

rather than for the stretching of a bond. The directions of maximum thermal vibration of the chlorine atom and the water molecule can also be understood when one considers their environment, the direction in both cases being that in which they make no bonds (Fig. 7).

Finally, we may comment on the very close agreement obtained between calculated and observed structure factors. Over the range  $\sin \theta/\lambda < 0.5$ , two sets of independent measurements on two crystal specimens were made, and the value of  $\Sigma |F_1 - F_2| \div \Sigma |F_1|$  was 0.026. Over the same range  $\Sigma |F_o - F_c| \div \Sigma |F_o| = 0.046$ . This is simply another indication of the fact that the actual electron distribution differs very little from that in a set of 'Hartree' atoms, so that the corresponding atomic scattering factors, including that of hydrogen, are nearly correct. Nevertheless, it is surprising to find that the average atomic scattering factor of an isolated atom is correctly represented by the values given by James & Brindley, to within 4% over this range, as these results suggest. However, it must be remembered that any error in  $f_0$ , which corresponded to a general spreading out of the calculated electron distribution such as results from a neglect of the exchange principle (Hartree & Hartree, 1936), would be at least partially compensated by our method of estimating the temperature-factor parameter.

I should like to conclude by thanking Prof. Sir Lawrence Bragg and Dr W. H. Taylor for their continued support and encouragement. I am indebted to Dr M. V. Wilkes for permission to use the Hollerith tabulator on which much of the computing work was done, and to Mrs Gill for her assistance with the latter.

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## The Structures of Pyrimidines and Purines. IV. The Crystal Structure of Guanine Hydrochloride and its Relation to that of Adenine Hydrochloride

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The crystal structure of guanine hydrochloride monohydrate has been established by X-ray analysis, employing two-dimensional Fourier methods. The cell dimensions and space group are different from those of adenine hydrochloride hemihydrate, but, in spite of this, the two structures are strikingly similar. From the disposition of intermolecular hydrogen bonds an attempt is made to deduce the positions of the hydrogen atoms covalently bound to nitrogen atoms of the purine molecules.

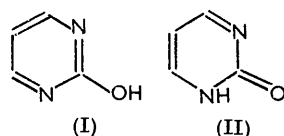
### 1. Introduction

An X-ray study of the hydrogen chloride salts of the purines adenine and guanine was undertaken as part of

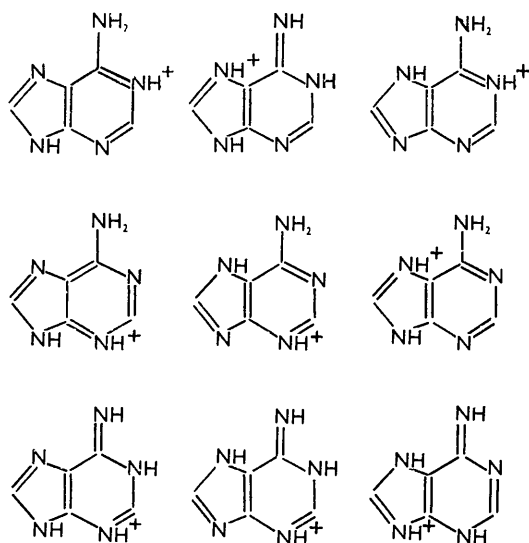
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a programme of investigation of a group of comparatively simple molecules which are constituents of nucleic acids. In this particular case the main object of the research has been to establish, if possible, which tautomeric forms of adenine and guanine exist in the solid

state. The nature of this problem may be illustrated by reference to the much simpler compound 2-hydroxy pyrimidine, whose formula can be written in the following alternative ways:



The evidence regarding the molecular structures of such prototropic pyrimidines has been reviewed by Kenner & Todd (unpublished), and, even when allowance is made for the different methods of investigation used, much of it appears to be conflicting. The complexity of the problem in the case of amino- or hydroxy-substituted purines is shown by the fact that if we formulate adenine hydrochloride as  $(HA)^+Cl^-$ , there are then nine possible tautomers of the adenine cation:



Some evidence on the molecular structure of amino pyrimidines in the solid state has been obtained by Clews & Cochran (1949). The crystal structure of adenine hydrochloride has been described in a previous communication (Broomhead, 1948). In this paper the structure of guanine hydrochloride is described, and an attempt is made to deduce the positions of the hydrogen atoms in both purine molecules. Photographic recording techniques and two-dimensional Fourier methods have been used throughout, and the limitations introduced by this become apparent in the discussion.

The experimental technique, and the method of determination of the structure, are described in §§ 2 and 3. The structure is described in § 4, and the significance of the special features of both adenine and guanine structures is discussed in § 5.

## 2. Experimental

Guanine hydrochloride was recrystallized from dilute hydrochloric acid and the crystals obtained were of

two forms. Needle-like crystals with approximately square cross-sections were found to be monoclinic, with space group  $P2_1/a$  and cell dimensions  $a = 14.67 \pm 0.1$ ,  $b = 13.39 \pm 0.1$ ,  $c = 4.84 \pm 0.05$  A.,  $\beta = 93^\circ 30' \pm 30'$ . The only well-developed faces were  $\{110\}$ . The density, found by flotation, was  $1.562 \text{ g.cm.}^{-3}$ , and, assuming four molecules in the unit cell, the molecular weight was found to be 223. According to *Beilsteins Handbuch* (1929), the hydrogen chloride salt of guanine may crystallize as guanine hydrochloride monohydrate, guanine hydrochloride dihydrate or guanine dihydrochloride. These compounds have molecular weights of 205.5, 223.5 and 223 respectively, and the measured value is, therefore, consistent with either of the last two formulae. Microanalysis showed that the crystals were of guanine hydrochloride dihydrate.

