of $HClO_4$ for $NaClO_4$. For the general reaction between two molecules, the measured rate constant can be related to activity coefficients by $k_2 = k_0(\gamma_A\gamma_B/\gamma_{\pm})$.[12] Assuming that the transition state is nonionic and that $\gamma_{\pm}$ approximates the activity coefficient of the alcohol leads to the relation that $k_2 = k_0\gamma_{Br_2}$. It is easily shown that the ratio of the experimentally determined distribution coefficients yields the ratio of the activity coefficients of Br_2 for the two salt solutions, 3.0 *M* $NaClO_4$ and 2.32 *M* $HClO_4$–0.68 *M* $NaClO_4$. This ratio is 1.55. The ratio of the rate constants for these solutions is 1.63. In view of both the assumptions and uncertainties involved, the two ratios are essentially the same, implying that the major factor determining the reduction in the second-order rate constant with increasing acidity is the effect of the change in medium on the activity coefficient of Br_2. While the activity coefficient of a nonpolar solute as a function of ionic strength can frequently be described by $\log \gamma = k_s\mu$,[13] the situation in mixed electrolyte solutions of constant ionic strength as a function of composition is less clear and quantitative. It is clear that if μ is constant and the k_s values for the electrolytes being considered are reasonably close, little effect will be observed upon the activity coefficient with replacement of one electrolyte for another. However, substantial differences in k_s values will materially alter the activity coefficient as one electrolyte is substituted for the other, and that at constant total ionic strength $\log \gamma$ may be approximately linear in the concentration of the electrolyte which is being substituted. The plot of $\log k_2'$ *vs.* $[HClO_4]$ shown in Figure 4b is linear and consistent with previously reported differences in the effect of $HClO_4$ and $NaClO_4$ on the activity coefficient of benzene.[14] On the basis of the results presented here, there would seem to be no necessity for the postulation of protonated 2-propanol and the effects observed can be described adequately by an activity coefficient effect.

While the uncertainties in the rate constants and the limited temperature range make meaningful calculations of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ impossible, $\Delta H^{\ddagger}$ can be crudely estimated as approximately 18 kcal and $\Delta S^{\ddagger} \cong -8$ eu in 3.0 *M* $NaClO_4$ solutions.

---

(12) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, Wiley, New York, N. Y., 1961, p 132.

(13) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," 3rd ed, Reinhold, New York, N. Y., 1958, p 532.

(14) W. F. McDevit and F. A. Long (*J. Amer. Chem. Soc.*, 74, 1774 (1952)) report from studies of the solubility of benzene in $NaClO_4$ solutions and $HClO_4$ solutions values of k_s of +0.119 and −0.041, respectively.

Interaction of Acylating Agents and Phosphorus(III) Sources. I. Intermediacy of Condensed Species in the Formation of Ethane-1-hydroxy-1,1-diphosphonic Acid

J. B. Prentice, O. T. Quimby, R. J. Grabenstetter, and D. Allan Nicholson*

Contribution from the Procter and Gamble Company, Miami Valley Laboratories, Cincinnati, Ohio 45239. *Received February 10, 1972*

Abstract: This work determines the main sequence of intermediates formed when acetylating agents react with phosphorus(III) compounds under anhydrous conditions. The capacity of the reactants to scavenge water is shown to be the driving force for such reactions. Under anhydrous conditions, the initial products are condensates; *i.e.*, two or more molecules of ethane-1-hydroxy-1,1-diphosphonic acid condensed *via* the removal of water. Five such condensates have been isolated and characterized. The existence of three others is inferred from ^{31}P nmr data. Three of the isolated condensates have been shown to be involved in the complex rearrangements which occur during reaction of acetyl groups and phosphorus(III) species. Interconversions among the isolated condensates are discussed. The condensed intermediates are quantitatively converted to $CH_3C(OH)(PO_3H_2)_2$ upon heating in water. One condensate not observed is the cyclic dimer containing a $\underline{\mathrm{C{-}O{-}P{-}C{-}O{-}P}}$ ring. This is thought to be due to the instability of such a diester relative to the C–O–C and P–O–P bonded condensates.

Chemistry is seldom as simple as it seems at first sight. A prime example of this is the preparation of ethane-1-hydroxy-1,1-diphosphonic acid (EHDP) from acetylating agents and phosphorus(III) sources. EHDP and its salts have been known since the classic studies of von Baeyer and Hofmann,[1] who correctly represented the structure of the acid as $CH_3C(OH)(PO_3H_2)_2$, calling it "acetodiphosphorous acid." The metal binding ability of EHDP, suggested by the studies of von Baeyer and Hofmann, has encouraged a closer examination of its preparation[2] and properties.[3]

Recently papers[4,5] have appeared describing cyclic condensates isolated from the reaction of acetylating agents with phosphorous acid, the usual reagents for EHDP synthesis. This prompts us to report our ex-

---

(1) H. von Baeyer and K. A. Hofmann, *Ber.*, 30, 1973 (1897).

