Hydrolysis of Diethyl Benzoylphosphonate in Aqueous and Hydrochloric Acid Solutions. Postulation of a Stable Pentavalent Phosphorus-Containing Intermediate

K. S. Narayanan[1] and K. D. Berlin*

Contribution from the Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma 74074. *Received March 9, 1978*

Abstract: The hydrolysis of diethyl benzoylphosphonate (**1**) in aqueous acid solutions was found to be pseudo first order in the substrate, by monitoring the $\pi \rightarrow \pi^*$ band. Products of hydrolysis were stoichiometric amounts of benzoic acid and diethyl hydrogenphosphonate. Correction was made for the absorption of benzoic acid. The reaction rate was retarded as the pH of the medium was lowered by adding hydrochloric acid (pH 2-4). The product of the pseudo-first-order rate constant and H_3O^+ ion concentration in solution was found to be reasonably constant [$(1.2 \pm 0.1) \times 10^{-8}$ mol s^{-1} L^{-1}]. Analysis of the ^{31}P NMR, UV, and Raman spectral data of solutions of **1** revealed the formation of stable hydrates of **1**, formed by a fast process. At very low pH (~1 N HCl), cleavage of the phosphonyl group occurred. A mechanism has been proposed in which **1** could exist in equilibrium with the two hydrates, a phosphonyl hydrate and a carbonyl hydrate. The C-P bond cleavage could occur by the attack of 2 or 3 equiv of H_2O on **1** in the rate-determining step, followed by an intramolecular proton abstraction by the phosphonyl oxygen atom in a fast step. The stable intermediate species proposed were reasonable precursors for the products resulting from phosphonyl ester cleavage. ^{31}P NMR signals for the above products were observed in highly acidic solutions of ester **1**. The experimental activation parameters [$\Delta H^{\ddagger} = 20 \pm 2$ kcal/mol, $\Delta S^{\ddagger} = -52 \pm 7$ eu (for 3 equiv of water in the rate-determining step)] and the solvent isotopic effect $k_{H_2O}/k_{D_2O} = 1.6$ as measured in solution were in conformity with the proposed mechanism.

Introduction

Considerable interest in the general structure and behavior of dialkyl acylphosphonates exists in the recent literature[2] since these reactive compounds are of use in a number of preparations involving nucleophilic substitution at carbonyl carbon and at phosphorus, some of which involved C-P bond cleavage.[3] Acylphosphonates also have considerable toxicity, although the mode of biological activity is not fully understood.[4a] Moreover, preliminary studies[4b] on diethyl benzoylphosphonate (**1**) showed possible immunostimulation in cancer therapy in mice. Hence a detailed study on the behavior of **1** in aqueous media was undertaken. Acylphosphonates undergo rapid base-catalyzed hydrolysis, whereas the acid-catalyzed reaction is considerably slower.[2a] Kinetic studies on general-base-catalyzed C-P bond cleavage of acylphosphonates, including ester **1**, by phosphate salts in water-dioxane medium have been recorded and a tentative mechanism has been postulated.[5,6] However, for reasons which we shall delineate in this paper, the conclusions[5,6] reached do not explain some of our observations. Initial nucleophilic attack by water on the carbonyl group followed by a general-base-catalyzed removal of proton as shown, with concerted C-P bond cleavage, was suggested to be involved in the rate-determining step (Figure 1).[5,6] Reported[5,6] kinetic data involved monitoring the less sensitive n $\rightarrow \pi^*$ band for **1** (λ 367 nm). Some of the half-lives determined were approximately 5 s and it was not clear what special techniques were adopted for these measurements. Also ester **1** has been observed to undergo photochemical trimerization on irradiation (n $\rightarrow \pi^*$ band) with photons of wavelength greater than 320 nm.[7] We have noted that a solution of **1** in dioxane or in a 1:1 water-dioxane mixture slowly decayed by about 7% in 24 h, an observation not cited previously.[5,6] In view of all of the above facts, studies were undertaken of the uncatalyzed, spontaneous hydrolysis of **1** in aqueous medium as well as of the acid-catalyzed process without buffer.

Experimental Section

Materials. All chemicals used were of reagent grade unless otherwise specified. Ester **1** was prepared in the laboratory by a known method[2a] and was vacuum distilled before use [bp 116-118 °C (0.15-0.2 mm), n^{24}_D 1.5080, lit.[8a] 141 °C (2.5 mm), n^{20}_D 1.5065].

$$p\text{-X-}C_6H_4C(O)\text{-}P(O)(OC_2H_5)_2$$

$$\mathbf{1},\ X = H;\ \mathbf{1a},\ X = Cl;\ \mathbf{1b},\ X = CH_3$$

Derivatives **1a** and **1b** were also similarly prepared [bp for **1a**, 132-134 °C (0.15-0.2 mm), n^{24}_D 1.5210, lit.[7] 159 °C (2 mm); and for **1b**, 128-130 °C (0.1-0.2 mm), n^{24}_D 1.5125, lit.[8b] 123-124 °C (0.05 mm)]. The esters showed only one spot when analyzed on a TLC plate made of 0.2-mm silica gel using a 1:9 acetone-chloroform mixture as the solvent system with I_2 as the developer. IR and NMR spectra were identical with those of authentic samples. Ester **1** was stored in a colored bottle in a desiccator over anhydrous $CaCl_2$. Approximately 5% decomposition was detected via a change in the optical density (OD) readings *over a period of 6 months.* Dioxane used as solvent for recording the UV spectra was of reagent grade and was freshly distilled over lithium aluminum hydride and stored over Linde molecular sieve 3A.[9] Hydrochloric acid solutions used were prepared by successive aqueous dilutions of reagent grade, concentrated hydrochloric acid to yield a stock solution, the concentration of which was checked periodically by titration with standardized sodium hydroxide. D_2O used was Aldrich gold label quality containing 99.8 atom % deuterium.

Procedure for Kinetic Studies. The concentration range used for **1** was 0.2-0.3 mM. A sample of ester **1** (5 μL) was withdrawn with a microsyringe from a vial and was placed in a previously weighed parafilm boat which was then weighed on a microbalance. This sample was dissolved (over a period of 60 s) in 100 mL of distilled water or in standard hydrochloric acid solutions, which were kept in a previously thermostated, stoppered Erlenmeyer flask. The temperature of the bath and the UV cells was maintained within ±0.1 °C of the specified temperature (Table I) by using a Magniwhirl constant temperature system. Aliquots of the reaction mixture were withdrawn at specified time intervals and placed in a 1-cm quartz UV cell, and the OD (268 nm) was measured using a Cary UV recording spectrophotometer, Model 14. The solvent was placed in an identical reference cell. Fresh samples of D_2O were used for *each run* while monitoring the OD of **1** in D_2O to estimate the solvent isotopic effect.

Treatment of Kinetic Data. Identification of Products in Aqueous Solutions. The electronic spectra of the reaction mixture after 10 half-lives was found to match exactly with the spectra of authentic standard solutions of benzoic acid (**2**), which strongly suggests the formation of stoichiometric amounts of **2** from the spontaneous hydrolysis of **1** in aqueous solutions. The other product was identified

0002-7863/79/1501-0109$01.00/0

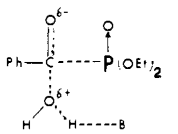


Figure 1. Postulated structure for the transition state in the general-base-catalyzed hydrolysis of **1**; see ref 5 and 6.

as diethyl hydrogenphosphonate (**3**) from ^{31}P NMR analysis of the reaction mixture. In these experiments, the characteristic ^{31}P NMR signal at +11.3 ppm (from 85% H_3PO_4; $^1J_{PH}$ = 720 Hz) for **3** was enhanced by the addition of an authentic sample of **3** (without solvent, **3** has a reported ^{31}P NMR signal at 8.0 ppm with a $^1J_{PH}$ = 687 Hz).[10]

Mathematical Formulations. Let the symbols OD, C, and ϵ represent the corresponding optical density, molar concentration, and molar absorptivity, respectively.

