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# Kinetics and Mechanism of the Hydrolysis of Aryloxyphosphonium Salts. Salt Effects

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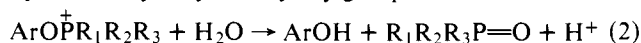
Abstract: The rates of hydrolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate, I, of methylphenyldiphenoxyphosphonium triflate, II, and of methyldiphenylphenoxyphosphonium triflate, III, are decreased 30-, 63-, and 83-fold, respectively, by the addition of 1.8 M lithium triflate in 34% aqueous acetonirile. These enormous salt effects are ascribed to a decrease in the activity of water in the mixed solvent. Substitution of triflic acid for lithium triflate at a constant ionic strength of 1.8 M further decreases the rate of hydrolysis of I and II by factors of 2.6 and 3.2, respectively, but has no influence on that of III. These data can most simply be interpreted to mean that the rates of hydrolysis of I and II are inhibited by acids per se, and that the observed decreases in rate with increasing concentration of acid at constant ionic strength are not simply caused by a difference between the effects of hydrogen and lithium ions on the activity coefficient of water. The inhibition by acid provides evidence that the hydrolysis proceeds by way of a phosphorane as intermediate.

Introduction

The hydrolysis of aryloxyphosphonium salts[1,2] provides a model for an essential step in the acid hydrolysis of phosphates, phosphonates, and phosphonites; the detailed mechanisms of such hydrolyses[3-5] are of interest because of the ubiquitous occurrence of phosphates in intermediary metabolism. Presumably phosphates are protonated to yield hydroxyphosphonium salts that in turn react with water:

$$(RO)_3PO + H^+ \rightleftharpoons (RO)_3\overset{+}{P}OH$$

$$(RO)_3\overset{+}{P}OH + H_2O \rightarrow products \tag{1}$$
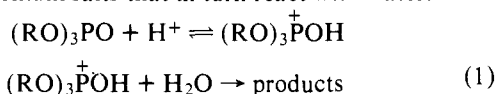
The reactions summarized by eq 2 model the second step in this mechanism; ArOH is a phenol, and R_1, R_2, and R_3 can represent alkyl, aryl, or aryloxy groups.

$$ArO\overset{+}{P}R_1R_2R_3 + H_2O \rightarrow ArOH + R_1R_2R_3P{=}O + H^+ \tag{2}$$

A major question arises as to whether the hydrolyses shown in eq 1 and 2 proceed by way of phosphoranes as intermediates, or by way of pentacoordinate transition states (or even, perhaps, through hexacoordinated intermediates).

The rates of hydrolysis of methyltriphenoxyphosphonium triflate, IV, and of methyltris(2,6-dimethylphenoxy)phosphonium triflate, I, as functions of the concentration of water and acid in aqueous acetonitrile have been measured previously by stopped-flow techniques.[1] The rates of hydrolysis in that solvent increase a millionfold between 0.2% and 34% water, but the rate at any given concentration of water is sharply diminished by added acid; 1.8 M triflic acid in 34% aqueous acetonitrile decreases the rate about 100-fold. The rates are also strongly inhibited by salts,[2] and, in particular, the rate of hydrolysis of I in 34% aqueous acetonitrile is decreased 30-fold by 1.8 M lithium triflate; the rate of hydrolysis is diminished
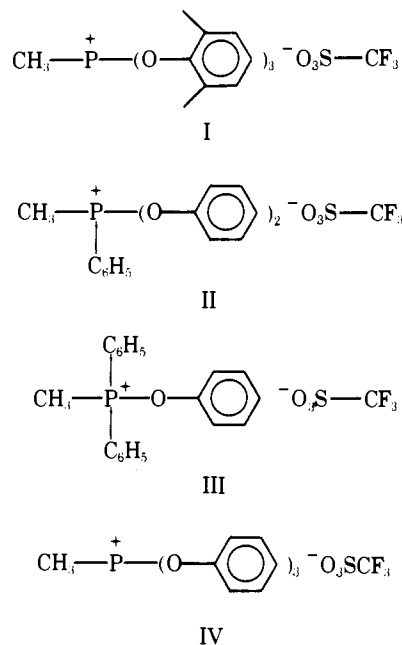
another factor of 2.6 by replacing the lithium triflate by 1.8 M triflic acid. The question naturally arises as to whether this further decrease in rate, caused by the substitution of hydrogen ions for lithium ions, is the result of an inhibitory effect of acid, per se, or whether it represents a difference between the salt effects of lithium and hydrogen ions on the activity coefficient of water or other reaction species. The mechanism of the hydrolysis of the phosphonium salts under study obviously depends on the answer to this question.

