Les nœuds à facteur de structure nul ne possèdent pas de domaine de diffusion mesurable. La grandeur du domaine de diffusion est en relation avec le facteur de structure, p.ex. le domaine de diffusion 020 est allongé parallèlement à l'axe [100] et atteint dans cette direction une longeur de 0,25 B_0 ($F_{020}=65$), le domaine de diffusion 040 possède dans cette direction la longeur 0,14 B_0 ($F_{040}=12$).

θ_i	$\theta_0-\theta_i$	ϕ
− 1,2°	7,4°	12,4°
− 0,8°	7,0°	12,4°
+ 0,8°	5,4°	12,4°
+ 1,2°	5,0°	12,4°
+ 3,2°	3,0°	12,4°
+ 4,2°	2,0°	12,4°
+ 5,2°	1,0°	12,4°
+ 6,6°	− 0·4°	12,4°
+ 8,8°	− 2,6°	12,4°
+ 10,8°	− 4,6°	12,4°
+ 12,8°	− 6·6°	12,4°

Nous avons mesuré l'intensité aprochée des réflexions diffuses en comparant le temps de pose nécessaire pour obtenir une réflexion de la même intensité quand le cristal est placé dans la position de Bragg. L'ordre de grandeur des intensités diffuses est à peu près le même pour les différents plans. Pour le plan 020 le rapport de l'intensité de la réflexion diffuse pour un angle d'incidence $\theta_i=2°$, à l'intensité de la réflexion de Bragg $\theta_i=6° 12'$ est de l'ordre de 1/14 000.

Le phénomène de la réflexion des rayons X en dehors des directions de Bragg admet pour le chlorate de sodium un centre de symétrie, les phénomènes sont les mêmes sur les deux côtés d'un même plan réticulaire.

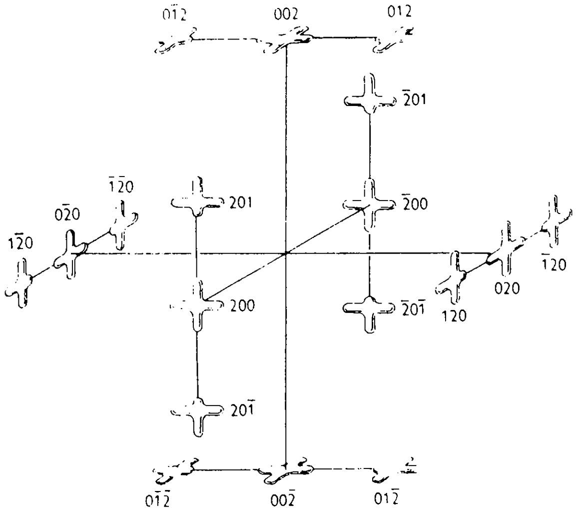

Fig. 2. Forme et position rélative des domaines de diffusion des plans (020) et (120)

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The Structures of Pyrimidines and Purines. I. A Determination of the Structures of 2-amino-4-methyl-6-chloropyrimidine and 2-amino-4, 6-dichloropyrimidine by X-ray Methods

By C. J. B. Clews and W. Cochran

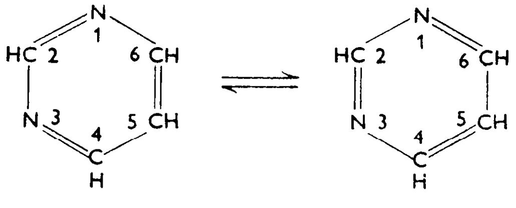
Crystallographic Laboratory, Cavendish Laboratory, Cambridge, England

(*Received* 10 *October* 1947)

The structures of two isomorphous pyrimidines 2-amino-4-methyl-6-chloropyrimidine and 2-amino-4,6-dichloropyrimidine have been studied by X-ray methods. The molecules are based on planar six-membered rings with the C–C and C–N bonds in the ring having approximately 50% double-bond character. It is found that for the compound containing the methyl group, the methyl groups and the chlorine atoms are distributed at random throughout the structure in two chemically, but not crystallographically, equivalent positions in the molecules. The structure is held together by the van der Waals forces between the chlorine atoms of adjacent molecules and by a system of hydrogen bonds.

Introduction

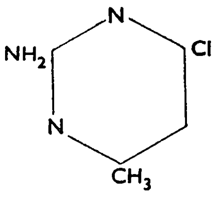
The pyrimidines and the purines are of considerable importance in relation to a group of biological substances, the nucleic acids, which are phosphoric esters of glucosides. These glucosides are, in turn, composed of sugars not known to occur in any other biological material and of pyrimidine and purine bases. Pyrimidine is a six-membered heterocyclic ring compound containing two nitrogen atoms, and, as in the case of benzene, resonance can occur between a number of structures, including the two Kekulé structures (I and II):



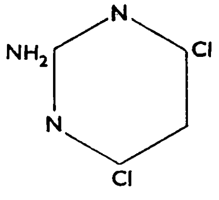
(I) (II)

In addition, with amino pyrimidines for example, tautomerism may occur through migration of an amino-hydrogen to a ring nitrogen atom. The present X-ray structure determinations were undertaken in close association with the chemical work of Prof. A. R. Todd and his collaborators, as it seemed possible that a knowledge of the dispositions of the bonds in the molecule and in the crystal structure might provide information of considerable chemical interest.

