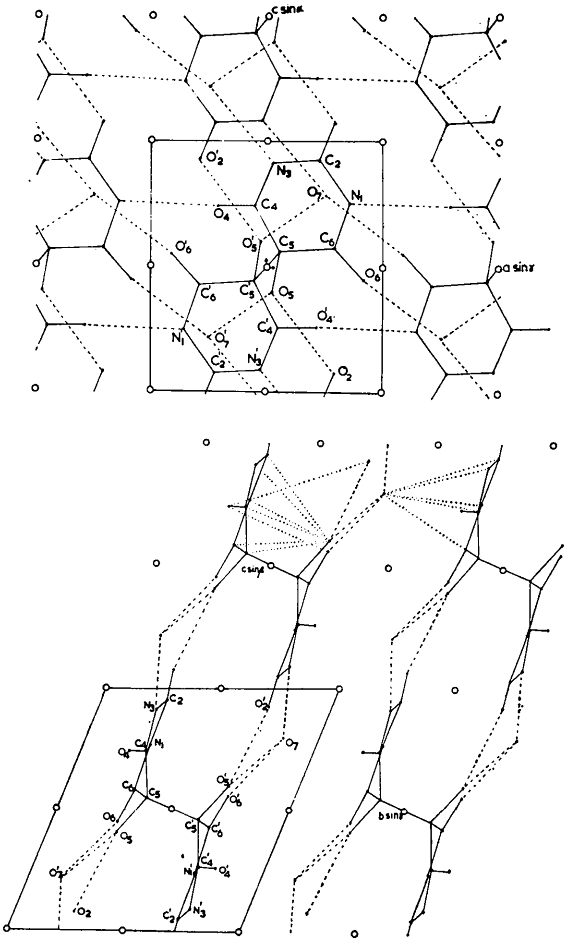


Fig. 5. Structure of alloxantin projected on (010) and (100) showing the hydrogen-bond network (dashed lines) and some van der Waals contacts (dotted lines).

Intermolecular contacts

A number of intermolecular approaches of less than 3·2 Å (Table 5), apart from the hydrogen bonds, occur between the water molecule and the half alloxantin molecule at height (*y* + 1) and between the hydroxyl oxygen, O(5), and the symmetry related half-molecule in the same cell (Fig. 5). The O(5) (I)–C(5) (I′) distance of 2·41 Å is significantly shorter than the van der Waals radii of carbon and oxygen, 3·1 Å, but this and the O(5) (I)–C(6) (I′) = 2·88 Å contacts are between atoms of the same molecule. The O(7) (I)–C(4) (II) distance of 2·83 Å between the water molecule and an atom from the adjacent molecule, though much shorter than the van der Waals distance, is most probably a van der Waals contact since the angular relations associated with it are not compatible with a hydrogen-bond formation.

Comparison of alloxan and alloxantin

The crystal structures of alloxan (Chatar Singh, 1965*a*) and alloxantin have a number of remarkably

Table 5. *Intermolecular distances less than* 3·2Å

General positions of the molecules are I(*x,y,z*); I′($\bar{x},\bar{y},\bar{z}$); II(*x,y* + 1,*z*); IV(*x* + 1,*y,z* + 1); V(*x,y,z* − 1).

O(7)(I) · · ·	C(4)(II)	2·833 Å
	C(6)(II)	3·061
	N(3)(II)	3·188
	O(2)(IV)	3·112
O(6)(I) · · ·	O(2)(V)	3·026
	C(4)(I)	3·071
	O(4)(I)	2·956
O(5)(I) · · ·	C(2)(I′)	3·122
	C(4)(I′)	2·938
	C(5)(I′)	2·411
	C(6)(I′)	2·884
	N(1)(I′)	3·035
	N(2)(I′)	2·964

similar features. Both are triclinic with two substituted pyrimidine rings per unit cell. The significance tests have shown that their mean molecular dimensions are identical. Both are in the triketo configuration with an equal number of single and double bonds. Perhaps the most striking feature is the similarity of the puckering of the ring; the displacements of the atoms being in the same sense. Even in their physiological actions both are diabetogenic.

