Hydrolysis of a Phosphonium Salt. Encounter-Limited, Rate-Determining Breakdown of a Pentacovalent Intermediate

David G. Gorenstein

Contribution from the Department of Chemistry, University of Illinois, Chicago, Illinois 60680. *Received July 2, 1973*

Abstract: The pH–rate profile for the hydrolysis of 1-methoxy-1-phenyl-2,2,3-trimethylphosphetanium hexafluorophosphate is presented. The rate of hydrolysis is proportional to the hydroxide ion concentration in the alkaline region, pH >9, and is pH independent in dilute acid. In the moderate to strong acid region (pH <1) the rate decreases with increasing acidity, attributable to a decrease in the activity of water. Of major interest is the sigmoidal titration curve between pH 3 and 8, with the rate increasing with increasing pH. This curve is ascribed to a change in the rate-determining step for hydrolysis, from rate-limiting hydration around neutral pH to rate-limiting breakdown of a pentacovalent intermediate in acid. Evidence is presented to suggest that this rate of breakdown of the intermediate approaches a value expected for an encounter-limited proton transfer reaction.

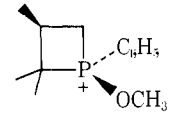
Studies on the nature of the pentacovalent intermediates in the reactions of phosphoryl compounds are complicated by the protonic equilibria which must be simultaneously accounted for in any proposed scheme. Thus, recent studies on the epimerization and exchange of a phosphetane oxide,[1] hydrolysis of methyl ethylene phosphate,[2,3] and hydrolysis of a bicyclic phosphinic acid[4] have produced very complex kinetic schemes. However, if one could "tie down" one or more of these illusive protons and therefore restrict the number of protonic equilibria, it might be possible to simplify and, thus, aid in the kinetic analysis. Experimentally this is often achieved by substituting a methyl group for one of these labile protons, and such an approach is the subject of this paper.

Previous studies[5-12] on the hydrolysis of alkoxyphosphonium salts have been concerned with either the

$$R_3P^+\text{–}OR' + {}^-OH \longrightarrow R_3P{=}O + R'OH \qquad (1)$$

position of bond breaking or the stereochemistry of the displacement reaction at phosphorus (assuming P–O bond breaking has been demonstrated). These studies have been conducted in either highly alkaline solutions or in the presence of a good nucleophile in nonaqueous solutions where reaction rates would be extremely difficult to measure. In acyclic alkoxyphosphonium salts both P–O and C–O bond breaking have been observed,[6b,12-14] as well as variable degrees of stereospecificity for attack at phosphorus. Thus, examples of complete inversion[6b] or even complete retention[7a] are known.

On the other hand, only P–O bond cleavage with retention of configuration at phosphorus has been observed in the alkaline hydrolysis of a strained four-membered monoalkoxyphosphetanium salt.[6a,15a] Pseudorotation theory[3,5] has been successfully applied to explain this very different behavior. While previous studies have presented various mechanistic schemes requiring pentacovalent intermediates. little actual kinetic evidence is offered to justify the structures proposed in these mechanisms. The present work has considered in detail the nature of the hydrolysis reaction of 1-methoxy-1-phenyl-2,2,3-trimethylphosphetanium hexafluorophosphate (**1**) over the entire acidity range in



trans-1

aqueous solution. Interpretation of the pH–rate profile and additional kinetic evidence have yielded new understanding about the nature of the protonic equilibria and about the role of the pentacovalent intermediates in the reactions of tetracovalent phosphorus compounds.

Most significantly, we present the first evidence for rate-determining breakdown of a pentacovalent intermediate,[15b] and further, suggest that this rate of breakdown approaches a value expected for an encounter-limited proton transfer reaction.

Experimental Section

Synthesis of 1-Methoxy-1-phenyl-2,2,3-trimethylphosphetanium Hexafluorophosphate (1). A solution of an equilibrium mixture of cis/trans (20:80)[16] 1-phenyl-2,2,3-trimethylphosphetane oxide[1,17]

(1) D. G. Gorenstein, *J. Amer. Chem. Soc.*, **94**, 2808 (1972).
(2) R. Kluger, F. Covitz, E. Dennis, L. D. Williams, and F. H. Westheimer, *ibid.*, **91**, 6066 (1969).
(3) F. H. Westheimer, *Accounts Chem. Res.*, **1**, 70 (1968).
(4) R. Kluger and F. H. Westheimer, *J. Amer. Chem. Soc.*, **91**, 4143 (1969).
(5) K. Mislow, *Accounts Chem. Res.*, **3**, 321 (1970).
(6) (a) K. E. DeBruin, G. Zon, K. Naumann, and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 7027 (1969); (b) *ibid.*, **91**, 7023 (1969).
(7) (a) N. J. De'Ath, K. Ellis, D. J. H. Smith, and S. Trippett, *Chem. Commun.*, 714 (1971); (b) N. J. De'Ath and S. Trippett, *ibid.*, 172 (1969).
(8) K. E. DeBruin and J. R. Petersen, *J. Org. Chem.*, **37**, 2272 (1972).
(9) (a) K. E. DeBruin and M. J. Jacobs, *Chem. Commun.*, 59 (1971); (b) R. A. Lewis, K. Naumann, K. E. DeBruin, and K. Mislow, *ibid.*, 1010 (1969).
(10) J. Michalski, M. Mikolajczyk, and J. Omelanczuk, *Tetrahedron Lett.*, 3565 (1968); 1919 (1966).
(11) L. P. Reiff, L. J. Szafraniec, and H. S. Aaron, *Chem. Commun.*, 366 (1971).
(12) K. E. DeBruin and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 7393 (1969).
(13) K. E. DeBruin and S. Chandrasekaran, *ibid.*, **95**, 974 (1973).
(14) A. Michaelis and R. Kaehnl, *Chem. Ber.*, **31**, 1048 (1898); L. Kgay, *J. Org. Chem.*, **28**, 1426 (1963).