The general equation of hydrolysis can be written as

$$\underset{\mathbf{1}}{C_6H_5C(O)P(O)(OC_2H_5)_2} + H_2O \rightarrow \underset{\mathbf{2}}{C_6H_5CO_2H} + \underset{\mathbf{3}}{HP(O)(OC_2H_5)_2}$$

From stoichiometry and mass balance it can be shown that

$$(C_1)_t = \frac{[(\mathrm{OD})_T]_t - \epsilon_2(C_1)_0}{\epsilon_1 - \epsilon_2} \tag{1}$$

and the rate equation from Scheme I would be given by (see Appendixes A and B)

$$\frac{-\mathrm{d}C_1}{\mathrm{d}t} = \frac{k_1k_2}{k_{-1} + k_2} C^n{}_{H_2O}C_1 \tag{2}$$

(where n = 2 or 3)

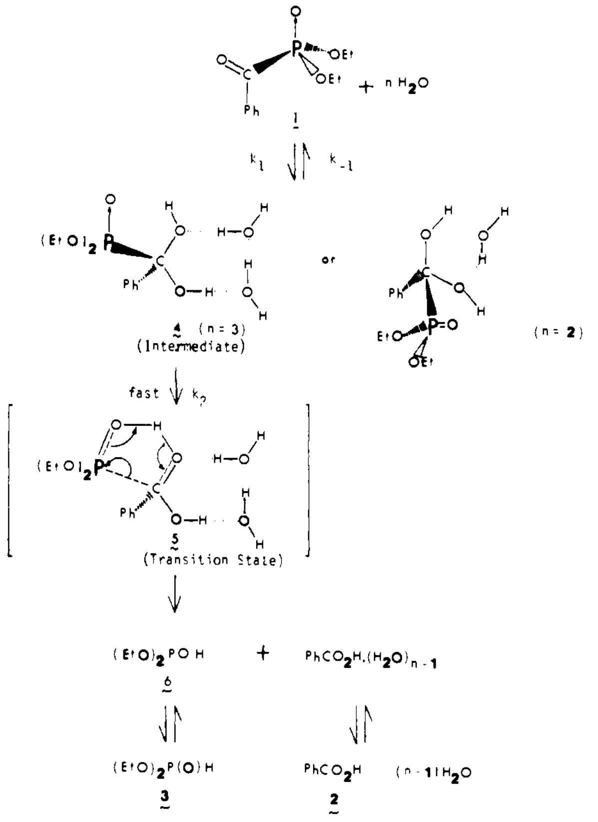
or

$$-\ln (C_1)_t = -\ln (C_1)_0 + k_{obsd}t \tag{3}$$

where

$$k_{obsd} = (k_1k_2/k_{-1} + k_2)C^n{}_{H_2O} \tag{4}$$

Scheme I



Thus, the reaction was followed to *90% completion* via monitoring the band at 268 nm at which **1** and **2** absorb. Since **1** underwent decay in aqueous solution, ϵ_1 was determined indirectly by following the initial rate to 8% of the reaction using various initial concentrations of **1** (ranging from 0.140 to 0.235 mM). Using a least-squares, linear

Table I. Pseudo-First-Order Rate Constants for the Hydrolysis of **1** in Aqueous and Acid Media

$(C_1)_0$, mM ($(C_1)_0$ calcd)[a]	$C°_{HCl}$, mM (pH ± 0.03)[b]	temp ± 0.1 °C	$k_{obsd} \times 10^5$, s^{-1}	R^2 [c]
0.235 (0.233)	1.06 (3.00)	25.0	1.18	0.999
0.233 (0.234)	0.795 (3.13)	25.0	1.57	0.999
0.231 (0.231)	0.530 (3.32)	25.0	2.37	0.999
0.235 (0.227)	0.265 (3.60)	25.0	4.31	0.999
0.235 (0.220)	0.106 (3.94)	25.0	10.8[d]	0.993
0.235 (0.209)	0.265 (3.60)	20.0	2.15	0.999
0.233 (0.218)	0.265 (3.60)	27.5	5.46	0.994
0.235 (0.224)	0.265 (3.60)	32.5	9.30	0.999
0.239 (0.207)	0.265 (3.60)	35.0	12.26	0.998
0.246 (0.182)	[e] (4.4)	25.0	32.1	0.987
0.231 (0.191)	[e] (4.4)	30.0	44.0	0.986
0.231 (0.191)	[e] (4.4)	32.5	63.4	0.993
0.233 (0.203)	[e] (4.4)	35.5	97.0	0.997

[a] Values in parentheses indicate those calculated from the least-squares line. [b] Values in parentheses are the experimental results. [c] R^2 is the least-squares correlation coefficient defined by $R^2 = [\sum xY - \sum x \sum Y/n]^2/[\sum x^2 - (\sum x)^2/n][\sum Y^2 - (\sum Y)^2/n]$ where $x = t$ and $Y = -\ln C_1$. [d] Value extrapolated from experimentally determined rate constant, 11.65 × 10^{-5} s^{-1} at 25.7 °C. [e] No external acid added, the approximated average of the experimental pH 4.4.

Table II. Experimental Values of ε (M^{-1} cm^{-1}) at λ 268 nm in Aqueous and Hydrochloric Acid Solutions for **1** and **2**

compd	water	concn of hydrochloric acid, mM				
		0.106	0.265	0.530	0.795	1.06
1	4350	5230	5420	5530	5500	5410
2	800	810	815	880	875	855

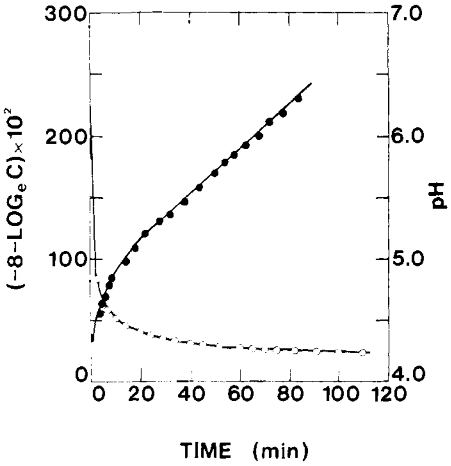


Figure 2. (●), pseudo-first-order plot for hydrolysis of **1** in H_2O at 25 ± 0.1 °C, $(C_1)_0$ = 0.235 mM; (○), pH as a function of time.

