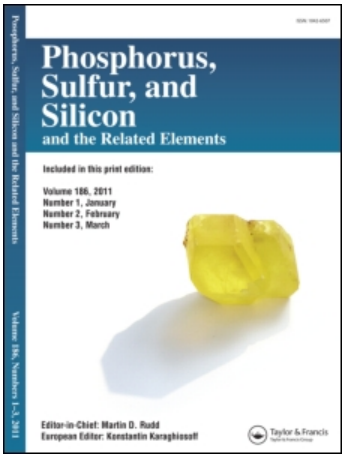

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Hydrogen bonded phosphate structures

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HYDROGEN BONDED PHOSPHATE STRUCTURES

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Abstract Some phosphate esters form structures containing infinite chains of hydrogen bonded units, others form discrete dimeric units, and still others form columns or chains of dimeric units. We have formed unique hydrogen bonded phosphorus ester systems which incorporate catechol molecules of crystallization, $[HOC_6H_4OP(Ph)O_2][PPh_4]\cdot$catechol, 1, and $[HOC_6H_4OP(Ph)O_2][C_5H_5NH]\cdot$catechol, 2. X-ray analysis shows a chain arrangement in 1 and dimeric phosphonate units in a chain structure for 2. By comparing our results with literature examples, a classification of hydrogen bonding in phosphates results which proves useful in interpreting orientational influences at enzyme active sites.

INTRODUCTION

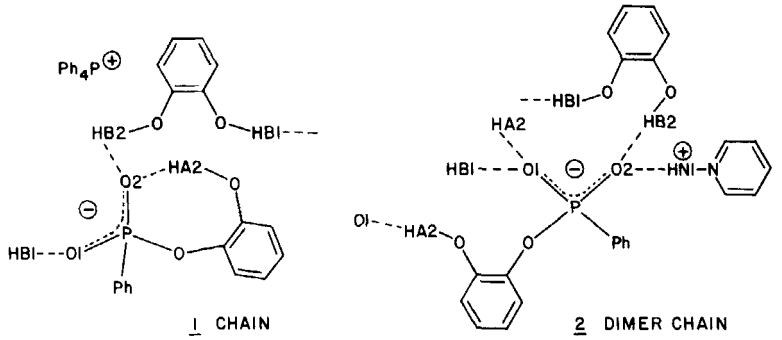
In modeling phosphoryl transfer enzyme reactions, it is necessary to incorporate hydrogen bonding between the phosphorus containing substrate and active site residues. The basis for estimating the magnitude of these terms and the conformational changes that are likely to occur as the reaction proceeds is usually limited. Our success in modeling ribonuclease action on uridylyl-(3'-5')-adenosine[1] was directly dependent on the inclusion of structural parameters into the modeling programs[2] based on earlier studies dealing with the structural determination of simpler tetra- and pentacoordinated phosphorus compounds.[3] The first step of action of this enzyme leading to a cyclic intermediate has limited phosphate-hydrogen bonding.[4] In staphylococcal nuclease, a system in which we are currently interested,[5,6] hydrogen bonding is more extensive.[7]

We wish to explore hydrogen bonding to model phosphate substrates that will allow an understanding of structural changes as the system becomes more complex. Examples from the literature[8-11] reveal phosphonate structures containing a variety of hydrogen bonding arrangements in simple chains, discrete dimeric units, and columns or chains of dimeric units. In some of these,

the hydrogen bonding takes place between phosphate units, while in others, a cationic base portion is interposed between phosphates.

RESULTS

We have prepared two unique hydrogen bonded phosphonate ester systems which incorporate catechol molecules that in one case isolate the phosphonate ester units from each other, $[(HOC_6H_4O)P(Ph)O_2][PPh_4]\cdot C_6H_4(OH)_2$, 1, and in the other, $[(HOC_6H_4O)P(Ph)O_2][C_5H_5NH]\cdot C_6H_4(OH)_2$, 2, isolate dimeric phosphonates from each other.



