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X-Ray diffraction study of choline chloride's β form*

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The organic salt choline chloride exists in two crystalline polymorphs. One (α form) is extraordinarily sensitive to ionizing radiation, the other (β form) is not The present report describes an x-ray diffraction study of the β form. The structure has been found to be highly disordered face centered cubic. Comparison with infrared, NMR, and calorimetric data indicates that the disordering is dynamic and is ascribable to rotations of the choline ion around crystallographic symmetry axes. Possible connections of the reorientation effects to the radiation stability of this form are discussed.

INTRODUCTION

Crystalline choline chloride, $[(CH_3)_3NCH_2CH_2OH]^+Cl^-$, is the most ionizing-radiation sensitive compound known. It decomposes by a chain reaction that gives $G_{(-M)}$ values as high as 55,000.[1] The anomalous sensitivity is shown only by the crystalline form; in solution, the compound exhibits normal radiation stability. In addition, the very high sensitivity is shown by only one of two known polymorphs of choline chloride. The radiation sensitive one, the "α" form, occurs at ambient temperatures, and up to about 75°. The radiation stable polymorph, the "β" form, appears at and above 78°. Clearly, an explanation of the α form's anomalous sensitivity must lie in some structural difference between it and the β form.

The crystal structure of the α form has been studied by Senko and Templeton[2] and, more recently, by Hjortas and Sorum.[3] According to these data the α form is orthorhombic, space group $P2_12_12_1$, with unit cell dimensions a = 11.21, b = 11.59, and c = 5.90 Å, with four molecules per unit cell. The structure is characterized by an unusually long bond between the N and C4 (Fig. 1) of 1.60 ± 0.03 [2] or 1.559 ± 0.01 Å [3] and a weak O-H...Cl bond with O-Cl distance of 3.03 ± 0.02 [2] or 3.070 ± 0.006 Å [3]. Collin[4], and Shanley and Collin,[5] investigated the structure of the β form of choline chloride. In these studies, the samples were either powder or single crystals grown in the α form at ambient temperatures and heated slowly above the transition temperature--however, the heating produced random fracturing of the crystals. The data were restricted to twelve reflections only. The authors found that the symmetry is disordered face centered cubic with axial length 9.48 Å. Furthermore, they calculated

approximately the phases of the various reflections by employing a spherical disordering model. The phases were in turn used for the location of the Cl and N atoms via an electron density map.

In the present study we report extensive high temperature x-ray measurements by using good quality crystals grown above the transition temperature. Our analysis, which is based on 42 unique reflections, has led to more-accurate electron density maps, and includes the positions of the four carbons bonded to the nitrogen.

EXPERIMENTAL

In our initial attempts to obtain the high temperature x-ray data, single crystals of choline chloride grown at ambient temperatures, mounted in sealed quartz capillaries, were heated slowly to ~90°. This process, which was used by previous authors,[4,5] was not very efficient, however, since the crystals were fractured during passage through the transition temperature. Therefore, we grew the crystals directly at about 100-120° from their solution in n-octanol. This was accomplished by means of a resistance wire distributed evenly over the surface of a Petri dish. The solution was in a mini vial mounted on top of the dish. The space above the dish and around the vial was heated by means of a heat gun. The dish and the vial were positioned under a microscope so that the size of the crystals could be continuously checked. Crystals of sufficient size were transfered from the solution to the hot surface of the dish where they could be handled. Crystals grown in this way over 15 hours were transparent cubes of very good quality with edges ranging between ∿0.3 and ∿2 mm. Special care was exercised to keep the temperature of the crystals above the transition point during all further handlings, including mounting on the x-ray diffractometer. Accidental

cooling would result in a fractured crystal with an opaque appearance. The crystals were non-hygroscopic in the air over periods of at least three days when kept at the high temperature.