(15) (a) Hydrolysis of a dialkoxyphosphetanium salt proceeds with lack of stereospecificity (see ref 9b). (b) As pointed out by a referee, the observation of a second-order hydroxide term in the hydrolysis of alkylphosphonium salts may actually represent the first example of rate-determining breakdown of a pentacovalent intermediate. These results, however, could be explained by a concerted hydroxide catalyzed attack of hydroxide upon the phosphonium salt which would avoid the formation of a pentacovalent intermediate: G. Aksnes and J. Songstad, *Acta Chem. Scand.*, **16**, 1426 (1962).
(16) Integration of the nmr signals as described in ref 1 was used to determine diastereomeric composition of the mixture.
(17) S. E. Cremer and R. J. Chorvat, *J. Org. Chem.*, **32**, 4066 (1967).

(2) (1.67 g, 8.05 mmol) in dichloromethane was added to a stirred suspension of Aldrich trimethyloxonium hexafluorophosphate (1.65 g, 8.0 mmol). The mixture was stirred under an argon atmosphere at room temperature overnight and a viscous oil was separated from the resulting solution by cooling in a Dry Ice–acetone bath. The oil was triturated several times with hexane and subsequently with ether until crystals of **1** first formed. The oily crystalline mass was recrystallized several times from ether–CH_2Cl_2 (1.5 g, 50%, mp 90–95°). The ^1H nmr of the salt in $CDCl_3$ showed signals attributable to what appeared to be an isomerically pure compound but probably still consisting of a mixture of isomers. This most likely resulted from accidental equivalence of the signals since kinetic and product studies indicated that a 20:80 cis/trans mixture of salts was still present: nmr (TMS) δ 1.14 and 1.50 ($PC(CH_3)_2$, doublet of doublets, $J_{PCCH_3} \approx 23$ Hz); δ 3.97 ($P-OCH_3$, doublet, $J_{P-OCH_3} = 12.1$ Hz); multiplets *ca.* δ 1.3 ($PCCCH_3$), 2–3 (ring protons), and 7.9 (aromatic protons).

Anal. Calcd for $C_{13}H_{20}OP_2F_6$: C, 42.40; H, 5.47; P, 16.82; F, 30.96. Found:[18] C, 42.46; H, 5.53; P, 16.67; F, 30.82.

Product Study in the Hydrolysis of 1. Acid or base hydrolysis of **1** (*ca.* 0.2 *M*) in 50% aqueous acetonitrile showed signals in the nmr only attributable to a cis/trans (20:80) mixture of 1-phenyl-2,2,3-trimethylphosphetane 1-oxide. In addition, the material was shown to be identical with the original phosphetane oxide by ir and uv spectroscopy. Hydrolysis of a phosphonium salt mixture prepared from a cis/trans (30:70) mixture of phosphetane oxides regenerated the same (30:70) isomeric ratio of oxides.

Determination of the Position of Bond Cleavage in the Hydrolysis of 1. The phosphetane salt (10.8 mg, 0.03 m*M*) was hydrolyzed in 200 μl of a 50% acetonitrile–$H_2{}^{18}O$ buffer solution at room temperature for over 10 half-lives. The phosphetane oxide was analyzed for ^{18}O incorporation by quantitative ir spectroscopy as previously described.[1,19] The results are presented in Table I.

Table I. ^{18}O Incorporation into 1-Phenyl-2,2,3-trimethylphosphetane 1-Oxide (**2**) for the Hydrolysis of **1** in 50% $CH_3CN-H_2{}^{18}O$ Buffer

	Atom % ^{18}O content of aqueous buffer[a]	Atom % ^{18}O content of **2**
pH 1.1, HCl	62.0 ± 1.0	62.0 ± 1.0
pH 8.0, 0.25 *M* Tris	56.0 ± 1.0	56.5 ± 1.0

[a] Determined by equilibration of the solvent with **2** and subsequent ir analysis of the $P{=}{}^{18}O$ and $P{=}{}^{16}O$ stretching frequencies (see ref 1).

Buffers. Reagent grade buffer salts and Matheson Coleman and Bell Spectroquality acetonitrile were used throughout without any additional purification. Redistilled water was employed. The pH's of the buffer solutions were measured at room temperature on a Radiometer PHM 26 pH meter fitted with a Type G2222C glass semimicro electrode and Type K4112 calomel electrode. The meter was calibrated against Fisher standard buffers. The pH's were measured on the 50% CH_3CN–buffer solutions before and after reactions, and those reactions in which the pH drifted by more than ±0.1 pH unit were discarded.

Kinetics. Conventional Uv Method. Hydrolysis of **1** in 50% acetonitrile–aqueous buffer (or strong acid) was followed by the change in absorbance at 265.5 mμ on a Cary 16K uv–visible spectrophotometer with an automatic sample changer and thermostated sample holder. For the slow and intermediate rate reactions (half-times 2–300 sec), a sample of **1** dissolved in 2–4 μl of CH_3CN was placed on the end of a flattened glass rod and inserted through a hole in the top of the sample compartment into a 1-cm quartz cuvette containing the buffer solution. The change in OD was monitored on a Cary modified Varian G2500 10-in. recorder where full scale pen travel represented 0.5 or 0.1 OD. The concentration of the phosphetanium salt was *ca.* 8×10^{-4} *M* ($\epsilon_{265.5}$ 1100) and the overall OD change was 0.1–0.3 OD ($\Delta\epsilon_{265.5} = 400$). Repetitive scan spectra of the slowly hydrolyzing samples were performed on a Pye Unicam SP 500 uv–visible spectrophotometer.

