Kinetics and Mechanism of the Methanolysis of Aryloxyphosphonium Salts

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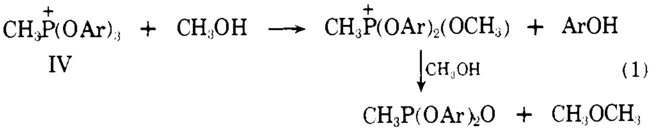
Abstract: The rate of methanolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate, I, in methanol–acetonitrile mixtures increases as the second power of the methanol concentration, and is decreased by factors of 14 and 9 by 2 M triflic acid and lithium triflate, respectively. At a constant ionic strength of 1 M, the rate is decreased twofold by 0.1 M acid, but remains constant at higher acid concentrations. The methanolyses of I, of methylphenyldiphenoxyphosphonium triflate, II, and of methyldiphenylphenoxyphosphonium triflate, III, proceed by way of methoxyphosphonium salts as intermediates. These data are explained in terms of a multistep mechanism with a phosphorane as an intermediate, and correlated with the kinetics and mechanism of the corresponding hydrolytic processes.

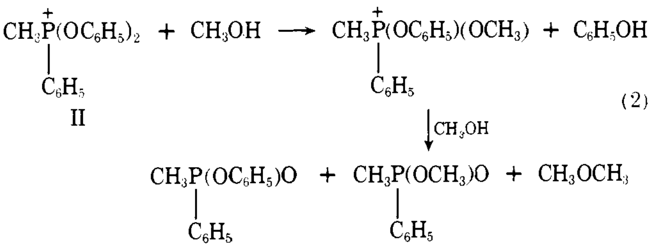
Introduction

The acid-catalyzed hydrolysis of phosphate, phosphonate, and phosphinate esters presumably proceeds by way of protonation of the phosphoryl oxygen atom of the ester, followed by the reaction of the hydroxyphosphonium cation with water.[1-4] The methanolysis presumably proceeds through parallel processes. A study of the methanolysis as well as that of the hydrolysis of the aryloxyphosphonium salts can help elucidate the mechanism of the hydrolysis of the esters.

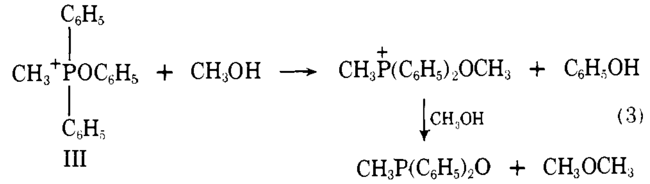
The chemical equations for the processes under discussion appear in eq 1-3.



$$\underset{\mathrm{IV}}{\mathrm{CH_3\overset{+}{P}(OAr)_3}} + \mathrm{CH_3OH} \longrightarrow \mathrm{CH_3\overset{+}{P}(OAr)_2(OCH_3)} + \mathrm{ArOH} \xrightarrow{\mathrm{CH_3OH}} \mathrm{CH_3P(OAr)_2O} + \mathrm{CH_3OCH_3} \qquad (1)$$



$$\underset{\mathrm{II}}{\mathrm{CH_3\underset{\underset{C_6H_5}{|}}{\overset{+}{P}}(OC_6H_5)_2}} + \mathrm{CH_3OH} \longrightarrow \mathrm{CH_3\underset{\underset{C_6H_5}{|}}{\overset{+}{P}}(OC_6H_5)(OCH_3)} + \mathrm{C_6H_5OH} \xrightarrow{\mathrm{CH_3OH}} \mathrm{CH_3\underset{\underset{C_6H_5}{|}}{P}(OC_6H_5)O} + \mathrm{CH_3\underset{\underset{C_6H_5}{|}}{P}(OCH_3)O} + \mathrm{CH_3OCH_3} \qquad (2)$$



$$\underset{\mathrm{III}}{\mathrm{CH_3{}^+\overset{\overset{C_6H_5}{|}}{\underset{\underset{C_6H_5}{|}}{P}}OC_6H_5}} + \mathrm{CH_3OH} \longrightarrow \mathrm{CH_3\overset{+}{P}(C_6H_5)_2OCH_3} + \mathrm{C_6H_5OH} \xrightarrow{\mathrm{CH_3OH}} \mathrm{CH_3P(C_6H_5)_2O} + \mathrm{CH_3OCH_3} \qquad (3)$$

