



Structural studies of cyclic organic phosphorus compounds
by Duane Douglas Swank

A thesis submitted to the Graduate Faculty in partial fulfillment of the requirements for the degree of DOCTOR OF PHILOSOPHY in Chemistry
Montana State University
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Abstract:

Using the Patterson synthesis and the "Symbolic Addition Procedure" the structures of three cyclic organic compounds of phosphorus were solved by x-ray diffraction.

Acetonediol cyclophosphate crystallizes in space group $P2_1/n$ with $a = 7.755\text{\AA}$, $b = 9.446\text{\AA}$, $c = 10.345\text{\AA}$, $\beta = 99.65^\circ$. The ring system is planar and the methoxy group lies directly above the ring with the carbon atom centered between the two ring oxygens. There appears to be some electron delocalization around the double bond. The O-P-O ring angle is 97.3° thus allowing for the formation of a trigonal-bipyramidal intermediate.

$P_3O_3(C_6H_5)_4(C_6H_4Br)C_5H_2$ crystallizes in space group $P2_1/C$ $a = 9.432\text{\AA}$, $b = 15.854$, $c = 19.094\text{\AA}$, $\beta = 102.01^\circ$. The five-membered ring is planar and the trigonal bipyramid is little distorted. The more electronegative atoms occupy axial positions, while the carbon atoms occupy the equatorial positions. The yellow color is apparently due to the conjugation in the 1,4-diphenyl butadiene portion of the molecule.

2,3,4-trimethylpentane-2,4-phosphinic acid monohydrate crystallizes in space group $C2/c$ with $a = 13.251\text{\AA}$, $b = 6.511\text{\AA}$, $c = 26.387\text{\AA}$, $\beta = 101.46^\circ$. The four-membered ring is slightly bent to form a very shallow V and is very highly strained. The phosphoryl oxygen is hydrogen bound to a water molecule across the two-fold screw axis and to the screw related water.

The screw related water is also hydrogen bound to the hydroxyl group of the phosphinic acid. This hydrogen bonding forms a network of zig-zag chains in the y-direction of the unit cell.

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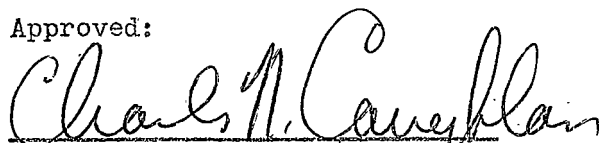
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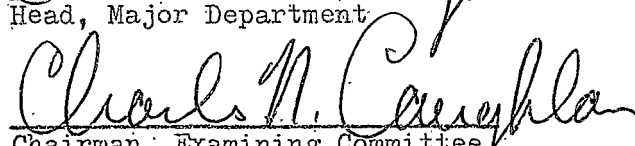
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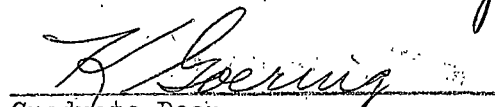
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ABSTRACT

Using the Patterson synthesis and the "Symbolic Addition Procedure" the structures of three cyclic organic compounds of phosphorus were solved by x-ray diffraction.

Acetionenediol cyclophosphate crystallizes in space group $P2_1/n$ with $a = 7.755\text{\AA}$, $b = 9.446\text{\AA}$, $c = 10.345\text{\AA}$, $\beta = 99.65^\circ$. The ring system is planar and the methoxy group lies directly above the ring with the carbon atom centered between the two ring oxygens. There appears to be some electron delocalization around the double bond. The O-P-O ring angle is 97.3° thus allowing for the formation of a trigonal-bipyramidal intermediate.

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INTRODUCTION

In 1905, Harden and Young demonstrated the dependence of alcoholic fermentation on the presence of inorganic phosphates. Since that time, biochemical research has revealed an amazing dependence of most biological systems on organic phosphates.

