The Crystal Structure of Spermine Phosphate Hexahydrate

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Recently, many interesting findings have been reported concerning the effect of spermine on various enzyme activities and on the relationship of this amine to nucleic acids and to problems of membrane stability.[1] Much of the evidence is indirect, but the data definitely indicate that spermine and nucleic acids have a strong affinity for each other.[2-4] The analysis of the crystal structure of spermine phosphate hexahydrate was, therefore, undertaken to provide information on the binding relation of this amine to phosphoric acid and water.

The unit cell dimensions were found to be: $a=7.95_5$, $b=23.21_6$, $c=6.87_0$ Å, and $\beta=113°39'$. The space group is $P2_1/a$. Density measurements indicated that two units of $C_{10}H_{26}N_4 \cdot 2H_3PO_4 \cdot 6H_2O$ are contained in a cell. The structure was solved by analysis of a three-dimensional sharpened Patterson function and was refined by the Fourier and least-squares methods. The final reliability factor for the 1747 non zero (*hkl*) data was 0.127.

From a consideration of the arrangement of hydrogen bonds and the bond lengths of the phosphate group, it has been concluded that the chemical formula of this compound can be written as $NH_3^+(CH_2)_3NH_2^+(CH_2)_4NH_2^+ \cdot (CH_2)_3NH_3^+ \cdot 2HPO_4^{2-} \cdot 6H_2O$. Two views of the structure, along the b- and c-axes, are shown in Figs. 1 and 2 respectively. The structure consists of parallel sheets of spermine molecules separated by a sheet of phosphate ions and water molecules. These two kinds of sheets are stacked alternatively parallel to the (001) plane and are held together by N–H···O hydrogen bonds. The latter sheet has the composition $HPO_4^{2-} \cdot 3H_2O$, containing hydrogen-bonded chains of phosphate ions, $\cdots O_2\text{–}P\text{–}O_4\text{–}H\cdots O_2\text{–}P\text{–}O_4\text{–}H\cdots$, running along the a-axis. As Fig. 2 shows, adjoining chains in the sheet are arranged antiparallel and are sparated by the distance $b/2=11.6$ Å. The water molecules form a hexagonal network of hydrogen bonds and fill up the spaces between the chains. In the molecular sheets of spermine, the molecules are tilted at about 33° from the a-axis and are arranged in parallel, keeping van der Waals distances, with adjacent molecules in the a-direction. Adjacent molecules in the b-direction are oppositely inclined and form a planar herring-bone arrangement with the spermine molecules. Along the backbones run the phosphate chains. Because of this tilting, the amino and imino nitrogen atoms on one side of a molecule are linked to the same phosphate chain. It is to be noted that of the ten such N–H···O hydrogen bonds, only two are those to the water molecules. All of the rest link the molecule strongly to the phosphate ions.

As for the arrangement of phosphate groups, we noticed a certain similarity between that found in crystalline DNA and that in spermine phosphate. Langridge et al.[5] have shown the arrangement of phosphate groups along the polynucleotide helices in the B-form of LiDNA (Figs. 13 and 14 in their paper). In this structure, two oxygen atoms O2 and O3 of a phosphate group which share one negative formal charge turned outwards and are readily available for interaction with proteins, water, etc. The distance between the O3 oxygen atoms of the successive phosphate groups along the helix is about 7.3 Å, which may be compared

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2) S. Razin and R. Rozansky, *Arch. Biochem. Biophys.*, **81**, 36 (1959).
3) H. Tabor, *Biochemistry*, **1**, 496 (1962).
4) D. Kaiser, H. Tabor and C. W. Tabor, *J. Mol. Biol.*, **6**, 141 (1963).
5) R. Langridge, D. A. Marvin, W. E. Seeds, H. R. Wilson, C. W. Hooper, M. H. F. Wilkins and L. D. Hamilton, ibid., **2**, 38 (1960).

