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Nucleophilic Catalysis in the Hydrolysis of 2,4-Dinitrophenyl Dibenzyl Phosphate

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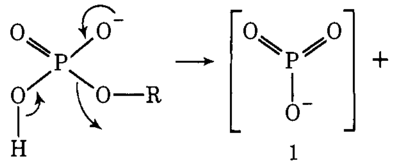
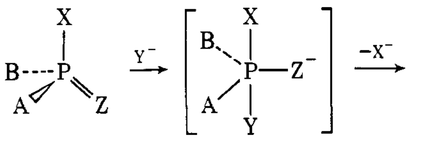
Abstract: The reaction of oxyanions with 2,4-dinitrophenyl dibenzyl phosphate involves nucleophilic catalysis in the cleavage of the P-O(aryl) bond. This conclusion is based upon irregularities in a Brønsted plot of the second-order rate constants for reaction of oxyanions and fluoride ion and observation of negligible solvent deuterium isotope effects. Inhibition of the reaction by organic solvents (1,4-dioxane and even the free acid component of formate and acetate buffers) is observed. Curved second-order plots with acetate, formate, and phosphate buffers are ascribed to a specific salt effect of the $NaClO_4$ electrolyte added to keep the ionic strength constant.

Our present understanding of the reactions of tetracovalent phosphorus (particularly phosphate esters) may be discussed in the context of two limiting general mechanisms.[2-4] The first of these may be called the $S_N1(P)$ reaction,[2a] which involves the unimolecular decomposition of a phosphate monoester to generate an unstable monomeric metaphosphate ion intermediate, **1**. The phosphorus-leaving group bond would be substantially broken in the transition state. At the other extreme, the phosphorus-leaving group bond is not broken at all in the transition state and this would be analogous to an addition-elimination mechanism,[5] proceeding through an unstable pentacovalent intermediate, **2**.



(1)

Of course, between these two extremes of elimination-



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(2)

addition and addition–elimination exists a whole spectrum of intermediate mechanisms involving varying degrees of bond making and breaking to phosphorus in the transition state. In recent years both the monomeric metaphosphate mechanism (eq 1) and the pentacovalent intermediate mechanism (eq 2) have gained wide acceptance.[6] While understanding of the structural and electronic factors which must determine the mode of reaction of a particular phosphorus compound has rapidly evolved, certainly much still remains unclear and difficult to explain within current theory. Thus, the role of the pentacovalent phosphorus intermediate in the addition–elimination mechanism for the hydrolysis of acyclic phosphate triesters has been a subject of controversy. The question whether the hydrolysis of phosphate triesters proceeds via an addition–elimination pathway or through a concerted $S_N2(P)$ mechanism still remains unravelled.[4]

In addition, the hydrolysis of trisubstituted phosphoric acid esters may be subject to general-base catalysis as well as nucleophilic catalysis, depending on the nature of the substituents, the nucleophiles, and the leaving groups.[2-4] A change in hydrolysis mechanism from nucleophilic to general-base catalysis as the nucleophile becomes markedly less basic than the leaving group has been demonstrated in a number of cyclic triesters.[7]

Since the reactions of acyclic triesters may differ from those of cyclic five-[5] and six-membered[7,8] ring triesters, and since the nature of buffer catalysis in the reactions of acyclic phosphate triesters is only poorly documented,[2-4] the purpose of this study is to examine the mode of reaction of an acyclic triester, 2,4-dinitrophenyl dibenzyl phosphate, with oxyanions and fluoride nucleophiles. It is hoped that this study and the one described in the following paper[9] on the hydrolysis of a phosphate monoester will provide information about the reaction pathways of acyclic phosphate esters.

Experimental Section

Materials. Reagent grade buffer salts were used throughout without any additional purification. Phenols were recrystallized.

1,4-Dioxane (Fisher Scientific Company) was passed through a column of acidic alumina and distilled to remove peroxides.

The heavy water (>99.8% D_2O) was purchased from Stohler Isotope Chemicals. Doubly distilled water was employed. The pH's and pD's (pD = "pH" + 0.41)[10] were measured on the 30% 1,4-dioxane-buffer (v/v) solutions before and after reaction on a Radiometer PHM 26 meter. Since the rates were unaffected by the pH, no pH meter corrections were made to account for pH effects in the mixed solvent system.