This paper is concerned with the kinetics of the hydrolysis of aryloxyphosphonium salts, with the effects of salts and acid on the rates of reaction, and on the mechanism of the hydrolytic process.

Experimental Section

Methods. Rates were measured by observing the change in UV absorption that accompanies the release of phenol (or 2,6-dimethylphenol) from the phosphonium salt during hydrolysis. Rates with $t_{1/2}$ > 10 s were measured with a Cary Model 15 or with a Gilford Model 240 spectrophotometer. Rapid solvolyses were measured with a stopped-flow spectrophotometer, consisting of a Durrum-Gibson Model 13701 stopped-flow mixing chamber (Kel-F) assembly, equipped with rotary valves and Teflon-tip drive-syringe plungers, a modified Zeiss Model PQ11 spectrophotometer, a Hewlett-Packard-Harrison Model 6515 DC power supply, a Tetronix Type 564 storage oscilloscope, a Tetronix Polaroid Model C-30 camera, and a Lauda K-2/RD refrigerated circulator, with Dow-Corning 200 silicon fluid. Kinetic data were analyzed on a Digital PDP 11/45 computer, equipped with a Calcomp 565 plotter.

^{1}H NMR spectra were recorded with Varian Models A-60 and HA-100 spectrometers and chemical shifts reported in ppm relative to tetramethylsilane. ^{31}P NMR spectra were obtained with a Varian XL-100 spectrometer in Fourier transform mode and chemical shifts reported relative to 85 percent phosphoric acid. Infrared spectra were determined with a Perkin-Elmer Model 137 spectrometer. Elementary analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn .

Phosphonium salts were recrystallized under argon in Schlenk glassware;[6] solvent was cannulated into the apparatus through stainless steel tubing inserted through Bittner serum stoppers.

Solvents and Reagents. Reagent grade solvents were dried prior to use by standard methods and distilled through a vacuum-jacketed helix-packed column into dried bottles. Burdick and Jackson's acetonitrile proved to be as dry and pure as any we could prepare and was used directly. Acetonitrile-d_3 (Stohler) was stirred for 2 h at room temperature with calcium hydride, refluxed over calcium hydride for an additional hour, and distilled through a dry short-path distillation apparatus. Triflic acid (3M Co., FC-24) was purified by vacuum distillation through a vacuum-jacketed helix-packed column, with a distillation head containing Teflon sleeves and stopcocks, bp 72 °C/24 mm. Lithium perchlorate (HEF Co.) was recrystallized from dry acetonitrile and dried under vacuum at 130 °C; sodium trifluoromethanesulfonate (Willow Brook) was recrystallized from ethanol and dried under vacuum at 70 °C. Deuterium oxide (Bio-Rad, 99.9% deuterium) was used without further purification. Trifluoromethanesulfonic acid-d_1 was prepared from the anhydride, which in turn was prepared by the method of Gramstad and Haszeldine;[7] its bp and infrared spectra corresponded with those in the literature. Addition of deuterium oxide to an equimolar amount of the anhydride yielded the deuterated acid, which was purified by vacuum distillation (bp 80 °C/28 mm).

Materials. Methyltris(2,6-dimethylphenoxy)phosphonium trifluoromethanesulfonate (triflate) was prepared according to Phillips et al.,[8] mp 193–194 °C (lit. 193–194 °C); bis(2,6-dimethylphenyl)-methylphosphonate was prepared according to Szele et al.,[9] mp 75–76 °C. Methylphenyldiphenoxyphosphonium trifluoromethanesulfonate melted at 152.5–154 °C (lit.[8,10] 151.5–152 °C; 155.5–157.7 °C). Methyldiphenylphenoxyphosphonium trifluoromethanesulfonate, recrystallized from methylene chloride-ether, melted at 102–103 °C (lit.[8,10] 99–100 °C, 100.5–102 °C). Diphenylmethylphosphine oxide, prepared by Dr. I. Sigal, had melting point and spectra in agreement with the literature.[11] Dimethyldiphenoxyphosphonium trifluoromethylsulfonate was prepared from methyl triflate (4.92 g) (Aldrich) and diphenyl methylphosphonite[12] (5.80 g) in methylene chloride by the same method used to prepare the other aryloxyphosphonium salts. The product was recrystallized from methylene chloride; yield, 61% of theory, mp 121–122 °C; ^{1}H NMR (CDCl$_3$) δ 2.50 (d, J = 15 Hz), 7.3–7.5 (m); ^{31}P [^{1}H] NMR (CD$_3$CN) δ −94.60. Anal. Calcd for C$_{15}$H$_{16}$F$_3$O$_5$PS: C, 45.46; H, 4.07; F, 14.38; O, 20.18; P, 7.82; S, 8.09. Found: C, 45.44; H, 4.20; F, 12.70; O, 21.30; P, 7.99; S, 8.25.