No previous X-ray structural work on the pyrimidines has been reported in the literature (see Clews & Cochran, 1947), so an extensive search was made for compounds which seemed likely to permit of a direct determination of structure without the necessity for any assumptions as to the nature of the pyrimidine molecule. A pair of isomorphous pyrimidines were selected, both of which contained heavy atoms, 2-amino-4-methyl-6-chloropyrimidine (III) and 2-amino-4,6-dichloropyrimidine (IV).



(III)



(IV)

Experimental

Both compounds crystallize from absolute alcohol as very thin laths or needles, with lengths parallel to the b-axes. There are four molecules in the monoclinic unit cell related by the space group symmetry $P2_1/a$ (C^5_{2h}). The accurately determined cell dimensions are given in Table 1.

Table 1. *Cell dimensions of the compounds*

Compound	a	b	c	β
III	16·426 A.	$4{\cdot}00_0$ A.	10·313 A.	109° 08′
IV	16·447 A.	$3{\cdot}84_5$ A.	10·283 A.	107° 58′

As unit cell dimensions obtained from measurements of the layer line separation on single crystal rotation photographs are generally not sufficiently accurate when bond lengths are to be determined to better than 1 %, a more accurate but simple method has been devised. A full account of this method, and of the precautions necessary to ensure accurate results, is being prepared for publication. The values given in the table are correct to ±0·005 A. and ±2′. (The wavelength of Cu $K\alpha_1$ radiation has been taken as 1·5405 A.)

Oscillation and zero layer line Weissenberg photographs were taken for both specimens. Copper $K\alpha$ radiation was used throughout.

The relative intensities of the reflexions were estimated by eye with the aid of calibration scales prepared from the crystal under investigation. These were corrected for polarization and Lorentz factors in the usual way, giving a set of coefficients proportional to the F^2's.

Determination of the structures

2-*amino*-4,6-*dichloropyrimidine*

Patterson projections for both compounds were computed by means of the Beevers-Lipson strips with a view to determining the positions of the common chlorine atom and the replaceable atom.

Two chlorine atoms situated at (x_1, z_1) and (x_2, z_2) produce peaks in the Patterson projection on (010) whose co-ordinates, for space group $P2_1/a$, are

$$\begin{array}{cccc} A & B & C & D \\ 2x_1, 2z_1 & 2x_2, 2z_2 & x_1+x_2, z_1+z_2 & x_1-x_2, z_1-z_2. \end{array}$$

Replacement of the second chlorine atom by a methyl group should not affect the height of A, but B should practically disappear, since it now corresponds to a vector between two carbon atoms. C and D should also be reduced in height. In fact, the two Patterson projections are strikingly similar in appearance, as is shown in Fig. 1 *a* and 1 *b*; the peaks A and B of equal height in the projection for the compound containing two chlorine atoms remain equal in height when a chlorine atom is replaced by a methyl group. This made it impossible to proceed with the analysis by the isomorphous replacement method, since the replaceable chlorine atom could not be identified. The peaks labelled A, B, C, D in Fig. 1 *a* can, however, be satisfactorily accounted for as arising from chlorine atoms at $x_1, z_1 = 0{\cdot}159, 0{\cdot}149$ and $x_2, z_2 = 0{\cdot}488, 0{\cdot}175$. If this interpretation is correct, it follows that the corresponding peaks in Fig. 1 *b* must arise from equal scattering centres having these same co-ordinates. This point will be discussed later.

As the space group is centro-symmetrical, a positive or negative sign is associated with each structure amplitude. A Fourier synthesis giving a first approximation to the structure projected on the (010) plane was carried out, the signs of most of the terms being determined entirely from the assumed positions of the chlorine atoms. The resulting electron density map showed the rest of the atoms clearly resolved. The parameters of all the atoms were refined by successive approximation. The fourth approximation is shown in Fig. 2.

A similar procedure was adopted in dealing with the projections parallel to the a and c axes, and the $[\bar{1}01]$ direction, i.e. a Patterson projection to determine the co-ordinates of the chlorine atoms followed by successive approximations on Fourier electron density maps. There was considerable overlap in these projections and it was necessary to compute three of them in order to resolve all the atoms.

The final atomic parameters are collected in Table 2.

The x and z co-ordinates have been determined from the b-axis projection in which all the atoms are clearly resolved. The y co-ordinates cannot be determined with the same accuracy, but the observed values are consistent with the assumption that the molecule is planar. Small departures of about 0·03 A. in y from a planar arrangement are within the limits of the experimental error in this co-ordinate.