2,4-Dinitrophenyl dibenzyl phosphate, DPDBP, was prepared by the method of Kirby and Varvoglis.[11] After two recrystallizations from ethanol, it gave colorless needle-like crystals, mp 65–66 °C (lit.[11] mp 65–66 °C).

Lithium 2,4-dinitrophenyl benzyl phosphate was prepared by debenzylation of the 2,4-dinitrophenyl dibenzyl phosphate with lithium chloride.[12] After recrystallization from ethanol-acetone, the melting point of this compound was 110–111 °C.

Kinetics. Spectrophotometric Method. Kinetic measurements were carried out on a Cary 16K UV-visible spectrophotometer equipped with an automatic sample changer and a Cary modified Varian G2500 recorder. The cell holder was maintained at a specific temperature by means of a Laude thermostat. A teletype which yielded a punch tape record of the time vs. absorbance data was also connected to the spectrophotometer via a specially constructed digital data system.

Reactions were followed by measuring the rate of appearance of 2,4-dinitrophenoxide at its absorption maximum at 360 nm, and in a few cases, confirmatory runs were also carried out at 250 nm. All reactions followed good first-order kinetics.

Table I. Mass Spectral Results for Acetate-Catalyzed Hydrolysis of Aryl-^{18}O-2,4-Dinitrophenyl Dibenzyl Phosphate

Reaction conditions[a]	% of oxygen-18[b] I	% of oxygen-18[b] II
1.0 M acetate (1/0.25)	93.2	89.0
0.4 M acetate, 0.6 M $NaClO_4$ (1/0.25)	92.7	90.7
2.0 M acetate (1/0)	91.7	91.0

[a] ^{18}O content in aryl-^{18}O-DPDBP, 93%. [b] Percent of ^{18}O estimated from (M + 2)/M ratio for peaks at m/e 184 and 154, respectively, by formulas I and II: (I) 186/(186 + 184) × 100%; (II) 156/(156 + 154) × 100%.

The first-order rate constants, k_{obsd}, were determined both by hand plotting of the absorbance data and by a weighted, iterative, nonlinear least-squares computer program.[13] Reactions were followed for at least 4 half-lives and allowed to proceed to completion (the infinity absorbance values were taken after 10 or more half-lives). Unless otherwise specified, all runs were carried out at 30.0 ± 0.1 °C and an ionic strength of 1.0 M maintained with sodium perchlorate.

Reactions of DPDBP, 2,4-dinitrophenyl benzyl phosphate, and dibenzyl phosphate with oxyanions were also determined on a Unicam SP 800A spectrophotometer, which automatically scanned the spectra between 450 and 200 nm for at least 3 days.

Titrimetric Method (pH Stat). The rate of hydrolysis of DPDBP was also studied by a titrimetric method in 30% 1,4-dioxane-water (v/v) at 30 °C. Kinetics were carried out by a pH stat using a Radiometer SBR2c Titrigraph combined with a SBU1a Syringe Burette, TTT11 Titrator and a TTA3 thermostated titration assembly. A K4112 calomel electrode was filled with saturated NaCl solution (KCl fouled the electrode in perchlorate solutions).

P–O/C–O Bond Cleavage Studies. Approximately 2.5–4.0 mM ^{18}O-2,4-dinitrophenyl dibenzyl phosphate[9] was hydrolyzed in acetate buffers under the conditions of the kinetic experiments at 30 °C. The solutions were acidified with a few drops of 61% $HClO_4$ to pH 1 after completion of the reaction and were extracted four times with methylene chloride. The extract was then evaporated to dryness under vacuum. The ^{18}O content of the resulting 2,4-dinitrophenol was determined by scanning and recording at least three times the mass spectrum on a AEI MS-30 or Perkin-Elmer Model 270 mass spectrometer. The oxygen-18 content was estimated by comparison of the m/e 186–184 and 156–154 peaks (Table I).

Product Studies. Identification and quantification of the benzyl alcohol product in the hydrolysis of DBDPP were determined by GLC analysis. After completion of the reaction of the triester (0.0096 M) in a series of 1,4-dioxane–acetate buffers, the hydrolysate (2 mL) was acidified with a few drops of $HClO_4$ to pH 1, and extracted four times with 2-mL portions of methylene chloride. The extract was evaporated to 1 mL and analyzed for benzyl alcohol on a F & M Scientific gas chromatograph Model 402 equipped with flame ionization detector and using a 15% Eggs-X on 100–120 mesh Chrom P, ⅛ in. × 6 ft column.