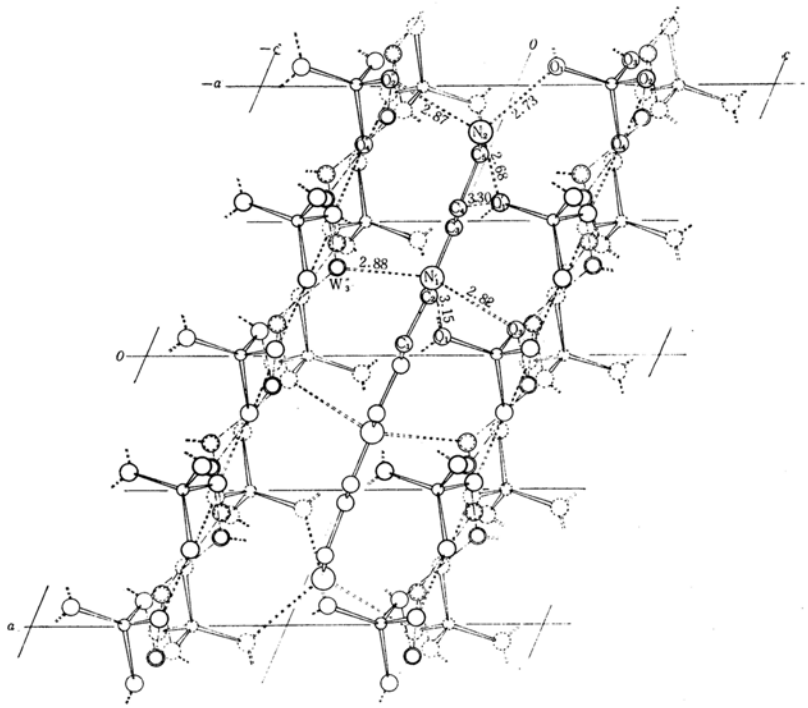

Fig. 1. Projection of the structure along the b-axis. Hydrogen bonds are indicated by double broken lines and by single chain lines. The water oxygen atoms are indicated by double circles. The atoms of the lower phosphate chains are indicated by broken circles. Only one spermine molecule is shown.

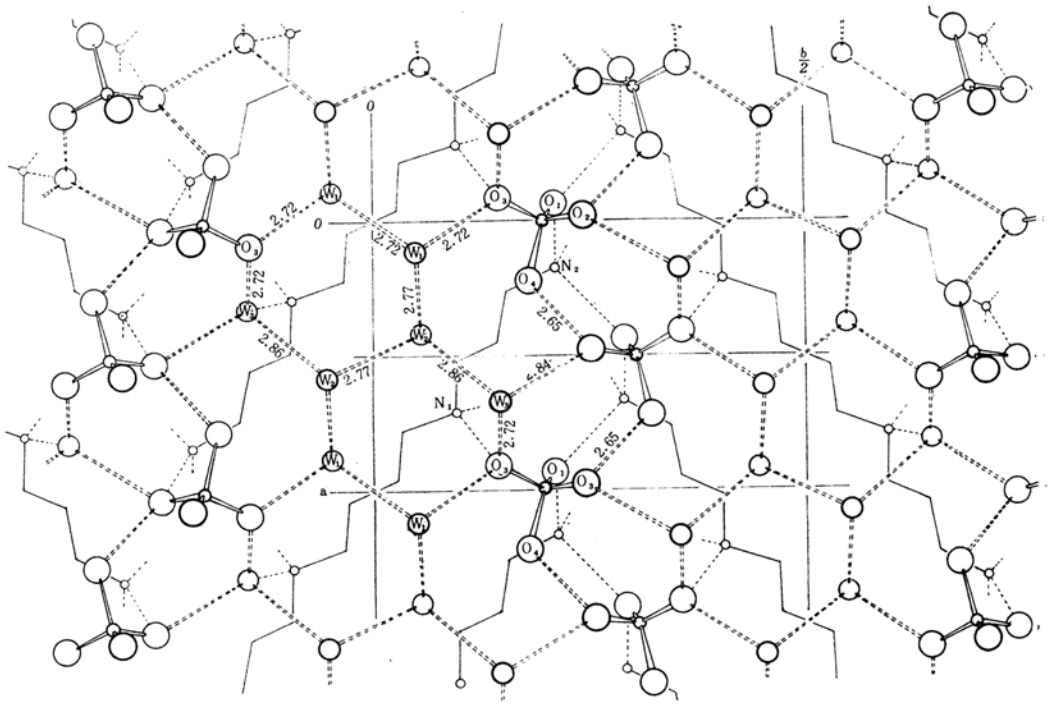

Fig. 2. Projection of the structure along the c-axis. The networks of hydrogen bonding within the phosphate-water sheet are shown. Hydrogen bonds from the spermine molecules are indicated by single broken lines.

with the a-translation period of 7.96 Å along the phosphate chains in spermine phosphate. The perpendicular distance between two nucleotide chains (chains A and B of the same molecule, measured across the shallow) in LiDNA is about 13 Å, while in the latter structure the separation of the phosphate chains within the same sheet is found to be about 11.6 Å.

Full details will be published later.

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