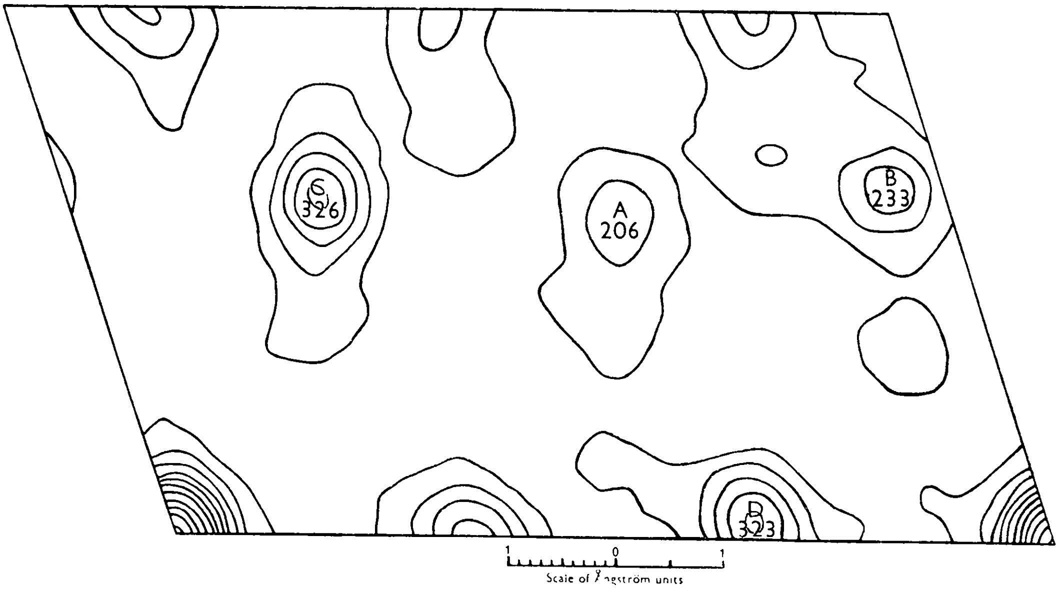


Fig. 1a. Patterson projection of $C_4N_3H_3Cl_2$ on (010)

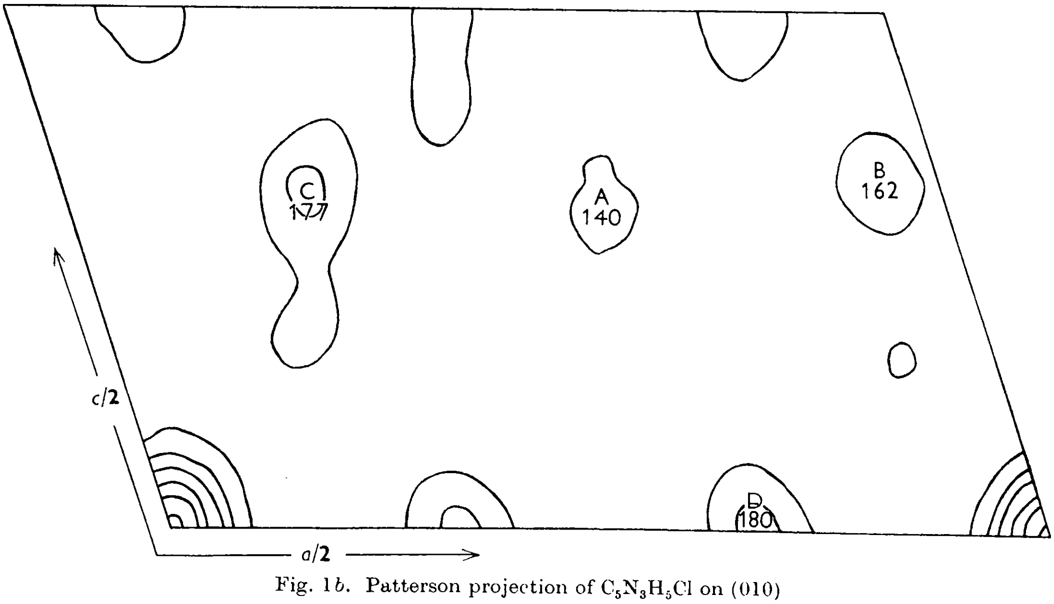


Fig. 1b. Patterson projection of $C_5N_3H_5Cl$ on (010)

Following the procedure suggested by Booth (1946) a b-axis Fourier synthesis was made using F values calculated from the atomic co-ordinates. This *theoretical* electron density map showed small displacements of the atoms of about 0·02 A. from the positions given in Table 2, which figure may be taken as a measure of the accuracy of the observations.

The general correctness of the structure is confirmed by the agreement between observed and calculated structure amplitudes for all observed ($hk0$), ($h0l$) and ($0kl$) reflexions, and for some reflexions of the type (hkl), illustrated graphically in Fig. 3.

The value of the factor $\Sigma \mid F_{\text{obs.}} - F_{\text{calc.}} \mid / \Sigma \mid F_{\text{obs.}} \mid$, which has been suggested as a criterion of accuracy, is 0·24 compared with 0·17 for the accurate three-dimensional geranylamine hydrochloride structure (Jeffrey, 1945).