Results and Discussion

Kinetics. Analysis of the observed buffer catalysis is complicated by the upward curvature of many of the buffer plots (see for example, Figure 1) at high buffer concentrations and (in the case of acetate and formate) small inhibition of the reaction by the free acid component of the organic buffers. A corrected, observed rate constant $k_{obsd}{}^{c}$ was obtained by subtracting this acid rate depression term from the observed pseudo-first-order rate constants, k_{obsd}:

$$k_{obsd}{}^{c} = k_{obsd} - \alpha(BH)(B) \qquad (3)$$

where α is the acid inhibition correction constant and BH and B are the concentrations of free acid and base components of the buffer, respectively. For acetate buffers, α = 0.084 and for formate buffers α = 0.130 and thus correction is only impor-

Table II. Second-Order Rate Constants for the Reactions of Oxyanions and Fluoride Ion with 2,4-Dinitrophenyl Dibenzyl Phosphate at 30 °C and I = 1.0 M ($NaClO_4$ added salt)

	Nucleophile (concn range studied: acid; base), M	No. of runs	pK_a[a]	pK_a[b]	$k_0 \times 10^3$, s^{-1}	$k_B{}^c \times 10^3$, $M^{-1}\ s^{-1}$
1.	H_2O		−1.7	−1.37	0.090	0.0001
2.	$H_2PO_4^-$ (0.025-0.4; 0.05-0.32)	24	2.12		0.110	0.065
3.	Fluoride (10^{-5}-4 × 10^{-5}; 0.005-0.02)	10	3.4	3.62	0.110	134
4.	Formate (0-4.0; 0.02-1.0)	46	3.7	4.03	0.105	0.37
5.	Acetate (0-4.0; 0.02-1.0)	116	4.76	5.17	0.105	0.27
6.	HPO_4^{2-} (0.025-0.4; 0.05-0.32)	24	7.2	6.83	0.110	0.39
7.	*p*-Chlorophenolate (0.00025-0.001; 0.005-0.02)	8	9.38	9.46		73.0
8.	Phenolate (0.0005-0.005; 0.005-0.02)	16	9.98	10.11		110.0
9.	*p*-Methoxyphenolate (0.0013-0.005; 0.005-0.02)	8	10.20	10.46	207.1	>117
10.	CO_3^{2-} (0.002-0.4; 0.0001-0.001)	50	10.30	10.14		2.30
11.	Hydroperoxide (0.001-0.01; 0.001-0.001)	10	11.6	11.78		50 000.0
12.	Hydroxide (-; 0.005-0.02)	16	15.7	16.06		485.00

[a] Values of pK_a at 25.0 °C taken from G. Kortum, W. Vogel, and K. Andrussow, "Dissociation Constants of Organic Acids and Bases in Aqueous Solution", Butterworths, London, 1961. [b] Values of pK_a at 25.0 °C measured in 30% 1,4-dioxane-buffer solutions. [c] Rate constant for bimolecular attack at the phosphorus atom.

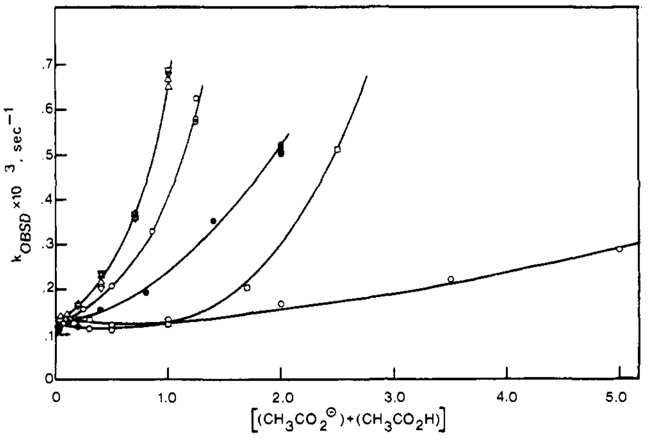


Figure 1. Uncorrected observed pseudo-first-order rate constants vs. total acetate buffer concentration in $CH_3CO_2^-/CH_3CO_2H$ buffer ratios: 1/1 (•); 1/4 (○); 1/0.25 (○); 1/1.5 (□); △ (1/0); ▽ (1/0.01).

