J. Am. Chem. Soc. 1981, 103, 6432–6436

Hydrolysis of Spirobicyclic Oxyphosphoranes. Associative and Dissociative Reactions

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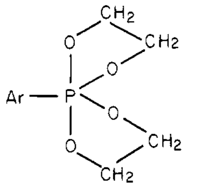
Abstract: The hydrolysis reactions of three aryl-substituted spirobicyclic oxyphosphoranes (Ia–c) have been studied in aqueous solution. These are characterized by an H^+-catalyzed reaction extending to about pH 9.54 sharply changing there to an OH^--catalyzed reaction. The acid reaction is general acid catalyzed ($\alpha = 0.74$) and appears to be a dissociative process directly analogous to the general acid catalyzed hydrolysis of an acetal or ortho ester. Features indicative of this type of reaction include a negative ρ value based on the variation of the aromatic substituent, a near-zero entropy of activation, and a slightly inverse solvent isotope effect. The hydroxide ion reaction appears to be an associative process proceeding through a hexacoordinated phosphoroxanide ion. Evidence for this includes a positive ρ value (+2.5) and a significantly negative entropy of activation. General base catalysis is also observed; this also appears to be an associative process on the basis of a positive ρ value.

The hydrolysis of phosphate esters[1,2] is thought to proceed in many cases by way of a pentacoordinate intermediate. A large number of analogues of this intermediate, commonly termed oxyphosphoranes, have now been prepared (see ref 3–10 for some recent examples including some observable hydroxyphosphoranes). The structural characteristics of these species have been studied extensively, particularly with respect to their tendency to undergo permutational isomerization, and a reasonable understanding of this aspect of their chemistry has emerged.[1,11,12]

The hydrolysis reactions of oxyphosphoranes, on the other hand, have seen little mechanistic study, principally because of the speed of the reaction.[13,14] A detailed investigation involving pentaaryloxyphosphoranes ($P(OAr)_5$) has been reported by Archie and Westheimer,[14] although a mixed aqueous organic solvent mixture was required to keep the rates in an observable range.

We report here a kinetic study of the hydrolysis of the spirobicyclic oxyphosphoranes Ia–c. We in particular felt it of interest to study an oxyphosphorane with an alkoxy leaving group rather than an aryloxy, since there should be a significant difference between the two, as indeed we have found. The aryl group directly attached to the phosphorus obviously provides a handle for relating charge buildup at the phosphorus in the transition state. The particular phosphorus Ia–c were chosen because of their ease of synthesis and also because of suggestions[15] that the general stability order of oxyphosphoranes is spirobicyclic > monocyclic > acyclic. We do find that Ia–c are sufficiently stable in wholly aqueous media for a detailed investigation over essentially the entire pH range.



Ia, Ar = $4\text{-}CH_3C_6H_4$
b, Ar = C_6H_5
c, Ar = $4\text{-}ClC_6H_4$

Experimental Section

Materials. Phosphoranes Ia–c were prepared following the general procedure of Cadogan and co-workers[5]. Aryldichlorophosphines (aryl = phenyl, commercially available (Aldrich), and aryl = 4-methylphenyl and 4-chlorophenyl, prepared according to ref 16) were converted[17] to 2-aryl-1,3,2-dioxaphospholanes. The freshly prepared phospholan (0.01 mol) was dissolved in 10 mL of dry methylene chloride, and to a stirred solution cooled in an ice bath, a solution of phenyl azide[18] (0.01 mol) in 5 mL of methylene chloride was added over 2 min. The ice bath was removed and the reaction mixture stirred at room temperature for 15 min. The flask was again cooled in an ice bath, and dry ethylene glycol (0.01 mol) was added all at once, followed by 10 mL of dry ether. This was allowed to stand at room temperature for 30 min. During this time a small amount of white powder precipitated. This solid[19] was removed by filtration in a water-free environment (glove box). (All filtrations were carried out in this way.) The filtrate was evaporated on a rotary evaporator to remove solvent, followed by evacuation at 0.1 Torr to remove aniline. Dry ether (15 mL) was added, and the oxyphosphorane was filtered. A white crystalline solid was obtained which could be recrystallized from ether containing a small amount of methylene chloride. The phosphorane Ib had mp 124–125 °C: 1H NMR δ 7.6–8.0 (m, 2 H), 7.3–7.5 (m, 3 H), 3.5–4.1 (symmetrical m, 4 H); ^{31}P NMR, δ −19.3. Anal. Calcd for $C_{10}H_{13}O_4P$: C, 52.64; H, 5.74; P, 13.57. Found: C, 52.73; H, 5.81; P, 13.45. Ia had mp 110–112 °C: ^1H NMR δ 7.73 (dd, J = 13 and 8 Hz, 2 H), 7.25 (dd, J = 5 and 8 Hz, 2 H), 3.5–4.1 (symmetrical m, 4 H), 2.37 (s, 3 H). Anal. Calcd for $C_{11}H_{15}O_4P$: C, 54.55; H, 6.24; P, 12.79. Found: C, 54.71; H, 6.21; P, 12.65. Ic had mp 122–123 °C: ^1H NMR, δ 7.60 (dd, J = 13 and 8 Hz, 2 H), 7.30 (dd, J = 5 and 8 Hz, 2 H), 3.5–4.1 (symmetrical m, 4 H). Anal. Calcd for

