Reversible Formation and Hydrolysis of Phthaloyl and Succinyl Monophosphates in Aqueous Solution[1]

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Abstract: Phthalic and succinic anhydrides are shown to be in facile reversible equilibrium with phthaloyl and succinyl monophosphate, respectively, in aqueous phosphate solution, the system favoring the anhydride under acidic conditions and the acyl phosphate species in neutral to alkaline solutions. Rate–pH profiles for formation and over-all hydrolysis have been determined. The hydrolytic mechanism appears to involve both direct hydrolysis and that mediated by formation of the anhydride.

Tendencies of dicarboxylic acid anhydrides to form acyl phosphates in aqueous phosphate solutions have been reported earlier by both Kaufman (succinyl phosphate)[2] and Avison (phthaloyl phosphate).[3] The present communication is concerned with results of rate and equilibrium studies designed to determine the reaction kinetics and free energy changes involved in these reactions, together with quantitative delineation of the hydrolytic pathways operating in these metastable systems. Data are presented in detail for the phthaloyl system, but essentially similar behaviors were noted for the succinyl case.

Spectral Changes Accompanying Formation of Phthaloyl Phosphate. The behavior of a freshly prepared aqueous solution of phthalic anhydride in the presence of phosphate ions can be conveniently followed in the ultraviolet. In Figure 1 absorbance changes at 305 mμ observed with time in a solution initially 2.5×10^{-4} *M* with respect to phthalic anhydride and containing 0.05 *M* phosphate at pH 5.6 are shown. The observed changes suggested rapid initial formation of a chemical species which subsequently underwent slower first-order loss. As the pH of these solutions was raised, the initial slope of plots similar to that shown in Figure 1 became sharper, while the final logarithmic loss appeared slower and slower, suggesting that with higher pH the intermediate species was more rapidly formed and became increasingly more stable. Since phthalic anhydride itself hydrolyzed much more rapidly than was observed for the second phase of the reaction under these conditions, a phosphorylated species more resistant to hydrolysis was apparently being produced.

To determine the spectral characteristic of the stable phosphorylated compound formed at higher pH values, two solutions were prepared differing only in the order in which the reagents were mixed. In the first solution 0.5 ml of an anhydride solution in dioxane was added to water and sufficient time allowed for it to hydrolyze before 50 ml of a 0.5 *M*, pH 7.5 phosphate buffer was added, the mixture then being brought to 100 ml with water. The phthalic anhydride solution was added directly to 50 ml of the buffer and the resultant solution brought to volume with water in the second solution. The spectra of these two solutions, compared in Figure 2, indicate the presence of some chemical species present in the second solution but absent in the first. This spectral difference provided a means of estimating the relative amounts of phthalic acid and the presumed phthaloyl monophosphate in these aqueous solutions.

Determination of Rate of Formation of Phthaloyl Phosphate, k_f. The initial rate of disappearance of phthalic anhydride in a phosphate buffer would evidently be the sum of its hydrolytic velocity and the rate of formation of phthaloyl monophosphate, *i.e.*

$$-\left[\frac{\mathrm{d(anh)}}{\mathrm{d}t}\right]_{t=0} = [k_{-1} + k_f(\mathrm{HPO_4}^{2-})](\mathrm{anh})_0 \quad (1)$$

where k_{-1} is the rate constant for the hydrolysis of phthalic anhydride in the system, k_f the second-order rate constant for the formation of phthaloyl phosphate, and $(\mathrm{anh})_0$ the initial phthalic anhydride concentration. Since phthalic anhydride is the only chemical species in this system which absorbs significantly at 305 mμ, the rate of disappearance of the anhydride may be followed exclusive of any other reactions in the system at this wavelength. Measures of the initial rates required for eq 1 can be obtained from the initial change in absorbance and the molar absorptivity at 305 mμ. Since the rate constant at $t = 0$ is $k^0_{\mathrm{obsd}} = k_{-1} + k_f(\mathrm{HPO_4}^{2-})$, we can write $k_f = (k^0_{\mathrm{obsd}} - k_{-1})/(\mathrm{HPO_4}^{2-})$.

In Figure 3 the values of $(k^0_{\mathrm{obsd}} - k_{-1})$ obtained in this fashion have been plotted *vs.* pH for a system containing 0.05 *M* phosphate at 25°. The smooth curve represents the fraction of phosphate in the diionic form based on the experimentally determined value for $\mathrm{p}K_{a_2}$ of 6.29 at an ionic strength of 1.5. It is evident from the obvious fit that the reactive species is $\mathrm{HPO_4}^{2-}$. The average value of the species-specific second-order rate constant, k_f, corresponds on this basis to 1.23 l./mole sec.

Hydrolysis of Phthaloyl Monophosphate (PMP). From the nature of phthaloyl monophosphate, it would appear that at least two reaction pathways may lead to its hydrolysis. The mixed acid anhydride would certainly be expected to undergo some direct hydrolysis either spontaneously or under the influence of hydrogen and/or hydroxyl ion. A second likely pathway is through re-formation of phthalic anhydride and subsequent hydrolysis of the latter compound. These

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[1] This study was supported in part by grants from the National Institutes of Health, GM05830, and from the Research Committee of the Graduate School from funds furnished by the Wisconsin Alumni Research Foundation.

[2] S. Kaufman, *Arch. Biochem.*, 50, 506 (1954).

[3] A. W. D. Avison, *J. Chem. Soc.*, 732 (1955).