The measurements were obtained with a Syntex $P2_1$ diffractometer with Mo radiation and a flat graphite monochromator. The LT-1 low temperature device was used to supply a stream of hot nitrogen gas around the specimen. The specimen was a ~0.5 mm edge cubic single crystal. The unit cell dimensions were determined by use of the Syntex autoindexing routine[6] and were found equal to 9.414 ± 0.008 Å --this is smaller than the reported[5], less-accurate value of 9.48 ± 0.003 Å. The axes were at right angles to each other, indicating a cubic structure. The calculated density, assuming four molecules per unit cell, was 1.11 g/cm^3, in very good agreement with reported direct density measurements.[7] The density at 25° is equal to 1.20 ± 0.02 g/cm^3 (ref. 3). Data were collected in the 2θ:θ mode up to h,k,l = 10,10,10. Systematic absences established a face-centered cubic structure, in agreement with the previous studies.[4,5] The collection of data was completed within a few hours. The unique reflections were repeatable after several hours, indicating no observable radiation damage to the crystal. Data taken on another crystal of somewhat smaller size were practically identical.

As has been pointed out in early investigations of the structure,[4,5] an overall characteristic of the high temperature form is that the maximum possible symmetry of the choline molecule itself (Fig. 1) is much lower than might be implied by any face-centered cubic space group. Therefore, the structure must be disordered and cannot be described by any specific space group. Systematic absences were used, however, to exclude a number

of high symmetry face-centered cubic space groups. The remaining probable space groups are either the centrosymmetric groups, Fm3, Fm3m, and F432, or the noncentrosymmetric one, F23. The position of the chlorine atom and of what turned out later to be the nitrogen atom were fixed at 0,0,0 and 1/2, 1/2, 1/2, respectively, by means of a Patterson map. The four carbon atoms bonded to the nitrogen were gradually located by means of a Fourier map. They all occupy the special positions x,x,x; this is unexpected because of their chemical non equivalence. A full matrix least-square refinement with the above centrosymmetric space groups resulted in x = 0.610 $\pm$ 0.002 with occupancy factor G = 0.101 $\pm$ 0.008 and isotropic temperature factor B = 18 $\pm$ 2 $\mathring{A}^2$, corresponding to R = 10.2%. The R factor dropped to 4.2% when we adopted the noncentrosymmetric group F23. The refined parameters in this case are x = 0.391 $\pm$ 0.007, G = 0.29 $\pm$ 0.06, B = 44 $\pm$ 7; and x = 0.602 $\pm$ 0.004, G = 0.31 $\pm$ 0.04, B = 25 $\pm$ 3.

The rather low value of R, which resulted by considering only six out of the eight non-hydrogen atoms of the choline chloride molecule, indicates that the remaining two atoms, C-O, do not give any substantial contribution to the intensities. As a matter of fact, an extensive search over the various possible positions of these atoms gave no indication of any prominent electron density due to the whole, or even a very small part, of their charge. This most probably implies that these two atoms either occupy general positions (a general position in F23 has 12 equivalents per molecule while one in Fm3, etc. has 24 equivalents) or rotate inside the unit cell. The latter possibility is supported by infrared and NMR data as is discussed in the next Section.

Table I summarizes the results obtained as described above. The strongest observed and calculated intensities in the centrosymmetric and noncentrosymmetric cases are listed in Table II. Plots of the electronic density as well as projections of the atomic positions in various intersections of the unit cell are given in Figs. 2, 3, and 4.

DISCUSSION

The present results have been based on a significantly larger number of reflections and more accurate data than reported earlier. This permitted the location of six out of the eight non hydrogen atoms of the molecule despite the disordered nature of the structure. Two of these atoms, namely the Cl and the N, occupy well-defined positions--0,0,0 and 1/2, 1/2, 1/2. The tetrahedron of the four carbon atoms, bonded to the nitrogen, has, however, at least two possible orientations in each molecule. Furthermore, all four carbons appear to be crystallographically equivalent, although one of them, C4, is not chemically equivalent to the others (Fig. 1). This is understandable as being a consequence of the disordering of this phase. An additional feature of the disordering is the apparent lack of specific location of the C-O group, which implies that the C and O atoms occupy rather general positions in the unit cell. This result is probably related to the reported substantial difference in the O-CH_2 infrared peaks between the α and β forms.[8,9] A similar difference may be noted also in the N-CH_2 peaks in these spectra. The N-CH_2 bond of the α form has been found to be unusually long[2,3], as we mentioned earlier, and this has been thought of as one of the causes of the radiation instabililty of choline chloride. Unfortunately, the N-C bond distances in Table I are not offered

for any comparison; their larger than usual values probably account for the disordering, the missing C-O groups, the temperature vibrations, etc. Another observation in the infrared spectra is that the O-H stretching frequency is present in both the α and β form, indicating that the H-bonding between the O and Cl, which has been found in the α form[2,3], most probably exists in the β form as well.