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(19) Cadogan and co-workers do not report the presence of this solid. We find it to be insoluble in all common organic solvents, and suspect that it is polymeric material. The relative amount formed of this product varied from preparation to preparation, with greater quantity forming when the 4-methylphenyl substituent was present, although even in this case the solid accounted for only 30% of the product.

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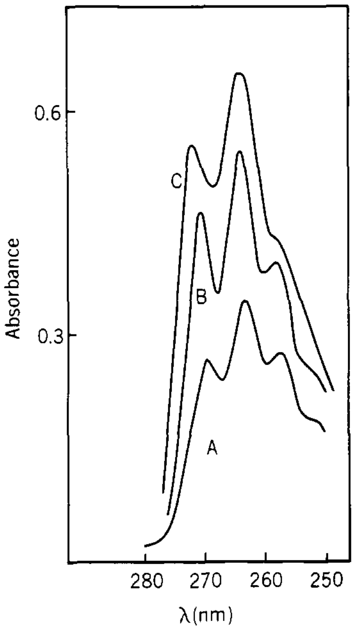


Figure 1. Absorbance changes. Curve A → curve B represents the spectral change observed with the phosphorane Ib in pH 6.5 buffer. Curve C → curve B represents the spectral change observed with the phosphonium ion IV in 0.1 M HCl. Concentrations in each case are about 10^{-3} M.

$C_{10}H_{12}ClO_4P$: C, 45.73; H, 4.61; P, 11.79. Found: C, 46.01; H, 4.71; P, 11.60.

Ethylene phenylphosphonate was prepared as previously described[20] from phenylphosphonic dichloride, ethylene glycol, and 2 equiv of pyridine. Dimethyl phenylphosphonate and di(2-methoxyethyl) phenylphosphonate were prepared in a similar manner, using in place of the glycol 2 equiv of methanol or 2-methoxyethanol. The latter ester had a ^1H NMR spectrum ($CDCl_3$) of δ 7.4–8.0 (m, 5 H), 4.1–4.4 (m, 4 H), 3.5–3.7 (m, 4 H), and 3.33 (s, 6 H).

Trimethoxyphenylphosphonium trifluoromethanesulfonate was obtained as an equilibrium mixture with dimethyl phenylphosphonate and methyl trifluoromethanesulfonate by mixing the latter two in dry methylene chloride. The reaction, which requires several hours to reach its equilibrium position, can be followed from the change in the CH_3–O protons in the ^1H NMR spectrum of the solution. The equilibrium constant, as determined by NMR integration, is near unity. For this reason a 2–3-fold excess of methylating agent was used in order to form as much salt as possible.

Products. Products were analyzed by adding to aqueous D_2O solutions a small quantity of phosphorane and recording the ^1H NMR spectra. Comparison spectra in the same solutions were obtained for di(2-methoxyethyl) phenylphosphonate, a model for di(2-hydroxyethyl) phenylphosphonate, one of the possible products, and ethylene phenylphosphonate, the other possible product. The cyclic ester undergoes hydrolysis to mono(2-hydroxyethyl) phenylphosphonate during the time required to record the NMR spectra. The diester is stable to further hydrolysis in acid, although a relatively rapid hydrolysis does occur in base.