Experimental Section

The general methods and materials were the same as those already described in the previous paper.[5]

The methanolysis reactions were followed by UV spectroscopy, in a fashion similar to that used for the hydrolyses. The rate for the hydrolysis of salt I was followed at 277 nm. The spectra[6] for the methanolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate and for methylphenyldiphenoxyphosphonium triflate resemble those shown in Figure 1 of the previous paper, in that the phenol produced in the methanolysis absorbs much more strongly around 280 nm than does the cationic starting material. The UV spectra for the methanolysis of methyldiphenylphenoxyphosphonium triflate are exceptional. The immediate products (see eq 3 and the section Products) are phenol and the methyldiphenylmethoxyphosphonium ion; the UV spectra for this system are presented in Figure 1; the spectrum of the intermediate products contrasts strongly with that of methyldiphenylphosphine oxide, shown in Figure 2 of the previous paper. Since the kinetics were followed by observing the appearance of phenol, the rate constants refer to reaction at phosphorus, and not to the formation of dimethyl ether.

Preparations. Bis(2,6-dimethylphenyl)methyl phosphite. A solution of methyl phosphorodichloridite[7] (10.0 g) in 20 mL of anhydrous ether was stirred at 0 °C. Over a period of 1 h a solution of freshly sublimed 2,6-dimethylphenol (18.38 g) and 2,6 lutidine (16.12 g, distilled from CaH_2) in 30 mL of anhydrous ether was added. After a half-hour's stirring, the white precipitate was removed by filtration and the filtrate extracted with water, 0.1 N NaOH, and again with water. The organic layer was dried with $MgSO_4$ and filtered and the solvent removed in vacuo. The resulting oil was vacuum distilled; the product boiled at 140–143 °C (0.05 mm): yield, 38% of theory; ^1H NMR ($CDCl_3$) δ 2.25 (s), 3.82 (d, $J = 8.5$ Hz), 6.93 (s); ^{31}P NMR ($CDCl_3$) 4.23 ppm.

A solution of methylbis(2,6-dimethylphenoxy)methoxyphosphonium triflate was prepared by mixing equal concentrations of bis(2,6-dimethylphenoxy)methyl phosphite and methyl triflate in chloroform-d_1 at −64 °C in an NMR tube. At −20 °C, two signals were observed, at +2.66 and −45.52 ppm; the former was identified as the phosphite starting material, whereas the latter was assigned to methylmethoxybis(2,6-dimethylphenoxy)phosphonium triflate.

Methanol (Mallinckrodt anhydrous, 150 mL) was dried under argon with 5 g of magnesium turnings (Fisher). Less than 0.1 g of iodine was added to initiate the formation of $Mg(OCH_3)_2$. After all the magnesium had reacted, ca. 800 mL of commercial anhydrous methanol was added and the solvent refluxed for 3 h. The methanol was then distilled through a 3-ft helix-packed vacuum-jacketed column, and the main fraction collected in a dry bottle. To make certain that no basic impurities contaminated the methanol, one batch of purified methanol was redistilled under argon from purified and dried sulfanilic acid. The rate of methanolysis of I in the redistilled methanol was 10% higher than that for the singly distilled product, probably because of traces of moisture in the former. Methanol-d_1 (Stohler) was dried by the same procedure as that for methanol.