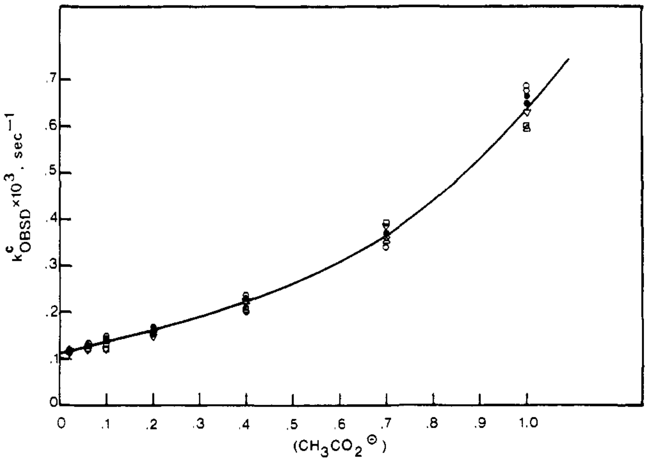


Figure 2. Corrected observed pseudo-first-order rate constants vs. acetate ion concentration. Symbols for points are given in Figure 1 legend.

tant at high total buffer concentrations. As a check on the validity of this correction, runs were also made using a pH stat where concentrations of the acid components of the buffer could be made vanishing small. As shown in Figure 2, the plot of the corrected rate constants vs. acetate ion is linear at low acetate (<0.4 M) and now is independent of the buffer ratio. Since at high buffer base concentrations (in acetate, formate, and carbonate) marked upward curvature was observed when sodium perchloriate was used to keep the ionic strength constant, only the slope in the linear region at low buffer concentration was used to determine the second-order buffer rate constants for catalysis by the free base, k_B.

As shown in Table II, the spontaneous hydrolysis rate between pH 3 and 7 is independent of pH. In the more basic buffers and at pH's > 11 in hydroxide ion solutions, the rate is proportional to the hydroxide ion concentration. Hence, the overall observed pseudo-first-order rate constant in the pH region 3-13 may be represented by

$$k_{obsd}{}^c = k_0 + k_{OH}(^-OH) + k_B(B) - \alpha(B)(BH) \qquad (4)$$

(The $H_2PO_4^-$ buffer rate constant is considered within the k_B term.)

Product Analysis and Reaction Scheme. The formation of both 2,4-dinitrophenol and benzyl alcohol in the first stage of the buffer-catalyzed hydrolysis of 2,4-dinitrophenyl dibenzyl phosphate indicates that at least two competitive reaction pathways must be considered. The ratio of the two isolated products varies with the concentration of the buffer in aqueous solution. At high acetate, formate, and phosphate concentrations 2,4-dinitrophenyl is produced predominantly, while benzyl alcohol is the major product at low buffer concentration (Table III).

In carbonate buffers, the products formed vary with the acid-base ratio of the buffers, and more than 90% of 2,4-dinitrophenol is formed in 1.0 M carbonate buffer. With phenolate, hydroxide, hydroperoxide, and fluoride ion, even at very low concentrations (≤0.02 M), very little benzyl alcohol is generated in these reactions.

As shown in Table III, the percentage of 2,4-DNP formed as determined spectrophotometrically agrees reasonably well (estimated error ±5%) with the percentage of 2,4-DNP formed as calculated from the kinetic data. This calculation assumes that the buffer-catalyzed path yields only 2,4-DNP and dibenzyl phosphate and the "spontaneous" water pathway yields benzyl alcohol and 2,4-DNP benzyl phosphate (Scheme I). None of the benzyl alcohol is formed from subsequent hydrolysis of either diester product, since under the conditions of the triester hydrolysis the diesters are stable. Actually this scheme neglects the ca. 6% of the water reaction in which the aryl ester bond is cleaved (Table III).