The characteristic features of these spectra are a multiplet at δ 4.1–4.5 associated with $-CH_2OP{=}O$ and a multiplet at δ 3.6–4.0 associated with $-CH_2OH$. The product mixture from the phosphorane also shows a sharp singlet on the edge of the upfield multiplet (δ 3.6) assignable to ethylene glycol. This product should be formed in an equal amount along with the monoester derived from further hydrolysis of the cyclic ester. If this is assumed to be the case, then the monoester:diester ratio can be calculated as $(2I_h - 2I_l)/(3I_l - I_h)$ where I_h and I_l are the NMR integrations of the high-field and low-field peaks, counting the ethylene glycol with the high-field multiplet.

Kinetics. (a) Phosphorane (pH 6–8). A 1-μL solution of the phosphorane in dry methylene chloride was injected into a thermostated 1-cm UV cell and the increase in absorbance at 263 nm (Figure 1) was monitored on a Unicam sp 1800 spectrophotometer. First-order rate constants were calculated as slopes of ln $(A_\infty - A)$ vs. time.

(b) Phosphorane (pH <6). The phosphorane dissolved in dilute (0.002 M) carbonate buffer, pH $\sim$9.5, was mixed in a Durrum-Gibson stopped-flow spectrophotometer with an appropriate acid or buffer, and the absorbance increase at 263 nm was monitored as in (a). The data from these experiments were digitized and fed directly to a Tektronix 4051 minicomputer for analysis.

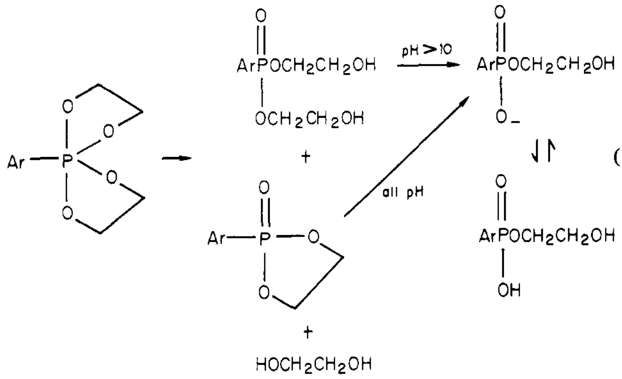
(c) Phosphorane (pH >9). In this pH region the subsequent hydrolysis of the ester products makes the direct spectrophotometric determination of the rate constant as in (a) and (b) difficult, and the following approach was therefore used. The phosphorane was dissolved in an appropriate buffer or base and rapidly loaded into one syringe of the stopped-flow apparatus, the other syringe of which carried an acetate buffer whose concentration was such that the pH after mixing in the stopped-flow apparatus was about 4.5. At appropriate times the stopped-flow apparatus was activated, and the first-order trace corresponding to the relatively rapid pH 4.5 hydrolysis was recorded. This process was repeated 8–10 times over a 5–50-min period. First-order rate constants for the hydrolysis at high pH were obtained from a plot of ln $(A_\infty - A_0)_t$ vs. t, where t is the time of firing of the stopped-flow apparatus, and $(A_\infty - A_0)_t$ is the total absorbance change which is observed in the hydrolysis in the pH 4.5 buffer.

The basis of this approach is that the phosphorane does undergo a reasonable absorbance change on hydrolysis at pH 4.5. This absorbance change is accurately first order and is unaccompanied by problems associated with subsequent hydrolysis of the ester products. The mixing experiment described above therefore results in the relatively rapid hydrolysis of unreacted phosphorane present in the high pH solution. The total absorbance change observed during this acid hydrolysis provides a measure of the quantity of phosphorane present in the base. The stopped-flow apparatus was used for this experiment for several reasons. By being able to see the first-order spectral change associated with the acid hydrolysis we could ensure that this change does correspond to the desired process, and is not associated with or complicated by some artifact. Excellent first-order traces were observed for the pH 4.5 hydrolysis, with the same rate constant being obtained on each mixing with the same base solution. The stopped-flow apparatus provides thermostating for the solutions in the drive syringes, with a limit of about 10 firings before reloading is necessary. Finally with the apparatus linked directly to a minicomputer, highly precise values of the two required absorbances could be obtained. Good first-order plots for the base hydrolysis were obtained using this approach. In one case, a solution of pH 7.6, rate constants were obtained using both the direct methods of (a) and (c) and excellent agreement was found.