Dialkyl phosphate groups are the structural units in deoxyribonucleic acids (DNA) and ribonucleic acids (RNA). The hydrolysis of the latter material under alkaline conditions proceeds through an intermediate which is formulated as a five-membered cyclic phosphate. This cyclization involves the neighboring hydroxyl group on the 2' position of the ribose ring and results in the cleavage of the phosphorus-oxygen bond attached to the 5' carbon of the ribose of the next nucleotide moiety (1). This is illustrated in Figure 1. Subsequent reactions of the cyclic esters with water produce a mixture of 2' and 3' phosphates. The cyclic esters are very reactive (42,43,44), in contrast to dialkyl phosphates and it is, therefore, instructive to investigate some of the simple cyclic phosphates. Previous to this work, the structures of two five-membered cyclic phosphates have been determined (2,3). The main conclusion of these investigations is that the rapid rate of hydrolysis of the five-membered cyclic phosphates compared to the open chain analogs is due primarily to the strain in the cyclic esters (58). This conclusion was subject to question when it was discovered that the acid-catalyzed hydrolysis of ethylene hydrogen phosphate in water enriched with O^{18} was accompanied by exchange of heavy oxygen into the unreacted ester (4). The exchange reaction was accelerated just as the hydrolysis was in the presence of a five-membered