Products. All of the reaction products were identified by ^{31}P NMR spectroscopy, as for the corresponding hydrolyses, except that no independent synthesis of methyl methylphenylphosphinate was carried out. Figure 2 shows the proton-decoupled ^{31}P NMR spectra at 0 °C for the methanolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate (I) in 19% methanolic acetonitrile-d_3 at 20 min after mixing and 12 h after mixing; these spectra are compared with the spectrum of the starting material in pure deuterated acetonitrile. (The chemical shift for the starting material depends to a small extent on solvent.) Although the phosphonate ester is the only material present after 12 h, after 20 min a small peak in addition to those for starting material (−41.27) and final product (−24.49) is visible at −45.28; this peak is assigned to methylmethoxybis(2,6-dimethylphenoxy)phosphonium triflate. The assignment of this signal to the methoxy salt is reasonable on the basis of the chemical shift; the assignment is strengthened by the appearance of the signal at the same position in the attempted synthesis of the salt, as described in the section on preparations. The

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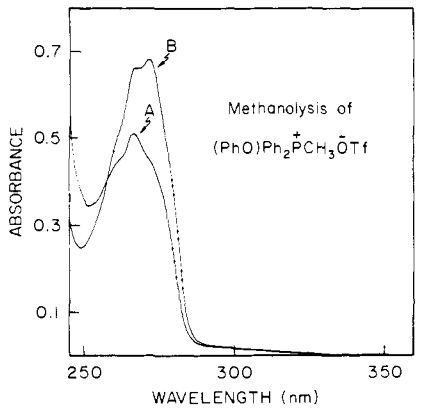


Figure 1. (A) UV spectrum of a ca. 10^{-3} M solution of methyldiphenylphenoxyphosphonium triflate in dry acetonitrile. (B) Corresponding spectrum of the intermediate products of methanolysis (methyldiphenylmethoxyphosphonium triflate, phenol, and triflic acid) after 30 min.

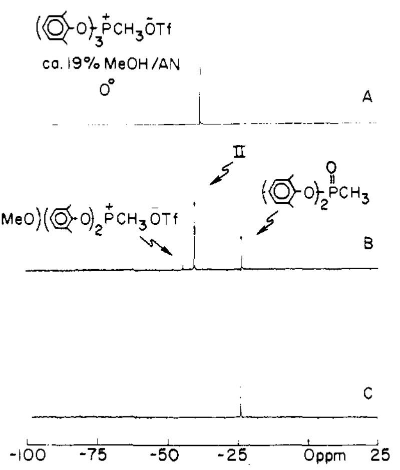


Figure 2. ^{31}P NMR spectra, relative to 85% phosphoric acid as standard, for the methanolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate. (A) Spectrum in dry acetonitrile. (B) Spectrum after 20 min in 19% methanolic acetonitrile at 0 °C. (C) Final spectrum, 12 h after mixing.

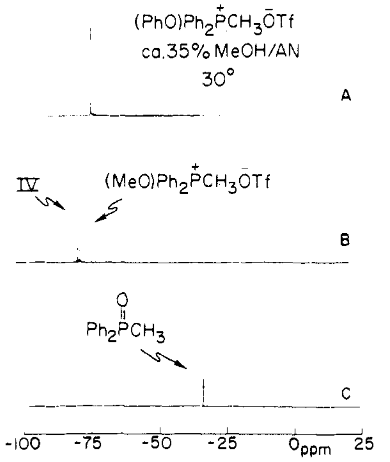


Figure 3. ^{31}P NMR spectra, relative to 85% phosphoric acid as standard, for the methanolysis of methyldiphenylphenoxyphosphonium triflate. (A) Initial spectrum in dry acetonitrile. (B) Spectrum after 30 min in 35% methanolic acetonitrile at 30 °C. (C) Spectrum of the final product, methyldiphenylphosphine oxide (3 months after mixing).