(d) Trimethoxyphenylphosphonium Ion. The methylene chloride solution in which this ion had been prepared was injected directly into a thermostated UV cell, and the absorbance decrease was monitored at 275 nm (Figure 1). Rate constants were shown to be independent of the actual ratio of reagents used in the preparation and were not affected by the excess methyl trifluoromethanesulfonate.

Results

Products. Both a di(2-hydroxyethyl) arylphosphonate and an ethylene arylphosphonate are formed as products of the hydrolysis of the phosphoranes Ia–c, the cyclic phosphonate ester being accompanied by an equivalent amount of ethylene glycol (eq 1).



(1)

The cyclic ester is not stable at any pH and is converted to a mono(2-hydroxyethyl) arylphosphonate. The diester is stable to further hydrolysis in neutral and acid solutions, although hydrolysis does occur in base.

Quantitatively, 50 ± 10% of the diester is produced in acid solutions (pH 1–3). This number seems relatively insensitive to the aromatic substituent, as well as to the acidity, although small variations may be hidden because of the imprecision of our analysis which is based on NMR integration of slightly overlapping peaks.

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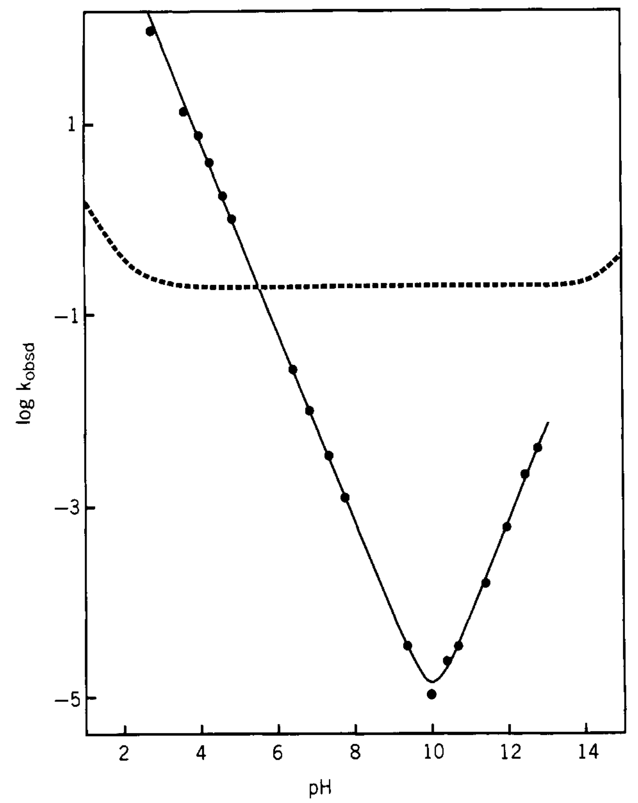

Figure 2. Rate constants (25 °C, $\mu = 0.1$) at zero buffer concentration in the hydrolysis of oxyphosphorane Ib. The line drawn is calculated as $5.3 \times 10^4[H^+] + 0.062[OH^-]$. The dashed curve refers to the hydrolysis of pentaphenoxyphosphorane in 75:25 dimethoxyethane:water[14] and is calculated as $16.4[H^+] + 0.202 + 12.0[OH^-]$.

We were unable to obtain a ratio in neutral solution because the phosphorane does not dissolve sufficiently to allow NMR spectra to be recorded. (Solution occurs in the strong acids only because of the speed of the hydrolysis). In base solution both ester products undergo hydrolysis more rapidly than the phosphorane, and it is not possible to determine what products are formed initially.

Kinetics. First-order rate constants for the hydrolysis of the phosphoranes were obtained over a range of pH and were found to obey the relationship of eq 2. Figure 2 depicts a rate–pH profile

$$k_{obsd} = k_H[H^+] + k_{OH}[OH^-] + k_{HA}[HA] + k_B[B] \qquad (2)$$

based on extrapolation to zero buffer concentration. Buffer catalysis is observed, representing general acid catalysis at pH <9 and general base catalysis at pH >10. Catalytic coefficients and some derived parameters are listed in Table I. A Brønsted plot for Ib based on H^+, HCOOH, CH_3COOH, and $H_2PO_4^-$ catalysts is reasonably linear (correlation coefficient = 0.998) with slope $\alpha = 0.74$.