Lithium Trifluoromethanesulfonate. Lithium hydroxide (25 g; Fisher) was dissolved in 400 mL of water, and the solution filtered. The alkali was titrated to pH 6.9 with an aqueous solution of vacuum-distilled triflic acid (100 mL of acid/400 mL of water). The water was removed in vacuo and the solid dried at 70 °C in vacuo

overnight. The salt was then recrystallized under argon from dry acetonitrile (45 g of salt in 120 mL of acetonitrile) in a large Schlenk double-tube recrystallizer. The salt was dried in vacuo at 60 °C; yield, 72%. A 0.1 M solution of the salt in deionized water showed a pH of 6.7.

Tetramethylammonium Trifluoromethanesulfonate. A 20% methanolic solution of tetramethylammonium hydroxide (Aldrich) was titrated to pH 6.9 with aqueous triflic acid (23 mL of acid/150 mL of water). The water was removed in vacuo and the resulting white solid was recrystallized from acetone, and dried in vacuo at 60 °C overnight: yield, 90% of theory, mp >300 °C; ^{1}H NMR (D$_2$O) δ 3.17 (s).

Kinetic Procedures. The various salts were weighed into dry volumetric flasks in an I^{2}R glove bag filled with nitrogen, or in a Labconco glovebox filled with nitrogen. The flasks were closed with rubber stoppers, and the required amount of water was added by cannulation. When the flasks had come to room temperature, they were filled to the mark with acetonitrile, again taking care to achieve thermal equilibrium. Solutions of triflic acid were necessarily prepared slowly, because of the large heat of mixing. A sample of the phosphonium salt for hydrolysis was transferred into a dry volumetric flask from the storage tube with the aid of a sample loader similar to Ace Glass no. 7782, while the tube was flushed with argon. The volumetric flask was capped with a rubber stopper and dry acetonitrile added by cannulation. For stopped-flow measurements, the solution of phosphonium salt (10^{-3} to 10^{-4} M) was transferred under argon pressure to one of the reservoir syringes of the stopped-flow apparatus by a Luer-lock needle. A solution of acid or salt, in aqueous acetonitrile, was then transferred to the other reservoir. Both 1:1 and 5:1 ratio syringes were used.

A number of troublesome artifacts plagued the stopped-flow measurements. When acetonitrile and pure water were mixed, the oscilloscope trace for 100% transmission appeared as an inverted tailing bell-shaped curve. The maximum negative[13] deviation appeared between 200 ms and 6 s and amounted to about 2% or 3% of full-scale deflection. The phenomenon may be caused by sharp gradients in refractive index; anyway, it did not appear when solutions of acetonitrile and of aqueous acetonitrile were mixed.

Another deviation occurred from 18 s to 10–15 min after equal volumes of pure acetonitrile and pure water were mixed. In this case, the deviation of 6–8% of full-scale was positive; this phenomenon has been described by Gibson et al.[14] for cases like the present one where mixing causes a drop in temperature; again, the phenomenon occurs through a change in refractive index. With reasonable care, the effects of these artifacts could be avoided; the data for the fast reactions were gathered before the negative deviation, with infinity points taken after the negative deviation had subsided but before the positive deviation occurred. Data for the slow reactions were gathered after the negative deviation but before the positive deviation, with infinity points after the positive deviation had subsided. The details of the experimental procedures are given elsewhere.[15] The data gathered from the Gilford and Cary spectrophotometers were not subject to these artifacts and were treated in conventional ways.

The change in absorption that occurs on the hydrolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate is shown in Figure 1a. The reaction was followed at 277 nm, the maximum for the absorption of the product. Similar spectra[15] were obtained for the hydrolysis of methylphenyldiphenoxyphosphonium triflate; again the phenolic product absorbed much more strongly than did the starting material; the rates were followed at 271 nm. However, the spectral change for the hydrolysis of methyldiphenylphenoxyphosphonium triflate to the corresponding phosphine oxide was atypical; the absorption of the phosphine oxide at long wavelengths is comparable to that of phenol (Figure 1b). In this instance, the rate was followed by observing the decrease in absorption at 245 mm that accompanies hydrolysis.