Stopped-Flow Method. The hydrolysis reactions of **1** which were too fast to measure on the Cary were followed on an Aminco-Morrow 4-8409 stopped-flow apparatus. One syringe contained the phosphetanium salt in dry acetonitrile and the second syringe contained the buffer solution; 100% T for the mixed solutions was set at 10 V as displayed on the 2 V/division scale of a Tektronix R564B storage oscilloscope. Reactions were monitored at 270 mμ (poorer signal to noise was experienced at 265.5 mμ) and at the concentrations of **1** normally employed (7×10^{-4} m*M*, ϵ_{270} 240, $\Delta\epsilon_{270} = 180$) relaxation of the system was conveniently followed on the 0.2 V/division (1.0% *T*/division) scale of the oscilloscope using a time base from 2 msec[20] to 5 sec/division. The oscilloscope record was photographed with a polaroid camera, the photograph traced onto graph paper, and the per cent *T* data converted into OD values. Unfortunately, a complication arose from use of the mixed solvent system necessitated by the reactivity of the phosphetanium salt. Thus, two *solvent* relaxation times were observed: an initial rapid increase in transmittance ($\tau_{1/2} \sim 53$ msec, amplitude ~0.3 V) followed by a slower decrease in transmittance ($\tau_{1/2} \sim 1.1$ sec, amplitude ~0.3 V). Since these changes in the solvent transmittance were independent of monitoring wavelength and only three times freeze–pump–thawed degassed solvents were used, these relaxation processes are most likely associated with some change in the bulk properties of the solvent. Mixing poorly temperature equilibrated samples is found to yield this type of change in transmittance of pure solvents and although our two syringes are previously temperature equilibrated in the thermostated housing of the mixing chamber, mixing of acetonitrile and aqueous solutions produces noticeable cooling. The two solvent relaxations must then result from the initial cooling followed by a slower temperature reequilibration.

Treatment of Kinetic Data. In addition to the solvent relaxation complication in the stopped-flow work, a second slower relaxation is generally observed in both Cary and stopped-flow kinetic studies. The amplitude of this second relaxation is *ca.* one-fifth that of the major reaction, and may be attributed to the slower hydrolysis of the *cis*-1-methoxy-1-phenyl-2,2,3-trimethylphosphetanium hexafluorophosphate. Examples of this biphasic behavior are shown in Figures 1 and 2. Since a cis/trans (20:80) mixture of phosphetane oxides was originally used in the synthesis of **1**, a 20:80 cis/trans mixture of the salts is presumably present. Confirming this interpretation, a sample of **1** prepared from a cis/trans (30:70) mixture of phosphetane oxides, **2**, upon hydrolysis showed two relaxations with amplitudes in the ratio of 30:70, and relaxation times comparable to those associated with the cis and trans isomers in the 20:80 mixture. In addition, only a single relaxation time was observed in the hydrolysis of an isomerically pure sample of **1** (>96%) trans).

The two relaxations were separated by fitting the data to eq 2 by

$$OD = Ae^{-k_\alpha t} + Be^{-k_\beta t} + OD_\infty \qquad (2)$$

use of an iterative, nonlinear least-squares program. The general purpose nonlinear least-squares program was written by Dye and Nicely[21a] and subsequently modified to fit on the UICC chemistry department's PDP-11/45 computer (16 K core). The program minimizes the sum of the squares of the residuals between the calculated OD's based upon eq 2 and the observed OD's using a weighting procedure described by Wentworth.[21b] Better convergence to realistic values of *A*, *B*, OD_∞, k_α, and k_β were obtained by first fitting only the very last portion of the kinetic data (the fast relaxation k_α was in its 8–10th half-life and thus represented only a very minor contribution to the change in the latter OD values) to a single exponential with the iterative, nonlinear least-squares program. This value of k_β was then included in eq 2 as a constant and only a best fit to a four-parameter equation was required. Because of the smaller amplitude of the k_β reaction and the fewer data points that could be used to determine k_β, errors in k_β are probably two times greater than errors in k_α.

In addition, the kinetics program was used to factor out the solvent relaxations observed in the stopped-flow work by including the two solvent decays in an expanded version of eq 2 (as constants only). In general, little if any improve-

(18) Microanalysis was performed by Galbraith Laboratories, Knoxville, Tenn.

(19) The molar extinction coefficients for a NaCl cell, path length 0.1 mm, for these analyses were $\epsilon_{1207\ cm^{-1}}(P{=}{}^{16}O)$ 2.42, $\epsilon_{1188\ cm^{-1}}(P{=}{}^{18}O)$ 2.21, $\epsilon_{1207}(P{=}{}^{18}O)$ 0.41, $\epsilon_{1188}(P{=}{}^{16}O)$ 0.53.

(20) The mixing time of the instrument is 2 msec (Aminco Instruction Manual).

(21) (a) J. L. Dye and V. A. Nicely, *J. Chem. Educ.*, **48**, 445 (1971); (b) W. E. Wentworth, *ibid.*, **42**, 162 (1965).