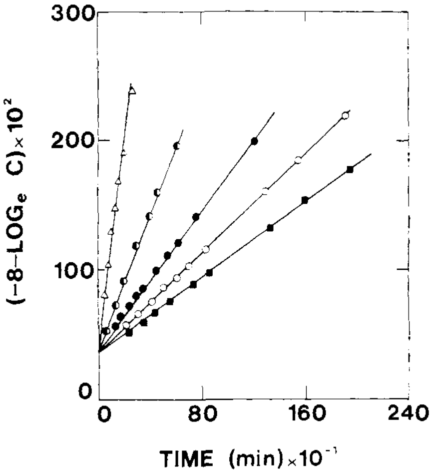


Figure 3. Pseudo-first-order plot for hydrolysis of **1** in aqueous HCl at 25 ± 0.1 °C, $(C_1)_0$ = 0.235 mM; C°_{HCl} (mM) (△) 0.106, (◐) 0.265, (●) 0.530, (○) 0.795, (■) 1.060.

fit between $-\ln [(OD)_T]_t$ and t for a pseudo-first-order behavior, the $[OD_T]_0$ could be evaluated for each reaction mixture of known initial concentration. From the above procedure of linear extrapolation, the correlation coefficient R^2 was found to be around 0.99 in most cases. This observation along with the fact that $\epsilon_1 \approx 6\epsilon_2$ (see Table II) indicated that OD arising from the stoichiometric amount of **2** formed from **1** was negligible (calculated to be within 1-2% of the OD contributed by **1**) for the above period (8%) of the reaction time. Applying a least-squares, linear fit between $(C_1)_0$ and $(OD_1)_0$ for each such reaction mixture, ϵ_1 was evaluated from

$$(OD_1)_0 = \epsilon_1(C_1)_0 \qquad (5)$$

These values of $(OD_1)_0$ were found to obey the Beer-Lambert law.

Values of ϵ_2 were determined[11a] separately and experimentally for **2** in aqueous and acid solutions at different concentrations of hydrochloric acid, since the electronic spectra of benzoic acid has been reported to be affected by pH.[12] The experimental values of ϵ_1 and ϵ_2 at λ 268 nm used in the present work can be found in Table II.[11b]

Pseudo-first-order eq 3 gave the best fit for the experimental data for reaction followed up to *90% completion*. Table I summarizes the values of k_{obsd} for 90% reaction calculated[11c] from eq 3 and 1. Appropriate rate equations corresponding to zero, second, or third order with respect to **1** did not produce a linear curve for the experimental data employed.

Instrumental Methods. Measurement of the pH of samples was achieved using a Corning Model 12 research pH meter with a Corning glass-reference, calomel combination electrode (Corning catalog no. 476021) and employing standard buffers for calibration.[13] Laser Raman spectra[14] were recorded using a Model 52, argon laser as a source, with a detector (Jarrell-Ash 20-100 dual monochromator) and with Hammer photon counting accessories (with a photon count rate of 2×10^3 s^{-1} and slits of width 3 cm^{-1} each). ^{31}P NMR spectra were recorded on a Varian XL-100(15) spectrometer operating at 40.5 MHz and equipped with Nicolet TT-100 pulse Fourier transformer accessory and using 85% H_3PO_4 as external standard. ^{31}P NMR spectra were obtained in the FT mode. The chemical shifts reported are from 85% H_3PO_4 as the standard. Positive values represent shifts downfield from the standard.

Error Analysis. A maximum deviation of 6% was observed in the rate constants (k_{obsd}) determined from 40 independent runs. The values reported included the average of three or more independent runs at each concentration with a deviation of a maximum of ±5%. Only two independent runs were made in those cases where the rate constants differed by ±2% or less. In those cases where no external acid was added, the deviations in k_{obsd} were found to be higher as compared with the observed deviation in k_{obsd} in acid solutions. Similarly the agreement between the calculated $(C_1)_0$ and experimental $(C_1)_0$ was much better for runs made in acid solution (Table I). For runs made in water, calculated $(C_1)_0$ were always less than the experimental $(C_1)_0$ by at least 15%. R^2 in all cases was close to unity. The discrepancies observed in aqueous solutions in the absence of acid could be attributed to the higher initial rate observed during the first 15% of the reaction (Figure 2) and the subsequent pH drop in the same region. After the initial period, a buffering region (may be due to self-protonation of substrate) was noticed. In an acid solution the pH was found to be steady (±0.03) and no initial rate was observed (Figure 3). It is clear from eq 1 and 3 that k_{obsd} would not depend on ϵ_1. However, computation of a reliable rate constant required an accurate value of ϵ_2, which was easier to evaluate. An estimated maximum error of 5% in the determination of $(C_1)_0$ or ϵ_2 would only give rise to an error of 4% in the final rate constant. The inherent error for the product of $C_{H_3O^+}$ and k_{obsd} (see Discussion section) would be 12%, the sum of the experimental uncertainties observed for k_{obsd} and $C_{H_3O^+}$.

Results

Kinetic Data. The spontaneous uncatalyzed hydrolysis of **1** in aqueous solution was examined by monitoring the $\pi \rightarrow \pi^*$ transition band at λ 268 nm, this band being more sensitive than the $n \rightarrow \pi^*$ band[5,6] (Table I). Also, since **1** was very slightly soluble in water (0.2 g/L),[8a] the $n \rightarrow \pi^*$ band could not be used for following changes in OD for such small concentration (0.2-0.3 mM) employed for reasons stated previously. The effect of UV radiation during the measurement was checked in view of the reported[7] trimerization of **1** and was found to be negligible in aqueous solution in the concentration range studied. Quantitative formation of benzoic acid (**2**) from **1** was observed at completion of the reaction by UV analysis and using standard solutions of **2**.

The rates of hydrolysis of **1** in hydrochloric acid (pH 3-4) were measured with a view to screen for any catalytic effect by H_3O^+, if an $A_{AC}1$ or an $A_{AC}2$[15] type of mechanism was operating with the $P(O)(OC_2H_5)_2$ moiety as leaving group. The rates of hydrolysis of **1** in acid solutions were found to decrease sharply with increasing concentration of acid [d log

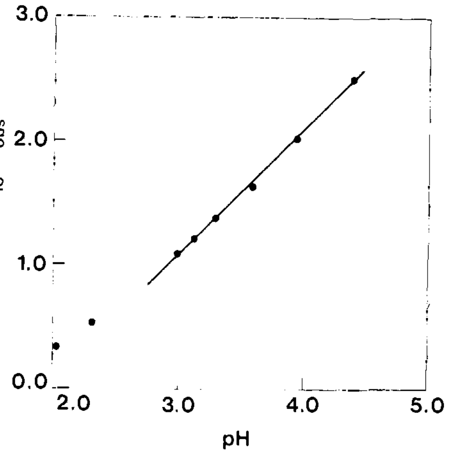


Figure 4. Log k_{obsd} (pseudo-first-order rate constant for the hydrolysis of **1** in aqueous HCl) vs. pH plot at 25 ± 0.1 °C.

k_{obsd}/d(pH) = 1.0, Figure 4]. The product of the pseudo-first-order rate constant and $C_{H_3O^+}$ was found to be reasonably constant [(1.2 ± 0.1) × 10^{-8} s^{-1} mol L^{-1}] over the range of acid concentrations used (up to pH 3) (Table I). The value for the product k_{obsd} $C_{H_3O^+}$ in 5.0 and 10.0 mM HCl (pH 2.33 and 2.04) solutions was found to be much higher (35 and 75%, respectively) (Figure 4). In these acid solutions (pH 2.04 and 2.33) simultaneous dealkylation (hydrolysis) of the phosphonyl ester groups in **1** and **3** could occur. Even at pH 3, 5% dealkylation was observed after 4 half-lives of **1** in the hydrolysis (see Spectral Data). Also, there is a known rate enhancement for the acid hydrolysis of **3** as the acid concentration increases.[16] This observation imposed a limit of acid concentration for effecting exclusive C-P bond cleavage without side reactions.

An Arrhenius plot for the rate constant k_{obsd} $C_{H_3O^+}$ can be found in Figure 5. A value for $\Delta H^{\ddagger}$ was found to be 20 ± 2 kcal mol^{-1} and the limiting values of $\Delta S^{\ddagger}$ were estimated to be −44 ± 7 eu for $n = 2$ and −52 ± 7 eu for $n = 3$ (see eq 2).