Crystals of the second form were monoclinic, with space groups  $P2_1/a$ , and cell dimensions (obtained using a Geiger-counter spectrometer) were

$$a = 19.297 \pm 0.02, \quad b = 9.941 \pm 0.01, \\ c = 4.494 \pm 0.005 \text{ A.}, \quad \beta = 107^\circ 54' \pm 2'$$

(wave-length of  $\text{Cu } K\alpha$  radiation taken as 1.5418 A.). The density was  $1.662 \text{ g.cm.}^{-3}$  and the experimental molecular weight of 205.2 suggested the formula guanine hydrochloride monohydrate.

$a$ -,  $b$ - and  $c$ -axis zero-layer-line Weissenberg photographs of both compounds were taken using  $\text{Cu } K\alpha$  radiation. Intensities were estimated visually. No correction for absorption was made, but the comparatively regular shape of the crystals used made the absorption factor approximately a function of  $\sin \theta$  only. The corrections for polarization and Lorentz factors were made in the usual way.

## 3. Determination of the structure

The structure of guanine hydrochloride dihydrate has not yet been determined successfully, and the work described below refers to the monohydrate. The methods adopted for the determination of this structure were similar to those used for adenine hydrochloride (Broomhead, 1948). In the case under consideration, however, it was realized that greater difficulty might be experienced in finding the position of the chlorine atom from Patterson projections, and, in addition, that the increased number of light atoms would cause the first approximation to the electron density, calculated from observed coefficients with phases fixed by the chlorine atom alone, to be less accurate than in the former case. Whether it would be sufficiently accurate to show the position of the guanine molecule could not be decided in advance.

### *c*-axis projection

The Patterson projection along the  $c$  axis suggested two possible positions of the chlorine atom. Two Fourier summations were computed from observed coefficients with phases determined by the appropriate chlorine

structure factor, but neither showed a clearly defined position for the guanine molecule. The correct position of the latter was eventually found by trial and error, and the successful solution involved placing the chlorine at (0.116, 0.042) (co-ordinates expressed as fractions of the appropriate cell edges), and the guanine molecule with its length along the  $a$  axis and in such a position that no atoms approached too closely to a centre of symmetry or to a chlorine atom. In this position (Fig. 1) all atoms of the molecule fell on or near regions of positive electron density on the distribution calculated from coefficients whose signs were given by the above chlorine position.

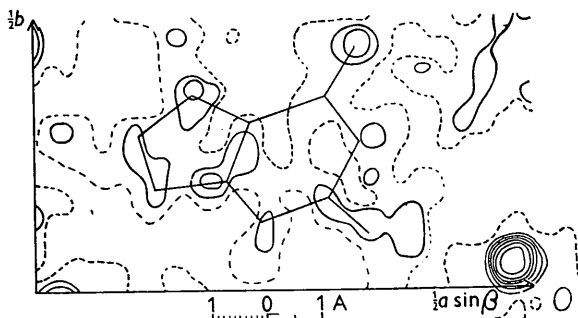


Fig. 1. First electron-density projection along the  $c$  axis. The final position of the guanine molecule is shown.

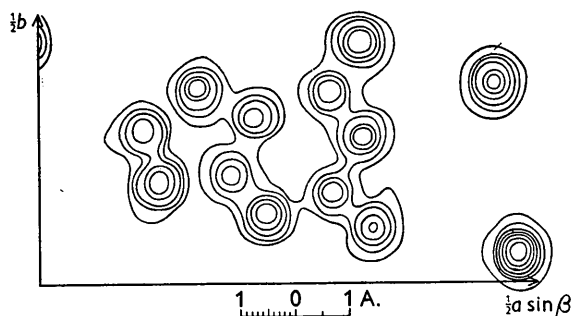


Fig. 2. Final electron-density projection along the  $c$  axis. Contour interval  $2 \text{ e.A.}^{-2}$  for carbon, nitrogen and oxygen atoms;  $4 \text{ e.A.}^{-2}$  for chlorine atom.

Parameter refinement was continued by the method of successive approximations and the progress of refinement was illustrated by the decrease in the value of  $\Sigma |F_{\text{obs.}} - F_{\text{calc.}}| \div \Sigma |F_{\text{obs.}}|$  from 0.58 to 0.17 between first and final approximations. The final electron-density projection is shown in Fig. 2. Atomic parameters taken from this projection were corrected for Fourier series termination by the 'back correction' method due to Booth (1946).

#### *b*-axis projection

The  $z$  co-ordinates of the chlorine atom and water molecule were found from a Patterson projection along the  $b$  axis, and approximate relative  $z$  co-ordinates of the atoms in the guanine molecule from a model of the molecule tilted until its image, projected on to a plane

perpendicular to the  $c$  axis, coincided with the map of electron density in this plane. Absolute  $z$  co-ordinates were determined by fixing the position of  $N_3$ . If it is assumed that this atom is separated from an equivalent atom across a centre of symmetry by a distance of about 3.1 Å., then the required separation in the  $c$ -axis direction can be calculated. Since, however, it is not known which of the two centres of symmetry will link these atoms, two possible  $z$  co-ordinates differing by 0.5 Å. are obtained. These two positions for  $N_3$  and the two possible directions of tilt of the molecule gave four sets of co-ordinates for atoms in the molecule. From a consideration of a possible hydrogen-bond system in the structure three of these were eliminated. Structure-amplitude calculations based on the remaining set of

