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The Crystal Structure of Histidine Hydrochloride Monohydrate*

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The structure of histidine hydrochloride monohydrate has been refined by three-dimensional least-squares methods. The amino acid part of the molecule is in the zwitter ion form; the imidazole ring is positively charged. The distances in the imidazole ring, combined with some previous results, are satisfactorily interpreted with the valence bond theory, and imply a carbon–nitrogen double-bond distance of 1·265 Å. All available hydrogen atoms form hydrogen bonds.

Introduction

The investigation of the crystal structure of histidine hydrochloride monohydrate was undertaken as part of a program on compounds related to proteins. In particular, the dimensions and tautomeric form of the imidazole ring part of the molecule are of importance because of the role of this group in coordinating zinc in zinc insulin (Tanford & Epstein, 1954), and information concerning this was immediately valuable in model building studies of the structure of insulin in which one of us was engaged (Lindley & Rollett, 1955). The approximate structure of histidine hydrochloride monohydrate was reported some time ago (Donohue, 1953). We wish now to describe in more detail how this structure was obtained, and to discuss the results of a subsequent parameter refinement by least-squares treatment of the general (*hkl*) data.

Experimental

Unit cell, space group, and intensity data

Crystals of histidine hydrochloride monohydrate were grown by slow evaporation of an aqueous solution. X-ray photographs obtained with Cu $K\alpha$ radiation ($\lambda = 1{\cdot}542$ Å) gave

Space group: $P2_12_12_1$ (D_2^4).
Unit cell: $a_0 = 15{\cdot}36$, $b_0 = 8{\cdot}92$, $c_0 = 6{\cdot}88$ Å.
Molecules per unit cell: 4 of $C_6H_9O_2N_3.HCl.H_2O$.
Density (obs.): 1·485 g.cm.$^{-3}$; density (calc.): 1·477 g.cm.$^{-3}$.

Our axial ratios may be compared with the goniometric values (Bauer, 1900):

Bauer: $a:b:c = 0{\cdot}7667:1:1{\cdot}7110$.
This paper: $c:b:a = 0{\cdot}771:1:1{\cdot}722$.

Intensities were determined by visual comparison between standard intensity strips and multiple films of equi-inclination Weissenberg photographs of the layers (*h*0*l*) to (*h*6*l*) and (*hk*0) to (*hk*4).

After the usual correction factors had been applied, correlation among reflections appearing on different films was used to bring all of the values $|F_{hkl}|^2$ on to the same arbitrary scale. The absolute scale and the temperature factor were then determined by the method of Wilson (1942). Of the 1,179 reflections within the limits described above, 935 were observed. Approximately 86 reflections accessible with Cu $K\alpha$, but with $k > 6$ and $l > 4$, were not recorded.

Trial structures

Although the intensity data were not collected over a spherical region in the reciprocal lattice, the consequent non-convergence in a three-dimensional Patterson function was not expected to lead to any serious difficulties. This function, sharpened and modified as previously described (Patterson, 1935; Shoemaker, Donohue, Schomaker & Corey, 1950) was calculated with punched cards and IBM machines at intervals of $\frac{1}{60}$ in *u* and $\frac{1}{30}$ in *v* and *w*. From the three Harker sections the parameters of the chloride ion were easily determined; they were then used in the construction of a vector convergence diagram (Beevers & Robertson, 1950) by placing the origin of the Patterson function at the four equivalent positions occupied by the chloride ion. Since it would have been tedious to do this by tracing the 31 levels in *w* of the $P(u, v, w)$ plot four times, a faster method was devised which made use of the fact that this function had been recorded on punched cards. The running

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coordinate on each card was *u*, a code giving *v* and *w*. It was consequently a simple matter to move the origin, since diagonal reproduction gave the desired change in *u*, and systematic change in the code shifted *v* and *w*. The four shifted $P(u, v, w)$ functions were then run through the IBM tabulator, which was wired to add, but to print the totals only if all four numbers making up the sum were positive. The resulting vector convergence diagram (Fig. 1) had 18 peaks, or 6 more than the expected number.

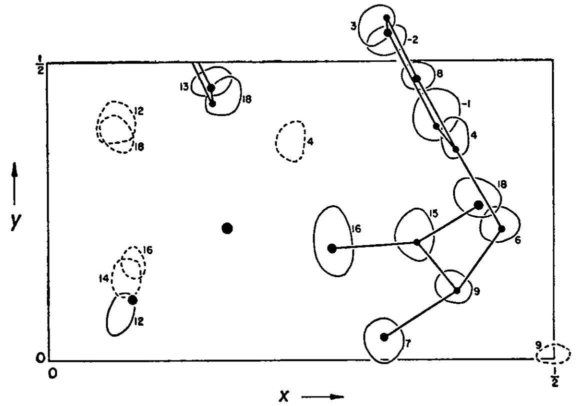

Fig. 1. The vector convergence diagram, based on the positions determined for the chloride ion. The numbers associated with each peak gives its *z* coordinate in 30ths. Compare with Fig. 5, which identifies the atoms.

It was of course obvious which 11 peaks corresponded to the histidine molecule, and the location of the water molecule was decided on the basis of interatomic distances, 6 of the 7 additional peaks being improbably close to other atoms. The parameters for these 12 atoms were then adjusted in order to improve the agreement with some of the resolved peaks in the Patterson function, and the structure factors for the three prism zones were calculated. The average discrepancy at this stage for the 256 observed reflections in these zones was 27%. Two Fourier projections, on (001) and (010), were prepared, using 89 of the 121 F_{hk0} and 57 of the 98 F_{h0l} reflections respectively. These were shown in the earlier note (Donohue, 1953). The structure-factor agreement and the appearance of the electron-density maps indicated that the trial structure was probably correct, but since only six atoms in the (001) projection and three atoms in the (010) projection might eventually be expected to be resolved, analysis making use of the general (*hkl*) data in subsequent refinements of the parameters was indicated.

There was also an ambiguity with regard to identification, as to kind, of the atoms of the imidazole ring. This decision, which perhaps could have been made on the basis of the approximate intermolecular distances then available, was deferred until a more direct indication could be used, e.g., either consideration of the peak heights in a three-dimensional electron density function, or an unequivocal change in the structure-factor agreement when the ring orientation was changed.

Refinement of parameters

The first parameter refinement consisted of a least-squares treatment of 170 of the prism zone reflections. These represent less than one-fifth of the total. They were chosen in such a way as to shorten greatly the computational time required—it was thought that these reflections would yield a satisfactory degree of resolution, since structure factors from all three zones were included, and, moreover, the form taken by both the structure factors and their derivatives is simpler when one Miller index is zero.

On the other hand, the use of three prism zones only does not lead to a set of normal equations in which the off-diagonal terms of the normal equations can be neglected, so it was necessary to calculate all of the 819 unique coefficients. This work was carried out with an IBM 604 multiplying punch. The resulting 39 normal equations were solved by iteration, and parameter shifts averaging 0·06 Å were obtained, the largest shift being 0·21 Å; the standard errors in the parameters were about 0·05 Å.

