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STRUCTURE OF DIVALENT ADENINE ION PROTONATED AT N(1) AND N(7)

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An X-ray study on the structure of adenine dihydrochloride has revealed that the base ions are protonated at N(1) and N(7). As a result of the protonation at N(7), the geometry of the imidazole ring differs significantly from those observed in neutral and N(1)-monoprotonated bases.

A series of X-ray studies on salts and metal complexes of nucleic acid bases was initiated in order to know the detailed structural change of base molecules in different environments. This paper presents a preliminary account of the structure of divalent adenine ion found in the crystals of adenine dihydrochloride.

Single crystals of adenine dihydrochloride, $C_5H_7N_5Cl_2$, were obtained by slow evaporation of a solution of adenine in concentrated hydrochloric acid in an ice box. At room temperature, on the contrary, adenine crystallized most easily as monohydrochloride hemihydrate. The crystals of dihydrochloride are orthorhombic, space group $Pna2_1$ or **Pnam** with four molecules in a unit cell of dimensions a= 13.461(10), b=9.382(8), c=6.649(12) Å. Intensity data were collected on a diffractometer of an equi-inclination type, around the c-axis up to the 8th layer. About 570 independent reflections were used for structure determination which had intensity larger than 3σ.

A Patterson map indicated that all atoms should lie at least nearly on planes z=1/4 or 3/4, corresponding to the space group Pnam. The positions of hydrogen atoms were found on difference Fourier maps. Least-squares refinements were made for both of the space groups Pnam and $Pna2_1$ to "R"-values of 0.045 and 0.043 respectively. In the non-centrosymmetric space group $Pna2_1$, the z-parameters of the non-hydrogen atoms were shifted slightly from 1/4 (or 3/4). At the present stage, the final conclusion cannot be drawn about the choice of the correct space group. However, all the corresponding positional parameters derived from the two space groups completely coincided with each other within their standard deviations, except for the z-parameters of chlorine atoms (in $Pna2_1$, $z \cong 0.246(2)$ and 0.254(2) for Cl(1) and Cl(2) respectively).

It has been established that the crystal consists of divalent adenine ions protonated at N(1) and N(7), and chloride anions. A number of X-ray analyses of crystals containing monovalent adenine ions, as well as of nucleosides, nucleo-

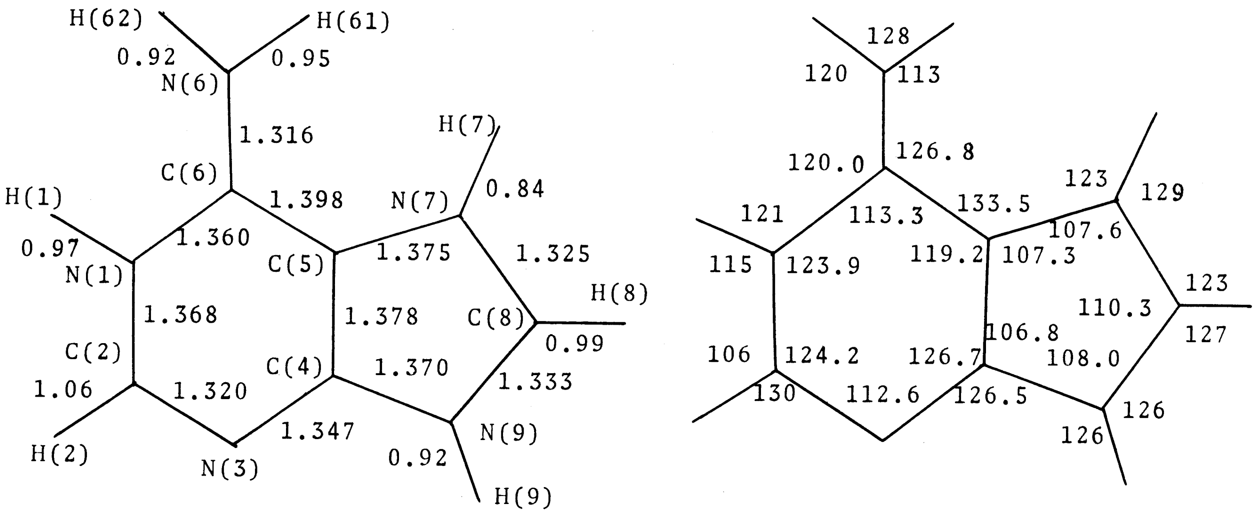
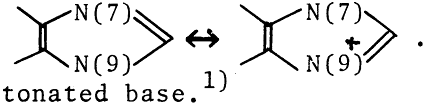


Fig. 1. Bond distances and angles (Å, deg.). Esd's: 0.008 Å, 0.5° for those not involving hydrogen atoms; 0.06 Å, 4° for those involving hydrogen atoms; and 6° for the angle H(61)-N(6)-H(62).

tides and metal complexes having adenine residue, have revealed that adenine is most easily protonated at N(1). N(7)-protonated adenine ligand has been observed in $[Cu_2(AdeH)_4(H_2O)_2]^{--}$ ion.[1] As far as the author is aware, the present result is the first conclusive X-ray evidence for the existence of divalent adenine ions in solid state. In connection with this it should be noticed that 9-methyladenine was presumed, on the basis of a two-dimensional analysis, to be protonated at N(1) and N(7) in the crystals of its dihydrobromide.[2]

The bond distances and angles obtained for the space group Pnam are shown in Fig. 1. Those obtained for $Pna2_1$ are in agreement with these values within standard deviations. The dimensions within the six-membered ring well agree with those in N(1)-protonated adenine residue, as in adenosine hydrochloride.[3] The geometry of the imidazole ring, on the other hand, differs significantly from those in neutral and N(1)-monoprotonated bases. The protonation at N(7) has an effect especially on distances N(7)-C(8) and N(9)-C(8), and also on angles C(4)C(5)N(7), C(5)N(7)C(8), C(4)N(9)C(8) and N(7)C(8)N(9); which are generally around 1.31 and 1.37 Å, and 111, 104, 106 and 114° respectively.[3,4] The introduction of the H(7) atom results in an appearance of an approximate symmetry C_{2v} in the geometry of the imidazole moiety, showing the resonance forms such as . A similar tendency has been observed in other N(7)-protonated base.[1]

All the hydrogen atoms attached to nitrogen atoms take part in hydrogen bonds of N-H...N or N-H...Cl type. Further refinement is now going on. The detailed molecular and crystal structure will be discussed elsewhere.

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