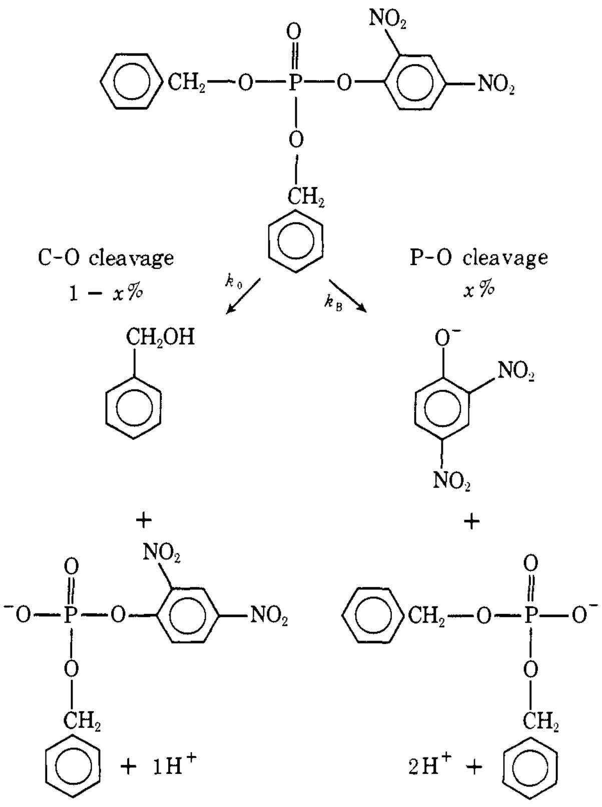
The ^{18}O labeling study (Table I) demonstrates that >98 ± 2% P-O cleavage occurs in the buffer-catalyzed cleavage of the aryl ester bond. In contrast, it is quite likely that C-O cleavage (via S_N2 attack on carbon) occurs in the hydrolysis

Table III. Hydrolysis Products in Acetate Buffer, $I = 1.0$ M[a]

Acetate, M (base/acid)	% of BzOH formed[b] (1/0.25)	% of 2,4-DNP formed (1/0.25)[c]	(1/0)[c]	(1/0)[d]
1.0	27.9	72.9	76.3	81.8
0.7	41.8	64.7	63.7	68.3
0.4	55.0	47.2	48.8	49.4
0.2		38.4	38.4	32.7
0.1	74.1	24.7	22.3	21.1
0.06		18.8	20.0	16.0
0.02		11.2	14.4	9.9
0			5.9	0

[a] $NaClO_4$ was added to maintain $I = 1.0$ M. [b] Experimentally determined by quantitative extraction of benzyl alcohol and analysis by GLC. 100% = 1 mol of benzyl alcohol formed/mol of triester hydrolyzed. [c] Experimentally calculated values from UV-visible A data at 360 nm. 100% = 1 mol of 2,4-DNP formed/mol of triester hydrolyzed. [d] Calculated values. Calculated on the basis of Scheme I and the rate constants given in Table II: % DNP = $(k_{obsd} - k_0)/k_{obsd}$.

Scheme I. Proposed Pathways for the Hydrolysis of 2,4-Dinitrophenyl Dibenzyl Phosphate



of the benzyl ester bond. Support for this presumption is provided by the Cl^--catalyzed hydrolysis of the triester,[15] which yields 2,4-dinitrophenyl benzyl phosphate and benzyl chloride. In contrast, the F^--catalyzed hydrolysis of the triester proceeds through attack on phosphorus and expulsion of the 2,4-DNP. Thus, in a trisubstituted phosphate ester in which both carbon and phosphorus centers are open to substitution, chloride and water will react at carbon, and fluoride and hydroxide will react at phosphorus. The results agree with Pearson's predictions[16] that hard nucleophiles such as oxyanions and fluoride tend to react with hard acids, such as the electropositive phosphorus center, and soft nucleophiles like water and chloride react with soft acids, such as the benzylic carbon center.

Further support for this reaction scheme is provided by the proton release study. By monitoring the amount of base consumed in the pH stat kinetic study of the acetate-catalyzed hydrolysis of the triester, the total number of protons released in the reaction can be determined. Since one proton is generated in the hydrolysis of the benzyl ester bond, whereas two protons are produced in the hydrolysis of the aryl ester bond when the pH is above ~6, the number of protons generated in the reaction may be calculated by

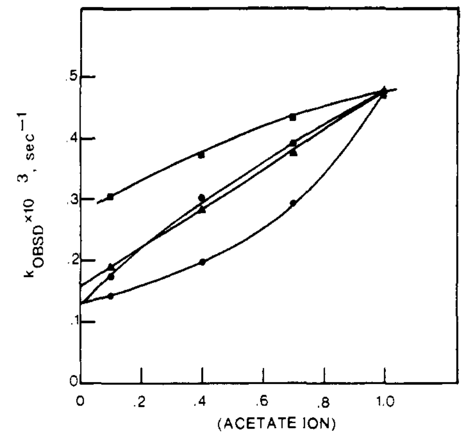


Figure 3. Uncorrected observed pseudo-first-order rate constants vs. acetate ion concentration in 1/1.5 buffer using $NaClO_4$ (●), Na_2SO_4 (●), $NaNO_3$ (▲), and KCl (■) to maintain $I = 1.0$ M.