Identification of Products. The products of the hydrolysis of the aryloxyphosphonium salts were isolated and identified by comparison of their melting points and infrared and NMR spectra with those of authentic samples. Thus, methyltriphenoxyphosphonium triflate yielded diphenyl methylphosphonate;[16] methylphenyldiphenoxyphosphonium triflate yielded phenyl methylphenylphosphinate;[8] methyltris(2,6-dimethylphenoxy)phosphonium triflate yielded bis(2,6-dimethylphenyl) methylphosphonate;[9] and methyldiphenyldiphenoxyphosphonium triflate yielded methyldiphenylphosphine oxide.[8] Although the products were isolated in good yield, in no case was isolation quantitative. However, the UV spectra (where measured)
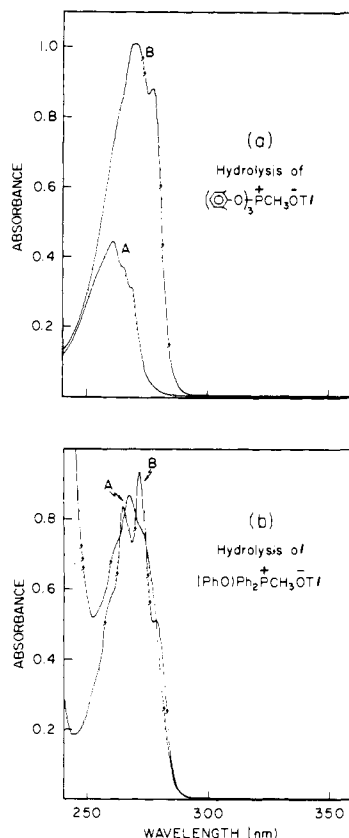
Figure 1. (a) A, UV absorption spectrum of a ca. 10^{-3} M solution of methyltris(2,6-dimethylphenoxy)phosphonium triflate in dry acetonitrile; B, spectrum of the products of hydrolysis (bis(2,6-dimethylphenyl) methylphosphonate, dimethylphenol, and triflic acid) in the same solvent plus ~2% water. (b) A, UV absorption spectrum of a ca. 10^{-3} M solution of methyldiphenylphenoxyphosphonium triflate in dry acetonitrile; B, spectrum of the products of its hydrolysis (methyldiphenylphosphine oxide, phenol, and triflic acid) in the same solvent plus ~2% water.

Figure 2. Logarithm of rate constants for hydrolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate (■, X) and of methyltriphenoxyphosphonium triflate (●, O) in aqueous acetonitrile at 25 °C vs. logarithm of the concentration of water. Open circles and X's refer to stopped-flow measurements; closed circles and closed squares refer to measurements with a Cary spectrophotometer. Note that the scales for the rate constants for the phenoxy salt are displaced, relative to those for the 2,6-dimethylphenoxy salt, by approximately two logarithmic units.

Figure 3. Logarithm of rate constants for hydrolysis of methylphenyldiphenoxyphosphonium triflate, of dimethyldiphenoxyphosphonium triflate, and of methyldiphenylphenoxyphosphonium triflate at 25 °C in aqueous acetonitrile vs. logarithm of the molarity of water.

were quantitatively what would have been expected for quantitative yields of the isolated products, and the ^{31}P NMR spectra of the reaction mixtures showed that, in each case, the only products formed were the expected ones.

Results

The effect of water in water–acetonitrile mixtures on the rates of hydrolysis of methyltriphenoxyphosphonium triflate and of methyltris(2,6-dimethylphenoxy)phosphonium triflate is shown in Figure 2 reprinted from our earlier communication.[1] The effect of water on the rates of hydrolyses of methylphenyldiphenoxyphosphonium triflate, of dimethyldiphenoxyphosphonium triflate, and of methyldiphenylphenoxyphosphonium triflate is shown in Figure 3.

A comparison of the rates of hydrolysis of the aryloxyphosphonium salts in 50% aqueous acetonitrile (extrapolated where necessary) is shown in Table I.

The rate data are also compared with the ionization constants of the corresponding phosphoranes, i.e., of the phosphoranes that ionize to the indicated cations and phenoxide ion. These constants had previously been determined conductometrically in dry acetonitrile.[10] The decrease in rate of association of the cations with water with increasing substitution at phosphorus parallels the increase in the dissociation constants of the phosphoranes.