At this stage in the investigation the work was interrupted for 18 months, and when the refinement was renewed a more rapid computer was available to us. Since the least-squares treatment on the partial data was carried through only one step, it is difficult to decide now whether this notion, if it had been con-

Table 1. *Final parameters and their standard deviations*

	x	σ	y	σ	z	σ
C_1	0·3642	0·00053	0·1935	0·00092	0·5034	0·00125
C_2	0·4022	0·00055	0·1176	0·00098	0·3243	0·00127
C_3	0·4531	0·00055	0·2210	0·00106	0·1891	0·00128
C_4	0·4016	0·00052	0·3603	0·00092	0·1304	0·00124
C_5	0·3417	0·00063	0·5245	0·00118	0·9303	0·00153
C_6	0·3669	0·00058	0·4743	0·00104	0·2375	0·00138
N_1	0·3291	0·00046	0·0386	0·00078	0·2171	0·00106
N_2	0·3835	0·00046	0·3945	0·00086	0·9392	0·00114
N_3	0·3302	0·00050	0·5749	0·00090	0·1136	0·00119
O_1	0·2845	0·00042	0·1834	0·00075	0·5393	0·00102
O_2	0·4207	0·00042	0·2604	0·00075	0·6074	0·00105
O_3	0·0812	0·00051	0·1010	0·00088	0·4093	0·00122
Cl	0·1760	0·00013	0·2278	0·00025	0·0302	0·00034