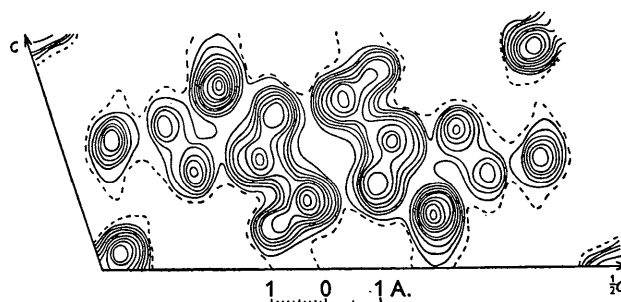


Fig. 3. Electron density projected on (010). Atoms can be identified with the help of Fig. 4.

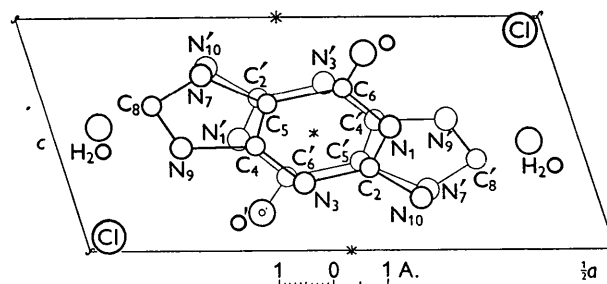


Fig. 4. Structure of guanine hydrochloride monohydrate projected on (010).

co-ordinates gave signs which were attached to the observed coefficients, and Fourier summation was computed. Refinement of the electron-density projection so obtained was carried out in the usual way and the final projection is shown in Fig. 3. During the refinement process the factor  $\Sigma |F_{\text{obs.}} - F_{\text{calc.}}| \div |F_{\text{obs.}}|$  decreased from 0.44 to 0.24.

The molecule is planar within the limits of experimental error, apart from  $N_{10}$  which appears to depart from the molecular plane by as much as 0.11 Å. (A similar departure of the amino group from the plane of the molecule was found in the crystal structure of 4-amino-2,6-dichloropyrimidine by Clews & Cochran (1949). Since only two of the eleven crystallographically independent atoms were well resolved in the  $b$ -axis electron-density projection (see Fig. 4), the molecule

was assumed to be planar (apart from N<sub>10</sub>) when bond lengths were calculated.

Final atomic co-ordinates are given in Table 1, and the observed and calculated values of the  $F(hk0)$ 's and  $F(h0l)$ 's in Table 2.

Table 1. Atomic co-ordinates

Co-ordinates expressed as fractions of the corresponding unit-cell dimensions; centre of symmetry as origin.

$$a = 19.30, \quad b = 9.941, \quad c = 4.494 \text{ \AA.}, \quad \beta = 107^\circ 54'.$$

Atom	<i>x</i>	<i>y</i>	<i>z</i>
N <sub>1</sub>	0.073	0.272	0.530
N <sub>3</sub>	-0.023	0.128	0.287
N <sub>7</sub>	-0.090	0.357	0.740
N <sub>9</sub>	-0.131	0.188	0.440
N <sub>10</sub>	0.083	0.106	0.193
C <sub>2</sub>	0.045	0.168	0.350
C <sub>4</sub>	-0.062	0.201	0.440
C <sub>5</sub>	-0.035	0.305	0.627
C <sub>6</sub>	0.037	0.353	0.690
C <sub>8</sub>	-0.148	0.280	0.617
O	0.072	0.443	0.842
H <sub>2</sub> O	0.205	0.370	0.467
Cl	0.229	0.054	0.940

#### 4. Description of the structure

The positions of the atoms are shown in Figs. 4 and 5. The molecule (Fig. 6) is planar within the limits of experimental error, apart from N<sub>10</sub> which appears to be displaced by 0.11 Å. from the plane containing the other atoms. The standard deviation of a measured bond length has been estimated to be about 0.04 Å. It follows that no useful comparison of bond lengths in the two structures adenine and guanine can be made, since a difference of even 0.1 Å. could be ascribed to experimental error. The bond C<sub>6</sub>-O in guanine, of length 1.20 Å., appears to have predominantly double-bond character. On the other hand, an error of 0.05 Å. in this value would make it comparable with C-O distances found, for example, in the molecules of diketopiperazine (Hughes, 1940) and glycine (Albrecht & Corey, 1939).

The guanine molecule is tilted in the unit cell so that C<sub>6</sub>-C<sub>2</sub> and C<sub>4</sub>-N<sub>1</sub> make angles of 40° and 9° respectively with their projections on the plane perpendicular to the *c* axis. The centre of symmetry at ( $\frac{1}{2}, \frac{1}{2}, 0$ ) is less than 0.03 Å. from the plane of the molecule, and molecules