The disordering of the β form, which is evident in the x-ray data, may be attributed generally to either different orientations of the choline ion from one unit cell to the other ("static disordering"), or to a rotation of the molecule or various parts of it around certain axes of symmetry ("dynamic disordering"). The latter possibility is supported by the observed unusual broadening of the infrared spectrum of the β form.[8,9] In recent NMR studies of three crystalline choline cholides, Graham and Hannon found a substantially decreased second moment of the choline chloride (0.96)[2] above the transition temperature.[10] They interpreted it as due to isotropic reorientation of the molecule. This finding is in agreement with the disordering of the β form and, moreover, implies that the origin of it is dynamic. Examination of the present structure results (electron density in Fig. 2) shows several possible ways that rotation of various groups, might lead to an overall cubic symmetry. Assuming that the Cl and N atoms remain fixed in the 0,0,0 and 1/2, 1/2, 1/2 positions, which span a NaCl like structure, and taking into account that the O-Cl bond (if indeed one is present) is very loose, we may easily imagine the choline ion rotating around the threefold or fourfold axes that pass through the nitrogen. During the rotations the C-O group spans the surface of a much larger sphere than the one which

is spanned by the other four carbon atoms. This explains why these two atoms cannot be located. Presumably the binding forces between the choline and the chloride anion favor discrete orientations of the choline ion instead of a spherical distribution. This is suggested by the fact that to each of the four carbons of the N-C4 group there correspond two distinct, practically equivalent, positions per molecule. Examination of Figs. 2 through 4 suggests that the missing C and O atoms probably lie along the diagonals [110] or [111] where more room exists in the unit cell. On the other hand, examination of the shape of the choline molecule[2,3] indicates that the O atom is hydrogen bonded--if bonded at all-- to the chloride lying closest to the nitrogen atom, that is, the one in the [001] direction.

The rotations of the choline ion probably are not restricted to those indicated above. Independent rotations of the C5,O atoms within the molecule are very plausible.

In order to check whether the choline ion retains its identity in the β form we have recently performed irradiation studies of the methyl-labeled-compound, $[(^{14}CH_3)_3\overset{+}{N}CH_2CH_2OH]$, at ambient temperature, following preheating at various temperatures above the transition point and for various times extending to 12 hours. The decomposition product acetaldehyde, which results from the $-CH_2CH_2OH$ group, was purified through a gas chromatographic column, and its radioactivity was measured. Although in certain cases a small ^{14}C content was found, indicating a possible sharing in the β form of the CH_2OH between the various methyl groups, it was concluded, in general, that this effect may be neglected and that the rotations described in the previous paragraphs are the most plausible ones.

The present results cannot be used for definite conclusions concerning the radiation sensitivity of the α form of choline chloride. It might be noticed, however, that the reorientation occurring above the phase transition may be related to the protonic conductivity[10,11] that has been suggested for the β phase.[8] Protons in turn may inhibit the decomposition chain mechanism by reaction with ethanol radicals.[8]

The α to β form crystallographic transition may be not the only one in choline chloride. As a matter of fact, both the infrared[9] and the NMR[10] data indicate the possibility of a weak crystallographic transition at subambient temperatures. This may be related to the low temperature radiation stability of choline chloride.[12] In a search for other phase transitions, as well as in order to determine the energy of the α to β form transition, we are presently making calorimetric studies of choline chloride using a DSC-2 Perkin Elmer apparatus. Preliminary results show a rather broad transition at 78°, which is identified as the α to β form transformation. The transition energy is approximately 27.5 cal/gram, corresponding to S = 10.9 cal/deg. x gram, which value agrees with the large energy needed for the reorientation to the β phase. These measurements show no indication of any additional transition in the range -60° to +150°C. Additional measurements are in progress.

