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Refinement of the crystal structure of histidine hydrochloride monohydrate.

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Recently, the structures of di-(L-histidino)zinc(II) dihydrate (Harding & Cole, 1963) and pentahydrate (Kretsinger, Cotton & Bryan, 1963) have been determined and refined by procedures which allowed anisotropic thermal motions of the heavy atoms and included the scattering of the hydrogen atoms. For purposes of comparison, it was felt that it would be worthwhile to extend the not very recent refinement of the structure of histidine hydrochloride monohydrate (Donohue, Lavine & Rollett, 1956) by allowing for both of these effects, especially in the light of the results reported by KC&B, who found that allowance for these effects in their refinement reduced the C(3)–C(4) bond length by 0·077 Å from 1·477 Å to 1·400 Å, and remarked that "DL&R gave a value of 1·53 Å for the corresponding bond in histidine hydrochloride but they did not take hydrogen atoms into account in their refinement".

To this end, the observed structure factors of DL&R were used in a full-matrix least-squares treatment which used the program of Gantzel, Sparks & Trueblood (1962). The scattering factor curves were those of Freeman (1959) for the carbon, nitrogen, and oxygen atoms, Tomiie & Stam (1958) for the chloride ion, and McWeeny (1951) for the hydrogen atoms. The weighting scheme was that of Hughes (1941), with $4F_{\min}=13$. The unobserved F's were not included in the calculations.

The refinement was started isotropically at the final parameter values of DL&R, omitting the hydrogen atoms. After three cycles, convergence was reached and R had dropped to 10·5%. The coordinates of the hydrogen atoms were then estimated by assuming C–H and N–H bond lengths of 1·0 Å, accepted bond angle values, and the NH_3^+ conformation derived by DL&R. These coordinates, together with the isotropic B values of the heavy atoms to which each hydrogen atom is bonded, were introduced in the computations as constants and the isotropic refinement was resumed. After four cycles, convergence was reached again, and R dropped to 9·5%. In the third and last stage of the refinement, the heavy atoms were treated anisotropically, while the hydrogen parameters were held constant. After four cycles (and full convergence: the largest value of the shift to e.s.d. ratio was 0·07) R had a value of 7·6%.

The values of the bond distances obtained at the three stages of refinement, together with the values from the previous authors, are presented in Table 1. The final set of parameters (AH) is given in Tables 2 and 3 for the heavy atoms, and in Table 4 for the hydrogen atoms.

Table 2. *Atomic coordinates*

($\times 10^4$)

	$x(\sigma)$	$y(\sigma)$	$z(\sigma)$
C(1)	3645(5)	1939(8)	5044(11)
C(2)	4020(5)	1169(9)	3240(12)
C(3)	4513(4)	2237(9)	1900(11)
C(4)	4016(5)	3625(8)	1321(11)
C(5)	3414(6)	5251(10)	9337(14)
C(6)	3680(5)	4766(9)	2392(13)
N(1)	3305(4)	384(7)	2173(10)
N(2)	3836(5)	3964(8)	9397(9)
N(3)	3301(5)	5734(7)	1123(12)
O(1)	2857(3)	1836(6)	5413(9)
O(2)	4204(4)	2628(7)	6055(9)
O(1)	802(4)	1001(9)	4083(10)
Cl^-	1758(1)	2276(2)	299(3)

Space group, $P2_12_12_1$

$a=15·36$, $b=8·92$, $c=6·88$ Å

Upon examination of Table 1, it may be noted that none of the bond lengths among our three sets differs significantly, the maximum difference being 0·018 Å. The average difference in bond length between those of our set AH and that of DL&R is 0·010 Å, and the largest, 0·038 Å. The C(3)–C(4) bond length remained fairly constant at a reasonable value throughout our refinement as contrasted to what happened during the refinement