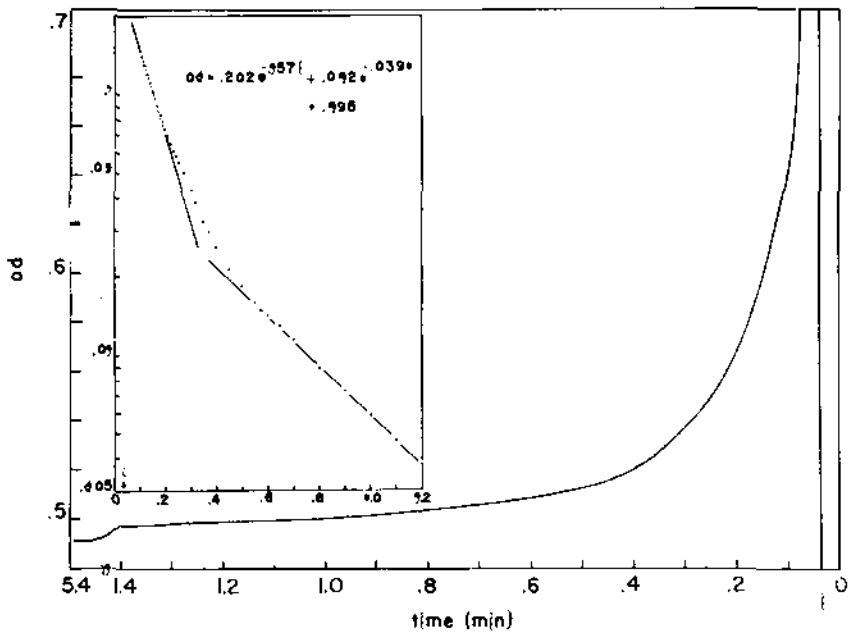


Figure 1. Cary uv kinetics for the hydrolysis of 1 (20:80, cis/trans) in pH 2.8 phosphate buffer–CH_3CN (50% v/v), 5.0°. Inset shows biphasic first-order kinetic plot.

ment in the fit of the stopped-flow data was achieved by this technique and rate constants reported are mostly uncorrected for this solvent effect. At worst, because of the solvent relaxations, the actual error in the rate constants may be 2–3 times as large as the normal linear estimate of the standard deviation of the stopped-flow data, ±20%. The error in the k_α rate constants is generally much better than this and in those cases where the Cary data overlapped with the stopped-flow work, good agreement was found. As a final check on the uv methods, an nmr method following the decrease in amplitude of the $POCH_3$ doublet and the increase in the CH_3OH signal gave good agreement (see Table II) with the Cary uv result.

Table II. Rate Constants for Hydrolysis of *trans*-**1** in 50% CH_3CN–Acid (v/v) at 5.0 ± 0.1[a]

pH (H_0)[b]	Acid concn	k_{obsd},[b,c] sec^{-1}
2.0	0.01 *M* HCl	0.101, 0.106 (0.022)
1.39	0.05 *M* HCl	0.0951, 0.0951
1.40	0.05 *M* HCl–0.2 *M* KCl	0.178 (0.030)
1.10	0.1 *M* HCl–0.2 *M* KCl	0.0890, 0.0834, 0.0850
0.20	0.5 *M* HCl	0.0708, 0.0792
−0.68	2 *M* HCl	0.0343, 0.0328
−1.40	4 *M* HCl	0.00696, 0.00611
−1.96	5.6 *M* HCl	0.00122
−1.96	5.6 *M* HCl	0.00165[d]

[a] H_0 values at 25° for aqueous solutions only: F. A. Long and M. A. Paul, *Chem. Rev.*, 57, 1 (1957). Unfortunately, the acidity function has not been determined for 50% CH_3CN–acid solutions. [b] Cary uv method. Rate constants for hydrolysis of *trans*-**1** (k_α). [c] Rate constants in parentheses for hydrolysis of *cis*-**1** (k_β). [d] Nmr method.

Buffer Catalysis. Pseudo-first-order rate constants, k_{obsd}, were determined at 3–8 different buffer concentrations at constant pH and a linear plot of k_{obsd} *vs.* total buffer concentration yielded k_0, the water rate constant as the intercept ($B_T = 0$), and k_{B_T}, the second-order buffer rate constant as the slope.

For several of the buffers, k_{B_T} was determined at different buffer ratios and a fit to a plot of k_{B_T} *vs.* per cent free base yielded k_B, the second-order rate constant for catalysis by the free base, and k_{HB}, the second-order rate constant for catalysis by the buffer acid component. Unfortunately, because of the simultaneous hydrolysis of the PF_6^-, low concentrations (<0.03 *M*) of buffer could generally not be used, and therefore errors in k_0 obtained from the buffer studies are quite large. Errors are all linear estimates of the standard deviations.

Results and Discussion

Rate constants for hydrolysis of *cis*- and *trans*-**1** are presented in Tables II and III and the pH–rate profile for hydrolysis of *trans*-**1** is presented in Figure 3.