Table 2. Comparison of observed and calculated structure factors

<i>hkl</i>	<i>F</i> <sub>obs.</sub>	<i>F</i> <sub>calc.</sub>	<i>hkl</i>	<i>F</i> <sub>obs.</sub>	<i>F</i> <sub>calc.</sub>	<i>hkl</i>	<i>F</i> <sub>obs.</sub>	<i>F</i> <sub>calc.</sub>
000	—	106	920	2	2	640	2	-1
200	12	16	10.2.0	5	4	740	9	9
400	7	9	11.2.0	5	6	840	2	3
600	19	-22	12.2.0	6	5	940	2	-3
800	8	-8	13.2.0	7	-6	10.4.0	8	-7
10.0.0	6	-6	14.2.0	0	1	11.4.0	0	0
12.0.0	5	-3	15.2.0	3	-2	12.4.0	4	3
14.0.0	9	8	16.2.0	3	-2	13.4.0	5	4
16.0.0	10	-8	17.2.0	9	9	14.4.0	5	5
18.0.0	5	-4	18.2.0	6	6	15.4.0	0	-1
20.0.0	10	-10	19.2.0	0	2	16.4.0	7	6
22.0.0	6	5	20.2.0	7	-6	17.4.0	0	1
			21.2.0	8	8	18.4.0	6	5
110	0	-1	22.2.0	3	4	19.4.0	10	-9
210	4	3	23.2.0	7	-8	20.4.0	0	0
310	2	-1				21.4.0	6	6
410	0	-1	130	1	-3			
510	7	7	230	14	-13	150	4	-3
610	13	-14	330	7	-6	250	7	-7
710	1	0	430	6	4	350	4	-4
810	14	12	530	9	8	450	5	-5
910	9	10	630	9	-9	550	0	0
10.1.0	4	5	730	8	-8	650	3	-3
11.1.0	9	-10	830	8	9	750	2	-1
12.1.0	3	3	930	9	7	850	11	12
13.1.0	7	7	10.3.0	6	-6	950	0	1
14.1.0	0	0	11.3.0	0	-2	10.5.0	2	-2
15.1.0	7	-9	12.3.0	12	12	11.5.0	3	-2
16.1.0	3	2	13.3.0	4	3	12.5.0	8	8
17.1.0	8	8	14.3.0	3	-3	13.5.0	3	-5
18.1.0	0	0	15.3.0	9	-8	14.5.0	13	-12
19.1.0	6	-5	16.3.0	3	3	15.5.0	6	6
20.1.0	0	0	17.3.0	4	-4	16.5.0	0	2
21.1.0	0	3	18.3.0	4	-2	17.5.0	6	5
22.1.0	4	3	19.3.0	0	1	18.5.0	13	-12
			20.3.0	4	4	19.5.0	4	5
020	10	-9	21.3.0	0	3	20.5.0	0	3
120	2	-3	22.3.0	0	-1			
220	18	-18				060	3	-1
320	3	4	040	11	-11	160	7	-8
420	12	12	140	11	-11	260	6	6
520	2	-3	240	6	-6	360	16	18
620	9	-7	340	9	11	460	0	-1
720	11	12	440	3	-4	560	4	-5
820	4	3	540	4	-5	660	5	6

Table 2. (cont.)

<i>hkl</i>	<i>F</i> <sub>obs.</sub>	<i>F</i> <sub>calc.</sub>	<i>hkl</i>	<i>F</i> <sub>obs.</sub>	<i>F</i> <sub>calc.</sub>	<i>hkl</i>	<i>F</i> <sub>obs.</sub>	<i>F</i> <sub>calc.</sub>
760	6	- 5	0.10.0	6	- 7	16.0.2	0	- 3
860	3	0	1.10.0	0	2	18.0.2	6	6
960	13	-13	2.10.0	5	6			
10.6.0	3	- 1	3.10.0	0	- 3	202	19	-21
11.6.0	10	-10	4.10.0	6	- 8	402	9	9
12.6.0	10	- 8	5.10.0	8	8	602	13	- 9
13.6.0	0	- 1	6.10.0	6	6	802	6	8
14.6.0	8	- 7	7.10.0	7	4	10.0.2	7	- 7
15.6.0	4	- 3	8.10.0	0	1	12.0.2	2	1
16.6.0	0	- 1	9.10.0	0	1	14.0.2	6	1
17.6.0	11	10	10.10.0	0	0	16.0.2	10	10
18.6.0	0	- 2	11.10.0	5	4	18.0.2	10	9
19.6.0	0	0	12.10.0	0	1	20.0.2	0	2
20.6.0	6	5	13.10.0	0	0	22.0.2	0	- 1
21.6.0	0	3	14.10.0	0	0	24.0.2	0	- 5
170	2	2	1.11.0	7	6	003	0	2
270	2	3	2.11.0	5	4	203	5	10
370	4	6	3.11.0	4	- 2	403	8	6
470	2	3	4.11.0	4	3	603	5	6
570	4	- 4	5.11.0	8	- 8	803	4	- 9
670	7	- 6	6.11.0	8	7	10.0.3	4	- 6
770	8	8	7.11.0	0	- 1	12.0.3	13	-15
870	0	0	8.11.0	5	4	14.0.3	7	- 2
970	8	-10	9.11.0	6	- 7	16.0.3	7	- 8
10.7.0	6	- 6	10.11.0	6	6			
11.7.0	3	4	11.11.0	5	5	203	6	- 7
12.7.0	5	4	12.11.0	4	- 6	403	7	3
13.7.0	0	- 2				603	5	3
14.7.0	5	- 6	0.12.0	10	-10	803	19	25
15.7.0	4	5	1.12.0	4	5	10.0.3	9	- 6
16.7.0	8	8	2.12.0	0	3	12.0.3	6	6
17.7.0	5	- 4	3.12.0	6	- 8	14.0.3	16	-16
18.7.0	0	- 1	4.12.0	4	- 4	16.0.3	0	- 5
19.7.0	0	0	5.12.0	5	- 3	18.0.3	6	- 9
			6.12.0	3	3	20.0.3	6	1
080	6	- 7	7.12.0	6	- 7	22.0.3	12	9
180	3	- 3	8.12.0	0	- 1	24.0.3	11	- 5
280	4	5						
380	0	2	001	15	-16	004	0	0
480	3	- 3	201	16	-17	204	0	1
580	5	- 5	401	8	8	404	4	- 5
680	5	6	601	4	- 2	604	0	1
780	4	4	801	9	10	804	5	- 8
880	0	- 3	10.0.1	9	9	10.0.4	10	16
980	0	3	12.0.1	4	2	12.0.4	0	3
10.8.0	8	9	14.0.1	0	- 1			
11.8.0	4	2	16.0.1	6	- 5	204	0	- 3
12.8.0	4	3	18.0.1	17	15	404	11	5
13.8.0	0	1	20.0.1	0	- 5	604	9	-11
14.8.0	0	- 2				804	4	2
15.8.0	0	2	201	12	-16	10.0.4	5	- 1
16.8.0	0	- 2	401	13	12	12.0.4	6	7
17.8.0	0	2	601	19	-18	14.0.4	11	-10
18.8.0	7	- 7	801	4	5	16.0.4	5	4
			10.0.1	6	- 6	18.0.4	0	- 1
190	0	1	12.0.1	15	13	20.0.4	4	5
290	3	- 4	14.0.1	0	- 1			
390	7	7	16.0.1	0	- 4	005	0	- 3
490	0	1	18.0.1	0	- 1	205	0	4
590	6	- 6	20.0.1	16	-12	405	4	- 9
690	5	- 4	22.0.1	10	6			
790	0	3	24.0.1	5	- 5	205	0	1
890	3	- 3				405	0	- 6
990	5	- 6	002	5	4	605	4	- 5
10.9.0	5	- 3	202	12	-15	805	4	0
11.9.0	10	11	402	0	2	10.0.5	13	-13
12.9.0	5	3	602	5	6	12.0.5	6	9
13.9.0	7	- 5	802	0	- 3	14.0.5	4	0
14.9.0	8	6	10.0.2	3	3	16.0.5	9	13
15.9.0	3	5	12.0.2	8	-10	18.0.5	7	- 8
16.9.0	0	1	14.0.2	14	13			