Table 2. *Observed and calculated structure factors*

h	k	ℓ	F_o	F_c
2	0	0	31.6	41.0
4	0	0	77.6	129.0
6	0	0	19.7	17.9
8	0	0	35.1	40.0
10	0	0	9.3	7.3
12	0	0	21.4	25.2
14	0	0	12.1	16.0
16	0	0	7.6	3.0
18	0	0	9.9	7.5
1	1	0	3.6	7.1
2	1	0	33.4	43.1
3	1	0	8.7	11.8
4	1	0	56.4	76.0
5	1	0	38.2	40.4
6	1	0	13.0	13.2
7	1	0	12.0	9.3
8	1	0	40.6	42.8
9	1	0	21.0	22.9
10	1	0	36.3	40.2
11	1	0	<4.9	3.9
12	1	0	12.5	14.7
13	1	0	<5.4	4.1
14	1	0	7.5	6.1
15	1	0	<5.4	2.4
16	1	0	8.4	11.2
17	1	0	<4.6	0.4
18	1	0	13.4	12.4
19	1	0	<3.1	0.0
0	2	0	38.5	49.4
1	2	0	18.2	16.1
2	2	0	6.3	2.0
3	2	0	19.4	19.3
4	2	0	29.3	24.4
5	2	0	46.8	49.3
6	2	0	13.7	15.1
7	2	0	3.6	6.4
8	2	0	27.8	30.3
9	2	0	9.6	8.1
10	2	0	10.8	8.1
11	2	0	12.2	12.2
12	2	0	<5.3	1.7
13	2	0	<5.4	4.7
14	2	0	5.5	6.1
15	2	0	<5.3	1.9
16	2	0	<5.1	3.8
17	2	0	<4.5	3.0
18	2	0	<3.9	0.6
19	2	0	5.0	3.5
1	3	0	46.9	54.6
2	3	0	13.0	10.4
3	3	0	4.5	3.9
4	3	0	43.8	49.7
5	3	0	14.0	11.6
6	3	0	22.6	21.6
7	3	0	13.2	13.5
8	3	0	8.2	10.1
9	3	0	9.2	7.0
10	3	0	<5.0	3.0
11	3	0	<5.2	2.0
12	3	0	22.9	25.1
13	3	0	9.1	8.8
14	3	0	<5.4	0.6
15	3	0	<5.2	2.3
16	3	0	15.5	14.7
17	3	0	<4.3	1.0
18	3	0	5.8	6.5
0	4	0	30.5	29.8
1	4	0	<1.4	3.0
2	4	0	22.5	23.2
3	4	0	28.4	26.2
4	4	0	<3.8	3.3
5	4	0	18.8	21.5
6	4	0	45.9	46.1
7	4	0	14.3	11.9
8	4	0	27.0	27.7
9	4	0	28.8	31.4
10	4	0	21.6	21.0
11	4	0	27.5	31.2
12	4	0	8.0	9.7
13	4	0	<5.1	2.5
14	4	0	<4.8	3.6
15	4	0	19.9	15.4
16	4	0	8.9	7.3
17	4	0	7.3	7.8
18	4	0	<3.0	1.5
1	5	0	34.8	35.1
2	5	0	21.3	19.8
3	5	0	15.1	18.7
4	5	0	31.4	31.5
5	5	0	20.0	18.5
6	5	0	<3.8	1.0
7	5	0	26.1	23.3
8	5	0	<4.5	0.9
9	5	0	<4.7	3.4
10	5	0	9.8	8.5
11	5	0	<5.2	4.0
12	5	0	12.2	12.4
13	5	0	<5.2	2.4
14	5	0	7.2	6.8
15	5	0	11.3	11.3
16	5	0	7.9	8.3
17	5	0	5.0	3.5
0	6	0	22.3	26.7
1	6	0	11.1	11.3
2	6	0	5.0	6.5
3	6	0	<2.8	0.0
4	6	0	8.2	11.3
5	6	0	4.7	5.2
6	6	0	4.7	3.3
7	6	0	<4.5	0.4
8	6	0	18.7	20.1
9	6	0	<5.1	4.5
10	6	0	<5.2	2.3
11	6	0	10.3	11.7
12	6	0	13.2	14.1
13	6	0	<4.9	1.4
14	6	0	12.5	11.1
15	6	0	<4.0	0.0
16	6	0	5.5	3.8
17	6	0	<1.8	2.7
1	7	0	20.7	19.8
2	7	0	9.8	11.0
3	7	0	6.4	3.9
4	7	0	24.8	26.3
5	7	0	7.6	7.9
6	7	0	9.8	9.3
7	7	0	10.8	11.3
8	7	0	7.6	9.6
9	7	0	<5.4	0.9
10	7	0	<5.3	5.0
11	7	0	<5.1	1.3
12	7	0	<4.7	1.7
13	7	0	<4.3	3.4
14	7	0	<3.7	0.7
15	7	0	5.9	5.3
0	8	0	9.4	10.4
1	8	0	6.5	7.1
2	8	0	8.6	8.6
3	8	0	19.6	19.0
4	8	0	8.8	10.1
5	8	0	12.1	11.1
6	8	0	7.9	7.7
7	8	0	<5.3	0.4
8	8	0	<5.2	3.5
9	8	0	14.0	10.8
10	8	0	9.9	6.7
11	8	0	15.6	13.1
12	8	0	<3.9	6.9
13	8	0	<3.3	2.0
14	8	0	<2.3	6.3
1	9	0	11.1	8.8
2	9	0	<5.3	4.6
3	9	0	<5.2	2.3
4	9	0	9.9	8.4
5	9	0	<5.1	2.9
6	9	0	4.9	3.2
7	9	0	15.6	11.8
8	9	0	4.5	4.3
9	9	0	6.5	5.8
10	9	0	6.2	4.9
11	9	0	7.3	4.2
12	9	0	<2.3	3.1
0	10	0	<4.6	1.7
1	10	0	8.0	5.6
2	10	0	<4.5	1.2
3	10	0	20.1	14.3
4	10	0	<4.3	1.0
5	10	0	7.7	5.6
6	10	0	<4.0	2.6
7	10	0	<3.5	1.3
8	10	0	8.2	5.0
9	10	0	<2.7	1.8
10	10	0	<1.8	0.7
1	11	0	8.7	5.5
2	11	0	10.3	6.6
3	11	0	<3.1	2.5
4	11	0	<2.5	2.1
5	11	0	8.2	6.1
6	11	0	<1.8	3.2
1	0	1	31.3	32.9
2	0	1	5.2	7.5
3	0	1	21.3	24.3
4	0	1	46.4	53.2
5	0	1	6.5	2.9
6	0	1	30.1	35.3
7	0	1	19.1	21.2
8	0	1	4.4	3.4
9	0	1	5.8	7.2
10	0	1	7.2	9.5
11	0	1	3.6	2.1
12	0	1	3.8	2.0
13	0	1	7.2	7.5
14	0	1	<4.0	0.0
15	0	1	7.4	8.3
16	0	1	<3.7	0.0
17	0	1	<3.3	0.7
18	0	1	6.5	8.2
19	0	1	5.6	3.4
0	1	1	8.6	6.4
1	1	1	33.5	37.9
2	1	1	14.9	13.9
3	1	1	50.3	65.0
4	1	1	14.1	10.9
5	1	1	10.0	7.5
6	1	1	44.1	46.8
7	1	1	16.5	19.8
8	1	1	13.6	14.4
9	1	1	4.3	4.4
10	1	1	5.9	5.1
11	1	1	4.9	1.0
12	1	1	9.9	10.6
13	1	1	6.7	7.1
14	1	1	24.4	28.3
15	1	1	8.6	7.7
16	1	1	10.7	9.6
17	1	1	6.4	5.5
18	1	1	9.4	8.1
19	1	1	5.0	3.9
0	2	1	45.0	43.8
1	2	1	30.9	35.2
2	2	1	73.4	102.2
3	2	1	51.8	61.7
4	2	1	52.1	58.8
5	2	1	17.5	19.0
6	2	1	9.0	9.3
7	2	1	43.4	45.6
8	2	1	14.0	16.1
9	2	1	6.7	7.6
10	2	1	24.0	27.1
11	2	1	18.6	19.5
12	2	1	9.7	9.4
13	2	1	8.3	9.8
14	2	1	10.5	10.3
15	2	1	4.9	6.0
16	2	1	4.9	6.1
17	2	1	<4.4	3.1
18	2	1	8.0	8.8
19	2	1	5.3	5.7
0	3	1	31.1	31.1
1	3	1	20.6	23.7
2	3	1	21.8	21.6
3	3	1	45.8	43.4
4	3	1	22.3	20.3
5	3	1	9.7	11.0
6	3	1	37.2	39.9
7	3	1	19.5	21.1
8	3	1	31.9	33.5
9	3	1	15.7	17.9
10	3	1	12.4	11.9
11	3	1	<5.3	3.2
12	3	1	18.8	21.2
13	3	1	6.9	6.0
14	3	1	14.6	17.0
15	3	1	9.6	9.1
16	3	1	<5.6	3.1
17	3	1	<5.1	3.1
18	3	1	5.2	4.7
19	3	1	<2.8	2.6
0	4	1	11.8	14.8
1	4	1	11.8	13.5
2	4	1	46.2	50.3
3	4	1	19.7	19.1
4	4	1	4.9	6.2
5	4	1	10.4	10.4
6	4	1	3.5	3.5
7	4	1	12.2	9.7
8	4	1	8.2	7.0
9	4	1	9.8	11.2
10	4	1	17.8	21.3
11	4	1	13.8	14.8
12	4	1	13.6	14.5
13	4	1	9.7	10.9
14	4	1	<4.8	4.1
15	4	1	10.0	10.6
16	4	1	5.0	6.6
17	4	1	4.5	3.3
18	4	1	7.6	8.4
0	5	1	9.9	9.8
1	5	1	11.6	11.6
2	5	1	19.2	20.0
3	5	1	23.6	26.0
4	5	1	8.4	9.6
5	5	1	23.1	23.5
6	5	1	20.9	22.2
7	5	1	16.4	16.0
8	5	1	10.6	11.8
9	5	1	12.2	13.6
10	5	1	10.6	9.4
11	5	1	<5.3	3.1
12	5	1	<5.3	2.8
13	5	1	7.3	6.6
14	5	1	6.8	7.3
15	5	1	6.2	4.7
16	5	1	5.5	4.5
0	6	1	5.4	5.4
1	6	1	23.8	24.7
2	6	1	<2.8	3.7
3	6	1	15.5	16.3
4	6	1	6.1	7.5
5	6	1	15.5	15.2
6	6	1	8.5	9.0
7	6	1	10.9	11.4
8	6	1	13.5	14.8
9	6	1	12.1	12.9
10	6	1	14.9	16.3
11	6	1	7.1	7.2
12	6	1	8.5	8.2
13	6	1	19.9	16.6
14	6	1	6.9	7.4
15	6	1	7.2	7.0
0	7	1	19.8	17.8
1	7	1	5.9	6.1
2	7	1	15.8	17.4
3	7	1	22.2	21.1
4	7	1	10.7	11.7
5	7	1	18.6	20.6
6	7	1	14.7	16.1
7	7	1	8.9	8.0
8	7	1	<5.4	2.6
9	7	1	12.0	11.9
10	7	1	5.2	5.0
11	7	1	8.5	6.5
12	7	1	6.1	4.5
13	7	1	<5.1	2.5
14	7	1	5.1	4.2
0	8	1	15.3	16.7
1	8	1	10.3	9.9
2	8	1	<5.5	4.8
3	8	1	5.9	6.2
4	8	1	8.5	7.8
5	8	1	7.3	6.1
6	8	1	6.7	6.1
7	8	1	12.2	14.0
8	8	1	5.9	5.3
9	8	1	11.8	10.0
10	8	1	15.4	12.4
11	8	1	4.5	3.3
12	8	1	5.8	4.9
13	8	1	7.3	7.2
0	9	1	14.2	10.7
1	9	1	14.4	10.6
2	9	1	8.4	6.7
3	9	1	15.0	13.0
4	9	1	8.6	7.6
5	9	1	11.1	9.9
6	9	1	7.2	4.1
7	9	1	7.2	5.5
8	9	1	6.5	3.2
9	9	1	6.3	5.0
10	9	1	4.6	3.1
11	9	1	8.5	7.5
0	10	1	<5.5	4.1
1	10	1	13.2	10.9
2	10	1	<5.5	1.6
3	10	1	5.6	4.7
4	10	1	<5.8	2.8
5	10	1	6.2	5.0
6	10	1	<4.7	1.8
7	10	1	12.1	10.4
8	10	1	5.6	4.5
0	11	1	<3.9	0.7
1	11	1	6.3	5.1
2	11	1	<3.7	1.4
3	11	1	7.2	6.0
0	0	2	56.8	69.7
1	0	2	35.5	41.5
2	0	2	39.4	45.3
3	0	2	15.3	10.7
4	0	2	13.5	13.5
5	0	2	<2.4	0.9
6	0	2	17.7	16.8
7	0	2.	31.2	32.9
8	0	2	14.9	14.0
9	0	2	10.8	11.4
10	0	2	6.6	7.7
11	0	2	8.0	8.4
12	0	2	8.0	8.2
13	0	2	5.1	7.3
14	0	2	<4.0	3.0
15	0	2	<3.9	3.9
16	0	2	<3.5	3.3
17	0	2	<3.2	2.7
18	0	2	<2.6	3.0
19	0	2	2.9	3.0
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1	1	2	31.1	31.4
2	1	2	33.5	30.6
3	1	2	27.5	25.8
4	1	2	18.3	18.7
5	1	2	24.9	25.9
6	1	2	29.2	26.0
7	1	2	32.8	32.6
8	1	2	23.5	25.9
9	1	2	6.0	6.2
10	1	2	32.7	35.8
11	1	2	5.9	6.7
12	1	2	16.2	18.6
13	1	2	14.9	13.7
14	1	2	5.9	5.7
15	1	2	6.5	5.3
16	1	2	14.0	15.2
17	1	2	11.4	9.9
18	1	2	5.1	5.3
0	2	2	64.7	70.7