Spectral Data. ^{31}P NMR spectral analysis of a solution of **1** (0.0235 M) in dioxane-hydrochloric acid solution (0.9 N in HCl, containing 16% D_2O for locking), when observed at different intervals of time (from t_0 + 0.75 h, t_0 + 9.75 h, t_0 + 16.75 h, t_0 + 143.25, 359, and 1438.5 h) gave signals corresponding to products **11** (triplet −2.3 ppm from 85% H_3PO_4) and **15** (singlet −2.9 ppm from 85% H_3PO_4). These signals were produced from **1** and, in addition, ^{31}P signals appeared corresponding to **19** [doublet of triplets +6.5 ppm ($^1J_{PH}$ = 680 Hz)], **20** [doublet + 4.0 ppm ($^1J_{PH}$ = 670 Hz)], and **21** [(triplet + 3.7 ppm) ($^1J_{PD}$ = 100 Hz)].[17] An authentic sample of **3** (0.2 M) gave identical signals due to **19**, **20**, and **21** (deuterated analogue of **20**) and also minor signals due to deuterium analogues of **3** and **19**, confirmed by decoupling experiments, when the spectra were observed at different intervals of time (from t_0 + 5 min to t_0 + 360 h). In Scheme II, intermediates **11** and **15** can also undergo cleavage of the C-P bond like **1** → **3** to give the corresponding phosphonic acids **19** and **20**. However, these steps might expectedly be slower owing to the greater stability of **11** and **15** (perhaps because of the H bonding) compared to **1**.

Under the conditions of our experiment in aqueous HCl (pH 3-4.4), no phosphonyl ester cleavage of **1** (or of **3** that formed) was observed in aqueous and acid solutions for a period of 4 half-lives. However, a moderately concentrated solution of **3** (0.4 M) in 1.06 mM HCl at room temperature gave ^{31}P signals corresponding to **19** and **20** [+6.7 ($^1J_{PH}$ = 660 Hz) and +4.2 ppm ($^1J_{PH}$ = 665 Hz), respectively] in addition to the parent signal for **3** [+11.3 ppm ($^1J_{PH}$ = 720 Hz)] when the mixture was analyzed after 28 h. From peak area ratios of **3**:**19**:**20**, it was estimated that 65% of the total hydrolysis of the phosphonyl ester groups had occurred.[16b,c] ^{31}P NMR analysis of **1** in 1.06 mM hydrochloric acid (pH ~3) observed after 15 h of signal accumulation gave the following signals. A doublet of quintets centered at +11.3 ppm ($^1J_{PH}$ = 720 Hz) was identified as from **3**. Addition of an authentic sample of **3** gave peak enhancement in the spectrum. Two more ^{31}P NMR signals (quintets at −0.3 and +17.9 ppm) appeared and were apparently due to intermediates **7** and **8**.[18] The spectra were observed at t_0 + 0.25 h, t_0 + 27.5 h, and t_0 + 52 h after 15 h of signal accumulation in each case. When the spectrum was observed immediately after dissolution of **1** in 1.06 mM HCl, only the intermediate signals (−0.3 ppm and +17.9 ppm) could be seen after pulsing for 1 h. The signal area ratios for the corresponding signals, evaluated from the above spectra, were **3**:(**7** + **8**):**19** = 1:1.8:0 (35% reaction), **3**:(**7** + **8**):**19** = 1:0.22:0 (85% reaction), **3**:(**7** + **8**):**19** = 1:0.12:0.06 (90% reaction). The area ratio of the two intermediate signals **8** and **7** was found to be constant (1.19 ± 0.02) within the experimental error throughout the course of the reaction. Similar signals were also observed in the ^{31}P NMR spectra of a suspension of **1** (17 mg) in 3 mL of water after 15 h of signal accumulation. The parent signal of **1** could be observed at −1.9 ppm in aqueous solutions only when a large excess of **1** was added to the above suspension. ^{31}P NMR signals from **19** (+6.6 ppm, $^1J_{PH}$ = 660 Hz) could be detected (5% as estimated from peak area ratios) only after 4 half-lives in a solution of **1** in 1.06 mM hydrochloric acid after signal accumulation for 15 h.

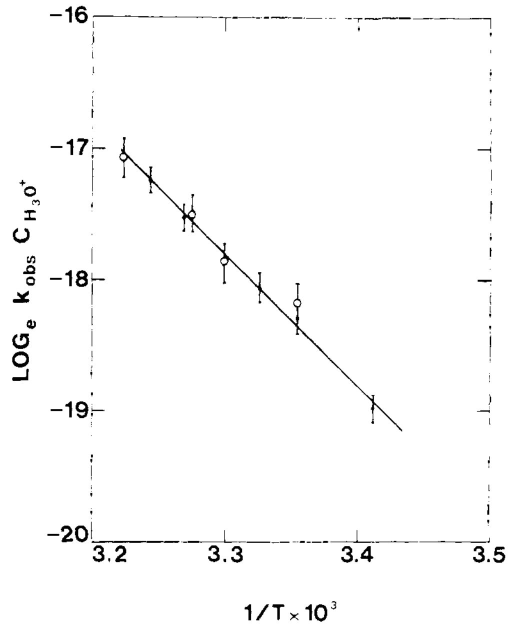
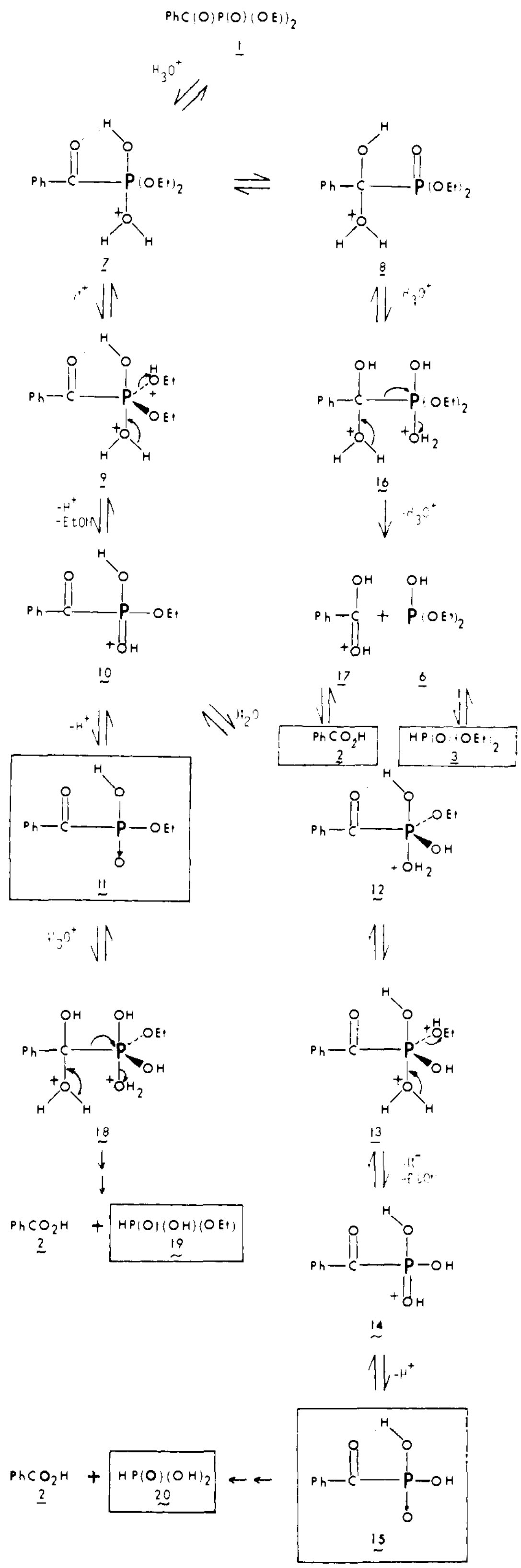


Figure 5. Arrhenius plot for the hydrolysis of **1** in aqueous HCl (●) at pH 3.6 ± 0.03: (○) represents data points calculated from data for hydrolysis of **1** in water and the experimentally observed average pH 4.4. $\Delta H^{\ddagger}$ = 20 ± 2 kcal/mol, $\Delta S^{\ddagger}$ = −44 ± 7 (n = 2), − 52 ± 7 eu (n = 3) using the expression $k = k_{obsd}C_{H_3O^+}/C^n_{H_2O}$ for the true rate constant. For the method used in the evaluation of standard deviation in $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ see ref 32.