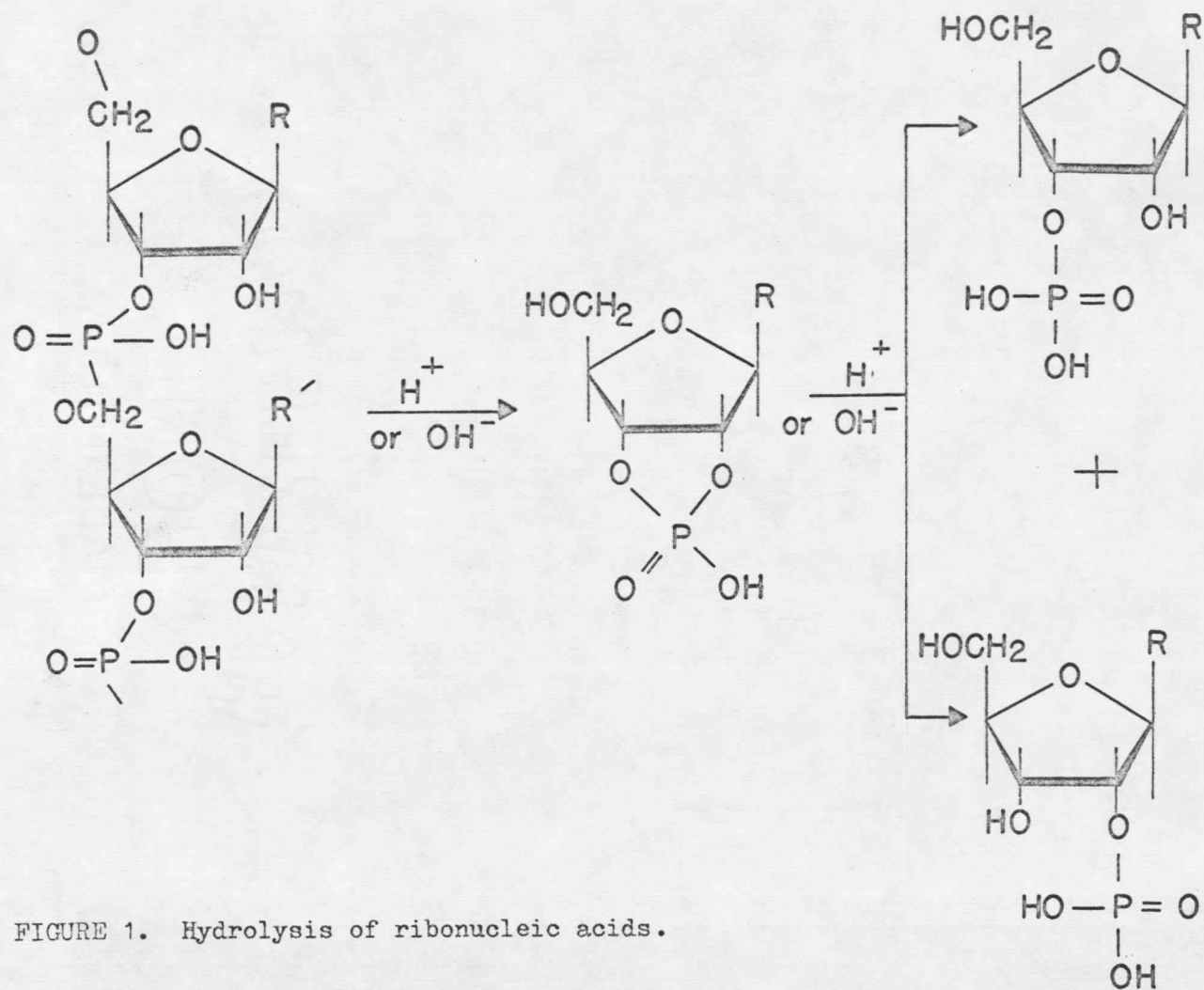


FIGURE 1. Hydrolysis of ribonucleic acids.

ring. Both of the structures reported were saturated rings and, therefore, it was of great interest to see if an unsaturated five-membered cyclic phosphate would exhibit the same properties in regards to the hydrolysis as the saturated systems. The structure of acetonediol cyclophosphate was, therefore, undertaken in hopes of obtaining more information about the hydrolysis of five-membered cyclic phosphates.

With the discovery of the O^{18} exchange phenomena thus leading to the conclusion that strain alone would not answer the question of the rapid hydrolysis, it was postulated that the hydrolysis of five-membered cyclic phosphates proceeded via intermediates with pentacoordinated phosphorus (5). This conclusion was based on certain considerations dealing with the phenomenon of pseudo-rotation in the trigonal-bipyramidal structure of the pentaoxyphosphoranes (45). Pseudo-rotation for trigonal bipyramids can be understood as being the intramolecular process whereby the molecule is transformed by deforming bond angles in such a way that it appears to have been rotated 90° about one of the interatomic bonds.

The ring opening hydrolysis does not require pseudo-rotation since it proceeds through an intermediate which resembles that of an S_N2 process.

The structure of a five-membered cyclic pentaoxyphosphorane was recently established by x-ray studies (6,7,8). The unsaturated five-membered ring occupies an apical-equatorial position in a trigonal bipyramid just as Haake and Westheimer (4) had postulated for the transition state in the acid-catalyzed hydrolysis of ethylene hydrogen phosphate where the ring is saturated. It seems reasonable that (a) if a five-membered cyclic phosphate ester is strained relative to an open chain

phosphate ester or an unstrained cyclic phosphate and (b) if the penta-oxyphosphorane which is derived by addition of water or another nucleophile to the phosphorus is less strained when it has a five-membered ring than when it lacks it, due to intramolecular crowding in the trigonal bipyramid (6,7,8), the hydrolysis of cyclic phosphotriesters (24) and cyclic phosphodiester could occur by the phosphoryl addition mechanism, at least under certain experimental conditions. This view has been recently expressed by several investigators (5,25,26,27,28). The mechanism is given in Figure 2.

This mechanism allows for (a) a path where the ring is apical-equatorial, (b) a ring angle of 90° , for intermediates leading to ring opening or hydrolysis external to the ring, and (c) a mechanism consistent with the principle of microscopic reversibility. The mechanism also allows the ring to occupy one apical position, while one group enters and another leaves from the second apical position.

Since the pentacoordinated complexes that have been determined were all pentaoxyphosphoranes, it was of interest to look at a complex with fewer oxygens attached to the phosphorus. The complex studied was $\text{PO}_3(\text{C}_6\text{H}_5)_4(\text{C}_6\text{H}_4\text{Br})\text{C}_5\text{H}_2$, a heterocyclic fused five- and six-membered ring system with two P-O oxygens. This would be a test case for two postulates, first that the more electronegative atoms should be found in the axial positions and, secondly, the five-membered ring should occupy the apical-equatorial position with the oxygens in the apical position. If this is true then the rings would both be apical-equatorial, fused at the equatorial carbon. If both oxygens are not apical then the six-membered ring