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TABLE I

Structural Parameters of the β Form of Choline Chloride

Face centered cubic. Unit cell edge = 9.414(8)Å. Four molecules per unit cell

	Space Group: F23; R = 4.2%				Space Group: Fm3, Fm3m, F432; R =10.2%			
Atom	Position	G Occupancy	B (Temperature factor)	C-N* Distance	Position	G Occupancy	B (Temperature factor)	C-N* Distance
Cl	0, 0, 0	0.0833	16.4(2)		0, 0, 0	0.0417	19.2(5)	
N	0.5, 0.5, 0.5	0.0833	25(1)		0.5, 0.5, 0.5	0.0417	35(2)	
C	0.391(1),0.391,0.391	0.29(6)	44(1)	1.78(4)	0.610(2),0.610,0.610	0.107(8)	18(2)	1.79
C	0.602(4),0.602,0.602	0.31(4)	25(3)	1.66(2)				

*C-N angles of any appropriately selected atoms = 109.5(5)°.

TABLE II. Certain Observed and Calculated Structure Factors of the β Form of Choline Chloride in the Noncentrosymmetric and Centrogymmetric Approaches

			F23				Fm3, Fm3m, F432			
h	k	l	|Fo|	|Fc|	A*	B	|Fo|	|Fc|	A*	B
1	1	1	19.77	20.14	-20.13	0.59	16.52	14.54	14.54	0.00
2	0	0	96.65	93.86	93.86	-0.00	80.78	74.15	74.15	0.00
2	2	0	52.38	53.66	53.66	0.00	43.78	46.50	46.50	0.00
2	2	2	38.74	38.48	37.26	-9.62	32.38	32.20	32.20	0.00
3	1	1	31.24	31.34	31.10	3.86	26.11	27.86	27.86	0.00
3	3	1	12.83	12.77	12.04	4.24	10.73	11.04	11.04	0.00
3	3	3	9.74	10.30	9.55	3.88	8.14	8.99	8.99	0.00
4	0	0	6.90	8.02	8.02	-0.00	5.77	8.90	8.90	0.00
4	0	2	18.62	17.53	17.53	-0.00	15.56	14.99	14.99	0.00
4	2	0	18.58	17.53	17.53	0.00	15.53	14.99	14.99	0.00
4	2	2	15.79	15.71	15.41	-3.04	13.20	12.37	12.37	0.00
4	4	0	12.79	12.93	12.93	-0.00	10.69	11.54	11.54	0.00
4	4	2	8.23	8.31	8.28	-0.71	6.88	6.19	6.19	0.00
4	4	4	4.10	3.24	3.24	-0.16	3.43	1.14	1.14	0.00
5	1	1	13.81	13.67	13.67	0.02	11.54	12.15	12.15	0.00

* Phases are given by arctg $(\frac{B}{A})$.

0 0 0 0 4 8 0 1 8 3 0

FIGURE CAPTIONS

Fig. 1. Molecular unit of the choline chloride.

Fig. 2. Electron density maps at two vertical planes a) z = 0.5 and b) x = y. Contours start at minimum density 0.2 eA^{-3}, with an interval of 0.2 eA^{-3}. Chloride contours end at maximum density 0.8 eA^{-3}.

Fig. 3. Positions of the various atoms in the unit cell corresponding to the space group F23. The radii of the various atoms were determined by the temperature factors (Table 1).

Fig. 4. Projections of the atoms (Fig. 3) on the plane (110).