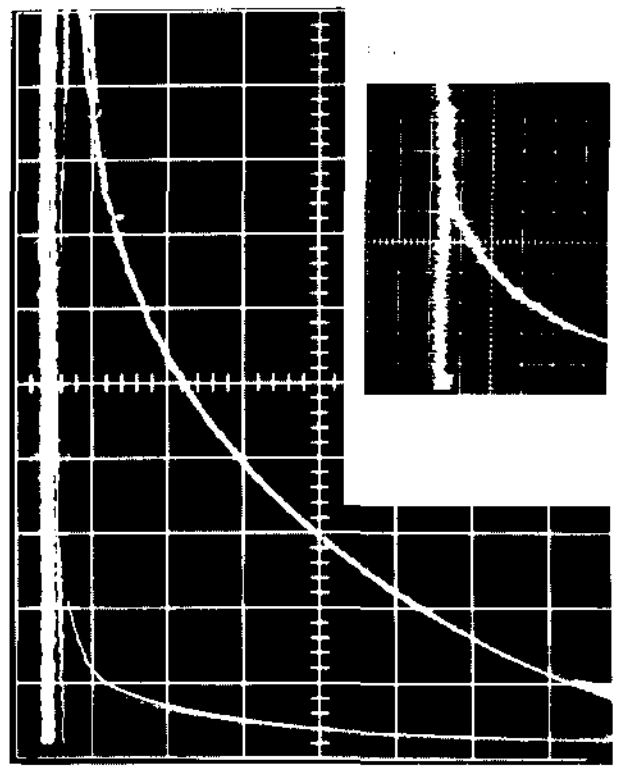
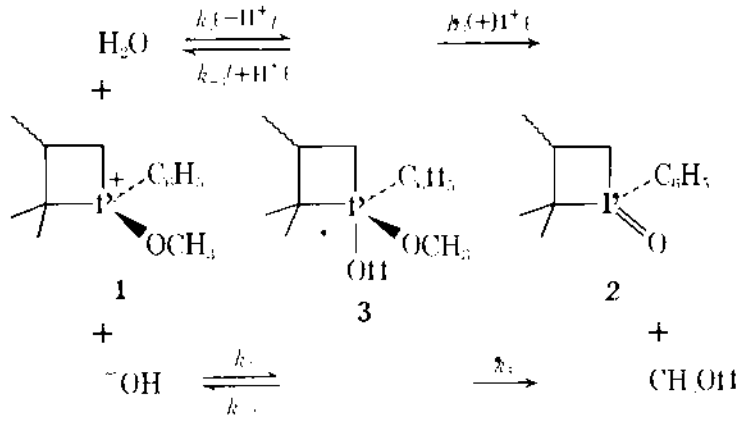


Figure 2. Stopped-flow relaxation spectra for the hydrolysis of **1** (20:80, cis/trans) in 50% 0.20 *M* phosphate buffer–CH_3CN, I = 0.25 *M*, 25.0°, pH 2.80. Slower relaxations in main figure and inset are associated with a 2 sec/division time base.

A mechanistic scheme consistent with the pH–rate profile and other supporting evidence is presented in Scheme I. Steady-state treatment of this mechanism

Scheme I



gives the rate law

$$k_{obsd} = \frac{k_a(H^+)}{1 + (H^+)/K_a} + \frac{k_b/(H^+)}{1 + K_a/(H^+)} + k_c(^-OH) \quad (3)$$

where k_a, k_b, k_c and K_a are defined by

$$k_aK_a = k_1k_3/(k_{-1} + k_3) = 0.5\ sec^{-1}$$

$$k_b/K_a = k_1k_4/(k_{-2} + k_4) = 11.0\ sec^{-1}$$

$$K_a = (k_{-3} + k_4)/(k_{-1} + k_3) = 1.29 \times 10^{-6}\ M$$

$$k_c = k_2k_3/(k_{-2} + k_4) = 5.6 \times 10^5\ M^{-1}\ sec^{-1}$$

The results of Table I show that within the experimental error (±2%) 1.0 atom of solvent oxygen is introduced into the phosphetane oxide product. Thus, water attacks only at phosphorus, and methanol loss occurs with exclusive P–O bond breaking. In addition, the product study (see Experimental Section) requires retention of configuration at phosphorus since a given cis/trans mixture of the phosphetanium salts produces the same isomeric ratio of oxides. The demonstration of exclusive P–O bond breaking with retention of configuration at phosphorus would require then a step involving initial addition of water to form an inter-

Table III. Pseudo-First-Order Rate Constants and Buffer Second-Order Rate Constants in 50% CH_3CN–Buffer (v/v) at 25.0 ± 0.1°

Buffer	pK_a[a]	I	[B]/[B]$_t$	pH	k_0, sec^{-1}	k_{BT}, M^{-1} sec^{-1}
Phosphate	2.80	0.25	0.5	2.80	0.5 ± 0.2	3.1 ± 0.6
Formate	4.48	0.05	0.39	4.30	1.0 ± 4.4	56 ± 5
		0.05	0.55	4.53		113 ± 32
		0.05	0.80	5.05	0.6 ± 0.2	123 ± 6
	4.28	0.25	0.44	4.13	0.5 ± 1.8	46 ± 5
		0.25	0.55	4.42	1.1 ± 0.5	56 ± 0.3
		0.25	0.66	4.60	1.0 ± 1.1	68 ± 5
	(D_2O)	0.25	0.80	5.54[b]	1.3 ± 0.6	45 ± 4
Acetate	5.80	0.05	0.50	5.80		251 ± 44
		0.05	0.70	6.00	1.4 ± 2	338 ± 42
	5.63	0.25	0.276	5.05	0.96 ± 4.6	89 ± 7
		0.25	0.375	5.30	3.75 ± 2.5	95 ± 7
		0.25	0.545	5.74	9.2 ± 3	86 ± 17
Phosphate	7.46	0.25	0.256	7.0		362 ± 66
Tris	8.17	0.25	0.244	7.65	13 ± 2	98 ± 11
		0.25	0.324	7.77	10 ± 3	89 ± 28
		0.25	0.50	8.17	10 ± 3	176 ± 31
Borate	9.94	0.25	0.56	10.00	60 ± 20	
		0.25	1.0	10.50	215 ± 50	