(2) (a) Henkel et Cie., Belgian Patents 619,619; 619,620; 619,621 (1962); (b) Albright and Wilson, Belgian Patent 672,168 (1966); (c) Procter and Gamble, U. S. Patents 3,366,675; 3,366,677; 3,400,147 (1968); Canadian Patents 770,173; 777,198 (1968); Monsanto, French Patents 1,521,961; 1,521,962; 1,521,963 (1968); and others.

(3) (a) Henkel et Cie., Belgian Patent 579,012 (1959); (b) *ibid.*, 591,066 (1960); (c) Procter and Gamble, U. S. Patent 3,159,581 (1964); and others.

(4) (a) B. Blaser, K.-H. Worms, H.-G. Germscheid, and K. Wollmann, *Z. Anorg. Allg. Chem.*, **381**, 247 (1970); (b) G. Brun and C. Blanchard, *C. R. Acad. Sci., Ser. C*, 272 (1970); *Chem. Abstr.*, **75**, 110372d (1971).

(5) Procter and Gamble U. S. Patents, 3,387,024; 3,400,151; 3,400,149 (1968); 3,621,081 (1971).

Table I. Phosphorus and Proton Nmr Data for EHDP and Its Condensates

		Phosphorus nmr spectra[b]				Proton nmr spectra[c]			
			multiplicity				multiplicity		
Compd	Cations	δ, ppm	No.	J_{PH}, Hz	% of P	τ′, ppm	No.	J_{HP}, Hz	% of CH_3
EHDP	H_4	−19.8	4	16.2	100	8.2	3	16.4	100
	H_2Na_2	−18.8	4	14.4	100	8.0	3		100
	HNa_3	−20.0	4	14.5	100	8.2	3	14.6	100
II[a]	H_4	−15.8			100	7.35	1		50
						7.65	3	15.5	50
	H_2Na_2	−14.8	4	14.1	100	7.33	1		50
						7.67	3	14.5	50
	HNa_3	−15	4	14	100	7.99	1		50
						8.42	3	14.6	50
	Na_4	−16.0	4	13		7.37	1		50
						7.75	3	13.0	50
IV[d]	Na_4	−5.5	5?	∼7	100	7.33	1		50
						7.57	5?	∼9	50
V[d]	Na_4	−12.0	6?	∼8[e]	100	7.40	M	15.5	100
III	H_6	−15.8	Complex		50	7.93	3?	15.2	100
		−5.2	Complex		50				
	H_2K_4	−16.1	Complex		50	8.0	3?	15.4	100
		−8.2	Complex		50				
	K_6	−13.5	Complex		Overlap	8.0	3?	13.8	100
		−11.3							
I[d]	1 Na-P	−16	Unresolved		100	Very broad unresolved peak			

[a] The roman numerals in the first column refer to the condensates of EHDP by the subdivision in which it was first described. [b] For phosphorus the chemical shifts (δ) are given in parts per million relative to 85% H_3PO_4 as external standard taken as zero without correction for difference in bulk diamagnetic susceptibility. [c] For hydrogen the chemical shifts (τ′) are given in parts per million relative to tetramethylsilane as external standard taken as 10.0 ppm without correction for the difference in bulk diamagnetic susceptibility. [d] Acids of these condensates are too readily hydrolyzed to allow nmr measurements on their aqueous solutions. [e] Dissimilar P atoms due to steric hindrance in V appear to cause a doubled quartet (six peaks), halving the true J_{H-P} (see ^1H nmr).

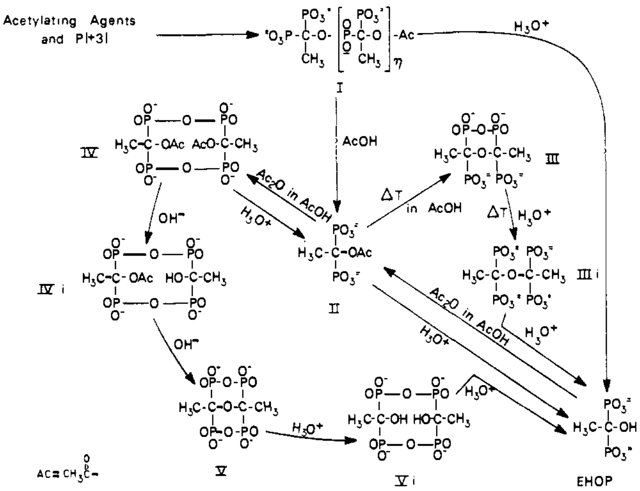


Figure 1. Formation of condensates.

tensive studies of the intermediates involved in the formation of EHDP.