related by it are coplanar within the limits of experimental error. On the other hand, the centre of symmetry at  $(\frac{1}{4}, 0, 0)$  is 0.2 Å. below the line of intersection of the molecular plane with (010). The planes of molecules related by this centre of symmetry are, therefore, not coincident and bonds between these molecules do not lie exactly in the plane of either. This may account for

what shorter than those previously reported in the literature (e.g. Albrecht & Corey, 1939), although Dyer (1951) reports one of length 2.55 Å. in the crystal structure of cysteylglycine. It seems probable that resonance structures in which the oxygen atom and N<sub>7</sub> are oppositely charged make a large contribution to the structure of the guanine molecule.

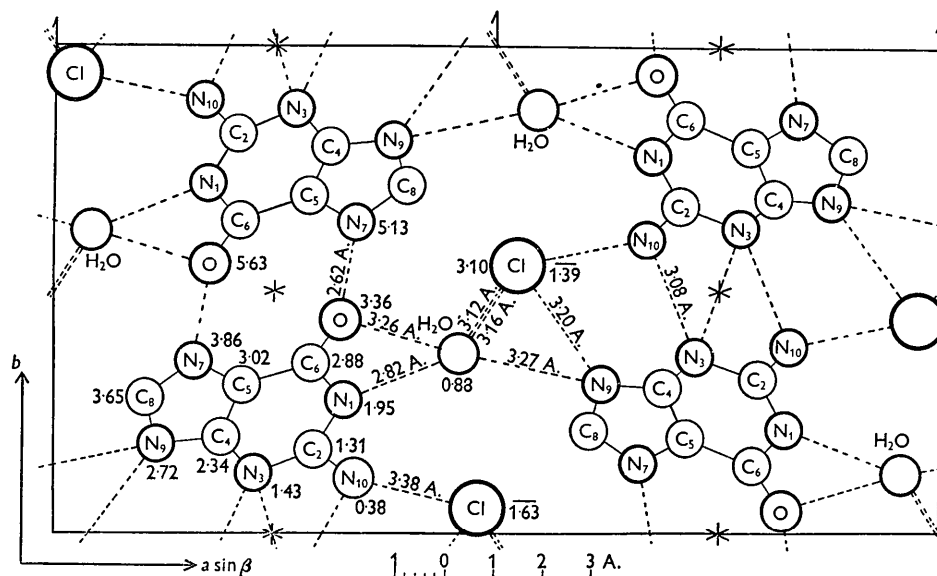


Fig. 5. Structure of guanine hydrochloride monohydrate projected on to a plane perpendicular to  $c$ ; distances of atoms above plane of projection indicated. Hydrogen bonds and short van der Waals contacts shown by broken lines.

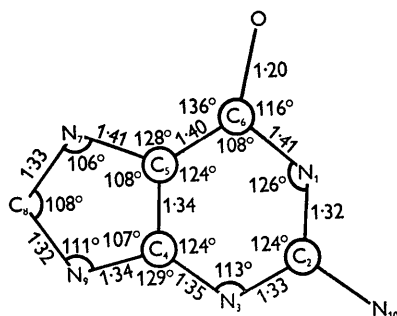


Fig. 6. Bond lengths and bond angles in the guanine molecule.

the displacement of N<sub>10</sub> from the plane of the molecule, for this is in such a direction that a stronger hydrogen bond is formed between N<sub>10</sub> and N<sub>3</sub> of the adjacent molecule. Thus sheets of molecules are not continuous as in adenine hydrochloride but have discontinuities of magnitude 0.4 Å. along the  $c$ -axis direction at each symmetry centre  $(\frac{1}{4}, 0, 0)$ . Alternate sheets of molecules are, as in adenine hydrochloride, linked through bonds to the chlorine atoms and water molecules.