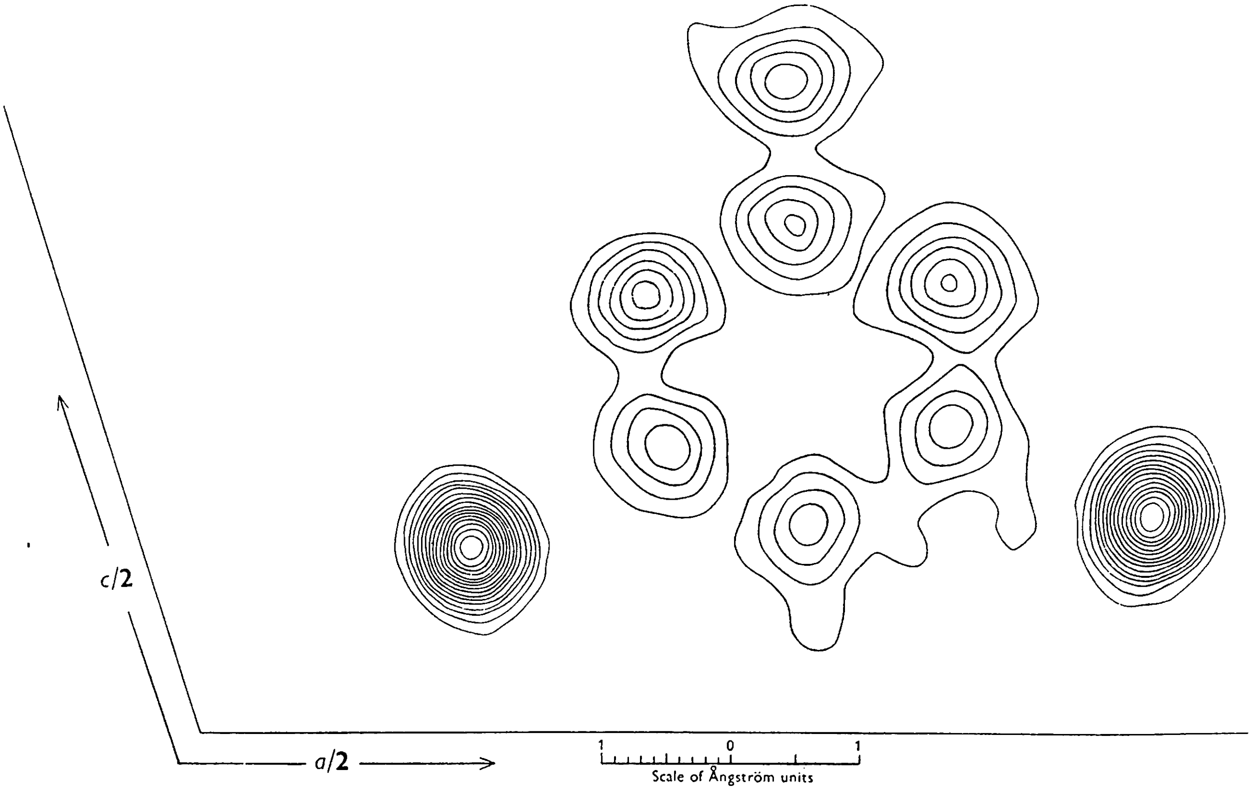


Fig. 2. Electron-density map of 2-amino-4,6-dichloropyrimidine projected on (010). Contours at an interval of two electrons per A.^{2}

Table 2. *Atomic co-ordinates in* 2-*amino*-4,6-*dichloropyrimidine expressed as fractions of the corresponding unit-cell dimension*

Atom	x	y	z
N_1	0·4250	0·292	0·3617
C_2	0·3608	0·353	0·4067
N_2	0·3758	0·518	0·5183
N_3	0·2800	0·250	0·3500
C_4	0·2667	0·100	0·2292
Cl_4	0·1587	−0·050	0·1492
C_5	0·3267	−0·017	0·1683
C_6	0·4042	0·133	0·2467
Cl_6	0·4875	0·025	0·1750

2-*amino*-4-*methyl*-6-*chloropyrimidine*

As already pointed out, the peaks of the Patterson diagram (Fig. 1*b*) can be satisfactorily accounted for only by assuming that the positions previously occupied by chlorine are now occupied by groups of smaller but equal scattering power. The first Fourier synthesis was therefore computed on the assumption that the signs of the terms were identical with those for the isomorphous compound. The resulting electron density map showed that the groups attached to the molecule in the 4 and 6 substituent positions were of equal scattering power. An electron count indicates that the group corresponds in scattering power to the mean of a chlorine atom and a methyl group. In succeeding approximations the *f*-curve for this group was taken as the mean of the *f*-curves for chlorine and carbon. The third approximation is shown in Fig. 4. It is suggested that the chlorine atoms and the methyl groups are distributed at random throughout the structure in the two chemically but not crystallographically equivalent positions. Although the methyl group and chlorine atom are chemically dissimilar, the effective radius (2 A.) of the methyl group is not greatly different from that of the chlorine atom.