Results

One can write a hypothetical reaction (eq 1) describing the formation of EHDP from acetic acid and 2 equiv of phosphorous acid.

$$CH_3COOH + 2HPO_3H_2 \longrightarrow CH_3C(OH)(PO_3H_2)_2 + H_2O \quad (1)$$

ing the formation of EHDP from acetic acid and 2 equiv of phosphorous acid. Experience has shown that this reaction does not occur. Partial replacement of phosphorous acid by phosphorus trichloride does, however, encourage the reaction to proceed in a few hours at 100–150°, as evidenced by the presence of EHDP when such a mixture is hydrolyzed.[2a] Alternatively, acetic acid can be replaced by acetyl chloride or acetic anhydride.[2c] In order to obtain EHDP, one of the reactants must contain a hydrolyzable linkage, *i.e.*, must react with water.

It appears as if the capacity of the reactants to scavenge water actually serves as a driving force for the reaction. Equation 1 suggests that the required water reactive site should be the equivalent of one hydrolyzable linkage per potential hydroxydiphosphonate unit. However, experience has shown that EHDP is obtained in but 50% yield under such conditions. To approach 100% conversion to EHDP even when 2 equiv of hydrolyzable linkage per potential EHDP are present requires a few hours of heating at 100–150°. When 2.5–3 equiv are present 1 hr or less of heating results in complete conversion.

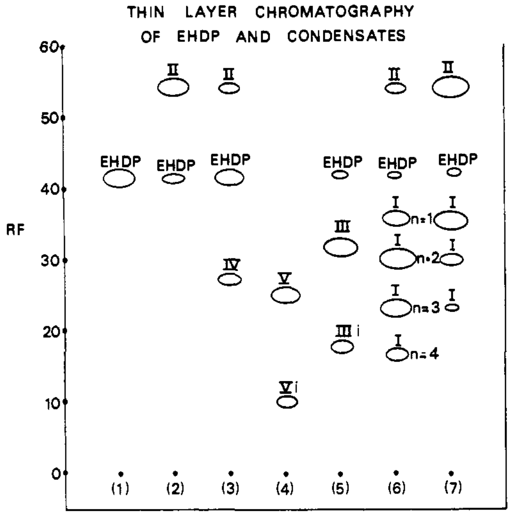
The products obtained under these highly anhydrous conditions are actually condensates, *i.e.*, two or more molecules of EHDP condensed *via* the removal of water. These condensates can be converted to EHDP by simply heating in water.

Figure 1 describes five condensates which have been isolated and positively identified in this work. The existence of three other condensates is inferred from ^{31}P nmr data. Three of the isolated condensates (I, II, and III) have been shown to be involved in the complex rearrangements which occur during reaction of acetyl groups and phosphorus(III) species.

Condensate I. In point of time this type of EHDP condensate was probably the first to be isolated as a solid product, for such a material was precipitated from a highly anhydrous liquid medium by Brooks,[6] who did not elucidate its structure. This polyester precipitates under a wide variety of conditions, but best at rather low temperatures (15–70°) when large amounts of acetic anhydride are combined with phosphorous

---

[6] B. T. Brooks, *J. Amer. Chem. Soc.*, **34**, 492 (1912).



Solvent: 5g Toluenesulfonic Acid: 150 cc H_2O : 150 cc Tetrahydrofuran : 200 cc n-butanol : 25cc Acetone

(1) EHDP acid (standard)
(2) Acetylated EHDP (II)
(3) Dimeric C-Acetylated Dianhydride (IV)
(4) Dimeric Ether Dianhydride (V)
(5) Dimeric Ether Monoanhydride (III)
(6) Chain Polyester (I)
(7) $Ac_2O + HPO_3H_2$ Reaction Mixture after 30 min. at 130°C.

Figure 2. Thin layer chromatography of EHDP and condensates.

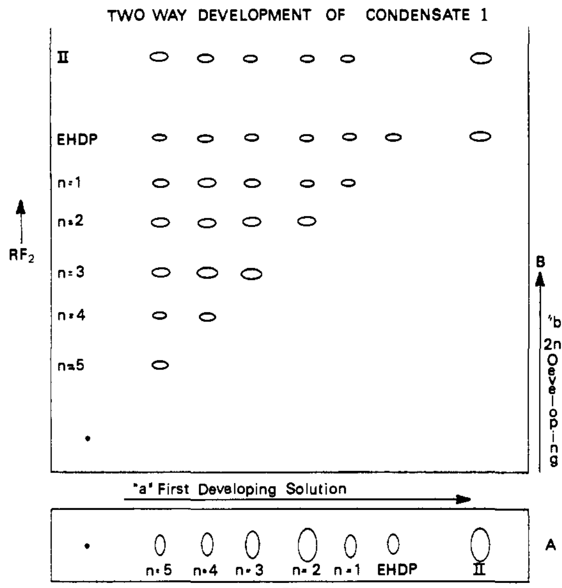
acid. When prepared at higher temperatures, it may also be contaminated with condensate III.