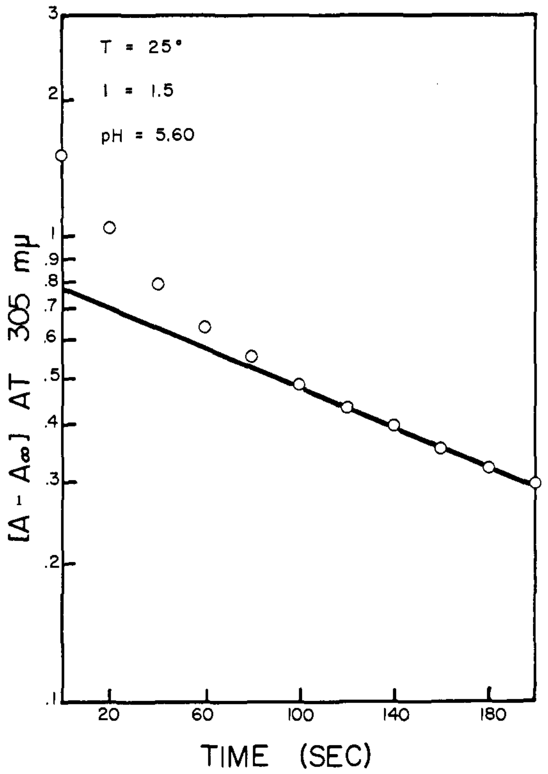


Figure 1. Plot showing the absorbance changes at 305 mμ when phthalic anhydride is introduced into a 0.05 M phosphate buffer of ionic strength 1.5 and pH 5.60 at 25°.

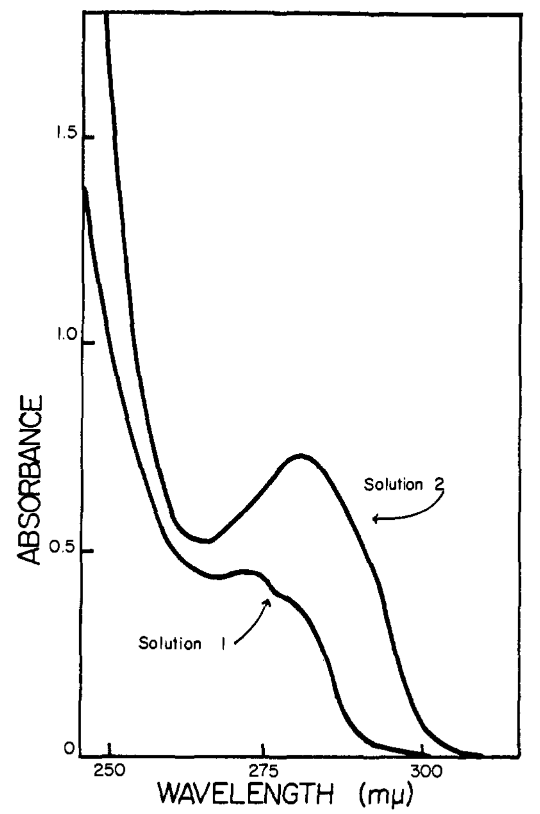
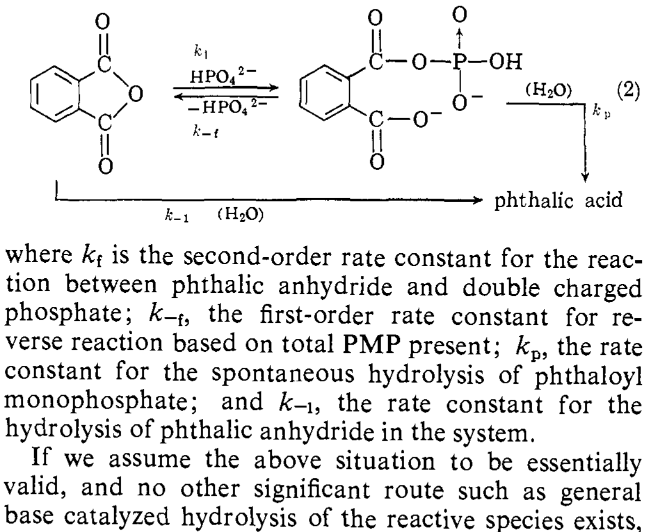


Figure 2. Spectra of phthalic acid (solution 1) and intermediate phosphate compound (phthaloyl monophosphate, solution 2) in 0.25 M, pH 7.5 phosphate buffers.

possibilities can be represented schematically as



where k_f is the second-order rate constant for the reaction between phthalic anhydride and double charged phosphate; k_{-f}, the first-order rate constant for reverse reaction based on total PMP present; k_p, the rate constant for the spontaneous hydrolysis of phthaloyl monophosphate; and k_{-1}, the rate constant for the hydrolysis of phthalic anhydride in the system.