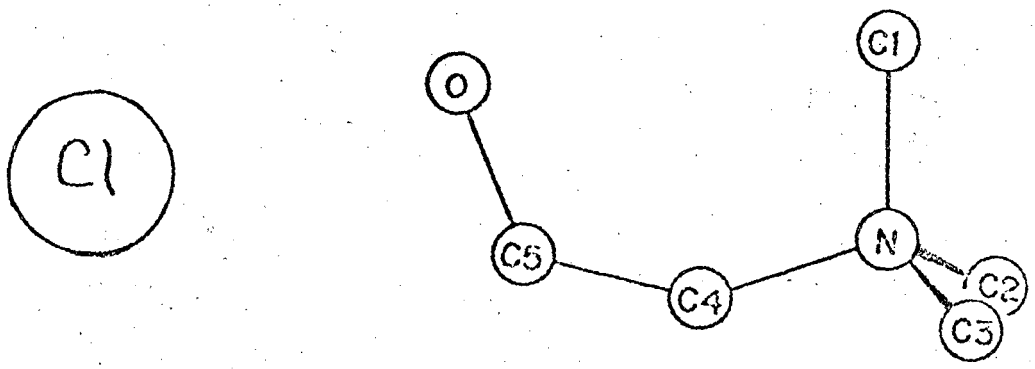

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