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3	2	2	30.0	29.5
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6	2	2	34.3	35.3
7	2	2	4.2	2.7
8	2	2	14.0	14.7
9	2	2	15.3	15.0
10	2	2	4.2	3.3
11	2	2	15.8	16.8
12	2	2	9.6	11.8
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14	2	2	6.2	7.7
15	2	2	7.4	7.7
16	2	2	4.6	5.6
17	2	2	<3.9	5.3
18	2	2	4.9	4.4
0	3	2	10.5	9.6
1	3	2	41.7	39.6
2	3	2	12.0	9.4
3	3	2	20.6	21.9
4	3	2	25.8	23.0
5	3	2	18.7	18.4
6	3	2	14.3	15.1
7	3	2	21.7	20.4
8	3	2	12.9	13.3
9	3	2	7.4	8.9
10	3	2	11.2	10.7
11	3	2	8.9	8.9
12	3	2	12.9	15.4
13	3	2	5.8	5.5
14	3	2	5.8	4.0
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16	3	2	13.7	12.5
17	3	2	<3.8	1.9
18	3	2	4.9	5.6
0	4	2	7.6	7.7
1	4	2	17.0	20.5
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3	4	2	25.8	27.7
4	4	2	5.1	3.4
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6	4	2	16.3	16.5
7	4	2	5.5	6.0
8	4	2	15.3	16.1
9	4	2	20.3	19.8
10	4	2	14.2	15.4
11	4	2	8.3	7.8
12	4	2	13.0	16.4
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16	4	2	<3.9	3.5
17	4	2	5.0	4.7
0	5	2	29.2	32.2
1	5	2	29.8	30.3
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3	5	2	10.1	10.5
4	5	2	31.5	31.1
5	5	2	22.4	21.9
6	5	2	9.5	8.0
7	5	2	<4.6	3.3
8	5	2	18.9	21.3
9	5	2	<5.1	1.0
10	5	2	7.9	10.0
11	5	2	7.4	8.0
12	5	2	7.2	8.9
13	5	2	4.6	3.2
14	5	2	<4.4	3.8
15	5	2	5.4	4.8
16	5	2	9.3	8.5
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1	6	2	5.8	5.3
2	6	2	4.6	2.7
3	6	2	4.7	4.1
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6	6	2	9.6	9.4
7	6	2	14.5	15.9
8	6	2	7.6	8.6
9	6	2	19.9	21.0
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11	6	2	15.9	16.3
12	6	2	8.1	8.4
13	6	2	<4.3	4.6
14	6	2	8.0	7.9
15	6	2	8.3	8.0
16	6	2	6.2	4.8
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6	7	2	11.3	9.7
7	7	2	11.8	11.2
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10	7	2	<4.7	4.8
11	7	2	<4.5	3.0
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13	7	2	8.8	7.6
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1	8	2	13.4	13.5
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3	8	2	12.9	12.0
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5	8	2	5.2	3.8
6	8	2	6.9	7.0
7	8	2	<4.7	0.4
8	8	2	8.3	7.0
9	8	2	6.7	5.2
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11	8	2	<4.0	3.2
12	8	2	7.3	6.1
13	8	2	2.6	3.0
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2	9	2	17.6	13.4
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6	9	2	10.0	8.3
7	9	2	14.2	11.5
8	9	2	5.9	4.1
9	9	2	5.8	4.6
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11	9	2	7.1	6.2
0	10	2	6.2	4.4
1	10	2	10.9	8.6
2	10	2	11.6	8.9
3	10	2	11.5	11.3
4	10	2	7.6	5.4
5	10	2	8.4	7.0
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7	10	2	4.5	4.5
0	11	2	<2.5	1.0
1	11	2	2.6	2.2
2	11	2	3.5	2.8
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2	0	3	41.9	48.6
3	0	3	37.8	45.4
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6	0	3	21.1	21.7
7	0	3	9.2	9.7
8	0	3	17.9	22.6
9	0	3	7.9	8.5
10	0	3	10.8	12.6
11	0	3	6.0	4.9
12	0	3	<4.0	3.0
13	0	3	4.7	3.1
14	0	3	<3.9	0.0
15	0	3	<3.6	0.4
16	0	3	9.5	9.8
17	0	3	<2.9	4.4
18	0	3	4.0	5.1
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2	1	3	13.0	13.4
3	1	3	12.4	11.7
4	1	3	15.5	16.3
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6	1	3	28.2	26.4
7	1	3	12.3	11.4
8	1	3	18.0	20.1
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10	1	3	19.3	20.1
11	1	3	7.2	7.0
12	1	3	17.5	22.1
13	1	3	11.3	11.2
14	1	4	16.0	15.9
15	1	3	3.9	4.7
16	1	3	<4.7	5.7
17	1	3	<3.1	3.0
18	1	3	<2.3	2.9
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1	2	3	11.4	9.9
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6	2	3	11.5	11.4
7	2	3	19.9	21.6
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11	2	3	8.3	9.1
12	2	3	5.5	5.5
13	2	3	12.7	12.1
14	2	3	4.7	3.0
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16	2	3	9.0	8.9
17	2	3	<3.0	3.8
18	2	3	<2.6	1.9
0	3	3	5.8	6.5
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2	3	3	25.9	24.5
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4	3	3	7.1	6.2
5	3	3	38.5	39.1
6	3	3	20.3	18.2
7	3	3	15.4	17.1
8	3	3	14.5	16.6
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12	3	3	13.7	14.7
13	3	3	7.0	8.8
14	3	3	6.8	7.0
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16	3	3	<3.3	3.7
17	3	3	<2.6	3.0
18	3	3	<2.4	2.5
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1	4	3	16.6	15.7
2	4	3	17.1	20.0
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6	5	3	7.5	9.3
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8	5	3	6.9	8.7
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16	5	3	5.4	5.5
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12	6	3	6.0	4.8
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13	7	3	<2.7	3.1
14	7	3	<1.9	2.3
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11	8	3	5.0	4.3
12	8	3	10.6	9.3
0	9	3	<3.9	3.2
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3	9	3	8.1	6.4
4	9	3	<3.6	1.3
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9	9	3	8.6	8.4
10	9	3	4.0	4.1
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1	10	3	12.6	10.3
2	10	3	<3.0	2.9
3	10	3	<2.9	0.6
4	10	3	<2.6	0.7
5	10	3	9.9	8.0
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1	0	4	10.9	9.4
2	0	4	28.2	31.6
3	0	4	19.4	23.3
4	0	4	<2.8	0.7
5	0	4	<3.2	1.2
6	0	4	35.1	35.9
7	0	4	8.6	7.1
8	0	4	3.9	1.1
9	0	4	14.8	15.6
10	0	4	8.1	8.8
11	0	4	<4.0	0.7
12	0	4	7.2	7.5
13	0	4	6.9	8.2
14	0	4	<3.5	2.8
15	0	4	<3.2	1.1
16	0	4	7.6	7.8
17	0	4	<2.2	0.6
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2	1	4	14.1	13.3
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7	1	4	18.0	18.8
8	1	4	11.9	11.0
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10	1	4	18.5	19.6
11	1	4	4.9	6.4
12	1	4	12.6	13.1
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14	1	4	5.2	5.4
15	1	4	5.3	5.3
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5	2	4	25.6	24.2
6	2	4	21.3	22.5
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17	2	4	4.2	4.1
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10	3	4	21.2	23.7
11	3	4	6.9	9.0
12	3	4	3.9	4.7
13	3	4	<4.3	3.0
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3	2	5	19.9	19.7
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5	2	5	14.6	15.5
6	2	5	<5.4	3.1
7	2	5	<5.4	1.4
8	2	5	7.9	6.8
9	2	5	8.7	8.2
10	2	5		3.3
11	2	5	<5.1	4.5
12	2	5	5.5	5.3
13	2	5	4.5	4.6
14	2	5	5.8	5.5
15	2	5	<3.3	3.6
0	3	5	9.2	8.5
1	3	5	12.9	12.1
2	3	5	8.9	8.6
3	3	5	13.2	16.1
4	3	5	14.2	13.7
5	3	5	7.0	8.4