If we assume the above situation to be essentially valid, and no other significant route such as general base catalyzed hydrolysis of the reactive species exists, it is experimentally possible to separate the contributions from each pathway to the total rate of hydrolysis, particularly in systems at higher pH where direct hydrolysis of the anhydride contributes little. Thus, we can write the rate of change of total unhydrolyzed phthalate species as

$$\frac{-\mathrm{d(TUPS)}}{\mathrm{d}t} = k_{-1}(\mathrm{anh}) + k\mathrm{p(PMP)} \qquad (3)$$

where (anh) and (PMP) refer to the respective concentrations of phthalic anhydride and phthaloyl monophosphate. At higher pH, (PMP) >> (anh) and the two species are essentially in equilibrium governed by the relationship

$$\frac{k_f}{k_{-f}} = \frac{(\mathrm{PMP})}{(\mathrm{HPO_4^{2-}})(\mathrm{anh})} = K$$

or

$$\frac{\mathrm{d(TUPS)}}{\mathrm{d}t} = \left[k_{-1}\frac{1}{1 + K(\mathrm{HPO_4^{2-}})} + k_p\frac{K(\mathrm{HPO_4^{2-}})}{1 + K(\mathrm{HPO_4^{2-}})}\right](\mathrm{TUPS}) \qquad (4)$$

and

$$k_{\mathrm{obsd}} = \frac{k_{-1}}{1 + K(\mathrm{HPO_4^{2-}})} + \frac{k_pK(\mathrm{HPO_4^{2-}})}{1 + K(\mathrm{HPO_4^{2-}})}$$

Thus

$$K(k_{\mathrm{obsd}} - k_p) = \frac{k_{-1} - k_{\mathrm{obsd}}}{(\mathrm{HPO_4^{2-}})} \qquad (5)$$

The over-all hydrolytic first-order rate constant for phthaloyl monophosphate in a given buffer system, k_{obsd}, was readily determined spectrophotometrically at higher pH values where (anh) << (PMP). The reaction when followed at 290 mμ exhibited the usual first-order behavior as shown in Figure 4. The particular data shown were obtained in 0.5 M phosphate buffers. According to eq 5, a plot of k_{obsd} *vs.* $(k_{-1} - k_{\mathrm{obsd}})/HPO_4^{2-}$ at a given pH or phosphate ratio should be linear with an intercept at k_p on the ordinate and $-Kk_p$ on the abcissa. A typical plot of this kind is shown in Figure 5 for data obtained at a phosphate ratio, $(HPO_4^{2-})/(H_2PO_4^-)$, of 1.0. The ordinate inter-

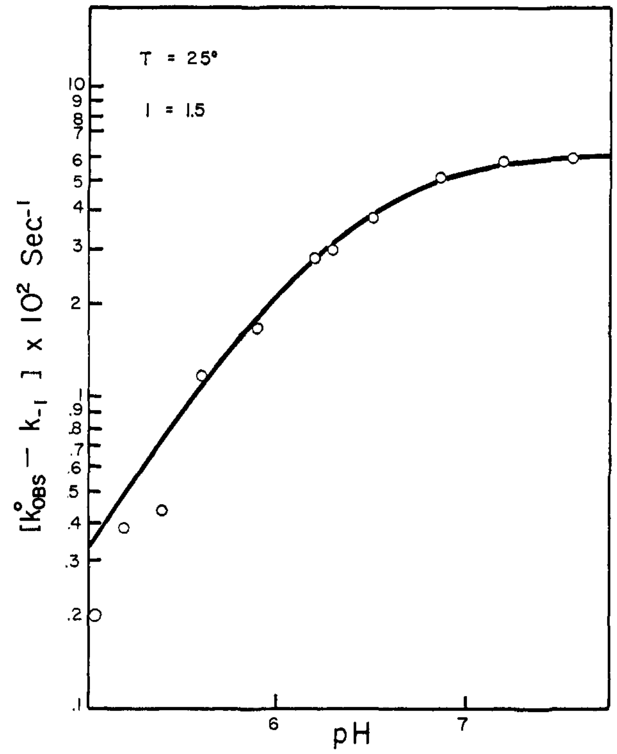


Figure 3. Plot of observed phthaloyl monophosphate formation constant, k_f, as a function of pH at 25° and in 0.05 M phosphate buffer.

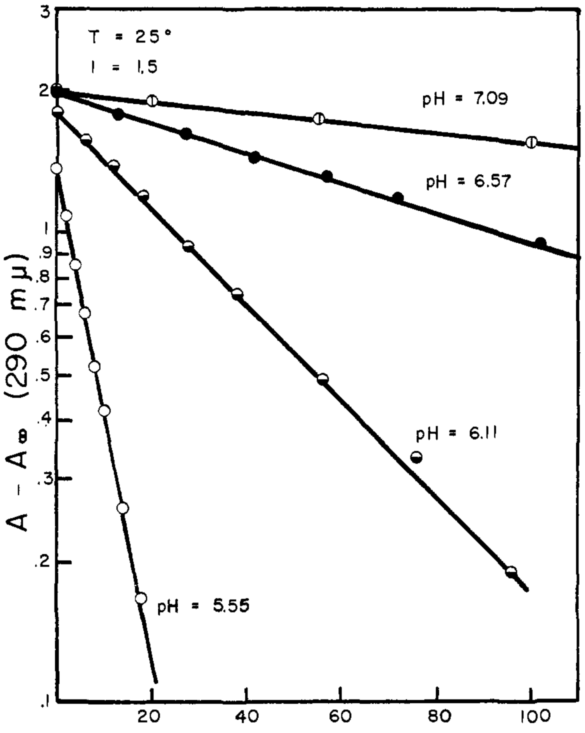


Figure 4. Plots showing the rate of disappearance of phthaloyl monophosphate in 0.5 M phosphate buffers at 25° for several pH values.