[a] pH of a 50% CH_3CN–buffer solution, [B]/[B]$_t$ = 0.5. [b] pD = "meter reading" + 0.4: T. H. Fife and T. C. Bruice, *J. Phys. Chem.*, **65**, 1079 (1961).

mediate or transition state in which the departing methoxyl group and entering water group are arranged in the equatorial/apical positions of a trigonal bipyramid, **3**. Pseudorotation theory and previous work on the epimerization and exchange reactions[1] of **2** have provided strong evidence to indicate that **3** would be a likely structure for the first formed kinetically significant *intermediate* in these reactions. Pseudorotation about the phenyl group pivot[3] of **3** would serve to move the methoxyl group of the phosphorane intermediate into the axial position, which would then allow for axial loss[3] of methanol and formation of the phosphine oxide, **2**. The four separate regions in the profile provide a convenient division for the following discussion of the proposed mechanism and the fate of this pentacovalent intermediate.

(1) **Neutral pH Region.** Considering only the portion of the proposed mechanism responsible for the plateau in the pH–rate profile between pH 6 and 8, eq 3 would simplify to $k_{obsd} = k_b/K_a = k_1k_4/(k_{-2} + k_4)$. As we point out later, attack of hydroxide cannot be occurring in this neutral pH region, and therefore the microscopic reverse of this process, k_{-2}, is disallowed as well. Hydration must be rate limiting, then, or $k_{obsd} = k_1$. It may appear that the assumed mechanism in this pH region violates the principal of microscopic reversibility since we are proposing that water attacks a positively charged molecule and methanol departs from a *neutral* species. If the k_4 decomposition of the intermediate were required to follow in the steps of a k_{-2} type process, we would indeed face microscopic reversibility difficulties (assuming methanol and water are sufficiently similar). Of course, the k_4 mechanism need not look at all like this higher energy k_{-2} process[22b] since the phosphorane acidic proton should be quite labile. The methyl group obviously is not. Therefore, a much more reasonable mechanism would require either a concerted proton transfer or formation of a zwitterionic intermediate, **4**. This structure would

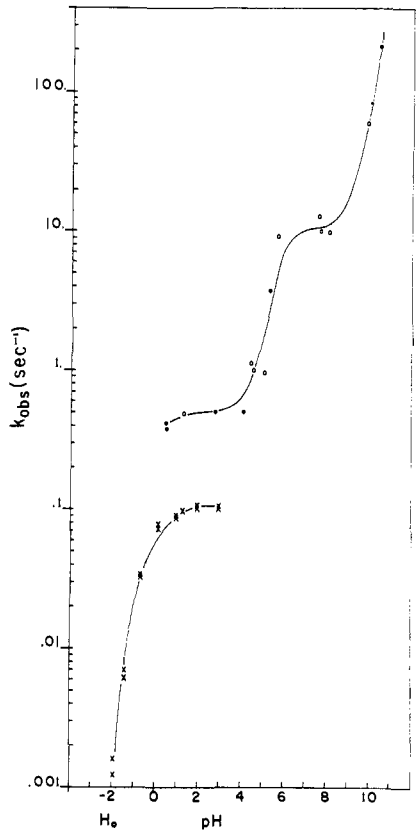
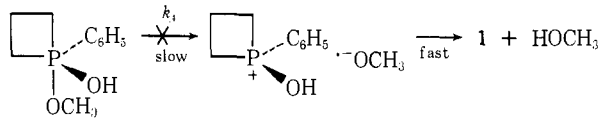
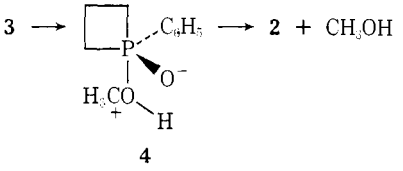


Figure 3. pH–rate profile for the hydrolysis of *trans*-**1** in 50% buffer (or acid)–CH_3CN, at 5.0° (×) or 25.0° and I = 0.25 M (○). The smooth curve for the 25.0°, I = 0.25 M points (○) was generated from eq 3. The curve in the moderate to strong acid region approximately follows a C_H+/h_0 dependency (see ref 1).



(22) (a) D. Z. Denney, D. W. White, and D. B. Denney [*J. Amer. Chem. Soc.*, **93**, 2066 (1971)] have shown that pseudorotation in related stable four-membered ring phosphoranes which allows permutation of alkoxyl apical and equatorial ligands is rapid on the nmr time scale down to −51°. Thus, this low energy pseudorotation process should be quite rapid relative to the overall rate of hydrolysis of 1. (b) Apical attack and leaving have been assumed (ref 1, 3, and 5).



4

agree with the polarity rule[23] whereby the most electronegative substituents prefer to occupy the apical positions in a trigonal bipyramid. Such a pathway is not possible for the k_{-2} step.