Table 2 (*cont.*)

h	k	l	F_o	F_c
6	3	5	9.6	12.9
7	3	5	<6.3	2.7
8	3	5	6.7	6.9
9	3	5	7.2	9.5
10	3	5	7.3	8.3
11	3	5	5.7	4.5
12	3	5	<5.4	1.0
13	3	5	9.9	9.8
14	3	5	7.9	6.8
15	3	5	6.1	5.4
0	4	5	5.5	2.9
1	4	5	6.6	6.1
2	4	5	8.4	11.1
3	4	5	6.7	4.9
4	4	5	19.7	20.2
5	4	5	16.6	19.1
6	4	5	7.3	9.3
7	4	5	7.7	8.7
8	4	5	8.8	10.6
9	4	5	16.2	14.7
10	4	5	<4.6	1.9
11	4	5	<4.4	3.6
12	4	5	7.8	6.2
13	4	5	4.3	4.9
14	4	5	3.5	4.4
0	5	5	25.5	28.0
1	5	5	16.6	21.0
2	5	5	12.1	13.0
3	5	5	12.0	12.8
4	5	5	12.5	13.8
5	5	5	11.8	12.4
6	5	5	5.5	6.4
7	5	5	6.9	8.5
8	5	5	7.2	8.8
9	5	5	<4.8	5.3
10	5	5	<4.5	0.9
11	5	5	<4.2	2.1
12	5	5	7.3	7.2
13	5	5	7.2	7.2
0	6	5	<5.1	1.2
1	6	5	5.4	5.5
2	6	5	5.9	5.7
3	6	5	7.8	8.6
4	6	5	7.4	8.4
5	6	5	<5.1	1.9
6	6	5	9.3	8.1
7	6	5	12.9	11.1
8	6	5	8.3	9.3
9	6	5	6.7	6.7
10	6	5	5.7	5.4
11	6	5	4.7	4.3
0	0	6	<4.0	0.9
1	0	6	14.2	14.1
2	0	6	<4.0	2.1
3	0	6	14.5	14.7
4	0	6	4.4	4.1
5	0	6	6.3	6.1
6	0	6	<4.0	3.3
7	0	6	19.2	21.6
8	0	6	<3.9	2.6
9	0	6	<3.6	0.8
10	0	6	<3.5	1.4
11	0	6	3.6	3.6
12	0	6	<3.0	1.3
13	0	6	<2.5	0.4
14	0	6	5.0	4.5
0	1	6	18.2	19.0
1	1	6	13.4	13.3
2	1	6	5.4	6.4
3	1	6	12.5	12.7
4	1	6	10.4	9.4
5	1	6	9.1	9.4
6	1	6	6.4	6.7
7	1	6	<5.1	1.7
8	1	6	5.4	5.6
9	1	6	7.6	7.2
10	1	6	6.0	5.9
11	1	6	18.1	15.2
12	1	6	6.3	5.8
0	2	6	18.2	19.9
1	2	6	17.3	16.7
2	2	6	6.6	6.9
3	2	6	7.3	6.9
4	2	6	10.9	10.3
5	2	6	15.3	13.0
6	2	6	12.8	12.5
7	2	6	14.1	14.2
8	2	6	7.1	7.2
9	2	6	5.8	6.5
10	2	6	10.6	8.6
11	2	6	<4.3	2.4
12	2	6	<4.1	0.0
13	2	6	<3.3	4.0
14	2	6	2.9	2.7
0	3	6	12.8	13.1
1	3	6	6.4	5.9
2	3	6	7.2	7.4
3	3	6	16.1	17.4
4	3	6	<6.3	1.9
5	3	6	13.6	13.7
6	3	6	<6.1	4.5
7	3	6	<5.9	4.1
8	3	6	<5.7	3.2
9	3	6	16.6	15.4
10	3	6	13.2	11.5
11	3	6	12.6	10.6
12	3	6	6.0	4.8
13	3	6	4.2	2.8
0	4	6	<4.9	0.9
1	4	6	14.2	15.5
2	4	6	<4.9	1.7
3	4	6	<4.9	3.2
4	4	6	5.5	6.5
5	4	6	9.0	10.2
6	4	6	4.7	4.3
7	4	6	6.4	7.6
8	4	6	7.7	6.4
9	4	6	5.0	3.8
10	4	6	5.6	6.1
11	4	6	4.1	3.9
12	4	6	3.8	4.4
0	5	6	7.8	9.7
1	5	6	6.2	6.4
2	5	6	7.7	9.1
3	5	6	5.0	3.3
4	5	6	<4.9	3.3
5	5	6	6.5	7.1
6	5	6	6.9	5.6
7	5	6	5.8	5.7
8	5	6	8.0	8.0
9	5	6	<4.8	3.6
10	5	6	<4.3	2.7
11	5	6	4.1	4.1
0	6	6	<4.7	0.0
1	6	6	5.8	1.9
2	6	6	7.0	6.0
3	6	6	5.7	4.8
4	6	6	5.7	5.7
5	6	6	5.4	2.8
6	6	6	6.7	6.0
7	6	6	6.8	5.4
1	0	7	3.8	3.0
2	0	7	14.9	14.3
3	0	7	24.2	22.7
4	0	7	5.5	6.0
5	0	7	14.4	15.0
6	0	7	3.8	3.3
7	0	7	8.2	7.5
8	0	7	9.8	8.0
9	0	7	3.9	4.9
10	0	7	<2.7	1.0
11	0	7	3.2	4.1
12	0	7	<1.7	1.8
0	1	7	<5.5	0.7
1	1	7	11.6	10.3
2	1	7	8.8	8.1
3	1	7	4.6	4.0
4	1	7	5.8	4.5
5	1	7	5.3	5.1
6	1	7	5.2	5.4
7	1	7	15.8	13.2
8	1	7	7.4	4.3
9	1	7	8.5	6.3
10	1	7	5.9	3.8
11	1	7	9.9	7.4
0	2	7	<5.1	3.9
1	2	7	<5.1	1.1
2	2	7	<5.1	3.5
3	2	7	13.1	10.6
4	2	7	6.9	5.4
5	2	7	12.9	10.3
6	2	7	<4.6	2.5
7	2	7	<4.3	0.4
8	2	7	<4.1	1.5
9	2	7	<3.9	2.8
10	2	7	<3.4	2.6
11	2	7	7.3	7.1
0	3	7	<5.7	2.9
1	3	7	11.8	10.7
2	3	7	7.3	5.5
3	3	7	7.1	5.3
4	3	7	10.6	10.0
5	3	7	<6.5	4.5
6	3	7	6.4	5.5
7	3	7	7.2	7.7
8	3	7	<5.5	3.0
9	3	7	5.0	3.4
10	3	7	<4.2	1.0
11	3	7	<3.0	3.4
0	4	7	5.4	4.9
1	4	7	<4.4	2.5
2	4	7	5.8	5.9
3	4	7	12.7	11.5
4	4	7	5.4	4.5
5	4	7	6.6	4.9
6	4	7	7.4	6.6
7	4	7	6.8	5.9
8	4	7	5.1	7.9
9	4	7	4.8	4.5
0	5	7	<5.1	2.8
1	5	7	11.0	9.2
2	5	7	12.0	10.0
3	5	7	<4.8	2.3
4	5	7	6.3	6.3
5	5	7	<4.5	1.7
6	5	7	<4.2	1.8
7	5	7	8.3	7.7
0	6	7	<3.6	2.6
1	6	7	4.5	2.7
2	6	7	4.3	2.2
3	6	7	5.9	5.7
0	0	8	<3.0	0.8
1	0	8	8.7	6.8
2	0	8	<3.0	1.8
3	0	8	4.6	4.4
4	0	8	3.4	3.7
5	0	8	3.4	2.6
6	0	8	<2.4	2.1
7	0	8	6.1	5.8
8	0	8	<1.9	1.1
0	1	8	<4.2	1.3
1	1	8	10.0	6.8
2	1	8	<4.2	0.4
3	1	8	11.0	8.0
4	1	8	<4.0	0.0
5	1	8	<3.7	3.0
6	1	8	4.4	4.0
0	2	8	<4.0	1.0
1	2	8	14.6	11.7
2	2	8	5.3	4.8
3	2	8	5.1	4.1
4	2	8	4.5	3.4
5	2	8	10.4	9.1
6	2	8	<3.1	0.0
7	2	8	11.2	9.5
0	3	8	7.6	6.2
1	3	8	<4.2	2.2
2	3	8	6.2	5.6
3	3	8	7.1	5.4
4	3	8	<4.6	0.6
5	3	8	6.8	6.7
6	3	8	5.8	5.7
0	4	8	3.6	1.7
1	4	8	4.3	4.2
2	4	8	<3.4	0.0
3	4	8	3.4	3.2
4	4	8	4.2	3.1
0	5	8	<2.4	5.4
1	5	8	<2.3	5.1