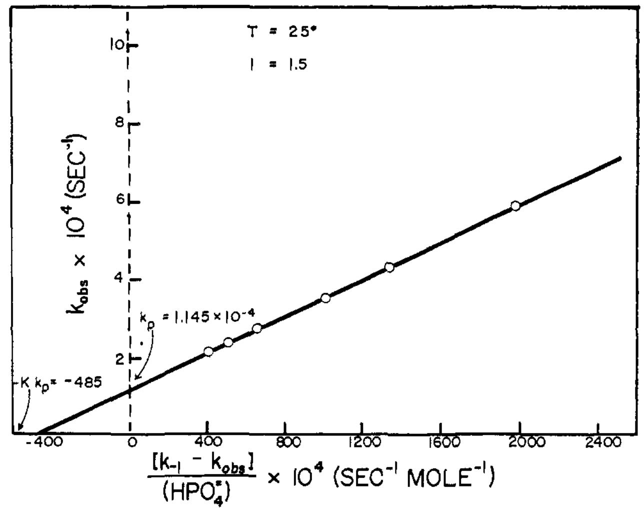


Figure 5. Plot according to eq 5 for a $HPO_4{}^{2-}/H_2PO_4{}^-$ ratio of 1.

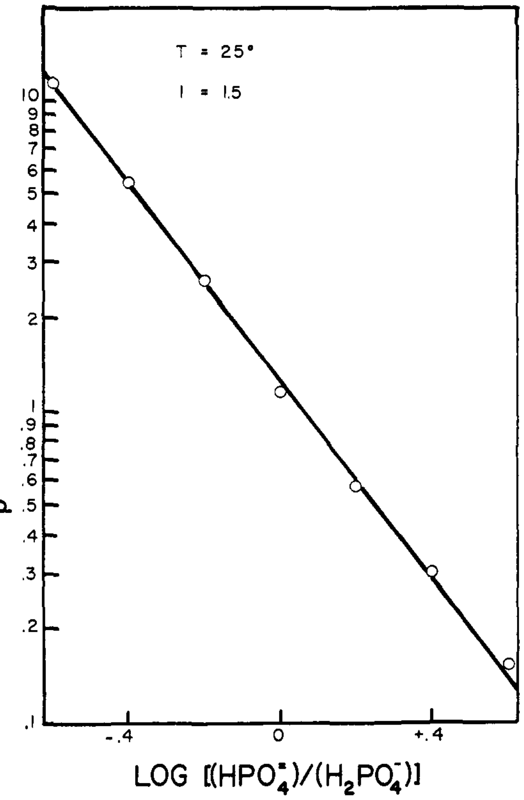


Figure 6. Plot showing dependence of k_p obtained from intercept values of plots similar to Figure 5 on the log of the phosphate ratio at 25°.

cept essentially represents response at an infinite phosphate concentration at which point k_{obsd} is equal to k_p.

In Figure 6 the values of k_p obtained from plots of data determined at several buffer ratios have been plotted logarithmically *vs.* the ratio. The log of the ratio of phosphate species was chosen as a parameter instead of pH because of slight but regular decreases in the pK_{a_2} of phosphoric acid as the total phosphate concentration was decreased although the ionic strength was kept approximately constant in these studies at 1.50. Although log k_p appeared to be a linear function of log (phosphate ratio) over the range studied, the slope of the line was not 1 but 1.54, suggesting contributions from several mechanisms.

Calculation of the Equilibrium Constant, *K*. In a similar fashion logarithms of K values calculated from slopes of plots, such as shown in Figure 5, plotted

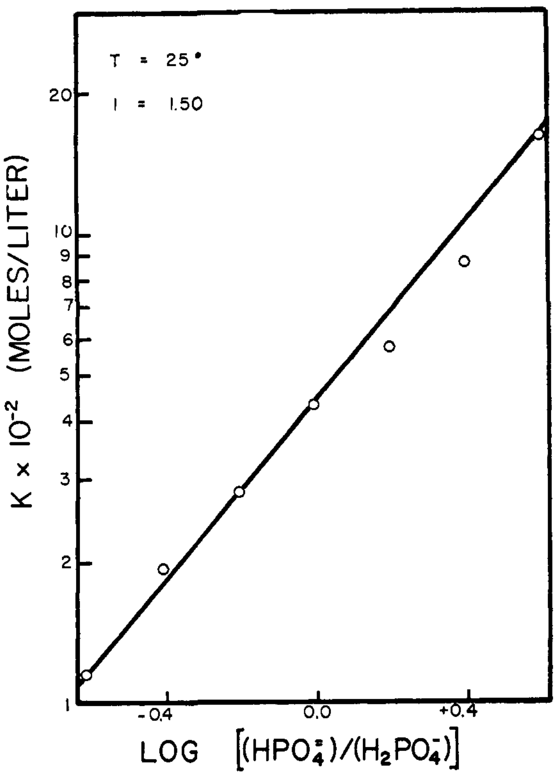
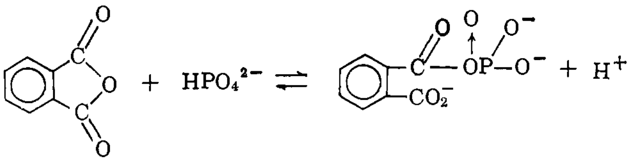


Figure 7. Plot showing dependence of K obtained from graphs similar to Figure 5 on the log of the phosphate ratio at 25°.

against the logarithms of the ratio of phosphate species, yielded a straight line as shown in Figure 7. In this instance, however, the points fell on a line having a slope of 1. On the basis of the K values shown, the percentages of total unhydrolyzed phthalate species represented by phthalic anhydride in 0.5 M phosphate buffer as a function of pH (assuming pK_{a_2} to be 6.37) were calculated from the relationship

$$\% \text{ anhydride} = 100\{1/[1 + K(HPO_4^{2-})]\}$$

These, for example, were 8.0% at pH 5.77, 0.91% at pH 6.37, and 0.15% at pH 6.97. The pH dependence of the equilibrium system suggests that it would be, over the pH range studied, more correctly written as



$$K_{eq} = \frac{(PMP^{3-})(H^+)}{(anh)(HPO_4^{2-})} = K(H^+)$$

The value of the newly defined constant, K_{eq}, can be readily obtained from the data shown in Figure 7. Since

$$K_{eq} = K[H^+] = KK_{a_2}\frac{(H_2PO_4^-)}{(HPO_4^{2-})}$$

the constant can be calculated from any value of K and the corresponding $(H_2PO_4^-)/(HPO_4^{2-})$. The mean obtained by averaging all of the points and based on pK_{a_2} = 6.29 came out to be 1.84×10^{-4} over the pH interval 4–7. This would indicate that at pH 6.7 and at a phosphate concentration of 0.001 M, roughly one-half of the anhydride introduced would exist in the phosphorylated form.