Raman spectra of **1** in the liquid state, in D_2O, and in a D_2O-hydrochloric acid suspension[19] were recorded. The C=O stretching frequency was observed at 1662 cm^{-1} for a neat sample of **1** which corresponds to the value observed in the IR spectrum. A reproducible shift of 4 cm^{-1} toward a smaller wavenumber was observed for the C=O stretching frequency in both D_2O and the D_2O-HCl suspensions of **1** as compared with the value for **1** neat.

Scheme II[a]



[a] In excess acid.

Discussion

The constancy of the product of the pseudo-first-order rate constant and $C_{H_3O^+}$ cannot be reasonably explained, in our opinion, by a general-base-catalyzed mechanism involving $\bar{O}H$ as the general base in a rate-determining step at pH ~3.0. Since the concentration of $\bar{O}H$ is calculated to be of the order of 10^{-11} M in such solutions, no significant contribution from this anion on the rate is likely, unless $K_{\bar{O}H} \gg k_0'$ in the following equation of the general form.[20]

$$k_{obsd} = k_0 + k_{\bar{O}H}C_{\bar{O}H} + k_BC_B \qquad (6)$$

$$(k_0 = \text{rate constant for reaction of } H_2O)$$

Assuming that a low concentration of $\bar{O}H$ is the only base that could exist in the acid solutions ($k_BC_B = 0$), calculated values of k_0' and $k_{\bar{O}H}$ from our experimental results (from a least-squares analysis using data from Table I) were $k_0' = k_0/C_{H_2O} = 2.16 \times 10^{-8}\ s^{-1}\ L\ mol^{-1}$ and $k_{\bar{O}H} = 1.1 \times 10^6\ s^{-1}\ L\ mol^{-1}$ at 25 °C. Thus, initially one might argue that $\bar{O}H$ could play a vital role in acid hydrolysis. However, such a low value for $k_0'/k_{\bar{O}H}$ would suggest a negligible catalytic effect due to H_2O from this analysis. Obviously this is unreasonable. An alternative mechanism which could explain the effect of pH on k_{obsd} might involve a fast equilibrium prior to the rate-determining step (Scheme III). The rate equations derived from Scheme III are identical in their mathematical forms with those derived from Scheme I (see Appendixes A and B). In certain carbon systems, some analogy could be found for our work. For example, Bell and co-workers[21] have shown that 3 equiv of water is involved in the rate-determining step in the reversible hydration of 1,3-dichloroacetone. Formation of an intermediate of the following structure was suggested (Figure 6). The strong electron-withdrawing chlorine atom on the α carbon was important for the formation of a stable hydrate. The reported equilibrium constant at 25 °C was 10.0 in favor of the hydrate.[22] Solvent isotopic effects for some of the analogous re-

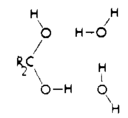
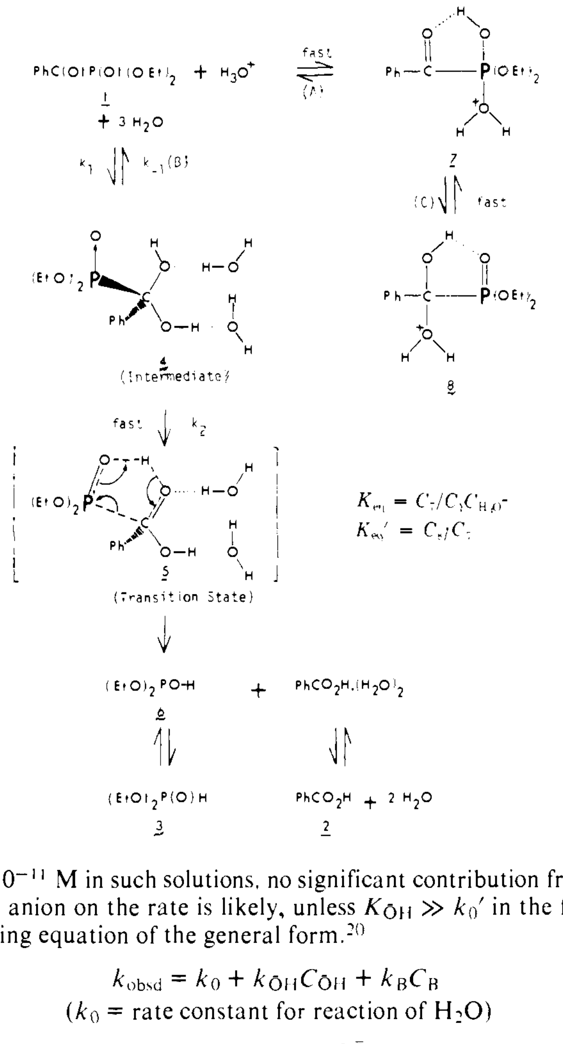


Figure 6. Postulated intermediate in the hydration of 1,3-dichloroacetone; see ref 21. R = CH_2Cl.

Scheme III



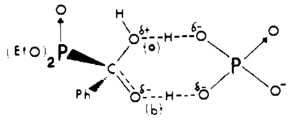
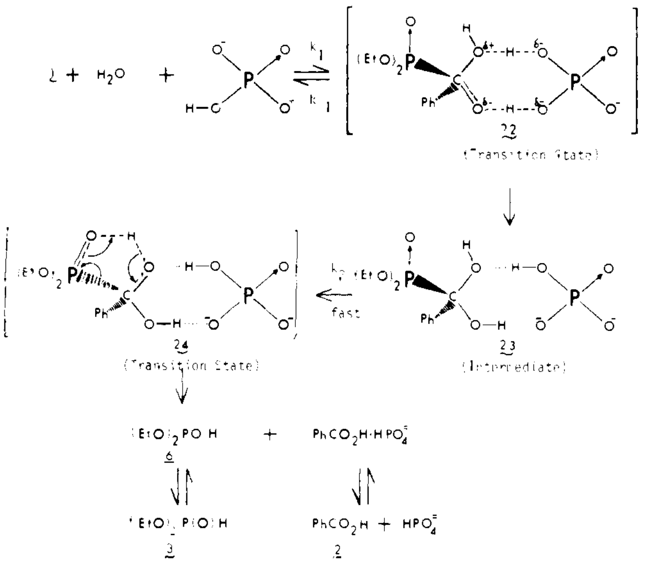


Figure 7. Modified structure for the transition state in the hydrolysis of **1** catalyzed by phosphate salt (HPO_4^{2-}).