Molecules related by the centre of symmetry at  $(\frac{1}{4}, \frac{1}{2}, 0)$  are linked by hydrogen bonds of length 2.62 Å. between the oxygen atom of one molecule and N<sub>7</sub> of the other. The separation between O and N<sub>7</sub> atoms of molecules in adjacent layers is 3.39 Å. The hydrogen bond O—H—N (or O—N—H) of length 2.62 Å. is some-

Molecules related by the centre of symmetry at  $(\frac{1}{4}, 0, 0)$  are linked by hydrogen bonds of length 3.08 Å. between N<sub>3</sub> of one molecule and N<sub>10</sub> of the other. The separation between N<sub>3</sub> atoms of these molecules is 3.93 Å. N<sub>3</sub> atoms of molecules related by the centre of symmetry at  $(\frac{1}{4}, \frac{1}{2}, 0)$  are separated by a distance of 3.15 Å. The perpendicular distance between molecules in adjacent layers is 3.36 Å.

N<sub>1</sub> is linked to a water molecule by a hydrogen bond of length 2.82 Å. and N<sub>9</sub> makes two relatively short contacts of length 3.20 and 3.27 Å. with a chlorine atom and a water molecule respectively. The bonds between N<sub>1</sub> and H<sub>2</sub>O, N<sub>9</sub> and Cl make small angles with the plane of the guanine molecule. The water molecule makes additional bonds of length 3.16 and 3.12 Å. with chlorine atoms in the same unit cell and in the adjacent unit cell below. The separation between the water molecule and the oxygen atom of a guanine molecule in the cell below is 3.26 Å. Three of the contacts of the chlorine atom have been mentioned; a fourth of length 3.38 Å. links it to N<sub>10</sub> giving the chlorine atom the usual co-ordination number of four.

#### Comparison with the structure of adenine hydrochloride

Adenine hydrochloride and guanine hydrochloride crystallize in unit cells of different dimensions and have different space groups, but in spite of this the structures are strikingly similar. This similarity is

shown in a convincing manner by Figs. 7 and 8 which are sections of the structures in the plane of one of the layers of molecules. (Fig. 8 is somewhat idealized since all the molecules of one layer in guanine hydrochloride are not exactly coplanar.) The position of the hydrogen atom covalently bound to  $C_8$  (and also to  $C_2$  in the case of adenine) has been calculated on the assumptions that  $C_8$ -H lies in the plane of the molecule in a direction

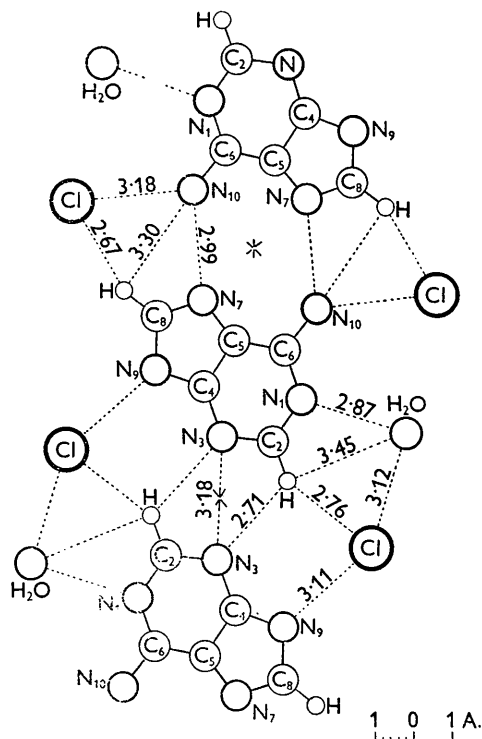


Fig. 7. A section of the structure of adenine hydrochloride hemihydrate in the plane of one of the layers.

which is symmetrical with respect to the other covalent bonds of  $C_8$  and is of length 1.08 Å. Perhaps the most striking feature shown in these figures is the replacement of the hydrogen atom attached to  $C_2$  in the adenine molecule by the amino group in the guanine molecule without altering the underlying structure in any way. In adenine hydrochloride this hydrogen atom is separated from  $N_3$  of a neighbouring molecule and from a chlorine atom by distances of 2.76 and 2.71 Å, respectively. The hydrogen atom covalently bound to  $C_8$  is separated from the chlorine atom by distances of 2.67 and 2.71 Å. in the adenine and guanine structures respectively. These van der Waals separations are similar to, but slightly shorter than, those found in the structure of 4-amino-2,6-dichloropyrimidine.

### 5. Discussion

The electron-density projections obtained are not sufficiently accurate to give directly any information concerning hydrogen positions. In compounds of the

type under discussion, however, the positions of hydrogen atoms can sometimes be deduced from the disposition of intermolecular hydrogen bonds. This has been done successfully in the case of glycine (Albrecht & Corey, 1939) and melamine (Hughes, 1941). Similar arguments are used here in an attempt to determine the positions of hydrogen atoms in the adenine and guanine molecules.