tinued, would really have reduced the computational effort significantly. It is worth noting that the parameters from this first least-squares treatment differed from the final parameters by an average of 0·032 Å, the maximum difference being 0·111 Å.

The refinement of the entire (*hkl*) data was carried out on a Datatron computer. The program used was that described by Lavine & Rollett (1956) for structures of class 222. Two stages of structure factors and least squares were first carried out, starting with parameters given by the earlier work. The shifts given by the second stage were considerably smaller than those from the first, and the structure-factor agreement was satisfactorily improved. At this point certain interatomic distances were calculated as a check on the assumed positions of the nitrogen atoms in the imidazole ring. It was found that the nitrogen atoms at the positions that had been chosen could form no hydrogen bond shorter than 4 Å but that one atom, taken to be carbon, was 2·68 Å from a carboxyl oxygen atom in another molecule. Furthermore, the two atoms that had been taken as nitrogens had higher apparent temperature factors (the program computed isotropic temperature factors for all atoms but did not, at this stage, apply these shifts) than the other ring atoms. For the next refinement stage, therefore, and in all further work, the alternative positions were taken for the nitrogen atoms. This change was confirmed by a bigger reduction of $\Sigma w(F_o-F_c)^2$ (7 units) in the third stage than in the second (5 units) in spite of the somewhat smaller positional shifts.

The positional shifts from the third stage were nearly as large as those from the second, indicating that one stage of work would have been saved if the alternate choice of positions had been made at the outset. The one extra stage of refinement by least squares, however, required considerably less time than would, for example, a three-dimensional electron-density calculation with the equipment available, and hence the method adopted for deciding this question was satisfactorily efficient.

The refinement was concluded after the seventh stage, in which no positional shift was greater than 0·011 Å (r.m.s. value 0·0039 Å) and the change in $\Sigma w(F_o-F_c)^2$ was small, indicating that further refinement would not improve the accuracy of the final parameters, which are shown in Table 1.

Even though the observed density of the crystals is 0·5% higher than that calculated, a check on the possibility that some loss of water had occurred was made by examination of F_o and F_o-F_c syntheses prepared with the (*hk*0) data. The former showed normal peak heights, and the latter gave no evidence of less than 1 H_2O, although both indicated that the vibration of the water molecule was anisotropic, the motion being greater along *b* than *a*.

In the first three stages the scale factor and the mean isotropic temperature factor for the whole structure were refined together, with allowance for their strong interaction. These parameters did not change appreciably after the first stage, and no change in scale factor was found when individual isotropic temperature factors were employed in the fifth and later sets of structure factors.

The average standard deviations in a parameter are 0·0089 Å for carbon, 0·0077 Å for nitrogen, 0·0071 Å for oxygen, and 0·0022 Å for chlorine.

The calculated and observed structure factors are presented in Table 2. The average discrepancy, R, for the 935 observed reflections is 12·0%. The agreement is in general quite satisfactory, although in the case of a few strong low-order reflections, viz. (400), (410), (020), and (221), the discrepancies between F_o and F_c are rather large. We feel these may be ascribed to extinction effects, and to the fact that the scattering of the twelve hydrogen atoms has been neglected.

Discussion of the structure

Configuration of the molecule

The intramolecular bond lengths and angles are listed in Table 3 and shown in Fig. 2. The molecule consists of two groups of very nearly co-planar atoms. The least-squares plane defined by the carboxyl group (C_1, O_2, O_1) and the α carbon atom (C_2) passes within 0·009 Å of these atoms and also within 0·029 Å of the amino nitrogen (N_1). The other least-squares plane is adjusted to the β carbon (C_3) and all five atoms of the imidazole ring (C_4, C_5, C_6, N_2, N_3). None of these six atoms lies more than 0·017 Å from this plane.

Table 3. *Intramolecular distances and bond angles*

Bond lengths		Bond angles	
$C_1{-}O_1$	1·252 Å	$O_1{-}C_1{-}O_2$	126·1°
$C_1{-}O_2$	1·274	$C_2{-}C_1{-}O_1$	120·1
$C_1{-}C_2$	1·522	$C_2{-}C_1{-}O_2$	113·7
$C_2{-}C_3$	1·526	$C_1{-}C_2{-}C_3$	115·0
$C_3{-}C_4$	1·528	$C_1{-}C_2{-}N_1$	108·4
$C_2{-}N_1$	1·517	$C_3{-}C_2{-}N_1$	111·2
$C_4{-}N_2$	1·379	$C_2{-}C_3{-}C_4$	112·8
$N_2{-}C_5$	1·327	$C_3{-}C_4{-}N_2$	122·4
$C_5{-}N_3$	1·352	$C_3{-}C_4{-}C_6$	131·7
$N_3{-}C_6$	1·360	$C_4{-}C_6{-}N_3$	108·4
$C_6{-}C_4$	1·365	$C_6{-}N_3{-}C_5$	108·2
		$N_3{-}C_5{-}N_2$	108·1
		$C_5{-}N_2{-}C_4$	109·8
		$N_2{-}C_4{-}C_6$	105·8

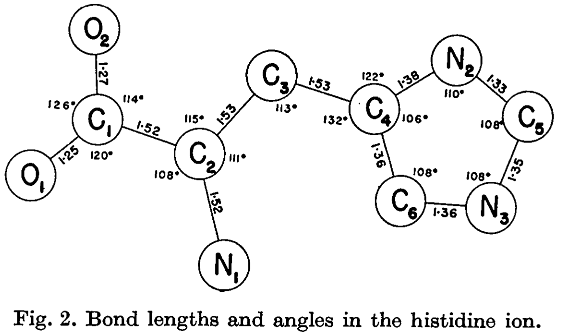
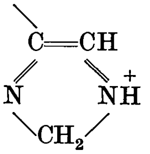


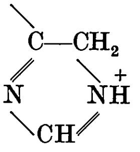
Fig. 2. Bond lengths and angles in the histidine ion.