Scheme IV



actions involving hydration of carbonyl groups can be seen in Table III.[23,24] Thus, the low isotopic effect $k_{H_2O}/k_{D_2O} = 1.5$ reported[6] for the phosphate-catalyzed hydrolysis of **1** in water-dioxane mixture might be explained more accurately by a modified structure for the transition state formed in the rate-determining step, as shown in Figure 7 in contrast to the structure shown in Figure 1. The primary effect due to deprotonation at point (a) would be reduced by the apparent inverse effect due to O-H bond formation at point (b). Conceptually, the structure in Figure 7 could give rise to an H-bonded intermediate, such as **23**, followed by a fast intramolecular proton abstraction by the phosphonyl oxygen atom as shown in Scheme IV.

In aqueous solution in the absence of a catalyst, formation of the intermediate could involve at least 2 equiv of water. In comparison with other carbonyl-containing systems[21,25] (Figure 6), structure **4** in Scheme I would be a reasonable intermediate for the spontaneous hydrolysis of **1** in water in the absence of a catalyst. In **4**, free rotation of the C-P bond could occur followed by fast abstraction of a proton in an intramolecular fashion as shown (via the P(O) group in **5**). This process may logically involve electron shifts resulting in C-P bond cleavage in a concerted step. Such a process of proton abstraction would be more probable, since the rate of C-P bond rotation would be much higher than the rate of collision between **4** and $\bar{O}H$ ions in such solutions of low concentration. The product diethyl hydrogen phosphite could quickly equilibrate to the stable phosphonate form.[26] Similarly, the other product would be solvated benzoic acid (hydrogen bonded with water molecules), which would be in equilibrium with free benzoic acid and water.[21b] Furthermore, the benzoic acid and diethyl hydrogenphosphonate could also exist as a 1:1 adduct.[27] In our work, the gross solvent isotopic effect for the hydrolysis of **1** carried out in H_2O and D_2O was experimentally measured and k_{H_2O}/k_{D_2O} was found to be 1.6 at 25 °C. The low isotopic effect is expected for a transition state involving strong hydrogen bonding between participants and is a situation in which the zero point energy could be conserved.[25]

In aqueous solution in the absence of a catalyst, formation of an intermediate involving only 1 equiv of water followed by a fast intramolecular proton abstraction by the phosphonyl oxygen (as in Schemes I, III, or IV) could not be ruled out. However, such a process is not likely, since it would be difficult to explain the observation of a general-base-catalyzed process reported elsewhere for this reaction.[6]

If a general-base-catalyzed mechanism is assumed operative with no participation of the *P=O group in acid solution*, much experimental data is difficult to defend. For example, ester **1** has a high dipole moment (2.76 D)[28] and would be expected to be protonated at P=O ($>P{=}O \rightarrow > P^+{-}OH$) in aqueous solutions.

^{31}P NMR data and the formation of stable species **11, 15, 19, 20,** and **21** in very high acid solution strongly suggested direct participation of the P=O group in acid solutions. In agreement with these observations was the Raman spectral data. The latter was also suggestive of a rapid initial structural modification (such as involving H bonding of the C=O group) when **1** was placed in aqueous and acid solutions. Unfortunately, the P=O stretching frequency could not be observed, since this region (1255 cm^{-1}) was masked by the broad absorption due to D_2O in the Raman spectrum.

Definite participation of the P=O group in phosphonates in forming hydrogen bonds in protic solvents and in association with carboxylic acids has been demonstrated in related systems via ^{31}P NMR studies.[27] Intermediates involving a hydrogen-bonded phosphonyl group[29] have been proposed for acid hydrolysis of certain phosphonated acetals and similar systems. Certain phosphonates, including diethyl hydrogenphosphonate, have also been reported[16] to undergo dealkylation in strong acid solutions at room temperature following an initial protonation of the P=O group. Interestingly, from ^{31}P NMR work on dialkyl hydrogenphosphonates in fluorosulfuric acid at −60 °C, Olah and co-workers[30] observed large deshielding effects on phosphorus upon protonation. It was concluded that in the protonated phosphonium species the positive charge was largely shifted from phosphorus to the oxygen atom. Such a

Table III. Solvent Isotopic Effect on Related Systems

reaction	medium	catalyst	k_{H_2O}/k_{D_2O}	ref
hydrolysis of **1**	dioxane-water v/v (1:4)	HPO_4^{2-} DPO_4^{2-}	1.5[a]	6
hydrolysis of *p*-nitrobenzoylimidazole	H_2O-D_2O	ImH-ImD	5.57[b] (2.01) 0.60[c] (0.94)	23
mutarotation of glucose	H_2O-D_2O	none	3.8 (3.16)	24
hydration of 1,3-dichloroacetone	dioxane H_2O-D_2O	none HCl	3.97 1.23	21b

[a] $k_{HPO_4^{2-}}/k_{DPO_4^{2-}}$ at pH 7.0. [b] $k_{1(H_2O)}/k_{1(D_2O)}$. [c] $k_{2(H_2O)}/k_{2(D_2O)}$ in the generalized equation $k_{L_2O} = k_1 + k_2\,[LO^-]$ where L = H or D. Numbers in parentheses are revised values.

situation could occur with **1** in acid and may be the cause of the occurrence of a ^{31}P NMR signal at lower field as is postulated for **7** or **8** in Scheme III.

The two additional ^{31}P NMR signals (−0.3 and +17.9 ppm from 85% H_3PO_4) observed in acid solutions of **1** at pH 3 were certainly suggestive of some structural transformation, such as hydration of **1**, in solution by a comparatively fast process. Unfortunately, no structurally related, known intermediates could be found in the literature for comparison of ^{31}P signals or any other property.

The following modified form of rate eq 7 could be derived from Scheme III (see Appendix A).

$$-\frac{\mathrm{d}(C_7 + C_8)}{\mathrm{d}t} = \frac{k_1 k_2 C^n{}_{H_2O}(C_7 + C_8)}{(k_{-1} + k_2)K_{eq}(1+K'_{eq})C_{H_3O^+}} \qquad (7)$$

Thus, if an aqueous solution of **1** is considered to be an equilibrium mixture of **7** and **8**, the observed rate of decay in terms of the total concentrations ($C_7 + C_8$) would be given by

$$-\frac{\mathrm{d}(C_7 + C_8)}{\mathrm{d}t} = k_{obsd}(C_7 + C_8) \qquad (8)$$

where from eq 7 we have

$$k_{obsd} = \frac{k_1 k_2 C^n{}_{H_2O}}{(k_{-1} + k_2)K_{eq}(1 + K'_{eq})C_{H_3O^+}} \qquad (9)$$

and after factoring out pH and water dependence

$$k'_{obsd} = \frac{k_1 k_2}{(k_{-1} + k_2)K_{eq}(1 + K'_{eq})} \qquad (10)$$

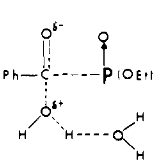
Equation 7 would predict a rate law of first order in **7** and **8** and also a dependence of k_{obsd} on $C_{H_3O^+}$. The overall rate constant would be related to k_{obsd} by eq 11. That is, from eq 9 and 10, we find

$$k'_{obsd} = k_{obsd}C_{H_3O^+}/C^n{}_{H_2O} \qquad (11)$$

The total concentration of the substrate species ($C_7 + C_8$) would be related to the experimental OD by eq 12 (see Appendix B).