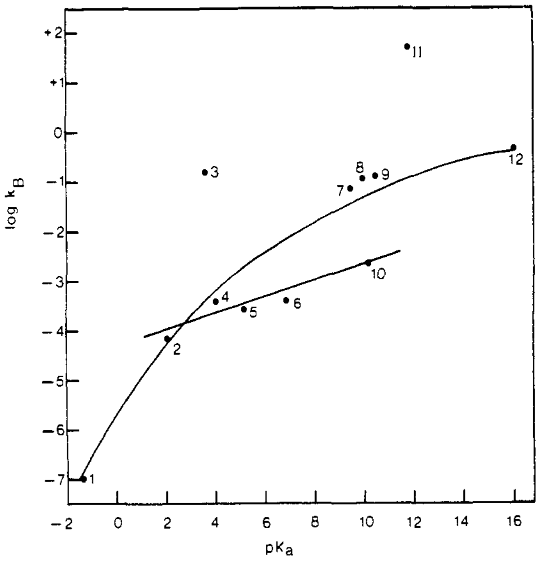


Figure 4. Brønsted plot of the second-order rate constants, k_B, for attack at phosphorus (numbers correspond to buffer labels in Table II).

$$\text{no. of H}^+ \text{ generated} = 2x + 1(1.00 - x) \qquad (5)$$

where x is the fraction of 2,4-dinitrophenyl formed, and $1.00 - x$ is the fraction of benzyl alcohol formed. As shown in Table IV, the observed and calculated number of protons generated in the acetate-catalyzed hydrolysis of the triester agrees with the proposed reaction pathway. At high acetate concentrations most of the reaction proceeds with aryl ester cleavage, while in the absence of added oxyanion buffers the water reaction proceeds with >94% benzyl ester cleavage.

Nucleophilic Catalysis. The question of nucleophilic vs. general-base mechanisms for the buffer-catalyzed hydrolysis of 2,4-dinitrophenyl dibenzyl phosphate may be answered in several ways. First, the scatter in the Brønsted plot (Figure 4) between the second-order rate constants for P-O(Ar) cleavage and the pK_a of the conjugate acid of the oxyanions and fluoride ion suggests that the buffer reaction proceeds via a nucleophilic

Table IV. pH Stat, Proton Release Studies

Acetate (1/0), M[a]	pH	$k_{obsd} \times 10^3$	No. of protons generated[b]	Estimate no. of protons generated[c]
1.0	8.272	0.5145 ± 0.0075	1.88	1.73
0.7	8.180	0.3763 ± 0.0031	1.67	1.65
0.4	8.150	0.1851 ± 0.0026	1.50	1.47
0.1	8.030	0.1556 ± 0.0038	1.34	1.25
0	8.150	0.0890 ± 0.0019	1.10	1.06

[a] Concentration is expressed in terms of ionic strength, $NaClO_4$ was added to maintain I = 1.0 M. [b] Number of protons generated = (OH^-) titrant consumed/($(BzO)_2P(O)ODNP$). [c] Number of protons generated is estimated by eq 5.

Table V. The Effect of 1,4-Dioxane on the Hydrolysis of 2,4-Dinitrophenyl Dibenzyl Phosphate in 1.0 M Formate (1/1) at 30 °C and I = 1.0 M

Dioxane, %	pH	ϵ^a	$k_{obsd} \times 10^3\ s^{-1}$
20	3.822	62.2	0.8616 ± 0.0032
30	3.960	53.5	0.7376 ± 0.0046
40	4.270	44.3	0.7141 ± 0.0039
50	4.540	35.6	0.6900 ± 0.0094

[a] Dielectric constants obtained from C. V. King and J. J. Josephs, *J. Am. Chem. Soc.*, **66**, 767 (1944).