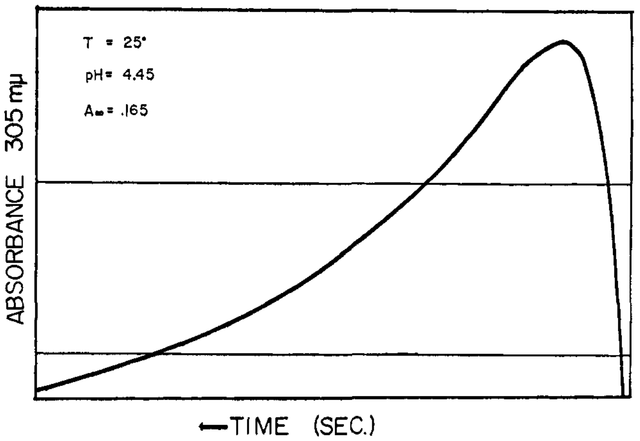
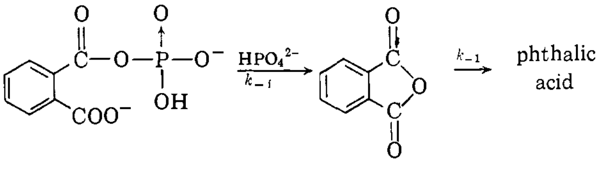


Figure 8. Plot showing absorbance changes at 305 mμ when a phthaloyl monophosphate solution was acidified to pH 4.45 at 25°.

Direct Measurement of Rate of Re-formation of Phthalic Anhydride from Phthaloyl Phosphate, k_{-f}. According to the proposed mechanism, acidification of solutions containing phthaloyl monophosphate should result in a shift in the phthalic anhydride–phthaloyl monophosphate equilibrium to the phthalic anhydride side. This was experimentally verified by acidifying phthaloyl monophosphate solutions to pH's below 3.5. Under these conditions phthalic anhydride is regenerated essentially quantitatively as determined from the spectra and the rate of change in absorbance of the resulting system.

The actual rate of re-formation of phthalic anhydride from phthaloyl monophosphate was determined between pH 4 and 5. When solutions containing the mixed anhydride were acidified at 25° with acetic acid directly in a Cary cell, a rapid initial increase in absorbance at 305 mμ followed by a slower decrease was observed, as is evident in Figure 8. A plot of the log of the absorbance, A, at time t, minus the absorbance of the completed reaction, A_∞, *vs.* time exhibited a linear limiting slope essentially that expected for hydrolysis of phthalic anhydride as shown in Figure 9.

If the formation of phthaloyl phosphate, which is a function of the diionized phosphate species present, is made negligible as it would be at low pH values, then we can write, ignoring for the moment the exact species involved, the reaction as



The system can be treated as two consecutive first-order reactions which would follow the logarithmic relationship

$$\log\left[e^{-k_{-1}t} - \frac{A_t - A_\infty}{W}\right] = \frac{-k_{-f}}{2.303}t$$

where W is the linear extrapolation of $A_t - A_\infty$ at time zero as shown in Figure 9. A plot of log $[e^{-k_{-1}t}$ −

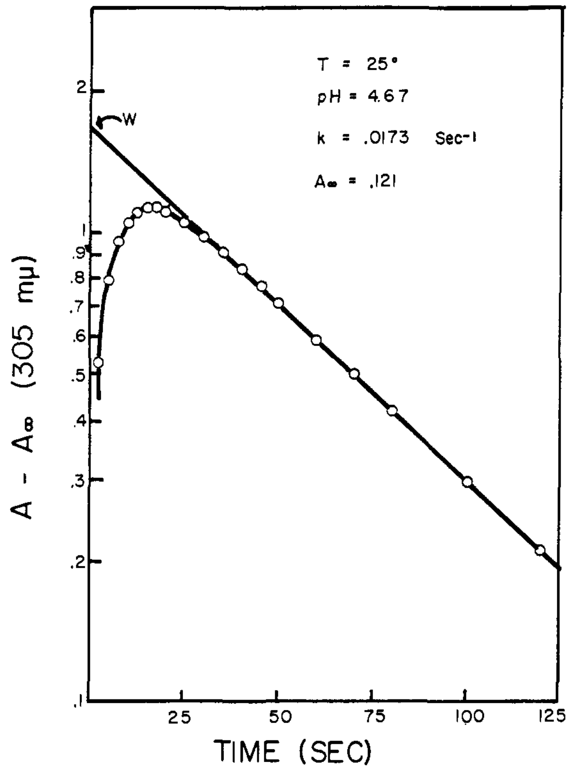


Figure 9. Semilogarithmic plot of absorbance change with respect to time for a phthaloyl monophosphate solution acidified to pH 4.67 at 25°.