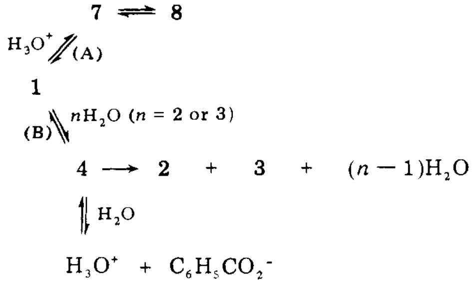
$$(C_7 + C_8)_t = \frac{(\mathrm{OD}_T)_t - \epsilon_2(C_1)_0}{(\epsilon_7/1 + K'_{eq}) - \epsilon_2} \qquad (12)$$

The observed rate constant k_{obsd} evaluated from eq 7, 9, and 12 or from eq 3 and 1 would be the experimental pseudo-first-order rate constant for either case where $n = 2$ or 3. Thus, we cannot eliminate the possibility of formation of a hydrate from **1** and water which involves 2 equiv of water as in **4**. There is evidence for 3 equiv of water participating in the hydration of 1,3-dichloroacetone as cited previously.[21] The high negative entropy of activation (−44 ± 7 eu for $n = 2$ or −52 ± 7 eu for $n = 3$) for the overall reaction supports this hydration process. Unfortunately, the hydration of **1** in 1:1 water-dioxane was too slow (only 10% change in the OD from the n → π* band after 37 h) for an accurate determination of n (molecules of water). If the second molecule of water were to act as a general base without the oxygen of the C=O group being involved (leading to a linear transition state) as shown, one would expect a *high* primary isotopic effect. On the other hand, if the proton of the water solvent matrix were to be linked to the carbonyl oxygen to give a cyclic transition state leading to the intermediate **4**, the primary isotopic effect would be reduced.[25] The gross isotopic effect for the hydrolysis of **1** in water and D_2O was observed to be 1.6 at 25 °C as stated previously. Consequently, the gross isotopic effect would be a total result due to L_3O^+, LO^-, and L_2O where L = H or D and these factors are not separable. Also other nonspecific effects due to differences in viscosity of H_2O and D_2O could add to the isotope value.[31] Any positive mechanistic conclusions based on gross solvent isotopic effect alone should be made with much caution.



Conclusions

On the basis of the experimental results obtained, we suggest that the hydrolysis of **1** in aqueous or aqueous acid solutions proceeds with the formation of a reactive intermediate **4** via the attack of **1** by 2 or 3 equiv of water. Cleavage of the C–P bond is postulated to occur by a fast unimolecular process initiated by intramolecular proton abstraction by the phosphonyl oxygen atom (Scheme I or III). Benzoic acid (**2**) and diethyl hydrogenphosphonate (**3**) are formed as major products in water. In acid solutions, **1** is apparently converted into a relatively stable species **7** and **8** in a rapid equilibrium process which reacts more slowly. At very low pH (<1), **7** and **8** may further protonate to give a series of products via phosphonyl ester cleavage from both **1** and **3** (as shown in Scheme II).



Formation of the proposed stable phosphorus intermediate **7** and **8** (pH 2-4.4) not only explains the rate law and the effect of pH on k_{obsd} (predicted by eq 7) but also accounts for the two additional ^{31}P signals (postulated for **7** and **8**) observed in solutions of **1** in hydrochloric acid (pH ~3).

Moreover, the conversion of **1** to **7** and **8** explains qualitatively the reduced value of ε observed in the UV spectrum of **1** in aqueous solution as compared with that found for **1** in hexane or pure dioxane (see Appendix C). In addition, other data which defend this situation include the shift of 4 cm^{-1} observed in the C=O stretching frequency of **1** in the Raman spectra of aqueous and acid solutions.

Acknowledgment. We gratefully acknowledge Professors L. M. Raff and G. J. Mains for most helpful discussions on various aspects of this work and for reading the manuscript.

Supplementary Materials Available: Appendixes A, B, and C and the derivations of eq 7 and 12 (8 pages). Ordering information is given on any current masthead page.

References and Notes

(1) Predoctoral candidate, 1975–1978. We gratefully acknowledge partial early support of this work by the USPHS, National Cancer Institute (Grant CA 14343), and the College of Arts and Sciences, Oklahoma State University. Part of this work was presented at the 23rd Pentasectional American Chemical Society Meeting, Norman Okla., on March 26, 1977, and at the 33rd Southwest Regional Meeting of the American Chemical Society, Little Rock, Ark., Dec 6, 1977.

(2) (a) K. D. Berlin and H. A. Taylor, *J. Am. Chem. Soc.*, **86**, 3862 (1964); (b) K. D. Berlin and D. H. Burpo, *J. Org. Chem.*, 1304 (1966); (c) P. E. Clark, K. D. Berlin, J. Mosbo, and J. G. Verkade, *Phosphorus*, **2**, 265 (1973); (d) K. D. Berlin, D. S. Rulison, and P. Arthur, *Anal. Chem.*, **41**, 1554 (1969); (e) K. Terauchi and H. Sakurai, *Bull. Chem. Soc. Jpn.*, **42**, 821 (1969); (f) E. A. Ishmaeva and A. N. Pudovik, *Vopr. Stereokhim.*, **1**, 141 (1971); *Chem. Abstr.*, **77**, 113723w (1972); (g) A. B. Remizov, R. D. Gareev, and A. N. Pudovik, *Zh. Obshch. Khim.*, **42**, 1238 (1972); *Chem. Abstr.*, **77**, 100549u (1972); (h) B. N. Laskorin, V. V. Yakshin, and L. I. Sokalskaya, *Zh. Obshch. Khim.*, **42**, 1261 (1972); *Chem. Abstr.*, **77**, 126780n (1972).

(3) (a) K. D. Berlin, R. T. Claunch, and E. T. Gaudy, *J. Org. Chem.*, **33**, 3090 (1968); (b) I. Shahak and J. Peretz, *Isr. J. Chem.*, **9**, 35 (1971); (c) A. P.

Pashinkin, T. Kh. Gazizov, and A. N. Pudovik, *Zh. Obshch. Khim.*, **40**, 28 (1970); *Chem. Abstr.*, **72**, 100827e (1970); A. N. Pudovik, I. V. Guryanova, and M. G. Zimin, *Zh. Obshch. Khim.*, **37**, 2580 (1967); *Chem. Abstr.*, **68**, 95890f (1968); (d) M. Soroka, and P. Mastalerz, *Zh. Obshch. Khim.*, **44**, 463 (1974); *Chem. Abstr.*, **80**, 121058k (1974); (e) T. Kh. Gazizov, V. E. Belškii, A. P. Pashinkin, M. V. Efremova, and A. N. Pudovik, *Sb. Nek. Probl. Org. Fiz. Khim., Mater. Nauchn. Sess., Inst. Org. Fiz. Khim., Akad. Nauk SSSR*, 33 (1972); *Chem. Abstr.*, **78**, 28807c (1973); (f) A. N. Pudovik, E. S. Batyeva, V. D. Nesterenko, and N. P. Anoshina, *Zh. Obshch. Khim.*, **44**, 1674 (1974); *Chem. Abstr.*, **82**, 4357n (1975); (g) I. V. Konovalova, L. A. Burnaeva, L. S. Yuldasheva, and A. N. Pudovik, *Zh. Obshch. Khim.*, **46**, 1733 (1976), and references cited therein; *Chem. Abstr.*, **85**, 177329v (1976); (h) A. Takamizawa and H. Harada, German Offen. 2 458 933 (June 26, 1975); *Chem. Abstr.*, **83**, 114384x (1975); (i) A. Takamizawa, Y. Matsushita, and H. Harada, *Chem. Pharm. Bull.*, **25**, 991 (1977), and references cited therein; *Chem. Abstr.*, **87**, 152064h (1977).