The effect of acid on the rate of the hydrolysis of I in 18.8 M (34%) water in acetonitrile (from our earlier work[1,2]) and the effect of lithium triflate on the hydrolysis of both I and III are shown in Figure 4. Although the rate of hydrolysis of III
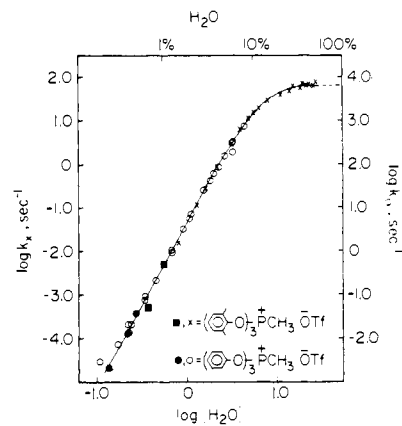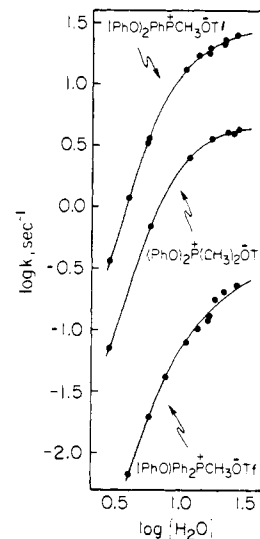
is only 3×10^{-3} as great as that of I, the shapes of the two curves are similar.

The rate of hydrolysis of III decreases by a factor of 83 between pure solvent and 1.8 M salt. On the other hand, and in sharp contrast to the behavior of methyltris(2,6-dimethylphenoxy)phosphonium triflate, the rate of hydrolysis of III at constant ionic strength is independent of acid; that is to say, the rate is the same at any given ionic strength in the range tested (i.e., up to 1.8 M) regardless of whether the electrolyte present is triflic acid or lithium triflate. The essential data, and the contrast with those obtained for the hydrolysis the salt, I, are shown in Figure 5. (In all of these figures, the rate in neutral solvent is marked on the ordinate. Since the abscissa is the logarithm of the concentration of acid or salt, the actual point for hydrolysis in the absence of salt should be displaced to negative infinity. Nevertheless, the plots show that the data do indeed extrapolate, as they should, to the point obtained in the absence of added electrolyte.)
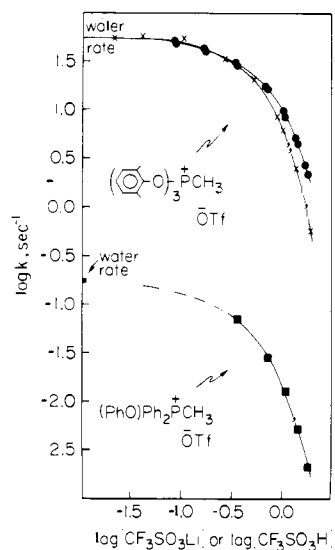
Figure 4. Effect of lithium triflate or of triflic acid on the rates of hydrolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate, 1, and of methyldiphenylphenoxyphosphonium triflate, 111, in 34% aqueous acetonitrile at 25 °C. The upper of the two curves for the hydrolysis of 1 refers to the effect of the salt, and the lower of the two curves to the effect of acid on the rate of hydrolysis.

Table I. Rates of Hydrolyses of Various Aryloxyphosphonium Triflates in 50% Aqueous Acetonitrile at 25 °C

cation	1st order rate constant, s^{-1}	K_{diss} in dry acetonitrile, M
$CH_3P(OC_6H_5)_3^+$ (1V)	6×10^3	$<4 \times 10^{-10}$
$CH_3P(OAr)_3^+$ (1)	55	
$CH_3P(C_6H_5)(OC_6H_5)_2^+$ (II)	25.2	8×10^{-9}
$(CH_3)_2P(OC_6H_5)_2^+$	4.3	
$CH_3P(C_6H_5)_2(OC_6H_5)^+$ (111)	0.237	5×10^{-6}

The salt effects obtained with a variety of salts are presented in Table II. These data show that lithium ion is far more effective than sodium ion in lowering the rate, whereas tetramethylammonium ion has little effect. (The limited solubility of tetramethylammonium triflate prevented us from using concentrations in excess of 0.93 M.) It should be noted, however, that, although both lithium triflate and lithium perchlorate produce enormous salt effects, the effect with perchlorate is greater by a factor of 2.7 for the hydrolysis of methyldiphenylphenoxyphosphonium triflate, and by a factor of 1.6 for the hydrolysis of methyltris(2,6-dimethylphenoxy)-phosphonium triflate.