The ^{31}P nmr spectra of aqueous solutions of the sodium salt (Table I) show but one somewhat broadened peak (δ -16 ppm). Since this peak shows no clear resolution into a multiplet such as would be expected from the coupling of each P with the CH_3C protons, it is probable that the two kinds of phosphorus in the polyester have nearly the same chemical shift. This is likely since replacement of acid hydrogens by simple alkyls often has only a small or negligible effect on the position of the ^{31}P nmr peaks.[7] The ^1H nmr spectrum shows only a broad unresolved peak in the region where CH_3C resonances normally fall.

The average chain length, $\bar{n} + 1$, usually ranges from slightly above 2 to about 4. Thin layer chromatography (Figure 2, lane 6) reveals the presence of polymers of differing n value plus some EHDP. The largest polyester detected chromatographically had a chain length of six EHDP units. These values may be considered lower limits because the acid developer is known to cause some reduction in chain length.

The sequential hydrolysis of the chain polyester to shorter chains is shown quite dramatically by two-dimensional thin layer chromatography (Figure 3). Two aliquots of a solution of I were spotted on the lower left corner of a plate and developed as shown by arrow a. Section A was removed and visualized to show the distribution of species in the sample. Section B was dried, turned 90°, and developed a second time as shown by arrow b. The hydrolysis of the chain polyester during the second development was probably more severe than normal as the toluenesulfonic acid from the first developing solution was not removed before drying.

Condensate I can easily be converted to EHDP by heating in water. The polyester chain structure can,



Solvent: 5g Toluenesulfonic Acid: 150 cc H_2O: 150 cc Tetrahydrofuran : 200cc n-butanol : 25cc Acetone.

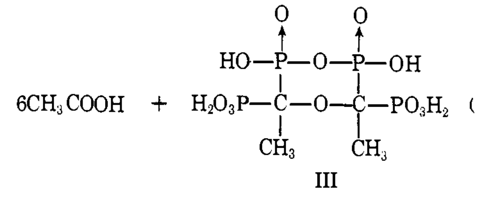
Figure 3. Two-way development of condensate I.

however, be stabilized by solution of the solid acid in sodium bicarbonate solution, taken in such amount that the final pH drops to about 5 (one acid hydrogen on each phosphonate group neutralized). The analytical sample was prepared in this manner followed by fractional precipitation of the sodium salt to remove C-acetylated EHDP (II).

Condensate II. With $n = 0$, I reduces to II. When condensate I is heated in acetic acid conversion to II is complete. Alternatively, EHDP acid can be treated with acetic anhydride or acetyl chloride to form the C-acetylated derivative. If an aqueous solution of the acid form of II is promptly neutralized to a pH of about 5, the resulting disodium salt, $CH_3(OCOCH_3)(PO_3HNa)_2$, is stable and can be isolated by fractional precipitation. It then analyzes in accord with the proposed formula. The nmr spectra (Table I) of this compound show one kind of phosphorus (quartet) and equal amounts of two kinds of methyl protons (singlet and triplet). Thin layer chromatography (Figure 2, lane 2) shows that this C-acetylated EHDP travels faster than EHDP or any other EHDP condensate; some degradation to EHDP during development of the chromatogram is again seen.

Condensate III. An equimolar mixture of acetic anhydride and phosphorous acid on prolonged heating at temperatures of 120–150° yields condensate III in accord with eq 2. The acetic acid which forms acts as a

$4(CH_3CO)_2O + 4HPO_3H_2 \longrightarrow$



$$6CH_3COOH + H_2O_3P-\underset{CH_3}{C}(-P(\overset{O}{\uparrow})(OH)-O-P(\overset{O}{\uparrow})(OH)-)-O-\underset{CH_3}{C}-PO_3H_2 \quad (2)$$

III

solvent from which III precipitates. It is probable that the low solubility of III directs the equilibrium. The solid acid is crystalline to X-rays.

---

[7] V. Mark, C. H. Dungan, M. M. Crutchfield, and J. R. Van Wazer, *Top. Phosphorus Chem.*, **5**, 227 (1967); phosphonate esters *vs.* phosphonic acids, pp 294–316.