The possibility of there being a fault structure present with blocks of the crystal consisting of molecules with CH_3 in one position and other blocks with CH_3 and Cl interchanged was considered, but there was no evidence for this. Long-exposure rotation photographs failed to show any additional layer lines and there was no diffuseness in the spectra.

A similar phenomenon has been reported by Hendricks (1933) for *p*-bromochlorobenzene, although in this case there are two molecules in a unit cell with space group $P2_1/a$, which requires a centrosymmetrical molecule. Hendricks suggested that there is a random distribution of bromine and chlorine in the two *para* positions throughout the structure. More recent work (Klug, 1947) using Fourier methods confirms Hendricks' hypothesis.

As the crystals are in the form of very fine needles it has not been possible to take photographs about other axes than the *b*-axis. Since, however, the two compounds are closely isomorphous it is certain that the

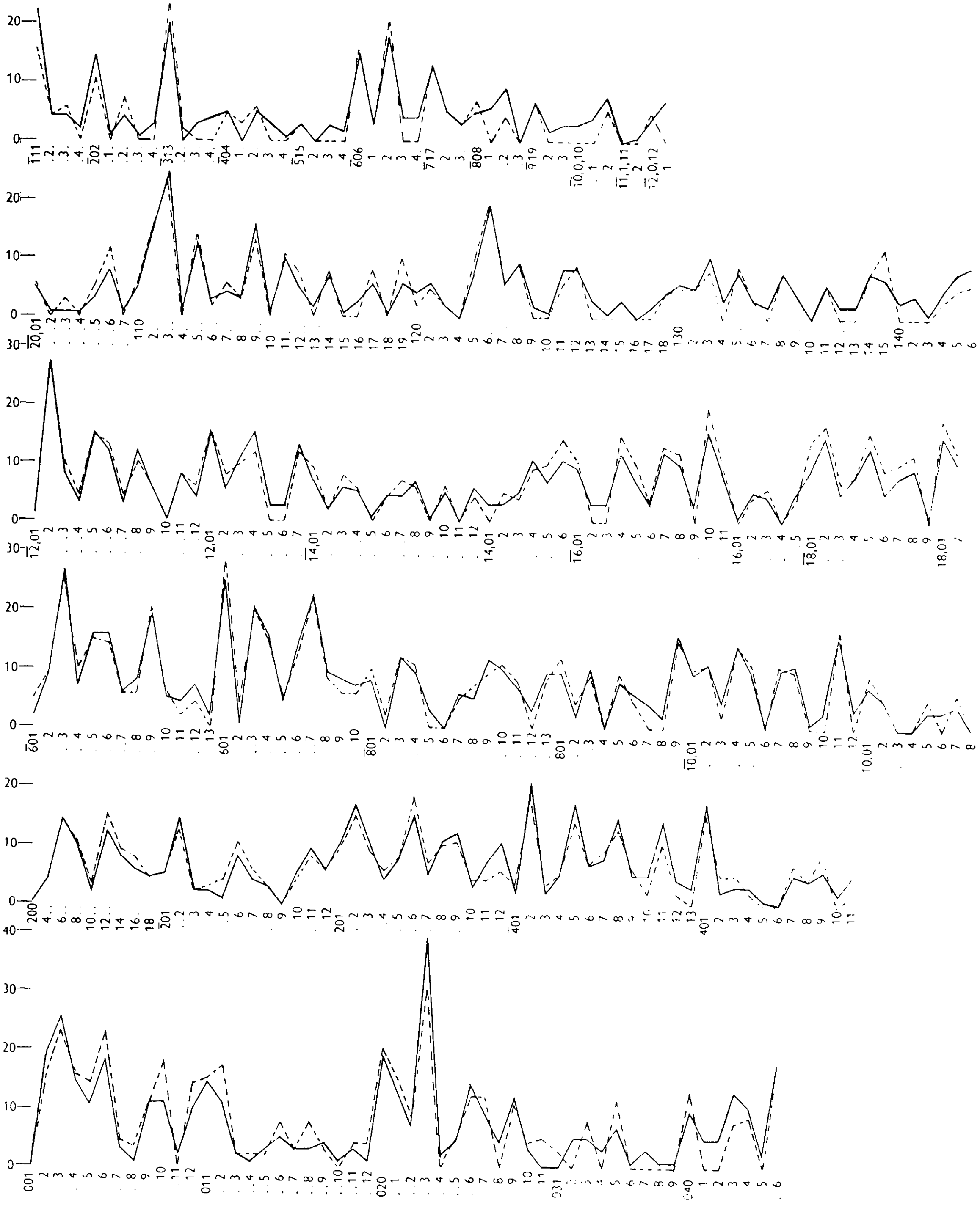


Fig. 3. Comparison of calculated (full line) and observed (dotted line) structure amplitudes for $C_4N_3H_3Cl_2$