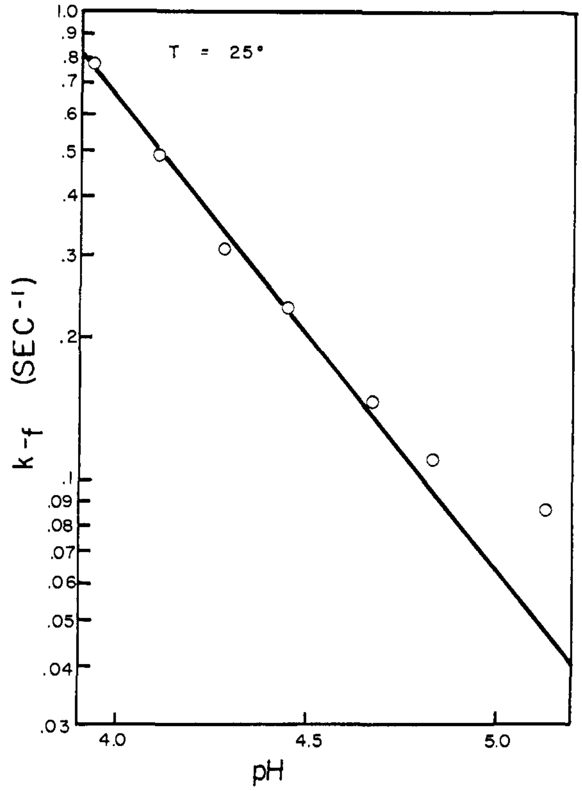


Figure 11. Plot of k_{-f} as a function of pH at 25°. k_{-f} values were obtained from plots similar to Figure 10.

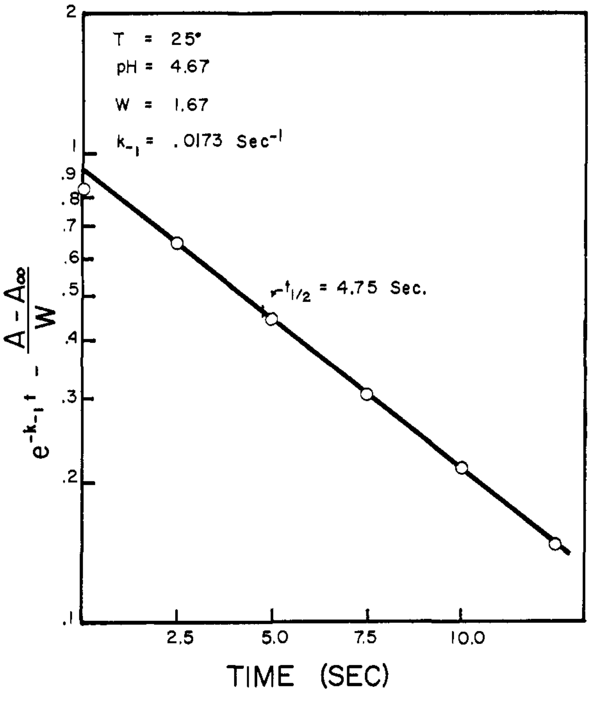
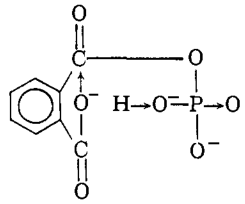


Figure 10. Semilogarithmic plot showing the linear relation of $e^{-k_{-1}t} - (A - A_\infty)/W$ and time for a solution acidified to pH 4.67 at 25°. The half-lives from such plots were used to calculate values of k_{-f}.

$(A_t - A_\infty)/W]$ against time should give a straight line with a slope of $-k_{-f}/2.303$. A typical plot of this type for the present system based on a known value for k_{-1} is shown in Figure 10. The pH profile for the formation of phthalic anhydride from phthaloyl monophosphate at 25° as determined from plots similar to Figure 10 is shown in Figure 11. Below pH 4 the reaction became too fast to be followed by this technique. As pH 5 was approached, the backward reaction apparently becomes appreciable, and this is seen in the large positive deviation at pH 5.13. The line drawn in Figure 11 has a slope of 1. It can be seen that the reaction reasonably approximates a linear dependency on hydrogen ion concentration in the more acid region.

It was, of course, also possible to estimate indirectly the rate of the reverse reaction, as measured by k_{-f}, from values determined above for k_f and the equilibrium constant for the reversible reaction. The indirect method yielded values which were in excellent agreement with the results discussed above.

On the basis of the observed pH-rate profile for formation of phthalic anhydride from phthaloyl phosphate, the reactive species appears to be the doubly ionized form of the phosphorylated acid. The direct dependence on hydrogen ion effectivity over the pH range 4–6.5 obtained by the direct and indirect procedures for determination of k_{-f} suggests that the relative composition of the ionic species does not change significantly over this pH interval, the phosphorylated acid probably existing essentially entirely in the triply ionized state. Although the three dissociation constants for phthaloyl phosphoric acid cannot be readily determined, it would appear reasonable to expect that all three pK_a values would lie below 4 at the high ionic strength employed. The microscopic mechanism can take the form of either a direct attack of the free carboxylate on the singly charged phosphorylated carboxylic group or equivalently coordinated attack of the free carboxylate on the singly charged phosphorylated carboxylic group or equivalently coordinated attack of the free carboxylic group on the doubly charged phosphorylated carboxylic function with simultaneous transfer of a proton as shown.