The hexasodium salt of III has a rather low water solubility, and is easily purified by crystallization from water, so as to give analyses in accord with the Na_6 salt of the above acid. For nmr spectra the more soluble potassium salts or the free acid are desirable; any one of them shows equal amounts of two kinds of phosphorus and essentially one kind of methyl protons (roughly a triplet).

Double resonance experiments on the hexamethyl ester[8] of the above acid show unequivocally that the downfield phosphorus peak (Table I) is that for the dangling phosphonate groups (P coupled with six methoxy protons), while the upfield peak is for the phosphonate groups in the ring (P coupled with three methoxy protons); this accords with expectation from the formation of P–O–P anhydride links, which usually displaces the phosphorus resonance upfield by 5–10 ppm. The two kinds of phosphorus are coupled with each other and with the CH_3C protons, giving phosphorus peaks of greater multiplicity than 4.

Condensate III is easily the most stable of the isolated condensates of EHDP. Long boiling of 30% aqueous solutions, either at pH 7 (K_5H salt) or at pH 12 (K_6 salt + an extra mole of KOH), caused no detectable change in the ^{31}P or ^1H nmr spectra. A boiling 30% solution of the acid hydrolyzes slowly nearing completion in 48 hr. The P-containing product of complete hydrolysis is $CH_3C(OH)(PO_3H_2)_2$, but partial hydrolysis gives evidence of 15% or less of the ether intermediate IIIi, indicating that the P–O–P linkage breaks a little faster than the C–O–C.

Hydrolysis of the acid form of III was followed by ^{31}P nmr. The area of both the -15 and the -5 ppm peaks decreases steadily while the -20 ppm peak [due to $CH_3C(OH)(PO_3H_2)_2$] appears and grows until it finally accounts for 100% of the phosphorus. During most of the hydrolysis period the area under the -15 ppm peak was larger than that of the -5 ppm peak by an almost constant amount. Numerical calculations showed such data to be consistent with the presence of the dimeric ether IIIi as an intermediate, a compound expected to show but one kind of phosphorus, the dangling phosphonate kind.

Thin layer chromatography (Figure 2, lane 5) of III shows the parent compound and its hydrolysis products, the dimeric ether IIIi and EHDP. The relative instability of III in chromatography is surprising as compared to its stability in aqueous solutions. We can only theorize that hydrolysis of this particular condensate is catalyzed by the cellulose surface.

Condensate IV. In the discussion of the process of preparing condensate II, it was stated that an acetic acid solution of EHDP will react with acetic anhydride or acetyl chloride to form II. However, if a large excess of acetic anhydride is present, two molecules of the C-acetylated species (II) will condense to form IV. For example, addition of acetic anhydride to a 6% solution of EHDP in acetic acid at 50–70° results in the rapid precipitation of a solid. This solid consists of IV solvated with acetic anhydride.

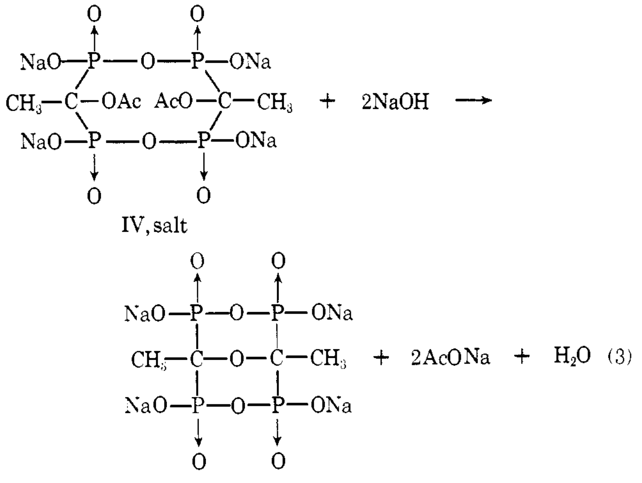
Just as IV forms rapidly under anhydrous conditions, it also cleaves rapidly in the presence of aqueous acid. The mere act of dissolving IV in unbuffered water at room temperature hydrolyzes the P–O–P anhydride links completely. The resulting condensate II can be isolated by neutralization and fractional precipitation.

In spite of its unstable nature, the eight-membered ring system of IV can be stabilized by careful dissolution of the solid acid in sufficient ice-cold aqueous sodium bicarbonate to neutralize the four acidic hydrogens. Fractional crystallization of this tetrasodium salt yields a product which analyzes properly for the suggested structure.

Aqueous solutions of the tetrasodium salt of IV show one kind of phosphorus (multiplet) and equal amounts of two kinds of methyl protons (singlet and multiplet) in accordance with the proposed structure. The ^{31}P chemical shift is about 10 ppm upfield from that of II as would be expected with the formation of P–O–P linkages.