Table 1. *Bond lengths* (Å) *in the histidine molecule*

		This work*			KC&B*			H&C*	
Bond	DL&R	*I*	*IH*	*AH*	*I*	*IH*	*AH*	*IH*	*AH*
C(1)–C(2)	1·522	1·526	1·532	1·530	1·530	1·520	1·537	1·518	1·519
C(2)–C(3)	1·526	1·517	1·522	1·527	1·519	1·551	1·553	1·554	1·539
C(3)–C(4)	1·528	1·525	1·507	1·508	1·478	1·427	1·400	1·495	1·486
C(4)–C(6)	1·365	1·362	1·369	1·358	1·378	1·350	1·332	1·361	1·369
C(6)–N(3)	1·360	1·363	1·351	1·359	1·408	1·387	1·368	1·375	1·374
N(3)–C(5)	1·352	1·331	1·319	1·314	1·324	1·306	1·290	1·313	1·324
C(5)–N(2)	1·327	1·324	1·323	1·319	1·308	1·271	1·278	1·337	1·329
N(2)–C(4)	1·379	1·381	1·387	1·386	1·378	1·390	1·404	1·412	1·417
C(1)–O(1)	1·252	1·247	1·250	1·240	1·199	1·187	1·193	1·241	1·243
C(1)–O(2)	1·274	1·274	1·265	1·265	1·252	1·243	1·231	1·263	1·260
C(2)–N(1)	1·517	1·509	1·492	1·495	1·500	1·498	1·487	1·474	1·473
R	12·0	10·5	9·5	7·6	10·8	11·3	—	12·7	10·5
σ C–C	—	0·014	0·013	0·011	0·025	0·025	0·025	0·023	0·020
σ C–N	—	0·013	0·013	0·011	0·023	0·023	0·023	0·023	0·020
σ C–O	—	0·012	0·011	0·010	0·021	0·021	0·021	0·023	0·020

* I = isotropic without H contributions, IH = isotropic with H contributions, AH = anisotropic with H contributions.

Table 3. *Temperature factors*
($\times 10^4$)

	$B_{11}(\sigma)$	$B_{22}(\sigma)$	$B_{33}(\sigma)$	$B_{12}(\sigma)$	$B_{13}(\sigma)$	$B_{23}(\sigma)$
C(1)	36(3)	53(8)	114(18)	5(9)	16(12)	23(21)
C(2)	20(3)	63(8)	150(17)	10(8)	−9(12)	−13(22)
C(3)	20(3)	76(9)	155(17)	9(9)	22(11)	−20(24)
C(4)	23(3)	45(8)	125(16)	−21(8)	13(12)	−17(19)
C(5)	29(4)	97(11)	187(22)	−12(10)	−19(14)	28(26)
C(6)	26(3)	74(9)	187(19)	−7(9)	14(15)	23(26)
N(1)	22(3)	60(7)	148(14)	2(8)	9(11)	−34(17)
N(2)	33(3)	95(9)	100(13)	−21(9)	13(11)	−10(20)
N(3)	35(3)	54(7)	213(17)	−2(9)	4(14)	20(20)
O(1)	26(2)	96(7)	171(12)	6(7)	32(10)	−34(19)
O(2)	35(3)	147(10)	136(12)	−26(10)	0(9)	−77(20)
O(3)	36(3)	187(12)	208(17)	29(11)	3(11)	112(26)
Cl⁻	34(1)	69(2)	126(4)	16(2)	−5(3)	4(5)