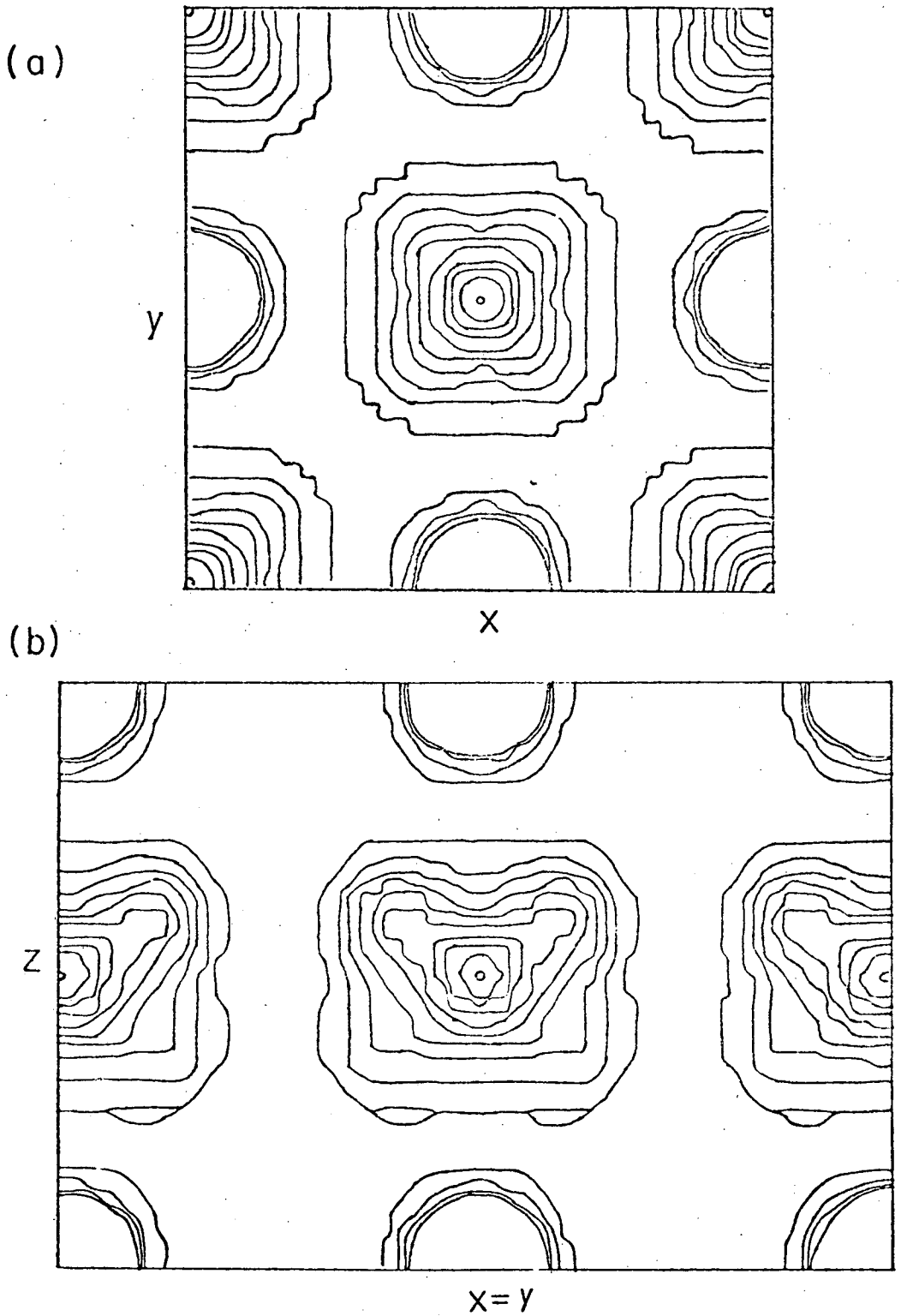
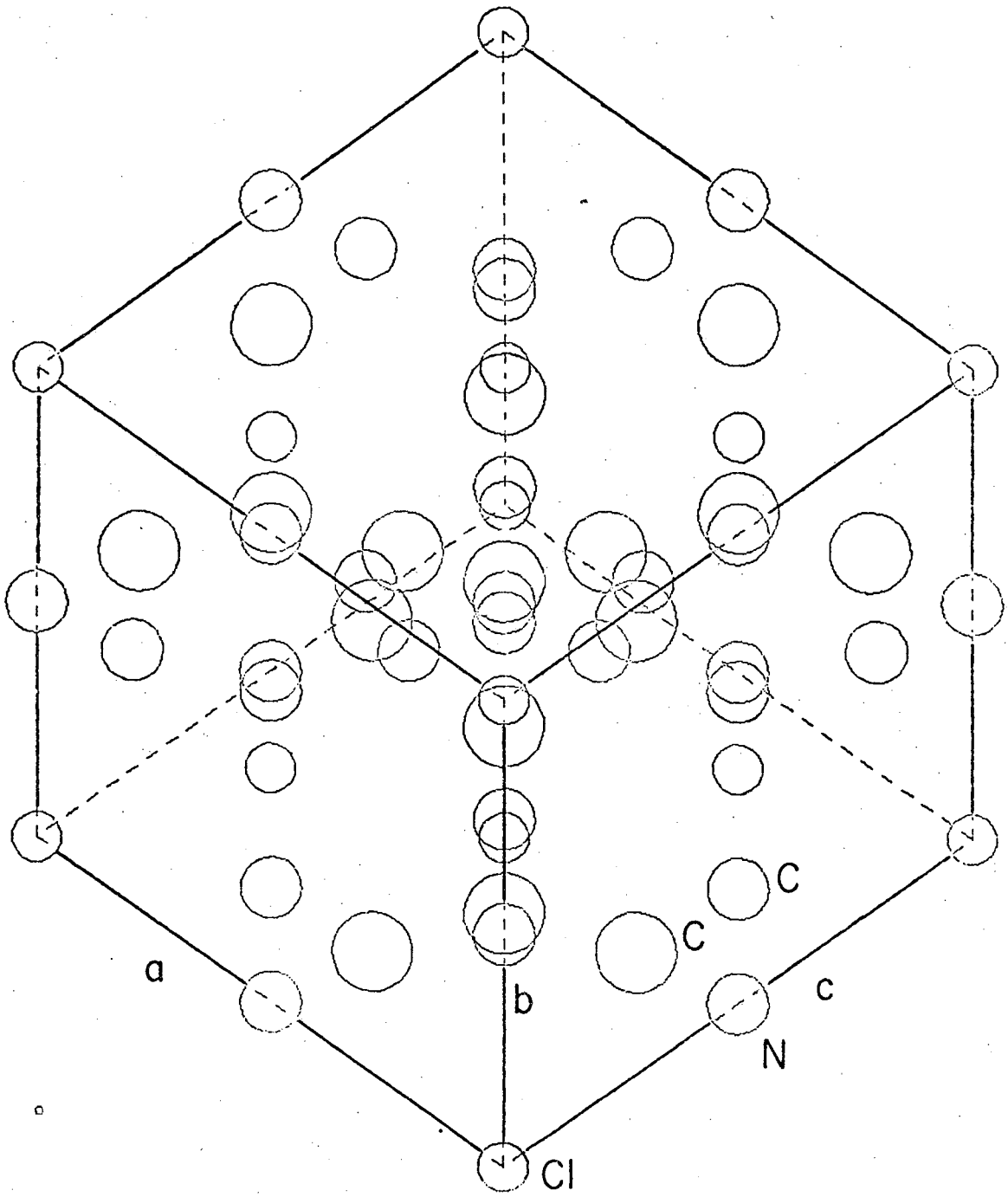
Fig. 1