1 CHAIN 2 DIMER CHAIN

In 1, there is an intraanionic hydrogen bond between the hydroxyl hydrogen atom, HA2, and a phosphonyl oxygen atom, O2, resulting in the formation of a seven-membered ring. The catechol moieties lie between translationally related anions forming infinite hydrogen bonded chains in which each of the catechol hydrogen atoms is hydrogen bonded to a different phosphonyl oxygen atom of the anions. The hydrogen bond lengths are HA2---O2 = 1.56(9)Å, HB1---O1 = 1.71(6)Å, and HB2---O2 = 1.59(6)Å, as compared to the van der Waal's sum of 2.6Å.

In 2, inversion related anions form dimeric hydrogen bonded units (HA2---O1 = 1.89(6)Å). Via hydrogen bonding, an inversion related pair of catechol molecules connects translationally related dimeric units (HB1---O1 = 1.69(6)Å, HB2---O2 = 1.99(6)Å), forming an infinite, doubly hydrogen bonded, zigzag chain to which the pyridinium ions are hydrogen bonded (HN1---O2 = 1.56(6)Å).

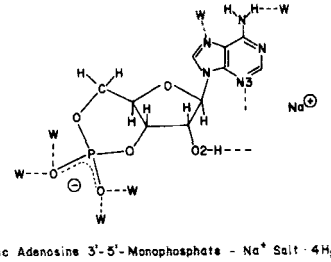
It is seen that 2 utilizes both phosphoryl oxygen atoms in forming two hydrogen bonds each while in 1 only one of the phosphoryl oxygen atoms is so utilized. In 2, the replacement of the Ph_4P^+ cation by the pyridinium ion with its hydrogen bonding

capability disallows the formation of an intramolecular hydrogen bonded ring system as in 1. This releases the attached catechol moiety in 2 which logically leads to the dimerization of phosphorus ester units via the released catechol hydroxyl group. The latter group hydrogen bonds to the phosphoryl bond of the second phosphonate making up the dimer. This additional hydrogen bonding made possible in 2 accounts for the presence of two hydrogen bonds per phosphoryl group in this case.

DISCUSSION

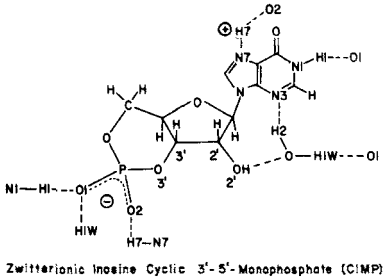
It is apparent from this study that the hydrogen bonded structures examined may be placed on a systematic basis regarding the number and types of interactions in relation to their resultant structures. In the more complicated hydrogen bonded nucleotide formulation 3,[10] a dimer is formed via N3---H——O2 hydrogen bonds. The authors[10] claim the dimer formulation is surprising. Relative to 4,[11] the result is expected. Similar to our observance that the pyridinium ion in 2 replaces the intramolecular hydrogen bonded ring in 1 and leads to the dimerization of 2, the water molecule present in 4 hydrogen bonds to the hydroxyl and amine functions that are involved in forming the dimeric units in 3.

The phosphoryl hydrogen bonds show a general correlation with the acidity of the proton that is involved. For the P=O---H——O



Cyclic Adenosine 3'-5'-Monophosphate - Na^+ Salt · $4H_2O$

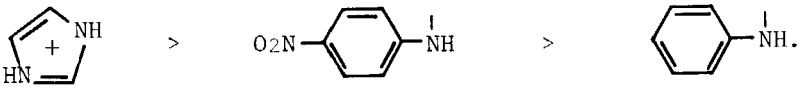
3 dimer



Zwitterionic Inosine Cyclic 3'-5'-Monophosphate (CIMP)

4 polymer network

hydrogen bonds, the O-O lengths increase with decreasing proton acidity in the order: $\overset{\circ}{-}CO_2H$ > PhOH > H_2O. The length changes from about 2.6Å to 2.9Å. In the related system, P=O---H——N, the O-N hydrogen bond lengths increase in the order: N_7-H^+ (of inosine) > imidazolium protons,



The lengths range from about 2.5Å to 2.85Å.

It is now possible to associate different hydrogen bond lengths to the variety of hydrogen bonds formed between phosphate substrates and active site residues. Using a bond length correlation, strengths of these interactions and their influence on substrate geometry may be estimated. With this basis, a more detailed mechanistic interpretation of the course of an enzymatic reaction should result.

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