The hydrogen-bonded network, which provides the attractive forces holding the molecules together in a compact arrangement, gives rise to comparatively high-density crystals and shorter than normal van der Waals approaches. Alloxan has two distinct types of hydrogen bonds whereas alloxantin has five. The hydrogen-bonded layers in alloxan, separated by $\frac{1}{2}c$, are interlinked by hydrogen bonds, whereas in alloxantin such layers, separated by $\frac{1}{2}b$, are linked only through the C(5)–C′(5) bond.

There is, however, a fundamental difference in the substituents at position 5. In alloxan there is a *gem*-dihydroxy group, whereas in alloxantin there is only one hydroxyl group. Alloxantin has two molecules of water in its structure, while alloxan has none.

The author is grateful to Professor Sir Nevill Mott, F.R.S. and Dr W. H. Taylor for the provision of research facilities and for interest and encouragement; to Dr W. Cochran, F.R.S., and Dr W. H. Taylor, my supervisors, for interest, advice and helpful criticism. Computations were carried out on EDSAC II by kind permission of Dr M. V. Wilkes, F.R.S., and Mr E. N. Mutch. My thanks are due to Dr M. Wells for kindly making available his crystallographic programs and to the staff of the Crystallographic Laboratory, Cavendish Laboratory for assistance.

The author wishes to acknowledge with gratitude the award of the 1957 Queen's Scholarship by the Federation of Malaya Government during the tenure of which this work was performed.

References

Chatar Singh (1965*a*). *Acta Cryst.* **19**, 759.
Chatar Singh (1965*b*). *Acta Cryst.* In the press.
Cochran, W., Srinivasan, R. & Tollin, P. (1963). *Crystallography and Crystal Perfection.* London: Academic Press.
Fuller, W. (1959). *J. Phys. Chem.* **63**, 1705.
Howells, E. R., Phillips, D. C. & Rogers, D. (1950). *Acta Cryst.* **3**, 210.
Maubasher, R. & Othman, A. M. (1950). *J. Amer. Chem. Soc.* **72**, 2667.
McDonald, T. R. R. (1956). *Acta Cryst.* **9**, 162.
McDonald, T. R. R. & Beevers, C. A. (1952). *Acta Cryst.* **5**, 654.
Merritt, L. L. & Schroeder, E. D. (1956). *Acta Cryst.* **9**, 801.
Pauling, L. (1960). *The Nature of the Chemical Bond.* 3rd Ed. Ithaca: Cornell Univ. Press.
Piloty, O. & Finckh, K. (1904). *Liebigs Ann.* **333**, 22.
Retinger, J. M. (1917). *J. Amer. Chem. Soc.* **39**, 1059.
Slimmer, M. & Stieglitz, J. (1904). *Amer. Chem. J.* **31**, 677.
Wöhler, F. & Liebig, J. (1838). *Liebigs Ann.* **26**, 241, 292.

Acta Cryst. (1965). **19**, 774

A Theoretical Study of the Least-Squares Refinement of Flexible Long-Chain Molecules, with Special Reference to α-Helical Structures

By Robert Diamond

Medical Research Council Laboratory of Molecular Biology, Hills Road, Cambridge, England

(*Received* 24 *February* 1964 *and in revised form* 13 *January* 1965)

We present the theory of a method of refinement which, like Scheringer's (1963), uses a minimum number of parameters, and also gives reason to believe that by partial refinement, *i.e.* by the use of selected eigenvectors, it may be possible to refine the main features of a chain at a much earlier stage in the analysis than is normally possible.

The method starts direct from the atomic coordinates, rather than from a matrix representation of these; it guarantees the integrity of the chains and preserves all the chemical information (bond angles *etc.*) which is implanted in the trial structure.

1. Introduction

Scheringer (1963) has shown clearly the advantages to be gained by refining certain group parameters describing the structure in preference to the x, y, z parameters of each atom. This approach is justified whenever one's foreknowledge of the configuration of various atomic groupings is more accurate than the results to be expected from a conventional refinement, or when the initial coordinates are far enough from the truth to