catalysis mechanism. In general, if hydrolysis involves general-base catalysis, a much better fit of the data for a wide range of nucleophiles to the Brønsted equation is usually obtained.[17] In addition, as expected, the nucleophilic reactivity of an anion toward the phosphorus center of the triester depends upon its basicity, except that, in particular, formate is more reactive than acetate, as indicated by Kirby and coworkers,[12,18] and hydroperoxide is exceptionally reactive as expected for an α-effect nucleophile.[2b,18] Additionally, fluoride is much more reactive than would be expected from its basicity as reported previously[3,8,19,20] and only a little less reactive than hydroxide toward the triester. These observations strongly indicate that this reaction involves a direct nucleophilic displacement at phosphorus by the anionic buffer component. This conclusion is further confirmed by a small solvent deuterium isotope effect on the second-order buffer rate constants, k_{H_2O}/k_{D_2O} = 1.0–1.6, which is within the range expected for nucleophilic catalysis.[3,8,12,21] Specifically, k_{H_2O}/k_{D_2O} for the reactions of the triester with formate, acetate, phosphate, and carbonate ions are 1.00 ± 0.2, 1.2 ± 0.2, 1.23 ± 0.2, and 1.58 ± 0.2, respectively. The solvent deuterium isotope effect for the spontaneous hydrolysis is 1.0 ± 0.1.

Attempts to verify the nucleophilic pathway by trapping of an intermediate with the hydroxamic acid test,[14] from the observation of a bad isosbestic point in the continuous scanning of the UV-visible spectrum, and deviations from good first-order kinetics in the pH stat runs were not successful. However, the possibility of nucleophilic attack could not be ruled out in view of the fact that the intermediate might not exist long enough to be detected both spectrophotometrically and titrimetrically prior to subsequent hydrolysis. In fact, both dialkyl acetyl phosphate and dialkyl phosphoryl fluoridate do hydrolyze faster than dialkyl 2,4-dinitrophenyl phosphate under comparable conditions.[2,22] Thus Kluger and Wasserstein[22] have shown that dimethyl acetyl phosphate hydrolyzes at pH 6.0 and 30.0 °C in 0.1 M KCl with an observed first-order rate constant of 0.068 s^{-1}. In 1 M acetate, the pseudo-first-order rate constant for acetate-catalyzed hydrolysis of our triester is 0.00027 s^{-1}. Thus breakdown of the presumed dibenzyl acetyl phosphate is likely much faster than its formation, and no intermediate will build up.

Khan and Kirby[7] have also concluded that the attack of various oxyanions on the cyclic triester, 2,4-dinitrophenyl-2-oxo-1,3,2-dioxaphosphorinan, involves nucleophilic catalysis and have calculated a Brønsted β (=0.30) for this reaction. Using the same four points used by Khan and Kirby (^-OH, carbonate, phosphate, and acetate) for calculating the Brønsted slope, we find β = 0.17 for the nucleophilic-catalyzed hydrolysis of 2,4-dinitrophenyl dibenzyl phosphate. However, perhaps a better analysis of the Brønsted plot shown in Figure 4 would suggest a curved best fit to the data. Weakly basic nucleophiles show a limiting Brønsted slope of ~0.8, while the strongly basic nucleophiles show a limiting $\beta \sim 0.1$.

Solvent Effects. Addition of organic solvent to the buffer solution hinders the rate of neutral hydrolysis of phosphate triesters.[23,24] In the reaction of 2,4-dinitrophenyl dibenzyl phosphate with formate ion in aqueous dioxane, the rate constant increases on going from 50 to 20% dioxane (Table V). In contrast, it is generally found that the rate constant decreases as the dielectric constant increases for the reaction of an anion with a neutral molecule in an S_N2 displacement reaction at carbon.[25] The opposite behavior for nucleophilic reaction at phosphorus could be due to a change in the ion-pair dissociation constants, which would result in a higher concentration of formate ion, rather than to a change in the dielectric constants. Alternatively, if the activated complex had greater charge density than the formate ion plus neutral triester, this result would be explicable. It would suggest a transition state with a fully formed nucleophile–ester bond and nearly a full negative charge on the single phosphoryl oxygen of a pentacovalent structure. In the formate ion this negative charge is delocalized over *two* oxygens. This rate decrease with decreasing dielectric constant of the medium also explains why we observe a rate depression with increasing concentrations of acetic acid or formic acid (the free acid buffer component, α term).