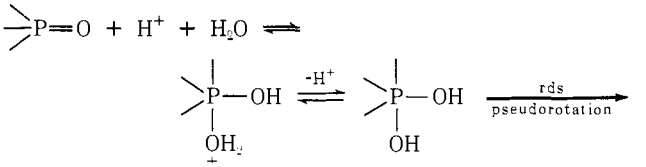
(2) **Intermediate Acidity Region.** The rate of hydrolysis of **1** decreases with increasing acidity, reaching a new plateau between pH 1 and 5 with the fall-off following a sigmoid titration curve with an apparent $pK_a = 5.89$. In this pH region eq 3 simplifies to $k_{obsd}^{acid} = k_aK_a = k_1k_3/(k_{-1} + k_3)$, again a pH independent rate term. Since $k_{obsd}^{neutral}/k_{obsd}^{acid} = 22 = (k_3 + k_{-1})/k_3$, $k_{-1} = 21k_3$ and, therefore, $k_{obsd}^{acid} \approx k_1k_3/k_{-1}$. The titration type profile arises then from a change in the rate-determining step, from hydration, k_1, around neutral pH to breakdown of the pentacovalent intermediate, *via* k_3, in dilute acid. Although the k_3 step is an acid-catalyzed process, the concentration of **3** is actually proportional to the hydroxide concentration and hence the *overall* rate would be independent of acid. It may appear unusual that an acid-catalyzed step should become rate limiting with *increasing* acidity, but, of course, the reason is that breakdown of the intermediate to starting material, *via* k_{-1}, is also acid catalyzed and occurs even faster than decomposition of **3** to products. Hence the concentration of the neutral pentacovalent intermediate must decrease directly in proportion to the increase in acidity. Only around neutral pH does the uncatalyzed breakdown of **3** (*via* k_4) compete successfully with the acid-catalyzed steps k_{-1} or k_3. Hydration then becomes rate limiting.

Simple calculation indicates that this rate-limiting breakdown of the pentacovalent intermediate may be diffusion controlled. Thus, in acid the rate of the reaction is given by

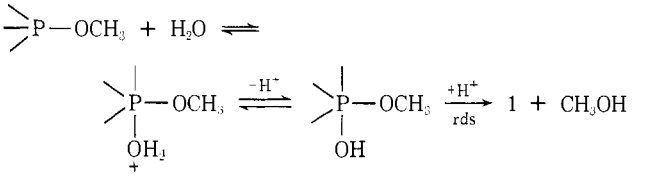
$$v = k_3[H^+][3]$$

and since there is no evidence in the nmr or uv spectra for the buildup of this intermediate, [**3**]/[phosphonium salt] < 0.1, $k_{obsd}^{acid} = 0.5\ sec^{-1} > 0.1\ [H^+]k_3$, or $k_3 > 0.5 \times 10^7\ sec^{-1}\ M^{-1}$ at pH ≈ 6 where the change in rate-determining step occurs. Furthermore, since $k_{-1} = 21k_3$, $k_{-1} > 10^8\ sec^{-1}\ M^{-1}$. If the concentration of **3** was actually smaller than our above crude estimate, these rate constants then may be approaching the encounter-controlled limit of *ca.* $10^9\ sec^{-1}\ M^{-1}$.[24] In addition, a similar calculation shows that [**3**]/[phosphonium salt] > 0.01–0.001 if decomposition of **3** is to be limited by the diffusion-control barrier. Thus, it may be possible under suitable conditions to actually observe the formation and breakdown of the pentacovalent intermediate (such studies are in progress).

(3) **Strong Acid Region.** The fall-off in rate in moderate to strong acid, [HCl] $> 0.1\ M$, is now a third example[1,4] of such dilute acid behavior in reactions of phosphorus compounds. In each case this fall-off has been interpreted to arise from a decrease in the activity of water superimposed upon a reaction which is overall *independent* of acidity. An important distinction, however, exists between the previous examples of this behavior and the present. In our previous study on the epimerization of the phosphetane oxide, **2**,[1] and Kluger and Westheimer's study on the hydrolysis of a strained bicyclic phosphinic ester,[4] pseudorotation of a neutral hydrate intermediate was shown to be rate limiting.



In the present study we have proposed that acid-catalyzed breakdown of a neutral intermediate is rate limiting, pseudorotation being rapid.[24b] This result



further confirms our interpretation of the strong acid (*ca.* 4 *M* HCl) rate maximum observed in the acid-catalyzed ^{18}O exchange of the phosphoryl oxygen of **2** with water. Thus, the methyl group in **1** functions in much the same way as a proton in the acid-catalyzed exchange reaction of **2**, and hence acid catalysis in the hydrolysis of **1** is not observed.

(4) **Base Region.** Around pH 8 the rate rises once again with increasing alkalinity of the solution. Unfortunately because the reaction soon becomes too fast to follow even in the stopped-flow spectrophotometer, data are necessary limited and the errors quite substantial. Nevertheless a first-order ^-OH catalyzed process is evident and represents the $k_6(^-OH)$ term of eq 3 and follows from the mechanism of Scheme I.

This second-order rate term presumably represents a simple bimolecular attack of hydroxide on the phosphetanium salt. It may be of interest to point out that the initial sigmoidal rise in the rate of hydrolysis around pH 6 cannot arise from bimolecular ^-OH attack since the rate constant for this term would exceed the diffusion control limit.[25]

Supporting Evidence. Although the mechanism of Scheme I has been shown to be consistent with the pH–rate profile and pseudorotation theory, certainly other schemes could be shown to be reasonable as well. Fortunately, a number of tests of this mechanism successfully reinforce our belief in this scheme.

The large entropy of activation (−41 eu, Table IV) and the large solvent isotope effect ($k_{H_2O}/k_{D_2O} = 3.5$, Table V) in 0.05 *M* HCl are consistent with a termolecular transition state involving proton transfer. The transition state for this water reaction in the region,

(23) E. L. Muetterties and R. A. Schunn, *Quart. Rev., Chem. Soc.*, 20, 245 (1966); D. Gorenstein and F. H. Westheimer, *J. Amer. Chem. Soc.*, 92, 634 (1970).