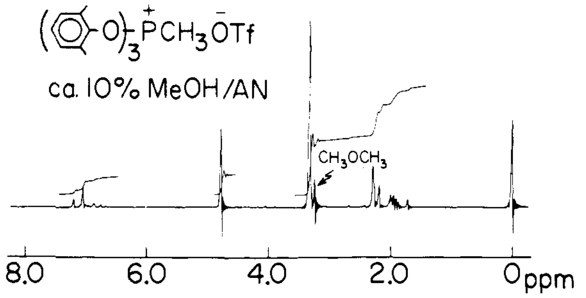


Figure 4. ^{1}H NMR spectrum, relative to Me$_4$Si as standard, for the methanolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate in 10% methanolic acetonitrile at room temperature; the reaction was ~90% complete. The small peak for dimethyl ether was identified by the addition of authentic material.

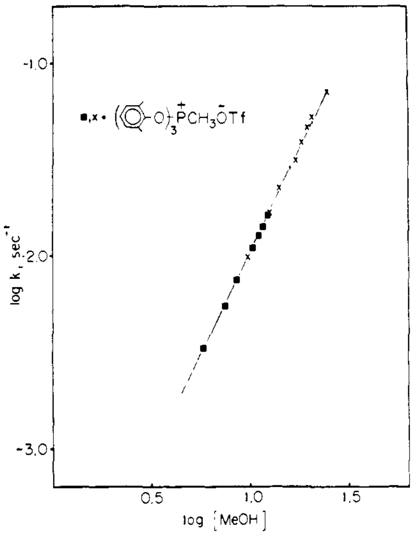


Figure 5. The logarithm of the rate constants for methanolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate at 25 °C vs. the logarithm of the molarity of methanol in acetonitrile. The highest point represents substantially pure methanol. The X's refer to experiments carried out by stopped-flow; the ■'s refer to those determined with a Cary spectrophotometer.

intermediate, which is stable at −20 °C, decomposes slowly at 0 °C in methanol to yield bis(2,6-dimethylphenyl) methylphosphonate. Similarly, the methanolysis of methylphenyldiphenoxyphosphonium triflate, II, showed a signal, in addition to those of starting material and final product, at −78.30; this appears close to the signal for the starting material, and is presumably that of methylphenylmethoxyphenoxyphosphonium cation; the signal is reasonably stable at room temperature. The relevant spectra, similar to those shown in Figures 2 and 3, are presented in detail elsewhere.[6] The methanolysis of methyldiphenylphenoxyphosphonium triflate, III, in 35% methanol in acetonitrile also led to the appearance of a new NMR peak at −74.86 close to that of the starting material. The signal presumably arises from methyldiphenylmethoxyphosphonium cation. In this methanolysis (Figure 3), the starting material was converted essentially completely to the methoxy salt before any substantial quantity of phosphine oxide was formed.

The ^{1}H NMR spectrum (Figure 4) of the reaction mixtures for methanolysis shows, in addition to the signals from starting materials and products, a peak at δ 3.24 that is assigned to dimethyl ether. The identification was made by the addition of authentic dimethyl ether (Matheson) to the NMR tubes.

Results

The rates of methanolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate in methanol–acetonitrile mixtures are shown in Figure 5. The rates are slow enough to be followed with a Gilford spectrophotometer as well as by stopped-flow methods; the fastest reaction—that in pure methanol—proceeded with a half-time of just under 10 s. The slope of the line drawn in Figure 5 is 2.1.

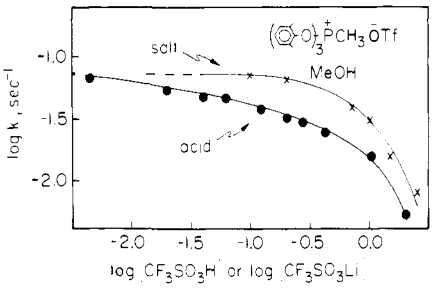


Figure 6. The logarithm of the rate constants for methanolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate in methanol at 25 °C, vs. the logarithm of the concentrations of added lithium triflate (upper curve) or triflic acid (lower curve).