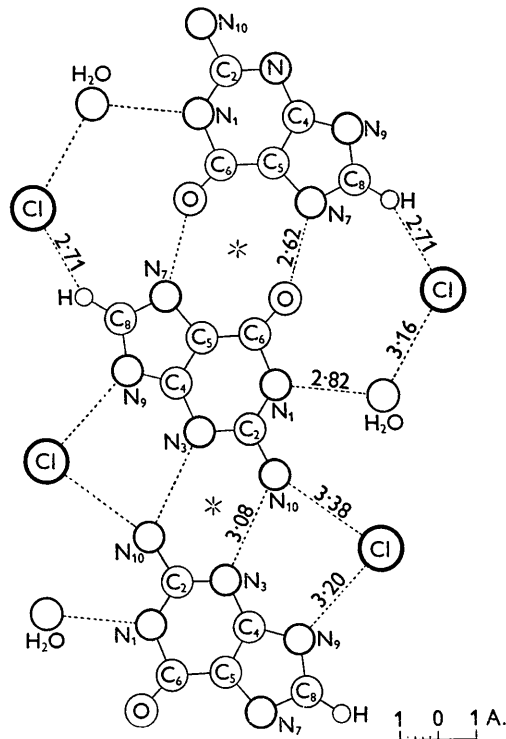


Fig. 8. A section of the structure of guanine hydrochloride monohydrate in the plane of one of the layers.

#### *Positions of hydrogen atoms in the adenine molecule*

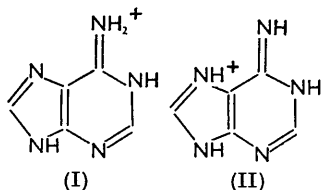
In the crystal structure of adenine hydrochloride we may assume the chlorine atom to be present as an anion  $Cl^-$  and the adenine molecule as a cation  $(HA)^+$ . The water molecule is probably uncharged, although an approximately tetrahedral distribution of two regions of positive and two regions of negative charge is to be expected. The positive regions will then be directed towards two chlorine atoms and the negative regions towards the  $N_1$  atoms of two adenine molecules.

In order to determine the tautomeric form of the adenine ion, we require to know the positions of four hydrogen atoms attached by covalent bonds to nitrogen atoms of this ion. Possible tautomers, in which the valency of each atom is completely satisfied, are shown in § 1. If it is assumed that hydrogen atoms attached to ring nitrogens lie in the plane of the molecule and in directions that make approximately equal angles with the two adjacent covalent bonds, and that hydrogen atoms attached to  $N_{10}$  lie in the plane of the molecule

and make angles of about  $120^\circ$  with the covalent bond  $C_6-N_{10}$ , then it is possible to eliminate several of the possible tautomers.

(i) If a hydrogen atom is covalently bound to  $N_3$  and the bond lies in the direction indicated above, the distances separating it from the hydrogen atom covalently bound to  $C_2$  of a neighbouring molecule and from the equivalent hydrogen atom across the centre of symmetry are 1.7 and 2.0 Å. respectively. These distances are both less than the required van der Waals separation of 2.4 Å. Furthermore, a hydrogen atom in this position would not be taking part in hydrogen-bond formation. If, however, the hydrogen atom is directed along the line joining  $N_3$  and  $N'_3$  and it is assumed that hydrogen atoms obey the laws of crystal symmetry, then two hydrogen atoms directed towards each other would approach to within a distance of 1 Å. These facts suggest that  $N_3$  does not form a covalent bond with a hydrogen atom.

(ii) The intermolecular bonds linking  $N_{10}$  to Cl,  $N_{10}$  to  $N_7$  of a neighbouring molecule,  $N_9$  to Cl and  $N_1$  to  $H_2O$  are presumably hydrogen bonds and are approximately the directions already indicated for covalent bonds involving hydrogen atoms. These are, therefore, the lines along which the four hydrogen atoms must occur, but the positions of the latter are not uniquely determined. Since, however, two hydrogen atoms cannot be directed towards each other along the same hydrogen bond, it is possible to eliminate all tautomers in which the position adjacent to  $N_7$  and the two positions adjacent to  $N_{10}$  are occupied simultaneously. We are then left with the possibilities (I) and (II) but to decide conclusively between them is not possible with the data at present available.



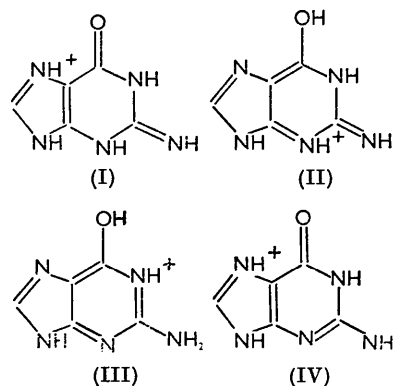
According to Hunter (1945) differentiation between the two forms is meaningless.  $N_7$  and  $N_{10}$  of adjacent molecules are linked to each other in the crystal structure by a hydrogen bond and the two tautomers are derived one from the other merely by proton interchange between these two atoms and a redistribution of the bonding electrons. Whether a proton can oscillate between one minimum of potential energy and another about 1 Å. away is not known in the present case. If, in the solid state, where  $N_7$  and  $N_{10}$  of an adjacent molecule are separated by 3 Å., this proton interchange is continually taking place then Hunter's interpretation is no doubt correct. Oscillation of the proton between these two positions, however, would not stabilize the system to any appreciable extent on account of the comparatively low frequency of the nuclear motion.