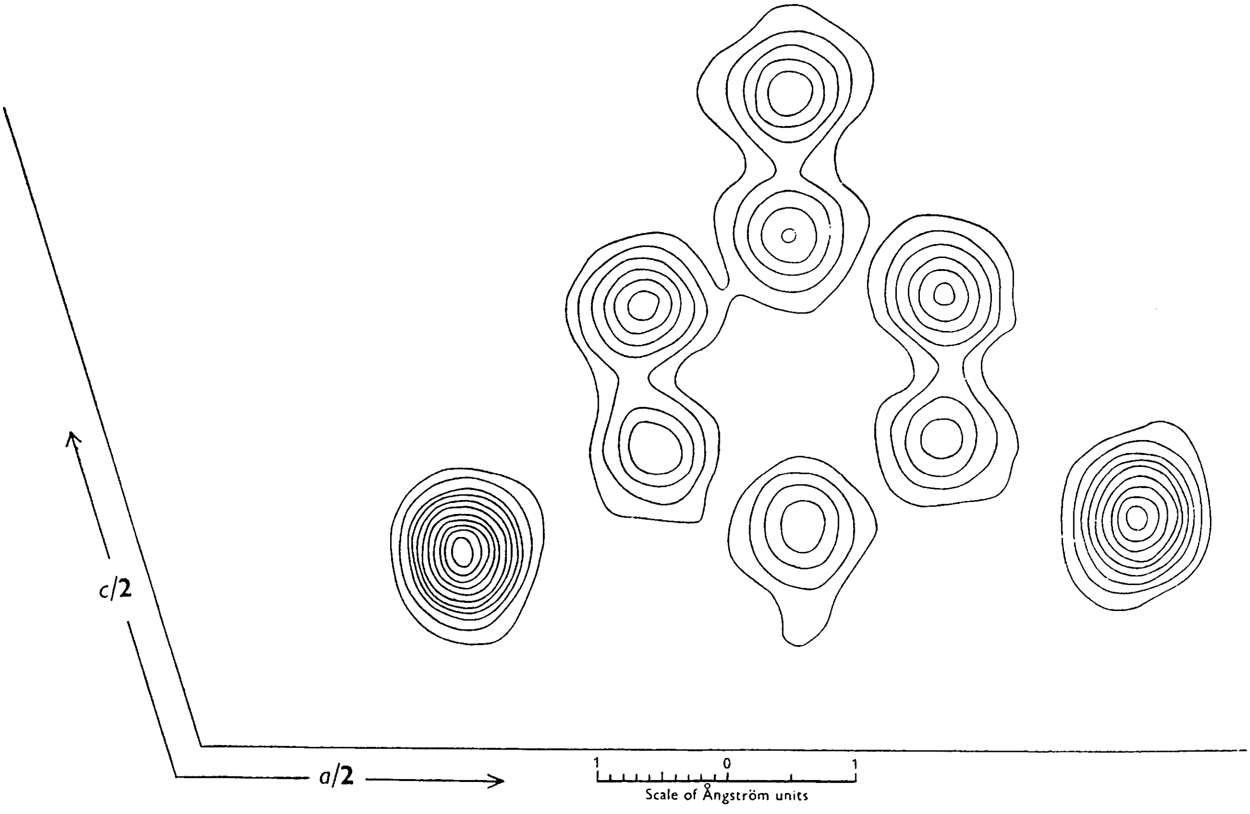


Fig. 4. Electron-density map of 2-amino-4-methyl-6-chloropyrimidine projected on (010). Contours at an interval of two electrons per A.^{2}

arrangement of the molecules in the cell will be very nearly the same in both cases. The bond lengths given below were calculated on this assumption, a small correction being made to allow for the increased length of the *b*-axis.

Discussion of the structure

The bond lengths within the molecule are shown on p. 10.