A few control kinetic experiments were carried out on the phosphonate ester products, using di(2-methoxyethyl) phenylphosphonate as a model for the diester product. These experiments were conducted in order to establish that the rates referred to in eq 2 and Table I do refer to oxyphosphorane hydrolysis, and not some subsequent ester hydrolysis. Ethylene phenylphosphonate does undergo an acid hydrolysis, but the rate is slower than that observed with the phosphorane by a factor of 10^4. The diester is stable in acid even over several days. Both esters undergo hydrolysis in sodium hydroxide ion solutions, at a rate which is greater than that associated with the oxyphosphoranes.

Kinetic experiments at 25 °C and $\mu = 0.1$ were also carried out for the hydrolysis of the trimethoxyphenylphosphonium cation to dimethyl phenylphosphonate and methanol. Over the pH range 1–6, rate constants at zero buffer concentration are independent of pH with $k_0 = 4.0 \times 10^{-3}$ s^{-1}. General base catalysis by added buffers is observed, with $k(CNCH_2COO^-) = 0.027$ M^{-1} s^{-1}, $k(MeOCH_2COO^-) = 0.085$ M^{-1} s^{-1}, and $k(CH_3COO^-) = 0.385$ M^{-1} s^{-1}. The Brønsted β value based on the three carboxylate catalysts is 0.51.

Table I. Rate Constants for the Hydrolysis of Phosphoranes[a]

phosphorane	catalyst	k (M^{-1} s^{-1})	derived parameter
Ib	H^+	5.25×10^4	
Ib	D^+	7.6×10^4	$k_H/k_D = 0.7$
Ib	H^+ (16.0°)	2.85×10^4	
Ib	H^+ (35.0°)	1.09×10^5	$\Delta H^\ddagger = 11.2$ kcal/mol
Ib	H^+ (45.0°)	2.10×10^5	$\Delta S^\ddagger = 1.2$ eu
Ia	H^+	7.2×10^5	$\rho = -1.0$
Ic	H^+	3.0×10^5	
Ib	HCOOH ($\mu = 1.0$)	9.9	
Ib	CH_3COOH ($\mu = 1.0$)	1.1	
Ib	$H_2PO_4^-$ ($\mu = 1.0$)	0.083	
Ia	$H_2PO_4^-$ ($\mu = 1.0$)	0.101	$\rho = -0.9$
Ic	$H_2PO_4^-$ ($\mu = 1.0$)	0.043	
Ib	HCO_3^-	~0.001	
Ib	Et_3N	0.002	
Ia	CO_3^{2-}	0.007	
Ib	CO_3^{2-}	0.016	$\rho = +2.1$
Ic	CO_3^{2-}	0.045	
Ia	OH^-	0.023	
Ic	OH^-	0.222	$\rho = +2.5$
Ib	OH^-	0.062	
Ib	OH^- (19.0°)	0.038	$\Delta H^\ddagger = 13.3$ kcal/mol
Ib	OH^- (32.1°)	0.106	$\Delta S^\ddagger = -19$ eu

[a] 25 °C, $\mu = 0.1$, unless stated otherwise.

The following experiment was carried out in an attempt to detect the cyclic phosphonium salt that we propose (see Discussion) as an intermediate in the acid hydrolysis of the phosphoranes. The phosphorane Ia in pH 9.5 buffer was mixed in a stopped-flow spectrophotometer with 1.0 M HCl. In the resultant acid solution, the first-order rate constant based on eq 2 is such that the process to which this rate refers is complete within the dead time of the stopped-flow instruement (2 ms), and indeed no absorbance change at 260–280 nm is seen on mixing, the absorbance which is observed corresponding to that of the products. The implication of this experiment is that the phosphonium ion intermediate also undergoes hydrolysis within the dead time, and we therefor place a lower limit of 10^3 s^{-1} on its rate of hydrolysis. The assumption being made here is that if the ion were to undergo hydrolysis more slowly, it would be detected from an absorbance decrease at 260–280 nm accompanying this hydrolysis, such as that which is observed with $PhP^+(OCH_3)_3$ (Figure 1).