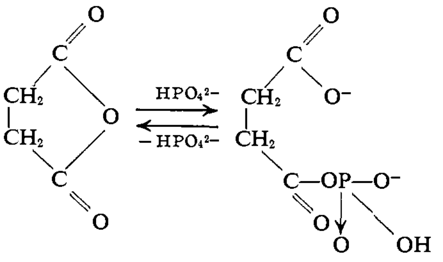
In any case the same intermediate structure should be responsible for both the forward and reverse reactions.

Over-all Hydrolytic Rate of Phthaloyl Phosphate. The total pH-rate profile for over-all hydrolysis of phthaloyl monophosphate obtained in 0.5 M phosphate buffers is shown in Figure 12. Although at the lower pH values the reaction occurred through at least two pathways, the velocity of the over-all reaction appears to be directly proportional to hydrogen ion concentration. In the plateau region, the half-life for the reaction was 45.7 hr and is roughly of the same order of magnitude as other acyl phosphates.

The phosphate dependency in the plateau region was found experimentally to be of somewhat different nature than that observed at lower pH's. Plots similar to Figure 5 did not yield straight lines in this pH region. The general behavior appears to reflect conversion of the phosphorylated acid to the triionized relatively stable form.

The value indicated in Figure 12 for k_{OH^-}, the second-order rate constant for hydroxyl attack or triply ionized phthaloyl phosphate, corresponds to 9.4×10^{-3} l./mole hr, and for k_{H_2O}, the spontaneous first-order hydrolytic rate constant of the same species, to 2.54 hr^{-1}. The relatively low ratio of k_{OH^-}/k_{H_2O} of 37 suggests that this compound is even more resistant to hydroxyl ion attack than acetyl phosphate, whose corresponding ratio is about 10^3 at 39°.[4] At very high pH values it is evident that phthaloyl monophosphate would be triply charged while acyl phosphates such as acetyl phosphate would carry only two negative charges. The highly negatively charged atmosphere surrounding the trianion may be expected to limit the approach of hydroxyl ions to an even greater extent than for acetyl phosphate.

Succinyl Systems. The general behavior of the reaction



appears to parallel that of the phthalate system. The reaction can be followed spectrophotometrically at 225 mμ but not as readily as the aromatic system.

The secondary rate constant for formation of the phosphorylated species as determined spectrometrically at 25° was found to be approximately 0.80 M^{-1} sec^{-1} compared to 1.23 M^{-1} sec^{-1} for the phthalate system. The pH profile for the reverse reaction was not determined, but measurement at pH 2.0 afforded a value of 0.024 sec^{-1} at 25°. It is evident on this basis that succinyl phosphate is significantly more stable than the phthalate derivative.

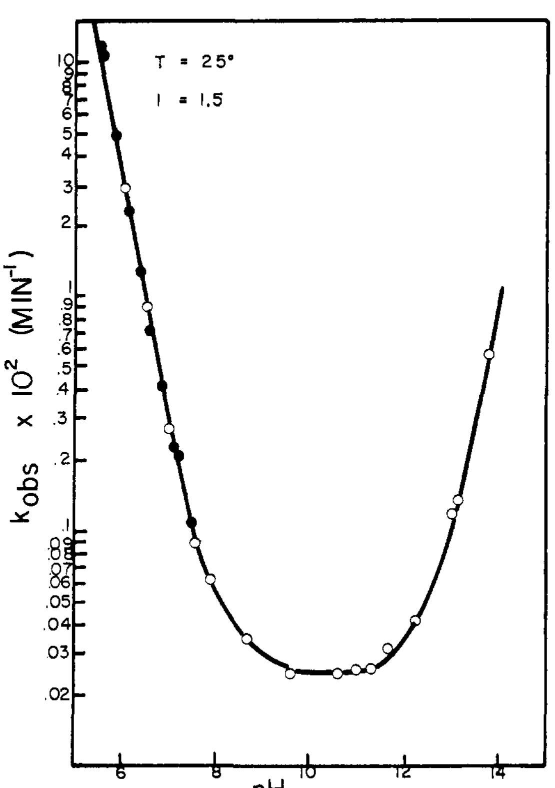


Figure 12. pH profile for the over-all hydrolysis of phthaloyl monophosphate in 0.5 M phosphate buffers at 25°. The theoretical curve has a slope of +1 and −1 in the pH-dependent regions: ●, values determined directly at 290 mμ; ○, values obtained by anhydride regeneration sampling.

The behavior of succinic anhydride in the presence of pyrophosphate, sulfite, and bicarbonate ions was also briefly investigated. The formation of a mixed anhydride species with pyrophosphate was clearly evident. Although sulfite has been shown to catalyze both the hydrolysis and formation of succinic anhydride from the acid,[5] no evidence of accumulation of an active intermediate species was noted when the anhydride was added to sulfite buffer. Bicarbonate also produced no visible effect.

Experimental Section

General. Temperature control was maintained at 25 ± 0.05°. Standard solutions for pH measurement were prepared as those outlined by Bates.[6] In most cases the pH was read to 0.001 unit.

The reagents used, whenever possible, were of analytical grade. It was necessary to purify the phthalic anhydride by washing it with chloroform.[7] Crude dioxane was purified according to Vogel's procedure.[8] Twice distilled water stored in a Pyrex vessel was used.

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(4) D. E. Koshland, *J. Am. Chem. Soc.*, 74, 2286 (1952).

(5) T. Higuchi, A. C. Shah, and J. McRae, *ibid.*, **88**, 4015 (1966).

(6) R. G. Bates, *J. Res. Natl. Bur. Std.*, **A66**, 179 (1962).