Deuterium Isotope Effect. The rates of solvolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate were also measured in D_2O–acetonitrile mixtures, in the presence and absence of lithium triflate and of triflic acid.[15] The rate of solvolysis increases with the third power of the concentration of D_2O in the mixed solvent, paralleling the results with water. The rate levels off at high concentrations of deuterium oxide in acetonitrile, as it does for high concentrations of water, but only at a somewhat higher concentration: about 50% D_2O, as compared with about 34% of H_2O. The difference is real and, presumably, is caused by a difference in the solvation of ions by the isotopic waters, leading to greater segregation of solvent molecules in the acetonitrile–H_2O mixtures. In view of this problem, the rates were compared only in solvent mixtures corresponding to the maximum rates, presumably equal to those in the pure solvent. In numerous experiments, with or
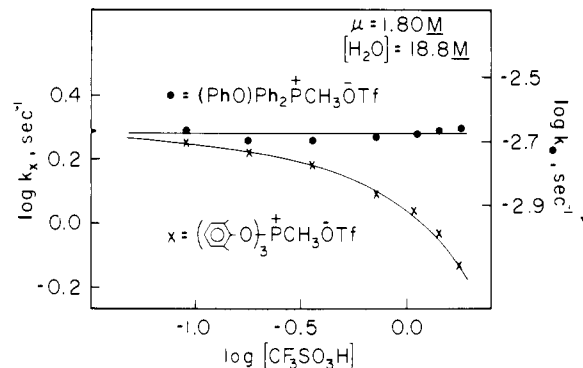

Figure 5. Effect of triflic acid on the rates of hydrolysis of methyldiphenylphenoxyphosphonium triflate, 111, and of methyltris(2,6-dimethylphenoxy)phosphonium triflate, 1, in 34% aqueous acetonitrile at 25 °C at a constant ionic strength of 1.8 M, maintained with lithium triflate. Note that the scale for the hydrolysis of 1 is displaced, relative to that for 111, by about 3 logarithmic units.

Table II. Salt Effects on the Hydrolysis of Phosphonium Triflates in ca. 19 M Aqueous Acetonitrile at 25 °C

substituents on phosphonium cation	$[H_2O]$, mol/L	[salt], mol/L	k_{obsd}, s^{-1}
methyltris(2,6-dimethylphenoxy) (I)	18.80	none	59.4
	18.80	0.93 M Me₄NOTf	49.3
	18.80	0.65 M Me₄NOTf	52.2
	18.80	0.37 M Me₄NOTf	55.1
	17.88	2.06 M NaOTf	13.0
	18.80	1.80 M LiOTf	1.94
	18.80	1.80 M LiClO₄	1.25
methyldiphenylphenoxy (III)	18.80	none	0.184
	18.98	1.80 M NaOTf	0.006 52
	18.98	1.80 M NaOTf	0.007 32
	18.80	0.90 M Me₄NOTf	0.121
	19.42	1.80 M LiOTf	0.002 21
	19.42	1.80 M LiOTf	0.002 18
	18.80	1.80 M LiClO₄	0.000 804
	18.80	1.80 M LiClO₄	0.000 803

without salt, and with or without acid, the solvent isotope effect, k_{H_2O}/k_{D_2O}, was 3.2 ± 0.2.

Discussion

The salt effect here noted is extraordinarily large, and perhaps unprecedented for such a low salt concentration. The large effect may, however, arise from the use of a mixed solvent. The ions, and especially the cations, are presumably hydrated, and combine much more strongly with water than with acetonitrile. Jordan[17] has suggested that, in mixed solvents of water and acetonitrile, the acidity can be approximated by assuming that the acetonitrile is inert. In the present instance, then, we should consider that 1.8 M salt in 34% aqueous acetonitrile will behave as if it were 5.4 M salt in water. Even

with this assumption, the salt effects here observed are large. The salt effects on the acidity function, H_0, in 60% dioxane–40% water, are comparable;[18] here the addition of 3.38 M LiCl to 3.2 M HCl decreased H_0 by 1.63 log units, corresponding to a factor in H_0 of 43. At high salt concentrations in water, enormous salt effects are well known.[19-23] For example, 9 M sodium perchlorate decreases the rate of hydrolysis of the acetylpyridinium ion[18] by a factor in excess of 1000, and 8 M sodium perchlorate decreases the rate of acid catalyzed hydrolysis of acetyl imidazole[19] by a factor of about 500. The rate of mercuration of benzene[25] is increased 100-fold by 7.5 M sodium perchlorate in the presence of a little perchloric acid (needed to prevent precipitation of mercuric hydroxide).