A further indication of the relative instability of cyclic phosphonium ions comes in our failure to prepare such a species. For example, treatment of ethylene phenylphosphonate with methyl trifluoromethanesulfonate results in no noticeable reaction. This is also true with triethyloxonium tetrafluoroborate or trimethyloxonium hexachloroantimonate, although with these alkylating agents extensive decomposition is observed over several days. Treatment of 2-phenyl-1,3,2-dioxaphospholane with all three alkylating agents in methylene chloride results in a rapid reaction, but the NMR spectra of the resultant solutions is very complex and shows little indication of the expected phosphonium salt.

Discussion

As is evident in Figure 2, the spirobicyclic oxyphosphoranes of this study differ considerably in their hydrolysis from a pentaaryloxyphosphorane. Particularly noteworthy is the complete absence[21] with the bicyclic compounds of a pH-independent or "water" reaction. This reaction dominates the rate–pH profile of the pentaaryl system and is obviously responsible for its relative hydrolytic lability. Archie and Westheimer have, in fact, found that the water rate constant increases with increasing water

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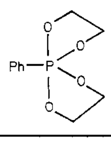
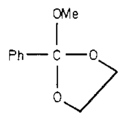
(21) An upper limit of 2×10^{-6} s^{-1} can be placed on the water rate constant. This limit is based on the consideration that at the rate minimum a 20% contribution to the overall rate constant would have been seen.

Table II. Acid-Catalyzed Hydrolysis of Phosphoranes and Dioxolane Ortho Esters

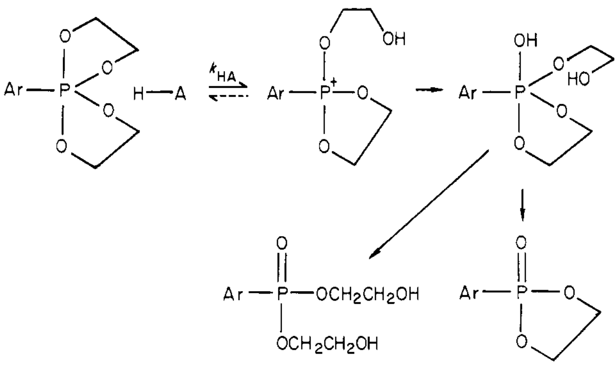
		
k_{H^+} (M^{-1} s^{-1})	5.3×10^4	5.4×10^3 [a]
k_{H^+}/k_{D^+}	0.7	0.46[b]
$\rho(H^+)$	-1.0	-1.60[c]
$\rho(H_2PO_4^-)$	-0.9	-1.93[c]
α	0.74	0.90[d]
$\Delta S^{\ddagger}$ (cal deg^{-1} mol^{-1})	+1.2	-3.0[e]

[a] Reference 30. [b] Reference 31. [c] Reference 32. [d] Reference 27. [e] Reference 33.

content,[14] so that the curve for the pentaphenoxy compound in a wholly aqueous solution would be even higher than that of Figure 2.

Both types of oxyphosphoranes do exhibit H^+-catalyzed and OH^--catalyzed hydrolyses, although with the bicyclic phosphoranes the former pathway is considerably more efficient. General acid and general base catalyzed reactions are also observed in the present case,[22] our results showing that the H^+-catalyzed and general acid catalyzed reactions are related, as are the OH^--catalyzed and general base catalyzed reactions.

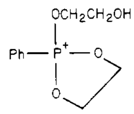
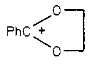
Acid Hydrolysis. The acid reaction appears to be the phosphorane analogue of general acid catalyzed hydrolysis of an acetal or carboxylic ortho ester,[23] proceeding with an initial dissociation to a phosphonium ion intermediate (eq 3). Acid-induced dissociative reactions of oxyphosphoranes have been suggested to account for isomerization in certain systems.[24] Archie and Westheimer argued against such a reaction for the acid hydrolysis of the pentaaryloxyphosphoranes,[14] although the dissociation of these species to a tetraaryloxyphosphonium ion could be observed and studied under nonhydrolytic conditions.[25]



(3)

Equation 3 is written with P–O bond cleavage and proton transfer concerted, in accordance with the currently accepted mechanism for general acid catalyzed acetal hydrolysis.[26-28] A stepwise reaction involving a discrete O-protonated oxyphosphorane intermediate can probably be ruled out in any event.