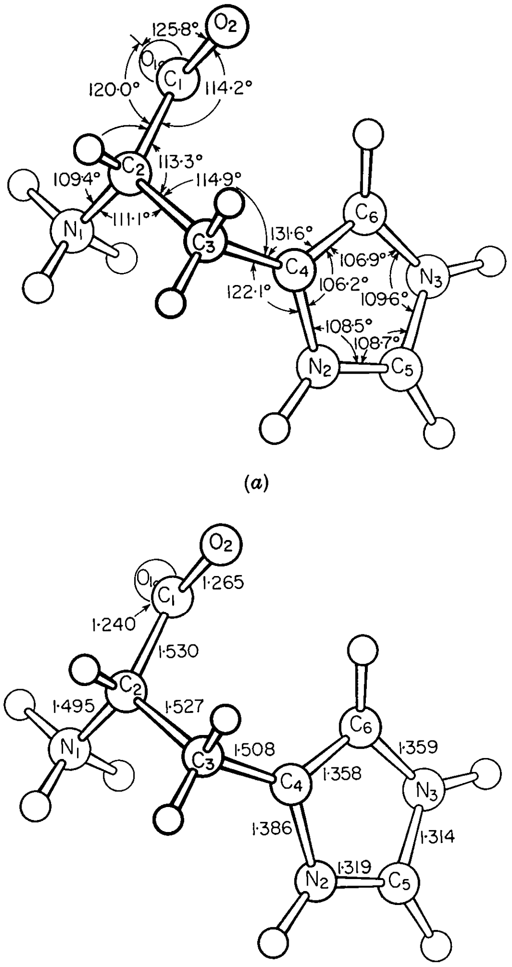

Fig. 1. (*a*) Bond angles and (*b*) bond distances in histidine hydrochloride.

Table 4. *Hydrogen parameters*
($\times 10^3$ except *B*'s)

	x	*y*	*z*	*B*
H(C2)	446	39	369	2·17 Å^2
H(C3)	472	163	75	2·36
H'(C3)	506	251	268	2·36
H(C5)	321	575	809	3·11
H(C6)	370	485	384	2·58
H(N1)	280	112	187	2·23
H'(N1)	350	0	87	2·23
H''(N1)	305	−45	296	2·23
H(N2)	402	333	821	2·57
H(N3)	299	670	150	2·80
H(O3)	111	142	297	4·17
H'(O3)	223	147	406	4·17

of KC&B. In spite of the fact that the conformation of the histidine cation is unlike that of the histidino groups in the zinc complexes, the bond lengths are very similar: ours differ from those of set *AH* of H&C by an average of 0·014 Å (maximum, 0·031 Å), and from those of set *AH* of KC&B by an average of 0·032 Å (maximum, 0·108 Å). It is interesting that there is better agreement between our set *AH* and set *I* of KC&B (average difference, 0·018 Å, maximum 0·049 Å) — this is the set which KC&B considered their best solution to the structure. We do not understand why introduction of the hydrogen atoms and allowance for anisotropy led to the rather large changes observed by KC&B.

In Fig. 1 the bond angles from our refinement *AH*

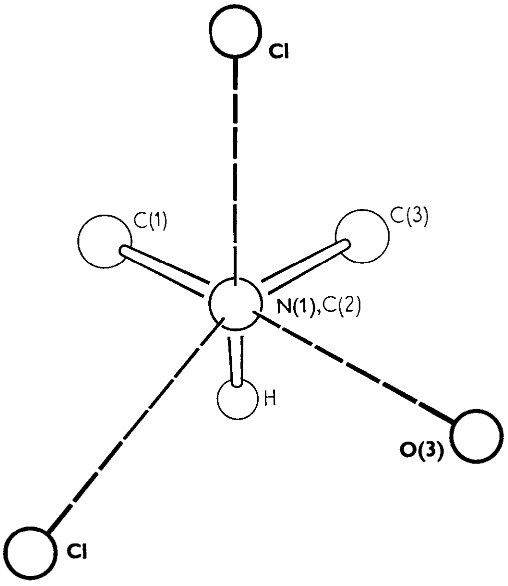

Fig. 2. View down N(1)–C(2) in histidine hydrochloride.