(24) (a) M. Eigen, *Angew. Chem., Int. Ed. Engl.*, 3, 1 (1964). (b) A referee has indicated that it may no longer be correct to assume that pseudorotation is fast compared with the very rapid breakdown of the pentacovalent intermediate. Since we do not know the rate of pseudorotation (see ref 22a), we cannot dispute this possibility. On the other hand, it would be difficult to rationalize the solvent isotope effect and the entropy of activation results if pseudorotation were rate limiting.

(25) Based upon $pK_w = 14.7$ for the 50% CH_3CN–H_2O solutions. Determined by pH measurements on 0.001–0.1 *M* NaOH–CH_3CN (50%) solutions using a Radiometer G2222B glass electrode.

Table IV. Activation Parameters

Conditions	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
0.5 *M* HCl–0.2 *M* KCl, 5° [a]	5.93 ± 0.69	−40.5 ± 2.4
pH 5.01, 0.0425 *M* HCO_2Na–0.2075 *M* KCl, 25° [b]	3.94 ± 0.5	−41.1 ± 2

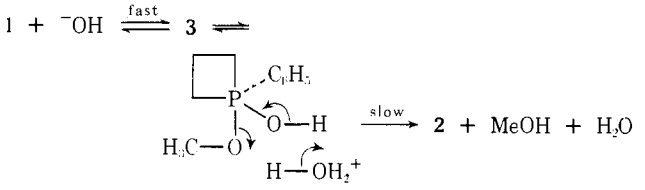
[a] Cary uv method. [b] Stopped-flow method.

Table V. Solvent Isotope Effects

pH/pD[a]	Conditions	k_{H_2O}/k_{D_2O}
1.37	0.05 *M* HCl–0.20 *M* KCl, 15.0°	3.25 ± 0.3
1.44	0.05 *M* HCl–0.20 *M* KCl, 25.0°	3.75 ± 0.3
~5	Formate buffers, I = 0.25, 25°	1.84 ± 0.2[b]

[a] pD = "pH reading" ± 0.4. [b] Isotope effect for formate catalysis.

pH <5, would thus likely contain two molecules of water, with one molecule of water necessarily serving as a general catalyst. Since we have already argued that the rate-determining step in the dilute acid region is k_3, that is, breakdown of the pentacovalent intermediate, then this solvent molecule (or really H_3O^+) must be functioning as a general acid catalyst rather than a general base catalyst. The "apparent general base catalysis" by water must then result from the kinetically indistinguishable specific base, general acid catalysis mechanism proposed in Scheme I and depicted more explicitly below.[26]



We have chosen to depict the general acid catalyzed breakdown of the pentacovalent intermediate as a cyclic, concerted process, although there is no reason to believe that the concerted reaction is any more reasonable than a number of alternative, stepwise processes.

The observation that only the base component of the formate buffer is catalytically active in the acid region (see Figure 4) and the reasonably large formate solvent isotope effect (Table V) would indicate that the buffer component serves as an apparent general base catalyst

(26) For this mechanism the observed solvent isotope effect must be shown to be consistent with both an equilibrium solvent isotope effect on the hydration preequilibrium step, and a kinetic solvent isotope effect on the general acid catalyzed step. Unfortunately, it is difficult to predict the magnitude of the equilibrium effect, although it is not unreasonable to assume that it would not be very large. This is supported by our observation of only a small solvent isotope effect on the epimerization of the phosphetane oxide, **2**, where, in acid, pseudorotation of the hydrated intermediate has been shown to be rate limiting.[1]

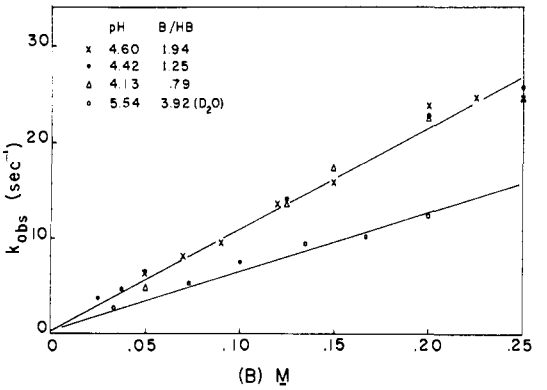
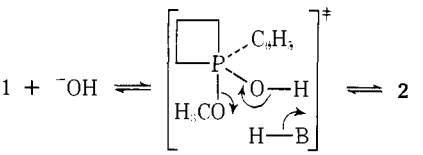
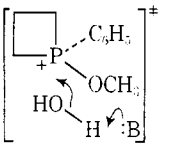


Figure 4. Plot of k_{obsd} *vs.* base concentration [B] for formate catalysis at 25.0°, I = 0.25 *M* (stopped-flow method).

in the hydrolysis of the phosphetanium salt. This general base catalysis by bases other than water may represent a similar specific base, general acid mechanism.



The kinetically indistinguishable, "true" general base catalysis might account for the rate-limiting hydration process in the neutral pH region.[27]



In the present study we have presented evidence that either formation or breakdown of a pentacovalent intermediate may be rate limiting for the hydrolysis of a phosphetanium salt. In the related system, epimerization of the phosphetane oxide,[1] we have previously shown that yet another step, pseudorotation of a pentacovalent intermediate, may be rate limiting as well. It would certainly appear that these phosphetane compounds offer a rich and exciting system for probing the role of the pentacovalent intermediate in the reactions of tetracovalent phosphorus compounds.

Acknowledgment. Partial support of this research by the National Science Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

(27) Although the data are limited and the errors substantial, it appears that both a general base and a general acid term may be found for acetic acid buffer catalysis. However, without better data, restricted by experimental difficulties, this general acid catalysis term cannot be considered definitely established.