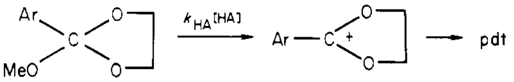
Table III. Rates of Hydrolysis of Oxyphosphonium Ions and Oxycarbonium Ions

ion	k, s^{-1}	ion	k, s^{-1}
$Ph\overset{+}{P}(OMe)_3$	4×10^{-3}	$Ph\overset{+}{C}(OMe)_2$	1.2×10^5 [a]
	$\geqslant 10^3$		1.7×10^4 [b]

[a] Reference 38. [b] Reference 30.

The pK_a of this intermediate should be large and negative (<–7),[29] and the rate of protonation of the neutral oxyphosphorane is therefore not likely to be as large as the observed rate of H^+-catalyzed hydrolysis ($\sim 10^5$ M^{-1} s^{-1}).

Evidence for the dissociative pathway is summarized in Table II where kinetic parameters obtained with the oxyphosphoranes are compared with those of 2-aryl dioxolane ortho esters. These are known to undergo initial exocyclic C–O bond cleavage in a general acid catalyzed reaction.[27,30] They were chosen for the comparison because they have a reactivity similar to that of the oxyphosphoranes in their H^+-catalyzed hydrolysis, a similarity which, as shown in Table II, extends to most aspects of the hydrolysis. The rate acceleration observed with electron donors is obviously the key indicator of the dissociative mechanism for the phosphoranes, pointing to the development of positive charge at the phosphorus in the transition state. The ρ values are small in magnitude, both with the ortho ester and oxyphosphorane, but this can be taken as an indication of a relatively early transition state for bond cleavage[34] or of a decreased interaction of the positive center and the aromatic ring owing to the inherent stability of the cation. The Brønsted α values are large in each system suggestive of a considerable degree of proton transfer in the transition state. Both systems also exhibit inverse solvent isotope effects. This behavior, which is more in accord with a specific acid reaction, has been noted previously in studies of general acid-catalyzed acetal hydrolysis, and a possible explanation advanced.[35]



(4)

There is some uncertainty in the oxyphosphorane reaction, in that the first step could be a preequilibrium because of the intramolecular nature of the reverse reaction. In this situation the rate-determining step would be the addition of water to the phosphonium ion. The observed ρ value would correspond to a relatively early transition state for the addition, so that the transition state would have a phosphonium ion character. The observed general acid catalysis would correspond to a kinetically equivalent specific acid:general base reaction, where the addition of water is assisted by bases, as it is in the hydrolysis of the trimethoxyphenylphosphonium ion. The one piece of evidence which is inconsistent with a preequilibrium ring opening is the near-zero entropy of activation. This is not the sort of value that would be expected for a rate-determining addition of water and is, in fact, very comparable to the value for the ortho ester where reversibility cannot be a factor. Moreover, these is an ortho ester

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(22) (a) The possibility of such catalysis was not investigated with the pentaaryl systems, perhaps because of the difficulty associated with buffer studies in mixed organic aqueous solutions.[22b] (b) Salomaa, P.; Kankaanpera, I.; Lahti, M. *J. Am. Chem. Soc.* **1971**, *93*, 2084–2085.

(23) For reviews of acetal and ortho ester hydrolysis, see (a) Fife, T. H. *Acc. Chem. Res.* **1972**, *5*, 264–272. (b) Cordes, E. H.; Bull, H. G. *Chem. Rev.* **1974**, *74*, 581–603.

(24) Reference 11b, pp 115–118.

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(29) For example, the pK_a values of protonated orthocarbonates, where there are also present three additional acid strengthening oxygen atoms, have been estimated to be in the range –6.3 to –8.5.[22b]

(30) Ahmad, M.; Bergstrom, R. G.; Cashen, M. J.; Chiang, Y.; Kresge, A. J.; McClelland, R. A.; Powell, M. F. *J. Am. Chem. Soc.* **1979**, *101*, 2669–2677.