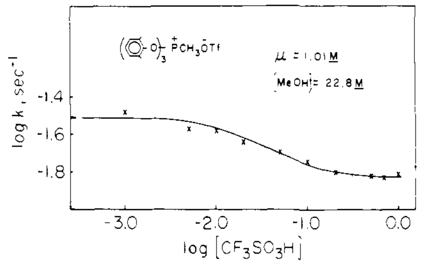


Figure 7. Logarithm of rate constants for methanolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate in methanol at 25 °C, at a constant ionic strength of 1.01 (maintained with lithium triflate) vs. logarithm of the concentration of triflic acid.

The effects of triflic acid and of lithium triflate on the reaction rate in pure methanol are plotted in Figure 6. In these experiments, where the highest concentration of acid or salt is 2 M, acid decreases the rate more than salt does. For example, the rate is depressed as much by 0.005 M acid as by 0.1 M salt—a statement that suggests that the acid has some effect per se, since one would not expect large salt effects in pure methanol at a concentration as low as 0.005 M. The effects of triflic acid and of lithium triflate on the rate of methanolysis in pure methanol at a constant ionic strength of 1.01 are shown in Figure 7. The incremental effect of acid relative to lithium triflate is fully expressed at 0.1 M acid, and then levels off. Similar results were obtained at an ionic strength of 2 M, where the decrease in rate caused by acid is fully expressed at 0.3 M acid; at the highest acid concentration (2 M) the rate was slightly higher than at 0.3 M, although nevertheless lower than in pure methanol.

Deuterium Solvent Isotope Effect. The rate of methanolysis of methyltris(2,6-dimethylphenoxy)phosphonium triflate was measured in CH_3OD, in the absence and presence of acids and salts. The rate ratio in methanol, as compared with that in deuteromethanol, was 4.4 ± 0.2. The result parallels that in water.

Discussion

The pathway for the methanolysis of the aryloxyphosphonium salts, as shown in eq 1–3, has been amply confirmed by NMR spectroscopy. The formation of methoxyphosphonium salts as intermediates in the process has been demonstrated (Figures 2 and 3, and ref 6) by observing the ^{31}P signal from these intermediates, including that from the unstable methylbis(2,6-dimethylphenoxy)methoxyphosphonium cation; the identity of that ion was confirmed by an independent synthesis. Even though the product of the synthesis proved to be unstable at 0 °C (as did the intermediate in the methanolysis), its method of preparation and its NMR spectrum leave little doubt as to its identity. The methoxyphosphonium salts react with methanol to undergo an Arbuzov reaction, leading to phosphoryl derivatives and to dimethyl ether; the ether was identified by ^1H NMR spectroscopy.

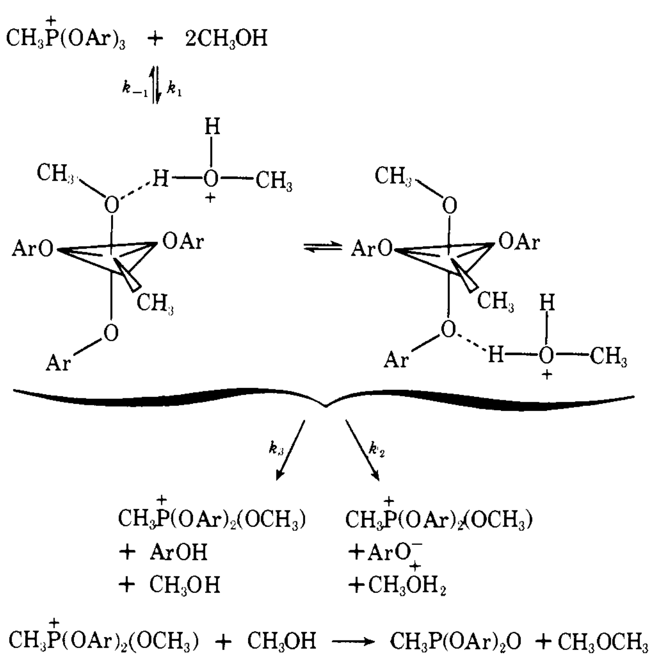
In the methanolysis of methylphenyldiphenoxyphosphonium triflate, II, the intermediate reacted both by an Arbuzov reaction and by methanolysis followed by an Arbuzov reaction, so that the final product mixture contained both phenyl methylphenylphosphinate and methyl methylphenylphosphinate;[6] this result merely shows that the methanolysis and the Arbuzov reaction of the intermediate ion proceed at comparable rates. By contrast, the methanolysis of methyltris(2,6-dimethylphenoxyl)phosphonium triflate, I, yields only the Arbuzov product. The reason for this contrast is not known; it may be related to steric hindrance at phosphorus for I. The methoxyphosphonium ions that have two and three carbon–phosphorus bonds are more stable than the ion with only one carbon to phosphorus bond. Our result is consistent with that of DeBruin, who isolated ethoxymethoxymethylphenylphosphonium hexachloroantimonate.[8] The rates of hydrolysis of the corresponding phenoxyphosphonium ions decrease in the same order as that in which their stability to methanolysis increases. Presumably aryloxy substituents are electron withdrawing at phosphorus relative to alkyl or aryl groups, and so increase the positive charge at phosphorus; the effect of positive charge is to increase the rates of both methanolysis and of the Arbuzov process.