The salt effects presumably arise because of the decrease in the activity of water with increasing concentrations of salt or acid. The enormous acidity of 100% sulfuric acid has been ascribed to the desolvation of the proton in the strong acid. The decrease in H_0 of 10 log units between 10% and 100% sulfuric acid has been correlated with the activity of water in those solutions;[26,27] presumably, the salt effects on H_0 are similarly derived. Furthermore, the rate of mercuration[25] has been correlated with the activity of water. In an analogous fashion, the reactivity of anions is increased by the use of solvents that dehydrate them.[28,29] Bunton[30] and Haake[31] and their coworkers have ascribed the salt effects on the hydrolysis of phosphate, phosphonate, and phosphinate esters at least in part to the decrease in the activity of water at high salt concentrations.
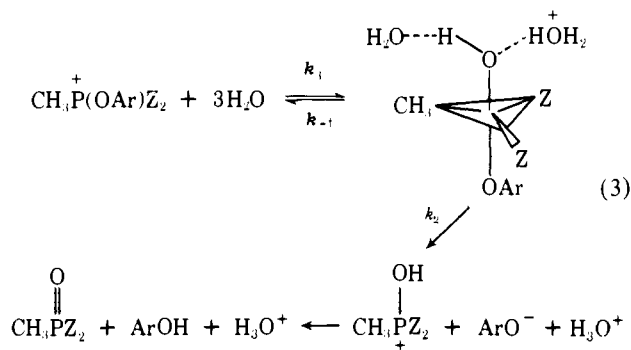
Since the salt effects are negative, they cannot readily be ascribed to an interaction of the anion (triflate or perchlorate) with the cationic reactant. For this explanation to hold, the equilibrium between phosphonium cation and the anion would have to favor the formation of a phosphorane. But even in pure acetonitrile, the triflate salts here under consideration are highly ionized,[10] and will presumably be even more highly ionized in the presence of 34% water. The decrease in rate in the presence of, say, lithium perchlorate must derive from a salt effect. The question then must arise as to whether lithium ions are reasonable surrogates for protons. Since sodium triflate is much less effective in reducing the reaction rate than is lithium triflate, and since tetramethylammonium triflate is even less effective, lithium triflate might be expected to prove less effective in reducing the activity of water than is triflic acid, and so produce a smaller "salt effect".

Furthermore, as is apparent from Figure 4, the effect of lithium triflate parallels the effect of triflic acid, and, although the actual difference in rates is about threefold at 1.8 M acid or salt, the curves are remarkably similar. The possibility that the difference is caused by a difference in the effects of hydrogen and lithium ions on the activity of water cannot be lightly dismissed. Such, however, does not seem to be the fact.

The critical data are those shown in Figure 5. Even though the salt effect on the hydrolysis of III is the largest we observed—a decrease in rate of over 80-fold with 1.8 M lithium triflate in 34% aqueous acetonitrile—the rate at constant ionic strength is independent of the concentration of triflic acid. Either the ionic strength principle holds rigorously in these solutions, or else the substitution of hydrogen for lithium ions has an effect on the activity coefficient ratio of the salt, III, and the transition state that, by coincidence, exactly compensates for its effect on the activity of water. Further, this compensatory effect must be absent for the other phosphonium salts here examined: methyltris(2,6-dimethylphenoxy)phosphonium triflate and methylphenyldiphenoxyphosphonium triflate. Although a coincidence is not impossible,[22] by far the simplest explanation for the data shown in Figure 5 is that, as between lithium ion and hydrogen ion in 34% aqueous aceotnitrile, the ionic strength principle is valid. Lithium ion and hydronium

ion have the same osmotic coefficient[32] in water up to 2 M. Blackburn and Jencks[21] have found that lithium ion is effective in maintaining constant ionic strength of 3.0 M for the aminolysis of methyl formate. Those data, however, refer to water as solvent, so that the concentration of salts, although formally similar to those in our study, in fact cause much smaller changes in activity coefficients. A repetition of the present work under "endostatic" conditions[33] might help to resolve the difficulties in comparing the effects of lithium ions and protons on the activity coefficient of water in these mixed solvents.

The simplest mechanism that accounts for the facts is that shown in eq 3, where Z is an alkyl, aryl, or aryloxy group.

$$CH_3P(OAr)Z_2 + 3H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \quad \overset{(3)}{}$$

$$CH_3PZ_2 + ArOH + H_3O^+ \longleftarrow \overset{+}{CH_3PZ_2} + ArO^- + H_3O^+$$
$$\quad\quad O$$

The rate equation for this process is shown in eq 4.

$$k_{obsd} = \frac{k_1 k_2 (H_2O)^3}{k_{-1}(H^+)\gamma_{H^+}/\gamma_x + k_2/\gamma_x'} \frac{\gamma_s \gamma_{H_2O}^3}{\gamma_x \gamma_x'} \quad (4)$$