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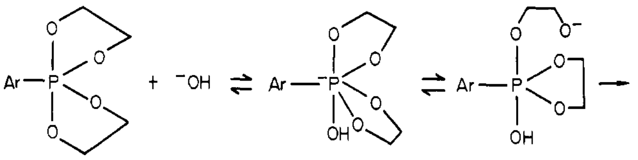
system, 2,4,10-trioxaadamantanes, whose hydrolyses are established to proceed with preequilibrium ring opening,[36,37] and their entropies of activation are significantly negative.[36]

Some comment can also be made regarding the relative stability of the cationic intermediates of the hydrolysis, as measured by their subsequent rates of hydrolysis. These are summarized in Table III, the lower limit for the cyclic phosphonium ion being based on the experiment described at the end of the Results section. The considerable difference between this cation and its acyclic analogue is reminiscent of the difference in reactivity between cyclic and acyclic phosphate esters,[1] and presumably the same factor or factors which are responsible for this difference are also present in the phosphonium ions. The major consequence of the decreased stability of the cyclic phosphonium ion is that it approaches in its reactivity a dialkoxycarbonium ion (Table III). This accidental similarity could also explain the close relationship between the acid hydrolysis of the bicyclic oxyphosphorane and the cyclic ortho ester (although there are undoubtedly other factors governing reactivity in the two systems). One implication is that an oxyphosphorane which would dissociate to an acyclic phosphonium ion (for example, $PhP(OCH_3)_4$) would be a much more reactive species. We are currently pursuing studies of such species to see if this is the case.

A further point of similarity between a cyclic phosphonium ion and a cyclic phosphate ester concerns their tendency to undergo hydrolysis to products derived from both exocyclic and endocyclic cleavage. Thus methyl ethylene phosphate at pH 1–3 also gives about a 50:50 mixture of products derived from the two modes of cleavage.[39]

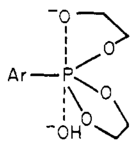
Base Hydrolysis. In contrast to the acid reaction the base hydrolysis appears to be an associative reaction, proceeding by way of a hexacoordinated phosphoroxanide anion (eq 5). This is the type of mechanism envisaged by Archie and Westheimer for the hydroxide-ion-catalyzed (and water-catalyzed) hydrolysis of pentaaryloxyphosphoranes.[14] Valence expansion of oxyphosphorane to phosphoroxanide anions is well estabilished in other cases, and such anions have been isolated as salts.[6,10,11,40]



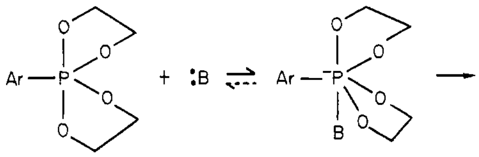
products (5)

The principal piece of evidence in the present work is the substantially positive ρ value (+2.5) observed for the hydroxide ion reaction, a value which points to a substantial development of negative charge on the phosphorus atom. The negative entropy of activation is also consistent with an associative reaction.

There is considerable uncertainty as to the exact details of the reaction after the formation of the hexacoordinated intermediate, and the scheme proposed in eq 5 is meant to represent only one possibility. Unfortunately, one useful piece of information, the nature of the initial products, is not obtainable in base because of their further hydrolysis. There is also the possibility that some of the initial steps could be reversible. As discussed for the H^+-catalyzed reaction, this could probably be accomodated by the observations. A mechanism where the hexacoordinated anion is a transition state and not an intermediate is also a possibility. This does, however, seem less likely in light of the substituent effect which points to a substantial buildup of negative charge on the phosphorus. A direct displacement would appear to place most of the negative charge in the transition state on the incoming and outgoing oxygen atoms.



One of the more interesting observations is the presence of a general base catalyzed hydrolysis, a reaction which on the basis of the substituent effect also appears to be associative. Two mechanisms can be envisaged to account for this, a general base catalyzed addition of water to the phosphorus to produce the same intermediate obtained upon addition of hydroxide ion, or a nucleophilic catalyzed reaction in which the base adds directly to the phosphorus. The former seems more attractive in that the anionic intermediate of eq 6 seems likely to preferentially expel the base which is the better leaving group. Interestingly, carbonate is considerably more efficient a base in this reaction than triethylamine, despite the somewhat greater basicity of the latter. This may reflect some steric crowding in the transition state, a possibility which we are currently investigating by studies with various other bases.[41]



(6)

Acknowledgment. Continued financial support of the Natural Sciences and Engineering Research Council of Canada is gratefully acknowledged. Support from the Research Corporation is also acknowledged.

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(41) Unfortunately, the choice of bases is somewhat limited since below pH 9 only acid catalysis is observed.