Thin layer chromatography (Figure 2, lane 3) reveals the presence of IV contaminated with EHDP and II. Again the instability of IV to acidic conditions is shown by substantial decomposition during development.

Condensate V. The ether link in this compound is made by further condensation of IV. The condensation occurs in basic solutions and yields the only bicyclic condensate of EHDP yet encountered. While the formation of an ether bond in aqueous base is unexpected, it is confirmed by all of the analytical data. After purification by crystallization, the salt has the analysis corresponding to the product shown in eq 3 (Ac=CH_3CO—). Nmr spectra on its water solution show but one kind of phosphorus (quadruplet) and one kind of methyl protons (multiplet).



Condensate V is considerably more stable toward hydrolysis than is IV, probably due to the two six-membered rings. Thin layer chromatographic analysis (Figure 2, lane 4) shows the parent compound and what is thought to be deacetylated dianhydride (Vi in Figure 1).

The presence of a phosphorus nmr peak at -8 ppm, noticed during both the preparation and the hydrolysis of V, suggests deacetylated intermediates. In the basic condensation the -8 ppm peak could be due to phosphorus in the nonacetylated half of IVi. In the hydrolysis it would be due to the fully deacetylated

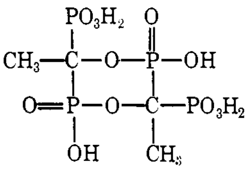
---

(8) The hexamethyl ester was prepared by the trimethyl orthoformate route; D. A. Nicholson, W. A. Cilley, and O. T. Quimby, *J. Org. Chem.*, 35, 3149 (1970).

dianhydride Vi. Neither compound was isolated in a pure state.

Discussion

Except for the cyclic diester



every dimer which can be imagined as forming by elimination of H_2O from 2 mol of $CH_3C(OH)(PO_3H_2)_2$ so as to yield oxygen bridges has been encountered. Most have been isolated in pure form. Only the chain polyester I was found to contain more than two EHDP units.

Among the isolated cyclic dimers held together by C–O–C ether and P–O–P anhydride links, two (III and V) have remarkably different stability toward hydrolysis. Examination of molecular models indicates that the bicyclic condensate V has its CH_3 and $P–O^-$ groups far apart and in such orientation as to leave its C–O–C and P–O–P links relatively exposed to attack by hydrolytic agents. On the other hand, the monocyclic condensate III has its CH_3 groups oriented in close proximity in space in a fashion which shields the C–O–C bridge from backside attack by hydrolytic agents. Attack of the C–O–C bridge in III is probably further hindered by its phosphonate groups. It seems likely that this compressed geometry results in the observed lower rate of formation of III as well.

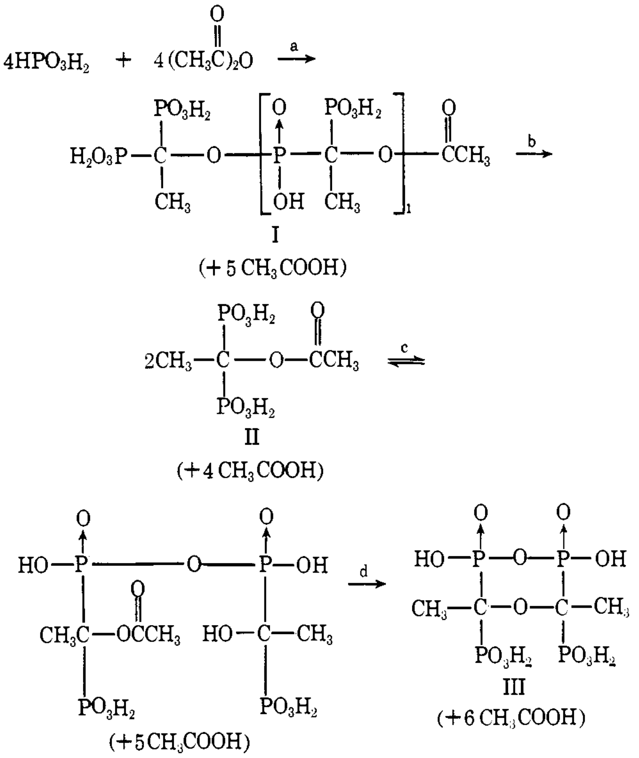
No way has been found to interconvert these two condensates. For instance, in the acid hydrolysis of V the C–O–C bridge breaks first, yielding Vi which is rapidly hydrolyzed to two $CH_3C(OH)(PO_3H_2)_2$ molecules. Again from models, it seems impossible (sterically) to cleave one of the P–O–P bonds of V without previously (or simultaneously) cleaving the C–O–C bridge, nor is it possible to force the formation of a second P–O–P anhydride link in III.