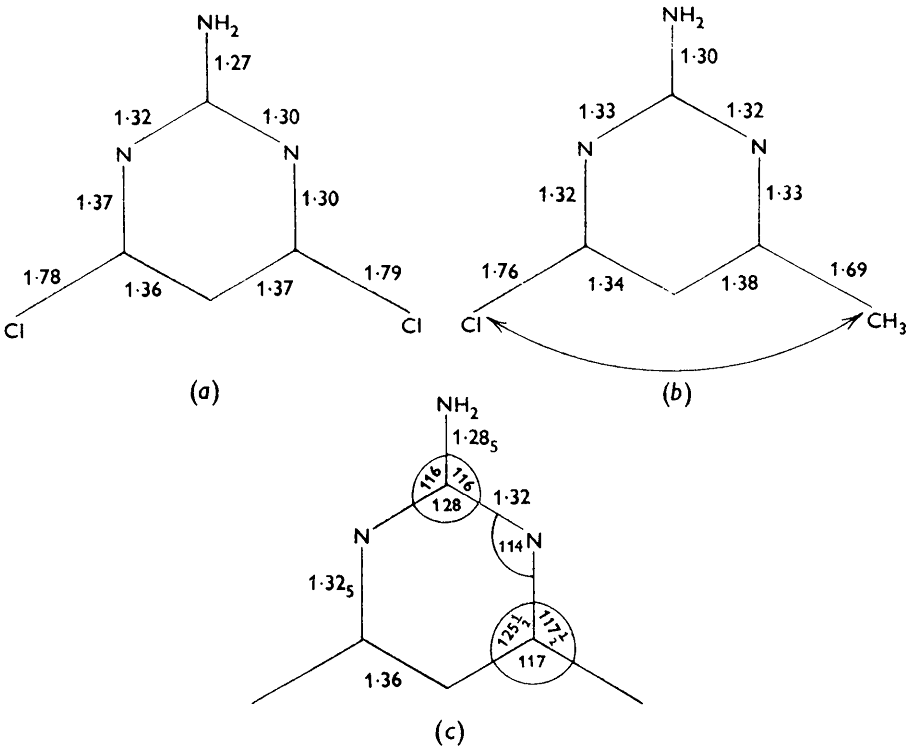
It is reasonable to suppose that both molecules will be symmetrical about an axis through the 2 and 5 positions especially in view of the fact that even the unsymmetrical molecules achieve statistical symmetry in the crystal structure. Thus, in deriving the most probable value of the C–C bond for example, the values 1·36, 1·37, 1·34, 1·38 A. have been treated as independent determinations of the same bond length. The bond angles have been similarly derived. The final values are shown in (*c*). The deviation of a single determination from the value finally accepted is at most 0·04 A. and is on the average $0{\cdot}01_5$ A., so that these values are probably correct to within ±0·02 A.

The arrangement of the molecules in the structure is illustrated in Figs. 5 and 6. The reference molecule *R* is tilted out of the (010) plane so that the line joining C_2 and C_5 makes an angle of about 31° with this plane.

The chlorine atoms are packed together about axes parallel to the *b*-axis passing through the centres of symmetry at (0, 0) and (0, $\frac{1}{2}$). The packing shown in Fig. 6 is such that Cl_6 is in contact with seven near neighbours, while Cl_4 touches six neighbouring chlorine atoms. Thus there are columns of chlorine atoms running through the structure in the direction of the *b*-axis, with the pyrimidine rings arranged in the intervening space. Certain of the Cl–Cl distances are abnormally short, and while no explanation is put forward to account for this behaviour it seems possible that it may be associated with the formation of hydrogen bonds discussed below. Other short intermolecular distances in the structure are those between the nitrogens of the amino groups and neighbouring ring nitrogens, i.e. N_2–$N_3' = 3{\cdot}37$ A. and N_2–$N_1'' = 3{\cdot}21$ A. All other interatomic distances are greater than 4 A.

It has already been pointed out that the molecule is planar to within the limits of experimental error. The C–N and C–C distances within the ring correspond to approximately 50 % double bond character as defined by Pauling (1945*a*), a result which is to be expected for a resonating ring system.

Chemical observations have established that 2, 4 or 6 substituted chloropyrimidines have the high reactivity associated with alkyl halides rather than that of the halogen-substituted aromatic compounds. The C–Cl distance of $1{\cdot}78_5$ A., which is close to that found in saturated aliphatic chlorine compounds (1·77 ± 0·02 A.) rather than to the value for chlorobenzenes (1·70 ± 0·02 A.), is in accordance with the chemical behaviour.



The intermolecular bonds N_2–N_3' (3·37 A.) and N_2–N_1''(3·21A.) are almost co-planar with the molecule *R*, and it is suggested that these are hydrogen bonds of the type N—H - - - N. (The idea of a hydrogen bond structure first arose during a discussion with Prof. L. Pauling.) This is consistent with the approach of the $N_{(2)}$–$C_{(2)}$ bond to full double-bond character. Although there are few data available on the length of N—H - - - N bonds, Pauling (1945*b*) quotes distances of 2·98 and 3·20 A. in ammonium azide and 3·38 A. for a weak bond in crystalline ammonia. This has an important bearing on the tautomeric behaviour of these pyrimidines as Hunter (1945) has suggested that the tautomeric character and molecular association of a large number of substances (amides, anilides, hydrazides, etc.) are due to one and the same cause, the intermolecular sharing