#### Positions of the hydrogen atoms in the guanine molecule

The guanine molecule is assumed to be present in the crystal structure of guanine hydrochloride as the cation  $(HG)^+$ . If the five hydrogen atoms are distributed among the seven available positions in such a way that the valencies of all atoms are satisfied, fourteen tautomers are obtained. The restricting condition that one proton must, but two cannot, occur along a hydrogen bond, eliminates ten of these characterized by one or more of the following:

- (i) no hydrogen atom covalently bound to  $N_7$  or O,
- (ii) hydrogen atoms covalently bound to  $N_7$  and O simultaneously,
- (iii) two hydrogen atoms covalently bound to  $N_{10}$  and one to  $N_3$ .

The four remaining possibilities are:



Neighbouring molecules in the crystal structure are linked by hydrogen bonds between O and  $N_7$ ,  $N_3$  and  $N_{10}$ . (I) would be changed into (II), and (III) into (IV), by proton interchange along the hydrogen bond  $O-H-N_7$ , and (II) would be changed into (III), and (I) into (IV), by proton interchange along the hydrogen bond  $N_3-H-N_{10}$ . According to Hunter (1945), therefore, these four tautomers are indistinguishable. It has been stated previously that the hydrogen bond  $O-H-N_7$  is shorter than those usually found in organic structures, and under normal conditions of thermal vibration it is conceivable that proton interchange might occur relatively easily along this bond. Such suggestions are speculative and more definite conclusions from this type of investigation await the application of more accurate techniques.

I wish to thank Prof. Sir Lawrence Bragg and Dr W. H. Taylor for their interest and encouragement. I am grateful to Dr W. Cochran for advice and many helpful discussions. Thanks are also due to Prof. A. R. Todd and his collaborators, in particular Dr G. W. Kenner, for their assistance and advice, and to Mrs J. K. Roberts for assistance with the computation. I am indebted to Newnham College for the award of a Research Studentship and to the Department of Scientific and Industrial Research for a maintenance grant.



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The Crystal Structure of *p*-Aminophenol

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The structure of crystalline *p*-aminophenol has been determined by the X-ray method. The dimensions of the orthorhombic unit cell, which contains four molecules of  $C_6H_4(OH).NH_2$ , are

$$a = 12.90 \pm 0.03, \quad b = 8.19 \pm 0.03, \quad c = 5.25 \pm 0.03 \text{ \AA.},$$

and the space group is  $P2_1nb$ , [ $a$ ] being the polar axis. The calculated specific gravity is 1.305, while that observed by flotation is 1.295. X-ray intensities were obtained from Weissenberg moving-film photographs for all layers of the three principal axes, and the approximate structure was derived by analogy from that of aniline hydrochloride. The atomic co-ordinates were refined by means of successive two- and three-dimensional Fourier syntheses using finally 605 experimental structure amplitudes as coefficients of the series. The bond lengths within the benzene ring are normal but the C-N bond is shorter (1.39 Å.) than that given by the sum of the covalent radii. Molecules of *p*-aminophenol are linked together by three hydrogen bonds of length 2.83, 3.13 and 3.18 Å.

## Introduction

During a survey of the unit-cell dimensions of organic crystals, it was observed that those of one form of *p*-aminophenol (Caspari, 1927*b*) bore some resemblance to those of aniline hydrochloride (Brown, 1949). As the atomic configuration of the greater part of the two molecules is the same, it was suggested that the crystal structures might be similar. The structure determination of aniline hydrochloride was carried only as far as two-dimensional projections because the unsuitable nature of the crystals gave reason to doubt the reliability of the X-ray intensities, and the bond lengths obtained might suffer in accuracy. It was considered therefore that a full three-dimensional determination of the structure of *p*-aminophenol would give necessary data on this class of compound, in particular, the lengths of C-O and C-N bonds attached to a benzene ring, and would provide further information concerning the lengths of N-H-O hydrogen bonds.

## Experimental

The crystals used in this investigation were grown from aqueous solution containing a small quantity of a surface-active agent. They were generally lath-shaped, elongated along [ $c$ ], and tabular on (010). The axial ratios given by Winchell (1943) reporting the work of Bolland (1910) are 0.785:1:0.721, and are only

partially correct, seeing that they are not consistent with our values (1.575:1:0.641). No cleavage or defects were observed and growth of suitable specimens was relatively simple. The crystals were the so-called stable  $\alpha$ -modification of Caspari (1927*b*); it has later been learned (Powell & Holmes, 1950) that the unstable  $\beta$ -modification reported by Caspari is actually a condensation compound of *p*-aminophenol with acetone.

The dimensions of the unit cell were obtained by measurement of the layer lines of single-crystal rotation photographs:

$$[a] = 12.90 \pm 0.03, \quad [b] = 8.19 \pm 0.03, \quad [c] = 5.25 \pm 0.03 \text{ \AA.}$$

For four molecules per unit cell, the specific gravity required is 1.305, while that observed by flotation is 1.295. Observed extinctions were  $\{h0l\}$  for  $(h+l)$  odd and  $\{hk0\}$  for  $k$  odd, whence the space group may be either  $Pmnb$  or  $P2_1nb$ . The impossibility of fitting the *p*-aminophenol molecule in the mirror plane in  $Pmnb$  confirms the correct space group as  $P2_1nb-C_{2v}^2$ .

X-ray intensity data were obtained from Weissenberg moving-film photographs about [ $a$ ] (zero and five layers), [ $b$ ] (zero and three layers), and [ $c$ ] (zero and two layers). As the temperature coefficient of the structure amplitudes was obviously moderately high, i.e. the intensities of the reflexions fell off to zero before  $\theta = 90^\circ$ , it was considered that all the experimental intensities