XBL 774 - 4355

Fig. 2



XBL 774 - 4354

Fig. 3

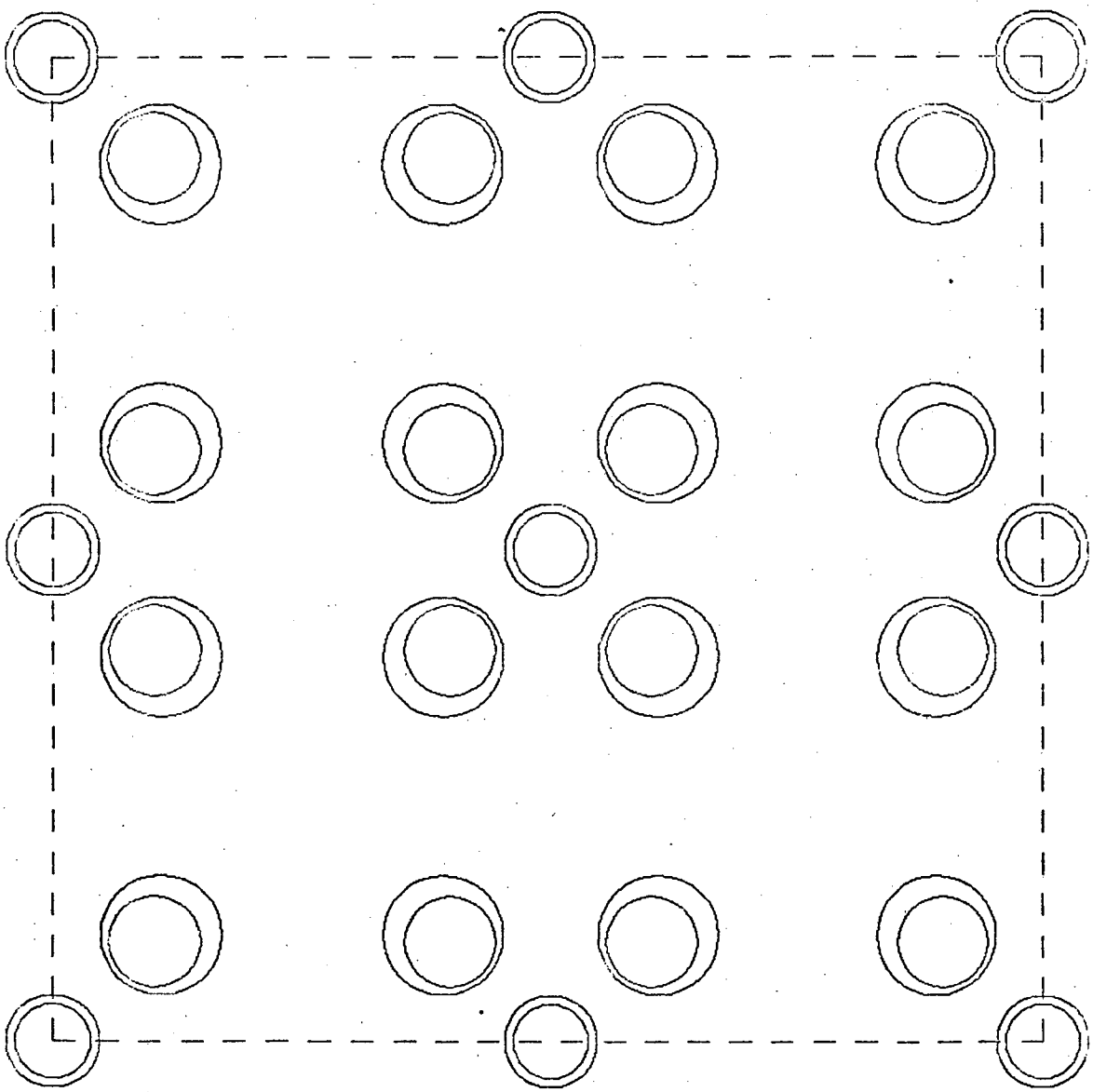


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Fig. 4

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