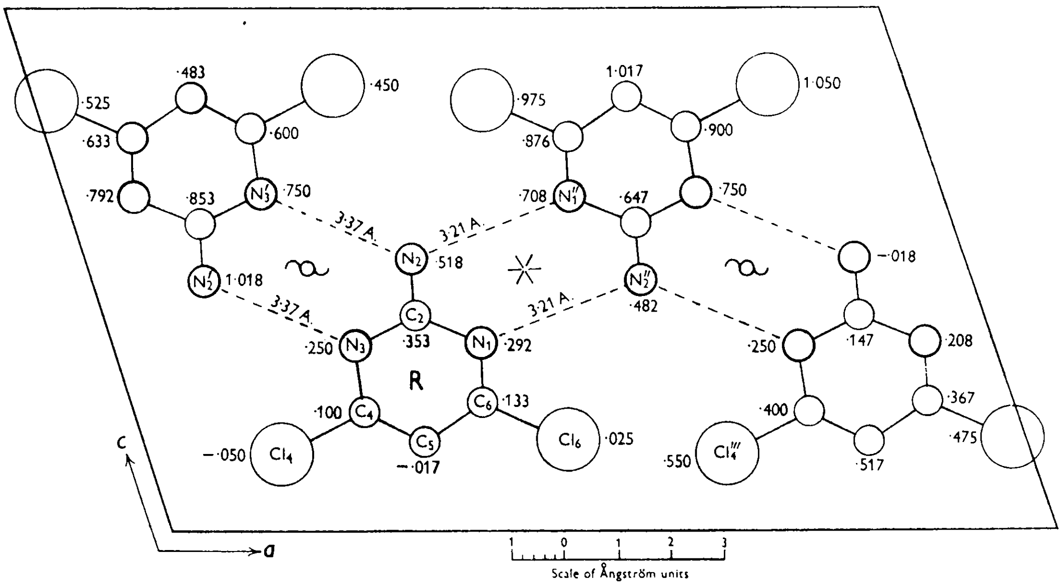


Fig. 5. Structure projected on (010), z-co-ordinates indicated. Hydrogen bonds are shown dotted

the hydrogen atom responsible for the tautomeric behaviour. Where tautomerism occurs due to the migration of a hydrogen atom, the system is usually

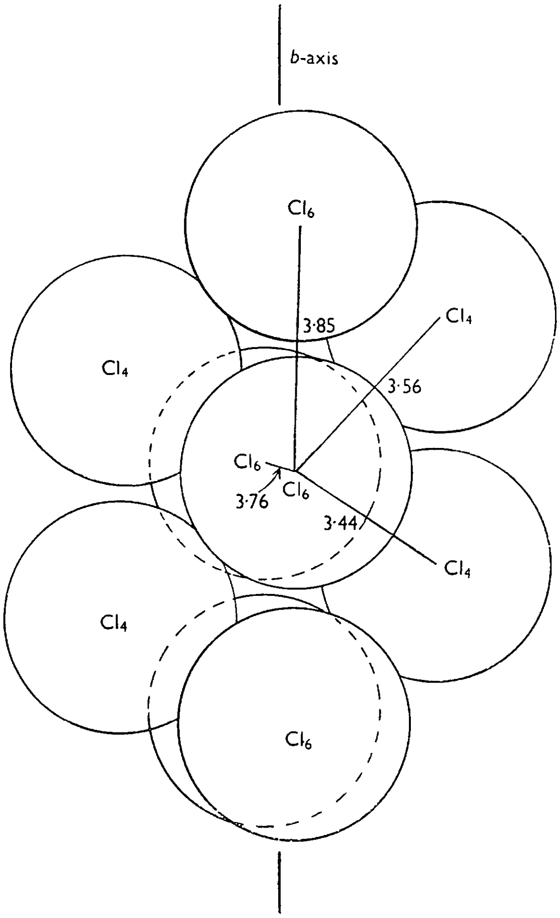


Fig. 6. Packing of chlorine atoms

represented $[\mathrm{H}]A\wedge\wedge\wedge B \rightleftharpoons A\wedge\wedge\wedge B[\mathrm{H}]$, the movement of the H atom being accompanied by a redistribution of valencies in the system $A\wedge\wedge\wedge B$. From his investigations Hunter concludes that if neither A nor B is carbon, the compound exhibits molecular association by operation of intermolecular bonds B—H—A. In solution or in the crystalline state such a compound consists of aggregates as below

$$---\mathrm{H}\text{——}A\wedge\wedge\wedge B---\mathrm{H}\text{——}A\wedge\wedge\wedge B--- \qquad (a)$$
$$\text{——}\mathrm{H}---A\wedge\wedge\wedge B\text{——}\mathrm{H}---A\wedge\wedge\wedge B\text{——} \qquad (b)$$
$$\text{(V)}$$

(Va) and (Vb) represent unperturbed states of which the true state is a resonance hybrid. Such a compound exhibits tautomeric behaviour due to the fact that the chemical and physical properties are intermediate between those expected of (a) and (b). The hydrogen bond system in the pyrimidines described here seems to present an example of such a mesohydric structure, with intermolecular sharing of the tautomeric hydrogen.

It is a great pleasure to thank Prof. Sir Lawrence Bragg and Dr W. H. Taylor for the facilities that they have placed at our disposal and for their continued interest and encouragement, and Prof. A. R. Todd and his collaborators for providing the specimens and for their ever-ready advice on chemical matters. One of us (C.J.B.C.) is indebted to the Managers of the I.C.I. Fellowship Fund of the University of Cambridge for the award of a Fellowship, and the other (W.C.) to the Department of Scientific and Industrial Research for financial assistance. Mrs Dalitz has assisted us with much of the computation.

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