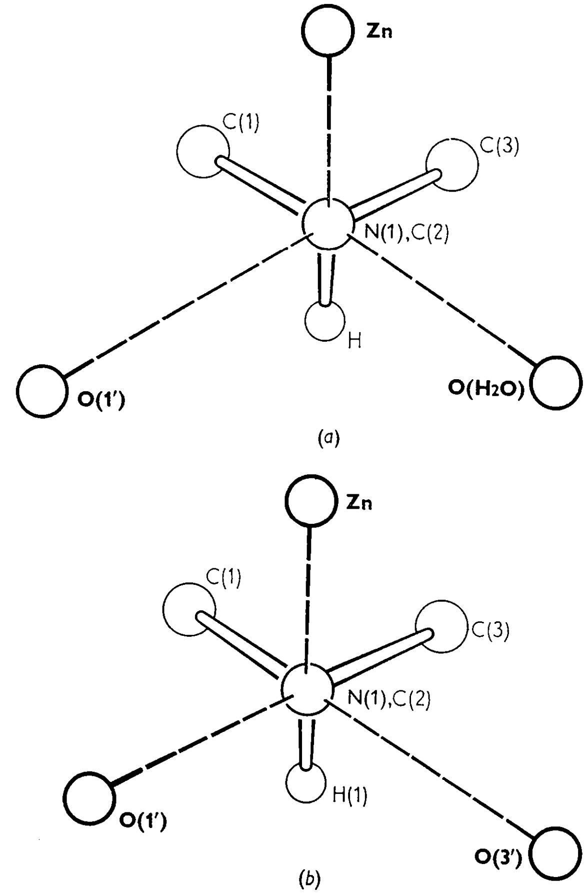

Fig. 3. View down N(1)–C(2) in histidino–zinc complexes: (*a*) in the dihydrate, (*b*) in the pentahydrate.

are shown. We feel it unnecessary to make the same detailed comparison among the various sets of bond angles as is done above for the bond distances.

There is an interesting point regarding the conformation of the histidino groups in the three compounds which has not been mentioned previously. DL&R pointed out that in histidine hydrochloride the disposition of the three proposed hydrogen bonds formed by the $-NH_3^+$ groups was satisfactory in terms of the angles C(2)–N(1)–H and H–N(1)–H, but they did not discuss the positions of these hydrogen atoms relative to the ligands of C(2). A view down the N(1)–C(2) bond is shown in Fig. 2, where it is seen that the conformation is the expected staggered one. Examination of the two histidino-zinc complexes shows that although in them the $-NH_2$ groups form, in addition to the N $\cdots$ Zn bond, two hydrogen bonds, one to an oxygen atom of a different histidino group and one to a water molecule, the conformation in each still closely approaches being exactly staggered, as shown in Fig. 3. We interpret these results to mean that preservation of the staggered conformation should be included in models proposed for larger molecules or complexes of which the histidino group is a part, unless stronger structural restrictions can be found which force relaxation of this condition.

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References

Donohue, J., Lavine, L. & Rollett, J. R. (1956). *Acta Cryst.* **9**, 655.

Freeman, A. J. (1959). *Acta Cryst.* **10**, 261.

Gantzel, P., Sparks, R. & Trueblood, K. T. (1962). I. U. Cr. *World List of Computer Programs.*

Harding, M. M. & Cole, S. J. (1963). *Acta Cryst.* **16**, 643.

Hughes, E. W. (1941). *J. Amer. Chem. Soc.* **63**, 1737.

Kretsinger, R. H., Cotton, F. A. & Bryan, R. F. (1963). *Acta Cryst.* **16**, 651.

McWeeny, R. (1951). *Acta Cryst.* **4**, 513.

Tomiie, Y. & Stam, C. H. (1958). *Acta Cryst.* **11**, 126.

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The Fourier transform of the regular tetrahedron.

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As a part of the work on the crystalline structure of proteins, an investigation on trypsin has been initiated in these laboratories (Kay, 1963). Both the PtI_6^{2-} and the HgI_4^{2-} ions have been used to prepare isomorphous heavy-atom derivatives of diisopropylphosphoryltrypsin by diffusion of the ions from solution into the crystals.

The effect of orientation of an octahedral ion such as PtI_6^{2-} on its Fourier transform has been examined (Stanford, 1962), and it seems advisable now to perform a similar investigation for a regular tetrahedron, such as the iodine atoms in HgI_4^{2-}.

The transform of four atoms, each with atomic scattering factor f and located at $(b/2, b/2, b/2)$, $(-b/2, -b/2, b/2)$, $(-b/2, b/2, -b/2)$, and $(b/2, -b/2, -b/2)$, is given by:

$$F = A + iB \,,$$

where

$$A = 4f \cos 2\pi h \cos 2\pi k \cos 2\pi l$$

and

$$B = 4f \sin 2\pi h \sin 2\pi k \sin 2\pi l \,.$$

The averaging of the function F is carried out on the

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