Study of the ways in which models can be assembled for condensate IV suggests that several different geometric isomers may exist. This may supply an explanation for the high apparent multiplicity of the proton and phosphorus nmr peaks observed on the actual products, which are presumably mixtures of isomers. Some models of IV have a geometry which prevents closing of the C–O–C link to form a condensate V isomer; such forms should lead, upon treatment with base, to the fully deacetylated dianhydride Vi referred to previously.

Reaction of P(III) sources and acetylating agents appears to involve condensates I, II, and III directly in the reaction sequences which form CP_2 units. Their order of formation during the course of the reaction is I → II → III. By proper choice of reaction conditions this sequence can be interrupted to give high yields of any of the three condensates. The other isolated materials, IV and V, and the two inferred, IVi and Vi, have not been detected in the anhydride reaction sequence which forms CP_2 units. They are instead prepared by independent interconversions of the sequence condensates.

Evidence for the proposed order of formation of condensates comes from thin layer chromatography of an actual reaction mixture. Consider the generation of CP_2 units from mixtures of acetic anhydride and phosphorous acid (1:1 *M*). Heating this clear solution to 130° for 30 min caused no visible change. By thin layer chromatography (Figure 2, lane 7) the materials present were condensates I, II, and a small amount of EHDP. Prolonged heating of this mixture at 130° caused 90–95% of the phosphorus to precipitate as III. Between these two extremes (after formation of the CP_2 units and before precipitation of III) the clear solution contains mostly II. It will be apparent from Scheme I that such a mixture soon generates a high molar concentration of acetic acid.

Scheme I



The low molecular weight form of polyester I formed by reaction a tends to be degraded to II by acetic acid attack on I as shown in reaction b. The remaining steps eventually lead to III *via* reaction c, which is fast (as shown by the rapid formation of IV from EHDP and an excess of acetic anhydride, and d).

At this point it could be argued that each step of the sequence is an equilibrium and that any of the three condensates could be the first CP_2 unit formed by the reaction. Note that in the above proposed sequence, all of the condensates are in equilibrium with acetic acid only. It thus becomes possible to determine the actual sequence of condensate formation by observing the behavior of each of the condensates separately in acetic acid.

When III is added to acetic acid, it remains insoluble and no change occurs even after prolonged heating. When II is added to acetic acid it dissolves to form a clear solution of II only; no I is observed. Heating the solution of II in acetic acid results in nearly quantitative precipitation of III. When I is added to acetic acid, it dissolves and is degraded almost quantitatively to a clear solution of II, which on prolonged heating precipitates III. These experiments supply evidence for the order of formation I → II → III in Scheme I, and suggest that reactions b and d are irreversible.

Scheme I can be interrupted to give high yields of I by taking advantage of two experimental parameters: (1) the insolubility of I in acetic anhydride and (2) the reduced rate of degradation of I to II by acetic acid. Thus, at lower temperatures and at high excesses of acetic anhydride I precipitates before degradation becomes too severe. Lower temperatures favor longer chain length products.

To synthesize longer chain polyesters of I it would appear desirable to add sufficient ketene to the acetic anhydride starting reagent to react with the acetic acid as it is formed (resulting in still more acetic anhydride). This does not prove practical, however, as the newly formed short chain polyesters, as well as many of the phosphite intermediates, precipitate from solution before the longer chain polyesters can form.

Condensate IV was never detected in an actual reaction product. This is somewhat puzzling since it has been shown that IV is rapidly formed from II in the presence of high acetic anhydride–acetic acid mixtures. Our rationalization is that the degradation of I to II does not occur when the acetic anhydride–acetic acid ratio is high enough to precipitate IV. Thus, II is not involved in the condensate sequence under highly anhydrous conditions.

Experimental Section

Elemental analyses and thin layer chromatographic runs were carried out by the Analytical Section in these laboratories. Phosphorus nmr spectra were recorded on a Varian HR-60 spectrometer operating at 24.3 MHz. Chemical shifts are accurate to ±0.5 ppm and were measured from an external 85% H_3PO_4 reference. Varian HA-100 and HR-60 spectrometers were used to obtain the proton spectra. Molecular weights of the sodium salts of the various condensates were obtained using the $Na_2SO_4 \cdot 10H_2O$ freezing point technique.[9] It has been our experience that this method gives fairly reproducible results (±5%), but generally about 5% above theoretical, for polyphosphonate salts.