The rate of methanolysis of the salt, I, increases as the second power of the concentration of methanol in acetonitrile, whereas the rate of hydrolysis increases as the third power[2,5] of the concentration of water. Furthermore, the salt effect of added lithium triflate on the rate of methanolysis, although large, is considerably less than that of the same concentration of salt, in acetonitrile–water as solvent, on the hydrolysis. In pure methanol, the maximum rate depression caused by 2 M lithium triflate is ninefold; in 34% water in acetonitrile (a solvent with a substantially higher dielectric constant than that of methanol), 1.8 M lithium triflate reduces the rate by a factor of 30. In the previous paper,[5] the large salt effects were correlated with the decrease in the activity of water, as water was withdrawn from solution by solvation by lithium ions and protons. Presumably, the decrease in the activity of water caused an exceptionally large decrease in rate because three molecules of water participate in the transition state; the activity coefficient of water in the rate equation is cubed. Since only two molecules of methanol participate in the transition state for methanolysis, the effect of salt in decreasing the activity of methanol is correspondingly less important than the corresponding effect in hydrolysis; the activity coefficient in the rate equation is squared. Although the quantitative agreement between the dependence of the hydrolysis on water and that of the methanolysis on methanol is quite good, we do not wish to stress the point, since the kinetic order of reactions with respect to solvent is necessarily quite uncertain.

The data for the methanolysis have here been correlated with the detailed mechanism shown in Scheme I. The mechanism as shown is unsymmetrical; that is, intermediates such as the phosphoranes shown in Scheme I lose phenolate ion rather than methoxide since of course phenolate ion is a much better leaving group than methoxide ion.

The facts are in accord with the transition states shown in this and the previous paper. Since a water molecule is comprised of an oxygen atom and two protons, whereas a methanol molecule holds only one proton, a nucleophilic water molecule can form two hydrogen bonds, whereas a methanol molecule can form only one. This is consistent with the dependence of the rate of hydrolysis on the third power of the concentration of water, whereas the rate of methanolysis varies as the second power of the concentration of methanol. The rate of methanolysis increases as the methanol concentration in acetonitrile

Scheme I



increases, all the way up to pure methanol, whereas the rate for the hydrolysis levels off at about 35% water in the mixed solvent of water and acetonitrile. Presumably cations are solvated by water so strongly, relative to acetonitrile, that the local environment near the ions in 35% water approaches that in pure water; by way of contrast, methanol and acetonitrile are more nearly alike, both in dielectric constant and because the hydrogen bonding in methanol is less important than it is in water, so that the segregation of solvent is severe in mixtures of acetonitrile with water, but not in mixtures with methanol.