Here γ_x is the activity coefficient of the transition state for the addition of water to the phosphonium salt, γ_x' is the activity coefficient for the transition state for the ionization of the electrically neutral hydroxyphosphorane, and γ_s is the activity coefficient of the substrate. The equation is based on the assumption that the reaction proceeds by way of a phosphorane as an intermediate, and is consistent both with the strong, apparently third-order, dependence of the rate on the concentration of water, with the salt effect, and with the effect of acid on the rate. At low acid concentrations, the observed first-order rate constant is represented by the equation

$$k_{obsd} = k_1(H_2O)^3\gamma_s \gamma_{H_2O}^3/\gamma_x \quad (5)$$

where the first step is rate-limiting, whereas at high acid concentrations

$$k_{obsd} = \frac{k_1 k_2 (H_2O)^3}{k_{-1}(H^+)} \frac{\gamma_s \gamma_{H_2O}^3}{\gamma_{H^+}\gamma_x'} \quad (6)$$

where the second step is rate limiting, and the concentration of the intermediate phosphorane is inversely proportional to the hydrogen ion concentration.

To fit this formulation with the available facts requires that the rate-controlling step in the hydrolysis of I change with acidity, whereas the rate-limiting step for the hydrolysis of III does not. This difference is a reasonable one. In the absence of added acid, the addition of water is rate limiting for the hydrolysis of both I and III. However, in the presence of acid, the hydrolysis of I is retarded, whereas that for I is not. These facts and eq 4 together imply that at high (H^+) the ratio of K_{-1} $(H^+)/\gamma_x$ to k_2/γ_x' is large for I but small for III. These are the rate constants that control the loss of protonated water and of phenoxide ion from the intermediate phosphorane in the hydrolysis process. Apparently the dissociation of the phosphorane from I is much more selective with respect to leaving group than that of the phosphorane from III. By contrast, the rate difference between loss of H_3O^+ and of phenoxide must be small for the dissociation of the phosphorane from III. But this is what one would expect from the thermodynamic dissociation constants that have been measured conductometrically (Table I). The constant for III is 10^4 greater than that for IV;

presumably it is also very large compared with that of I. This suggests a much greater rate of dissociation of leaving groups—and consequently much less selectivity with respect to the leaving group—for the dissociations from III as compared with those for I. Thus, the data are consistent with the finding that the rate for I is sensitive to acid at constant ionic strength, whereas that for III is not.

The deuterium isotope effect[34,35] is also consistent with the mechanism shown in eq 1. The transition state for the first step requires the transfer of a proton from a nucleophilic water molecule to a solvent molecule. By contrast a large solvent isotope effect would not be expected for a displacement reaction, since the hydrogen to oxygen bonds might not be substantially weakened in the transition state. Although the solvent isotope effect is thus consistent with the intervention of a phosphorane as intermediate in the solvolysis, some question must arise because the k_{H_2O}/k_{D_2O} ratio is the same in neutral solvent as for the solvolysis that is retarded by acid. For the neutral solvent, the rate-limiting step is presumably the attack of water on the salt, controlled by the rate constant, k_1, whereas for the rate in the presence of acid, the rate-limiting step is presumably the breakdown of the intermediate, controlled by the rate constant ratio, $k_1 k_2/k_{-1}$. One would not expect a large solvent isotope effect on k_2, or (as discussed below) on k_{-1}, so that the solvent deuterium isotope effects are substantially those for k_1 regardless of the acidity. The reason why one does not anticipate a large solvent effect on k_{-1} is that D_3O^+ is a considerably stronger acid than H_3O^+, so that the equilibrium for the formation of the phosphorane can reasonably be favored in H_2O as compared with D_2O by a factor similar to that demonstrated for k_1.

The difference in behavior between I and III is hard to interpret without assuming that a phosphorane is an intermediate in the hydrolysis. The data, then, support the mechanistic formulation of the hydrolysis by way of a phosphorane as intermediate. Prior to this study, the intervention of phosphoranes in the hydrolyses of cyclic phosphates, phosphonates, and phosphinates had been firmly established.[3,5,36,37] The only example where definitive evidence has been found for a phosphorane in the acid hydrolysis of an acyclic ester of an acid of phosphorus is for the hydrolysis of diphenylmethylphosphonate, where the hydrolysis is accompanied by substantial exchange of oxygen atoms between the substrate and solvent.[38] To the extent that the present study models phosphate hydrolysis, it lends support to the conclusion that these reactions proceed by way of phosphoranes as intermediates, rather than by way of trigonal bipyramidal transition states.

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