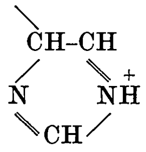
The molecule is in the zwitter ion form, as evidenced by the near equality of the two C–O distances in the carboxyl group, and by the three hydrogen bonds formed by N_1, which are discussed in more detail below. The three aliphatic C–C distances are sensibly equal, and, in agreement with previous results on amino acids (Corey & Donohue, 1950; Corey & Pauling, 1953), slightly shorter than the standard diamond value of 1·541 Å. The α-carbon–amino-nitrogen bond ($C_2{-}N_1$) with length 1·517 Å is longer than the standard value of 1·47 Å. For comparison here we have $\alpha C{-}NH_3^+$ values for the following: alanine, 1·496 Å (Donohue, 1950), serine, 1·491 Å (Shoemaker, Barieau, Donohue & Lu, 1953), threonine, 1·490 Å (Shoemaker *et al.*, 1950), hydroxyproline, 1·503 Å (Donohue & Trueblood, 1952), glutamine, 1·51 Å (Cochran & Penfold, 1952), α and β methionine, 1·52 Å and 1·50 Å (Mathieson, 1952), diglycylcystine, 1·46 Å (Yakel & Hughes, 1954), glycylasparagine, 1·463 Å (Pasternak, Katz & Corey, 1954), β-glycylglycine, 1·51 Å (Hughes & Moore, 1949), norleucine, 1·50 Å (Mathieson, 1953), and glutamic acid hydrochloride, 1·52 Å (Dawson, 1953). The weight of the above evidence appears to indicate that a somewhat long $C{-}NH_3^+$ bond may well be expected in amino acids. The two shortest values above are for peptides, and the average value for the ten amino acids is 1·505 Å.

Since both nitrogen atoms of the imidazole part of the molecule enter into hydrogen bonding with neighboring carboxyl groups, the formula of the salt is established as $RH^+NH_3^+COO^-.Cl^-.H_2O$, rather than $RNH_3^+COO^-.Cl^-.H_3O^+$ or $RNH_3^+COOH.Cl^-.H_2O$.

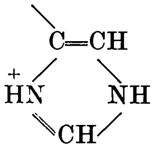
Likewise, tautomeric forms of the positively charged imidazole ring, such as



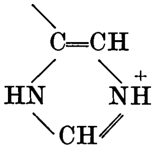




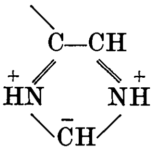
are eliminated. The most probable resonance forms for the correct tautomer are



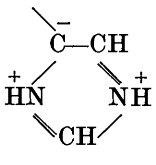
(*A*)



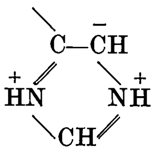
(*B*)



(*C*)



(*D*)



(*E*)

We may fix the total contribution of forms (*A*) and (*B*) at 72% directly from the observed C_4–C_6 distance (see Fig. 2 for the numbering of the atoms) and the well known bond character length curve for carbon–carbon bonds (Pauling, 1940). The preponderance of these forms over the others is expected since they do not involve charge separation. The carbon–nitrogen curve has not been established so firmly, however, so that it is appropriate to fix the parameters of this by using our C–N distances together with the results of Hughes (1941) for melamine (one-third double-bond character, 1·346 Å) and Wheatley (1955) for *s*-triazine (one-half double-bond character, 1·319 Å). There are three parameters for the double-bond characters in the ring (i.e., the contributions of (*A*), (*C*) and (*D*), (*B*) and (*E*) being fixed by difference) so that there are two degrees of freedom. The best agreement is given by (*A*) = 40%, (*B*) = 32%, (*C*) = 23%, (*D*) = 5%, (*E*) = 0%, which correspond with the bond lengths in Table 4 if we use the order–length relation

$$r_x = r_1 - (r_1 - r_2)(3x)/(2x+1)$$

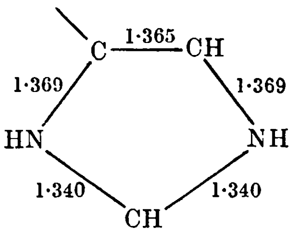
as for the carbon–carbon curve.

Table 4. *Carbon–nitrogen bond-order–length relation*

Bond character	Observed length (Å)	Calculated length (Å)	Error (Å)
1·00	(1·470)	1·474	+0·004
1·23	1·379 (C_4–N_2)	1·375	−0·004
1·28	1·360 (C_6–N_3)	1·362	+0·002
1·32	1·352 (C_5–N_3)	1·352	0·000
1·33	1·346 (melamine)	1·349	+0·003
1·45	1·327 (C_5–N_2)	1·325	−0·002
1·50	1·319 (*s*-triazine)	1·317	−0·002
2·00	—	*1·265*	—

It may be seen that the agreement between the various measurements is as good as we could expect. Furthermore, the contributions assigned to the various resonance forms are reasonable. The larger weight of (*A*) than of (*B*) is in accordance with the formation of a stronger hydrogen bond by N_2 (2·64 Å) than by N_3 (2·83 Å). The charge distribution for (*C*) is more favorable than for (*D*) or (*E*), and (*E*) is particularly unstable because it places a negative charge on C_6, which is only 3·1 Å from the negatively charged O_1 in the same molecule.

The above deductions do not depend, moreover, on differences between the lengths C_4–N_2 and C_6–N_3, or between C_5–N_2 and C_5–N_3. Normally one would expect an imidazolium ring to have a plane of symmetry perpendicular to the bond C_4–C_6, passing through the midpoint of this bond and C_5. Because the apparent absence of such symmetry may not be statistically significant, it is desirable to point out that the bond-character–length curve is practically unaltered if these differences are disregarded. We can average the bond lengths now assumed to be symmetrically equivalent, and obtain the following:



If we use the same nomenclature as before, we have (*A*) ≡ (*B*), (*D*) ≡ (*E*). The contributions which now give closest agreement are (*A*) = (*B*) = 36%, (*C*) = 24%, (*D*) = (*E*) = 2%, leading to the values 1·473 Å and 1·266 Å for the single and double C–N bond lengths respectively, in complete agreement with the results above.*

The curve given by the analysis, assuming no symmetry in the ring, is shown, together with all the experimental points, in Fig. 3.

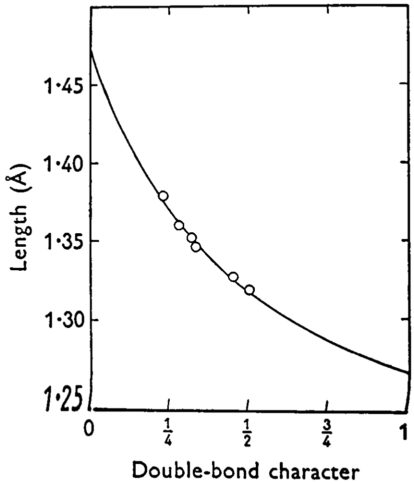


Fig. 3. Bond-lengths versus bond-character curve for carbon–nitrogen bonds, based on the data of Table 4.

The single-bond distance is 0·004 Å larger than the standard (Pauling, 1940) value of 1·47 Å. It is possible, however, that this value is somewhat short, in line with the values quoted above for the amino acids. At any rate, the agreement supports the validity of the extrapolations. The double-bond distance is 0·015 Å shorter than the value obtained by Wheatley (1955), who extrapolated the melamine and *s*-triazine distances in one direction only. It is interesting that the experimental values for carbon–carbon and nitrogen–nitrogen double bonds, combined with a modified Schomaker–Stevenson (1941) rule, give 1·26 Å (Donohue, 1947) or 1·265 Å (Gordy, 1947) for the C=N distance.

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* To illustrate the sensitivity of the extrapolation with the valence bond weights, if we assign (*A*)=(*B*) = 36%, (*C*) = 28%, (*D*)=(*E*) = 0%, we get 1·485 Å for C–N and 1·260 Å for C=N. If (*A*)=(*B*) = 36%, (*C*) = 20%, (*D*)=(*E*) = 4%, then C–N is 1·458 Å and C=N is 1·275 Å.