(7) A. I. Vogel, "Practical Organic Chemistry," 3rd ed, John Wiley and Sons, Inc., New York, N. Y., 1962, p 507.

(8) Reference 7, p 177.

The Formation of Phthaloyl Phosphate. A series of solutions, 0.05 M in total phosphate and varying from pH 5.05 to 7.56, were prepared; 3-ml of the respective phosphate solution was injected into 10 ml of a 3% solution of phthalic anhydride in dioxane, and the change in anhydride concentration with respect to time was followed in a thermostated Cary 11 system.

The Hydrolysis of Phthaloyl Phosphate. The reaction was followed by two different methods. The solutions were prepared by injecting 1 ml of a 2% phthalic anhydride solution in dioxane into 100 ml of phosphate buffer of ionic strength 1.5. At pH values below 7.5, calculated amounts of K_2HPO_4, NaH_2PO_4, and NaCl were weighed out on an analytical balance to give the desired phosphate ratio and an ionic strength of 1.5. At pH values greater than 7.5, the phthaloyl phosphate was prepared by injecting into 100 ml of Na_2HPO_4 solution of the desired concentration and then adding solid sodium hydroxide to the ionic strength of 1.5 based on phosphate being totally in the diionic form. The reaction was then followed directly on the Cary 11 at 290 mμ or indirectly by quantitatively regenerating phthalic anhydride by injecting 2.6 ml of solution into 0.5 ml of concentrated HCl. The former method was used at low pH values where the reaction was relatively fast; the latter was used at high pH values to avoid waiting for an equilibrium value. In the indirect technique the amount of anhydride produced in any sampling was directly proportional to $A_0 - A_\infty$ at 302 mμ. The A_0 value was obtained by extrapolating back to the injection time as seen on the Cary chart. In all cases the pH of the reaction mixture was measured after the anhydride had been added.

The Formation of Phthalic Anhydride from Phthaloyl Phosphate. The method consisted of a slight modification of the direct technique for following phthaloyl phosphate hydrolysis as described above. Acetic acid solutions of varying strength were used instead of hydrochloric acid solutions. A 2.6-ml portion of phosphate solution containing phthaloyl phosphate was injected into 0.5 ml of acetic acid of varying concentrations. The appearance of phthalic anhydride was followed at 302 mμ. After completion of the reaction, the pH of the solution in the cell was measured with microelectrodes.

Mechanisms of Nucleophilic Substitution of Propargyl and Allenyl Halides. Base-Promoted Reactions of 3-Bromo-3-methyl-1-butyne and 1-Bromo-3-methyl-1,2-butadiene in Aqueous Ethanol[1]

V. J. Shiner, Jr., and J. S. Humphrey, Jr.

Contribution No. 1421 from the Department of Chemistry, Indiana University, Bloomington, Indiana 47405. Received April 18, 1966

Abstract: Evidence is presented which shows that both the propargyl and the allenyl bromides (Ib and IIb) react with aqueous alcoholic base by rapid, reversible removal of the terminal proton followed by rate-determining loss of the halide ion and formation of the same allene–carbene intermediate. Although this species is attacked by lyate ions to form only propargyl products, its reaction with added thiophenoxide or azide ions gives both acetylene and allene derivatives. Proton magnetic resonance spectra indicated that the propargyl and allenyl azides initially formed subsequently reacted *in situ* to produce other materials. Salt effects and solvent and reactant secondary deuterium isotope effects have been used to elucidate some of the mechanistic details, and a tentative hypothesis is offered to explain why different nucleophiles give such widely differing acetylene/allene product ratios.

In 1951 Hennion and Maloney[2] proposed that the second-order base-promoted solvolysis of 3-chloro-3-methyl-1-butyne (Ia) and the isomeric allenyl halide, 1-chloro-3-methyl-1,2-butadiene (IIa), involved as a common intermediate the propargyl zwitterion–allene carbene species, III. The suggested mechanism was essentially that shown in Figure 1 with the slow step in each case being the formation of the conjugate bases in steps 1 and 2.

In 1952 Shiner and Wilson[3] offered conclusive kinetic evidence for the intermediacy of the species III in the solvolysis of the propargyl halides Ia and Ib in basic aqueous ethanol. They showed that Ib exchanged the acetylenic hydrogen in basic 80% ethanol-*d*-deuterium oxide solution much faster than it solvolyzed and that the rate of the second-order solvolysis in the nondeuterated medium was depressed by added sodium salts in the order: $Br^- > Cl^- > NO_3^- \sim ClO_4^-$. These results are consistent with the Hennion mechanism only if the rate-determining step is the ionization of bromide from the conjugate base of Ib, step 3 in Figure 1.

Gas chromatographic analyses of distillates from the reaction mixture of Ib in basic aqueous ethanol indicated that the propargyl ether VI was the predominant product (90% *relative* yield) accompanied by only small amounts of the propargyl alcohol V (7%) and volatile olefin IV (3%).[3] In comparison, the first-order, initially neutral solvolysis of Ib, characterized as an SN1 process,[3,4] yielded an entirely different distribution of these same propargyl products: VI, 43%; V, 22%; and IV, 35%.[3] "The difference in product proportions is apparently dictated by the different reactivity, and therefore selectivity, of the two intermediates, the carbonium ion and the zwitterion–carbene.

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[1] (a) Taken from the thesis submitted by J. S. Humphrey, Jr., to the Graduate School of Indiana University in partial fulfillment of the requirements for the Ph.D. degree, 1965. (b) Presented in part before the Division of Organic Chemistry at the 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., March 1966. (c) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

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