As in the previous paper, an important mechanistic question is whether the reaction proceeds by way of a phosphorane as intermediate, or whether a trigonal bipyramidal structure is present only as a transition state. The criterion is the effect of acid; it would be difficult to formulate a one-step mechanism that included inhibition by acid. Although acid strongly decreases the rates of methanolysis, as it does for the rates of hydrolysis, again a question arises as to whether the effect of acid is merely that of an especially large salt effect. The salt effect might be greater for the proton than for the corresponding lithium salt because the proton is more heavily solvated.

The decrease in rate by acid is clearly observed at 0.005 M acid, where salt effects in pure methanol cannot be large. Further, at constant ionic strength, maintained with lithium triflate, the effect of acid is maximal at 0.1 M acid; at that concentration of electrolyte in pure methanol the ionic strength principle should hold quite well. Furthermore, increasing the acid concentration beyond 0.1 M, at constant ionic strength of 1 M maintained with lithium triflate, does not affect the rate. If the difference in rate at 0.1 M acid had been caused by a difference in activity coefficient between protons and lithium ions, then that difference would presumably have been emphasized as the concentration of acid, at constant ionic strength, was increased from 0.1 to 1.0 M. The leveling of the effect at 0.1 M, as well as the low absolute value of concentration at which an effect of acid is noted, substantiate the conclusion that the effect of acid is inherent in the chemistry, and not simply an activity coefficient effect. These data then corroborate the conclusion drawn from the kinetics of hydrolysis and provide strong evidence that a phosphorane intermediate intervenes in the hydrolysis and methanolysis of the acyclic phosphonium salts here under discussion.

One further point needs clarification. In the hydrolysis of the aryloxyphosphonium salts, the effect of acid relative to salt was not limited to low concentrations, whereas, in the methanolysis at an ionic strength of 1 M, the effect of acid levels off at 0.1 M. This has been rationalized by the hypothesis (Scheme I) that the methanolysis includes a term in acid-catalyzed loss of phenol from the phosphorane intermediate, whereas the hydrolysis proceeds only by loss of phenoxide ion. (Perhaps an acid-catalyzed mechanism obtains in both cases; if so, the kinetic term for that pathway in hydrolysis must be small.)

These explanations can be put on a quantitative basis through the kinetic equations derived for Scheme I. Disregarding activity coefficients (and salt effects) for the moment

$$k_{\text{obsd}} = \frac{k_1(k_2 + k_3[\text{H}^+])[\text{MeOH}]^2}{(k_{-1} + k_3)[\text{H}^+] + k_2} \tag{4}$$

At low acid concentration, the first-order rate constant is then given by the expression

$$k_{\text{obsd}} = k_1[\text{MeOH}]^2 \tag{5}$$

and at high concentrations by the expression

$$k_{\text{obsd}} = \frac{k_1 k_3[\text{MeOH}]^2}{k_{-1} + k_3} \tag{6}$$

In the absence of acid, the rate-limiting step is the addition of methanol to the cation. As the acid concentration is increased, the concentration of the postulated phosphorane decreases, and the rate-limiting step becomes the acid-catalyzed loss of phenol from the phosphorane.

The first-order rate constant at low acidity will exceed that at high acidity by the ratio:

$$\frac{k_{\text{obsd}}{}^{\text{low acidity}}}{k_{\text{obsd}}{}^{\text{high acidity}}} = \frac{k_{-1} + k_3}{k_3} \approx 2.0 \tag{7}$$

so that $k_{-1} \approx k_3$; at intermediate acidities, the observed first-order rate constant will of course decrease from one limit to the other. Phenol, of course, is a better leaving group than is methanol; however, the methoxy substituent is more basic than the phenoxy substituent, and will be more readily protonated. Since these two effects operate in opposite directions, it is reasonable that they should more or less balance one another.

The solvent deuterium isotope effect is likewise similar to that described for hydrolysis. Its magnitude is about the same in acid solution as in neutral solution; the reasons for this presumably parallel those already discussed for hydrolysis.[5]

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References and Notes

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