Activation Parameters. A complication to the activation energy analysis is the concurrent reaction pathways. Although no attempt has been made to separately calculate the activation parameters for the water and buffer terms, the absence of any biphasic character to the plots of the observed rate constants indicates that the parameters are not very different for the two competitive reactions. In addition, throughout the temperature range studied, a constant 75% of the hydrolysis reaction proceeds through P-O(Ar) cleavage, again indicating similar activation parameters for the two pathways. For reactions of formate and acetate with 2,4-dinitrophenyl dibenzyl phosphate, activation entropies are large and negative (−22 and −26 eu; Table VI). These results are in good agreement with those generally found for reactions with phosphate triesters.[24,26,27]

Comments on Specific Salt Effects and Curved Buffer Kinetic Plots. Inorganic salts, potassium chloride, sodium nitrate, sodium sulfate, and sodium perchlorate were used in maintaining unit ionic strength for the kinetic studies. Specific salt effects are observed for the reaction of acetate ion with 2,4-dinitrophenyl dibenzyl phosphate; a linear second-order plot

Table VI. Activation Parameters[a] for the Reactions of Acetate and Formate with 2,4-Dinitrophenyl Dibenzyl Phosphate

Nucleophile	pH[b]	E_A, kcal/mol	$\Delta H^{\neq}$, kcal/mol	$\Delta S^{\neq}$, eu
Acetate	5.356	15.73	15.1	−26.36
Formate	4.012	16.06	15.5	−21.69

[a] Reference: A A. Frost and R. G. Pearson, "Kinetics and Mechanism", Wiley, New York, N.Y., 1961. [b] pH of 30% 1,4-dioxane-water (v/v) which contains 1.0 M of acetate (1/1) or 1.0 M of formate (1/1); T = 25.0 °C.

is obtained only in sodium nitrate salt media, whereas sodium perchlorate gives an upward curving second-order plot, and sodium sulfate and potassium chloride gives a downward curving plot (Figure 3).

Traditionally, upward curving buffer plots have been interpreted in terms of a second-order ($[B]^2$) catalytic term.[17] This is clearly mechanistically unreasonable for the present reaction, except possibly for an acetate ion (or formate ion) catalyzed breakdown of a pentacovalent intermediate involving addition of another acetate (or formate) ion. Since upward curvature of the buffer plots is not observed when the other salts are used, a second-order term explanation is definitely ruled out.

The upward curvature is not due to a specific water-$NaClO_4$ interaction affecting the activity of the water, since nearly identical upward curvature is found in the acetate-catalyzed methanolysis reaction (100% methanol).

The upward curvature with $NaClO_4$ added salt indicates that the $NaClO_4$ depresses the acetate-catalyzed reaction. (Also compare the acetate reaction in the presence of Na_2SO_4 and $NaNO_3$, ($k_B = 0.27\ M^{-1}\ s^{-1}$ for $NaClO_4$, $k_B = 0.32\ M^{-1}\ s^{-1}$ for $NaNO_3$, and $k_B = 0.42\ M^{-1}\ s^{-1}$ for Na_2SO_4). The salts also have a moderate effect on the k_0 term (the intercepts to Figure 3). The KCl added salt reaction, as already indicated, presents even further complication, since the Cl^- specifically reacts with the triester, hence increasing the rate at low acetate (high Cl^-) concentrations.

The slight downward curvature in the buffer plots using Na_2SO_4 is not likely due to a change in rate-determining step with buffer, as this sort of downward curving behavior is traditionally interpreted.[28]

These "anomalous" curved plots point out the importance of testing for specific salt effects before much confidence can be placed in interpretations based upon second-order buffer terms or a change in rate-determining step. This is especially crucial when large (>0.1 M) concentrations of added salt are used to "keep constant" the ionic strength of buffer solutions. It is likely that when fairly substantial solvent effects are noticed, activity coefficients of reactants and transition states in a 1 M acetate ion solution are not identical with a 0.01 M acetate-0.99 M added salt solution. Recent reemphasis[29,30] on the pitfalls of the poor assumption of the validity of the Debye-Hückel theory at high salt concentration demonstrates the requirement for caution in the interpretation of curved buffer plots.

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