Condensate I. Phosphorous acid (416 g, 5 mol) was dissolved in 4 l. (42.4 mol) of acetic anhydride and the solution was heated at 50° for 15 min. This clear solution was cooled to 25° and allowed to stand. A precipitate formed after about 45 min. The slurry was digested overnight and filtered, and the solids were washed with ethyl ether and dried (yield, 400 g).

Sodium bicarbonate (30.6 g) and 40 g of the above acid were dissolved in 250 ml of H_2O. The resulting salt was precipitated by adding 400 ml of methanol. The solid sodium salt (*ca.* 1 Na–P) of condensate **I**, $n = 2$, was filtered and dried (yield 32 g, 67%).

Anal. Calcd for $C_8H_{16}O_{20}P_6Na_6$: C, 12.85; H, 2.13; P, 24.54; Na, 18.22; mol wt 757. Found: C, 13.2; H, 2.4; P, 25.1; Na, 18.1; mol wt 768.

Condensate IV. A solution was prepared consisting of 100 g of $CH_3C(OH)(PO_3H_2)_2 \cdot H_2O$ and 1.4 l. of acetic acid. Acetic anhydride (1.4 l.) was added at 50°. A precipitate formed immediately. This slurry was digested overnight and filtered, and the crystalline solid was washed with ethyl ether and dried under nitrogen (yield 88 g, 76%).

This acid (80 g) was added slowly to 4 equiv of a cold 10% solution of $NaHCO_3$. Vigorous stirring was maintained during the addition. The solution was degassed to remove residual CO_2 and then fractionated into three crystal fractions by adding increments of methanol and acetone. The last fraction was rich in the desired sodium salt (as judged by ^{31}P nmr). This fractional crystallization was repeated four times, each time with the fraction richest in the desired material (final yield 36 g, 42%).

Anal. Calcd for $C_8H_{12}O_{14}P_4Na_4$: C,17.53; H, 2.21; P, 22.61; Na, 17.53; mol wt 548. Found: C, 17.5; H, 2.3; P, 22.6; Na, 17.1; mol wt 601.

Condensate II. The acid form of IV (75 g) was dissolved in 500 ml of H_2O and neutralized to pH 5 with NaOH. The Na_2H_2 salt of **II** was precipitated by adding 2.5 volumes of methanol and then 3 volumes of acetone. The resulting crystals were filtered and dried. The sample was recrystallized twice from H_2O–CH_3OH–acetone (yield 77 g, 91%).

Anal. Calcd for $C_4H_8P_2O_8Na_2$: C, 16.45; H, 2.76; P, 21.22; Na, 15.74; mol wt 292. Found: C, 16.4; H, 2.9; P, 21.8; Na, 15.9; mol wt 300.

Condensate III. Phosphorous acid (1.0 mol) was added to 101 ml of acetic anhydride (1.07 mol) and the solution was heated at 135° for 6 hr. The crystalline precipitate which had by this time formed was removed by filtration, washed with ether, and dried (yield 90.5 g, 96%).

Anal. Calcd for $C_4H_{12}O_{12}P_4$: C, 12.78; H, 3.22; P, 32.95. Found: C, 13.1; H, 3.7; P, 33.2.

Hexamethyl Ester. The Na_6 or acid Na salts of III (above) were too insoluble in melted $Na_2SO_4 10 \cdot H_2O$ to allow molecular weight measurements. The acid was converted to the hexamethyl ester by heating in trimethyl orthoformate.[8] The hexamethyl ester was purified by crystallization, mp 141–144°.

Anal. Calcd for $C_{10}H_{24}O_{12}P_4$: C, 26.10; H, 5.26; P, 26.92. Found: C, 26.4; H, 5.5; P, 26.0.

The molecular weight was determined by the benzene boiling point elevation procedure. Average of seven determinations was 464 with a standard deviation of 9 (theory 460).

Condensate V. The acid form of IV (10 g) was dissolved in 217 ml of cold 1 *N* NaOH solution. The clear solution was diluted with 200 ml of MeOH and then slowly with 500 ml of an equal volume mixture of acetone and MeOH. The crystal fraction which formed was removed by filtration and recrystallized in a similar manner (yield 5 g, 58%).

Anal. Calcd for $C_4H_6O_{11}P_4Na_4$: C, 10.77; H, 1.36; P, 27.78; Na, 20.62; mol wt 446. Found: C, 10.5; H, 2.3; P, 25.8; Na, 19.8; mol wt 477.

Acknowledgment. The nmr work was provided with the guidance of T. J. Flautt and the technical assistance of I. Calvert. The thin layer chromatographic work was directed by R. A. Libby and executed by W. R. Gehling. It is a pleasure to acknowledge their very capable assistance.

---

(9) H. J. Muller, *Ann. Chim. (Paris)*, **8**, 143 (1937).