The hydrogen bonding

There are five hydrogen atoms per histidine molecule, plus two from the water molecule, which are available for hydrogen bond formation. The classic method for locating hydrogen bonds, when the positions of the hydrogen atoms have not been found by direct methods, is to assign as hydrogen bonds the short N · · · O, O · · · O, O · · · Cl, etc., distances, providing that the angles of the sort C–N · · · X do not differ too much from the expected value of about 110°. For an ionized amino group the angles X · · · N · · · X should also be nearly tetrahedral. In the present case, the amino nitrogen (N_1) has four close neighbors, two oxygen atoms at 2·82 Å and 2·91 Å, and two chloride ions at 3·17 Å and 3·20 Å, but the oxygen atom at 2·91 Å cannot be involved in a hydrogen bond, since the respective C–N · · · X angles are 102°, 165°, 92°, and 120°. The angles X · · · N · · · X for the three remaining contacts are 101°, 107°, and 130°, and it is possible to find positions for the hydrogens of the NH_3^+ group so that the C–N–H and H–N–H angles are 109° and the NH lines pass close to the one O and two Cl atoms. This may be seen clearly in Fig. 4, which is a stereogram of the environment of the N atom, viewed down the C_2–N_1 bond.

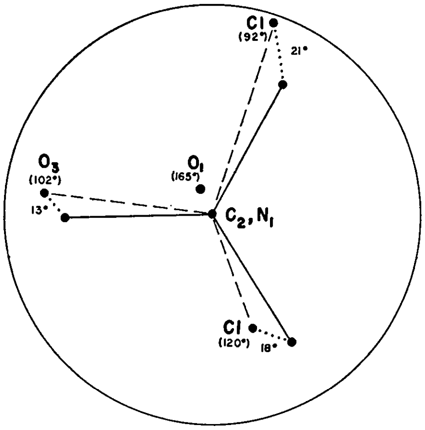

Fig. 4. Stereographic projection of the environment of the NH_3^+ group, viewed down the bond Cα–N.

Each nitrogen of the imidazole ring forms one hydrogen bond, to carboxyl groups in different molecules, the N · · · O distances being 2·64 Å and 2·83 Å. The bonded hydrogen atoms may be assumed to lie in the plane of the ring, and if they are placed so that the N–H bonds make equal angles with the C–N bonds, the angles H–N · · · O are found to be 7° and 29°, the smaller angle corresponding to the shorter N · · · O distance. The nitrogen atom (N_3) also has a second moderately close neighbor, a chloride ion at 3·36 Å, a distance rather longer than has been observed for the N–H · · · Cl type of bond (Donohue, 1952) and furthermore the angle H–N · · · Cl has the unacceptably large value of 47°.

There remains the water molecule (O_3), which in addition to accepting a hydrogen bond from the amino group forms two, one to a carboxyl oxygen, at 2·76 Å, and the other to the chloride ion, at 3·18 Å. The angle between these two hydrogen bonds is 102°.

The hydrogen bonding system is such that the crystal is essentially a three-dimensional network, in agreement with the absence of any marked cleavage. Two views of the structure, showing the hydrogen bonding, are presented in Fig. 5. Data on the hydrogen bond lengths and on intermolecular distances short enough to be classed as van der Waals contacts are given in Table 5. The conventional notation of M, A, B, etc. for the four equivalent molecules is used in Fig. 5 and in Table 5.

Table 5. *Intermolecular distances*

Hydrogen bonds		Other	
$N_1(M) \cdots O_3(C_{0\bar{1}\bar{1}})$	2·817 Å	$O_1(M) \cdots O_3(M)$	3·33 Å
$N_1(M) \cdots Cl(M)$	3·168	$O_1(M) \cdots Cl(M)$	3·79
$N_1(M) \cdots Cl(C_{0\bar{1}0})$	3·208	$C_5(M) \cdots N_3(C_{00\bar{1}})$	3·54
$N_2(M) \cdots O_2(M_{00\bar{1}})$	2·639	$C_5(M) \cdots C_6(C_{00\bar{1}})$	3·47
$N_3(M) \cdots O_1(C_{00\bar{1}})$	2·831	$O_2(M) \cdots O_3(C_{0\bar{1}\bar{1}})$	3·83
$O_3(M) \cdots Cl(M)$	3·194	$Cl(M) \cdots C_4(M)$	3·74
$O_3(M) \cdots O_2(A_{\bar{1}00})$	2·760	$Cl(M) \cdots C_5(M)$	3·74
		$Cl(M) \cdots C_6(M)$	3·93
		$Cl(M) \cdots N_2(M)$	3·57
		$Cl(M) \cdots N_3(M)$	3·94
		$O_1(M) \cdots Cl(C_{0\bar{1}0})$	3·72
		$O_1(M) \cdots Cl(M_{001})$	3·90

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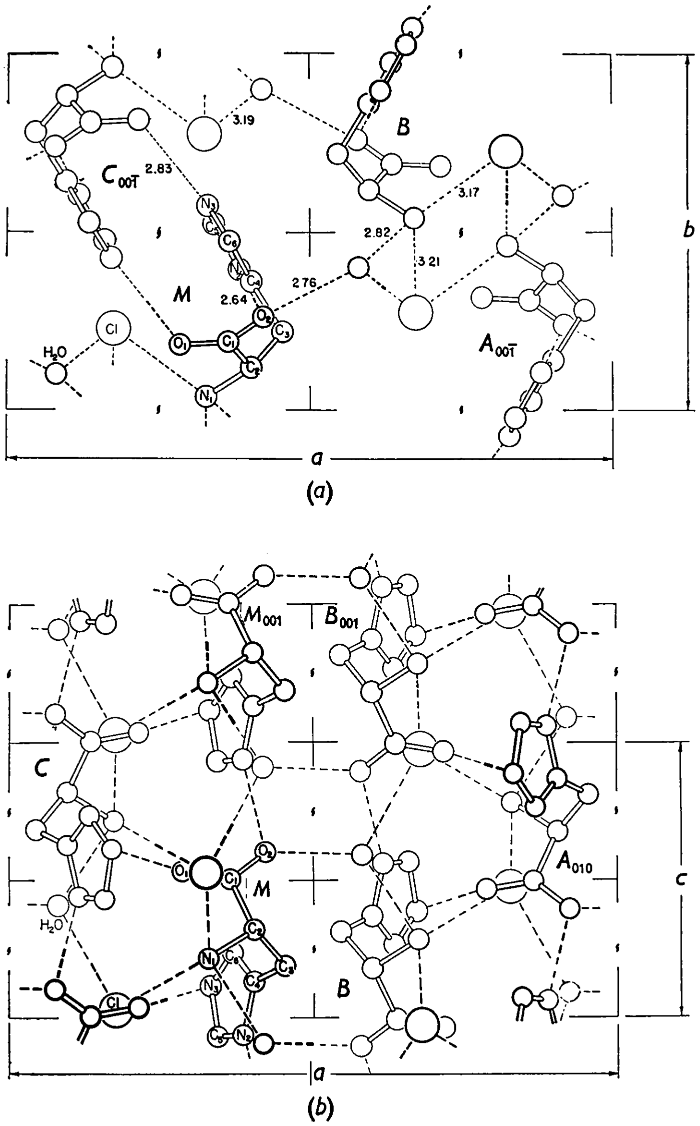

Fig. 5. (*a*) The structure viewed down *c*, showing the hydrogen bonds and their lengths. (*b*) The structure viewed up *b*, showing the hydrogen bonds.

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