(4) (a) Biological studies of the half ester salt, sodium methyl acetylphosphonate, revealed it to be a competitive inhibitor of pyruvate dehydrogenase; see R. Kluger and D. C. Pike, *J. Am. Chem. Soc.*, **99**, 4504 (1977); (b) T. Trenbeath, K. Carraway, N. N. Durham, K. S. Narayanan, and K. D. Berlin, unpublished results.

(5) W. Von Jugelt, S. Andreae, and G. Schubert, *J. Prakt. Chem.*, **313**, 83 (1971).

(6) S. Andreae and W. Von Jugelt, *Z. Chem.*, **13**, 136 (1973).

(7) K. Terauchi and H. Sakurai, *Bull. Chem. Soc. Jpn.*, **43**, 883 (1970).

(8) (a) I. L. Burger and R. M. Wagner, *J. Chem. Eng. Data*, **3**, 310 (1958); (b) A. Takamizawa, Y. Sato, and S. Tanaka, *Yakugaku Zasshi*, **85**, 298 (1965); *Chem. Abstr.*, **63**, 9941*a* (1965).

(9) R. L. Augustine and J. A. Caputo, *Org. Synth.*, **45**, 80 (1965).

(10) M. M. Crutchfield, C. H. Dungan, and J. R. Van Wazer, *Top. Phosphorus Chem.*, **5**, 11 (1967). A downward shift in the ^{31}P chemical shift and a corresponding increase in $^{1}J_{PH}$ for dimethyl hydrogenphosphonate and also for diethyl hydrogenphosphonate in solvents of varying protonic acidity have been reported.[27] For example, the reported shift difference for the ^{31}P signal for dimethyl hydrogenphosphonate in CCl_4 as compared to F_3CCO_2H is 3.6 ppm and there is an increase in coupling constant as the solvent is changed from CCl_4 ($^{1}J_{PH}$ = 691.9 Hz) to F_3CCO_2H ($^{1}J_{PH}$ = 744.3 Hz). These observations are attributed to the formation of intermolecular hydrogen bonds between the phosphoryl oxygen atom and the hydrogen directly attached to phosphorus in CCl_4,[27] and formation of 1:1 adduct with carboxylic acid from solvent through hydrogen bonding at the phosphoryl oxygen atom.

(11) (a) Values of ϵ_2 were determined by measuring the OD for several standard solutions of **2** of various concentrations and extracting the slope by a least-squares analysis. (b) Validity of Beer-Lambert's law was also tested for solutions of **1** in standard hydrochloric acid. Since hydrolysis of **1** in hydrochloric acid was found to be slow, values of ϵ_1 were also determined from measurements of OD of solutions of **1** in standard hydrochloric acid (0.265 mM). OD of the solution were measured exactly after $t_0 + 30$ min in each case. The OD values were corrected for the decay of **1** and OD for **2** produced from 1 in 30 min, using the rate constant given in Table II. ϵ_1 was calculated using a least-squares fit between $(\mathrm{OD})_1$ and C_1. The values of ϵ_1 so obtained agreed within ±2% with those obtained by extrapolation method described earlier and reported in Table II. (c) All calculations were programmed in the University IBM 370 computer. We gratefully acknowledge the help rendered by Dr. B. N. Sureshbabu, Department of Electrical Engineering, Oklahoma State University, in writing the computer program.

(12) H. Hosoya and S. Nagakura, *Spectrochim. Acta*, **17**, 324 (1961).

(13) Certified buffer tablets (pH 2 and 4) supplied by Coleman Instruments, Inc., Maywood, Ill., were used as the standard.

(14) We thank Dr. J. P. Devlin, Department of Chemistry, Oklahoma State University, for obtaining the laser Raman spectra.

(15) C. K. Ingold, "Structure and Mechanism in Organic Chemistry", 2nd ed., Cornell University Press, Ithaca, N.Y., 1969, p 1131.

(16) (a) H. R. Hudson and J. C. Roberts, *J. Chem. Soc., Perkin Trans. 2*, 1575 (1974); (b) V. E. Belškii, G. Z. Motygullin, V. N. Eliseenkov, and A. N. Pudovik, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **6**, 1297 (1969); *Chem. Abstr.*, **71**, 80416u (1969); (c) V. E. Belskii and G. Z. Motygullin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2551 (1967); *Chem. Abstr.*, **68**, 108353k (1968); (d) A. Francina, A. Lamotte, and J. C. Merlin, *C. R. Acad. Sci., Ser. C*, **266**, 1050 (1968); *Chem. Abstr.*, **69**, 58642b (1968); (e) D. Samuel and B. L. Silver, *J. Phys. Chem.*, **72**, 1809 (1968).

(17) E. Fluck and H. Binder, *Z. Naturforsch. B*, **22**, 805 (1967); *Chem. Abstr.*, **68**, 25325b (1968).

(18) The two signals at δ −0.3 and +17.9 ppm could be attributed to structures **7** and **8**, respectively. These could exist in an equilibrium, but slow enough on the NMR time scale to be seen as separate signals. Similar signals were also observed in the ^{31}P NMR spectra of suspensions of diethyl *p*-chlorobenzoylphosphonate (**1a**) and diethyl *p*-toluoylphosphonate (**1b**) in 1.0 mM hydrochloric acid. After signal accumulation for 1–15 h, **1a** gave signals at −1.9 (parent), −0.6 and +17.5 (intermediates), and +11.3 ($^{1}J_{PH}$ = 720 Hz) (**3**). **1b** gave signals at −1.4 (parent), 0.0 and 18.1 (intermediates), and +11.5 ($^{1}J_{PH}$ = 730 Hz) (**3**).

(19) Composition of the solution used for obtaining the Raman spectra was 4 μL of **1** + 5 mL of D_2O + 0.05 mL of 0.1 N HCl.

(20) L. P. Hammett, "Physical Organic Chemistry", 2nd ed., McGraw-Hill, New York, N.Y., 1970, pp 316–345.

(21) (a) R. P. Bell, J. P. Millington, and J. M. Pink, *Proc. R. Soc. London, Ser. A*, **303**, 1 (1968); (b) R. P. Bell and J. E. Critchlow, *ibid.*, **325**, 35 (1971).

(22) T. H. Lowry and K. S. Richardson, "Mechanism and Theory in Organic Chemistry", Harper and Row, New York, N.Y., 1976, p 404.

(23) (a) J. P. Klinman and E. R. Thornton, *J. Am. Chem. Soc.*, **90**, 4390 (1968); (b) R. L. Schowen, *Prog. Phys. Org. Chem.*, **9**, 275 (1972); (c) W. Palaitis, Ph.D. Dissertation in Chemistry, University of Pennsylvania, 1969; *Diss. Abstr. B*, **31**, 1210B (1970).

(24) K. B. Wiberg, *Chem. Rev.*, **55**, 713 (1955).

(25) (a) C. A. Bunton and V. J. Shiner, Jr., *J. Am. Chem. Soc.*, **83**, 3214 (1961). (b) R. P. Bell "The Proton in Chemistry", 2nd ed., Cornell University Press, Ithaca, N.Y., 1973, pp 183–190. (c) Possible existence of open trimers in water has been indicated by CNDO/2 calculations which show an energy minimum. See C. N. R. Rao in "Water. A Comprehensive Treatise", Vol. 1, F. Franks, Ed., Plenum Press, New York, N.Y., 1972, Chapter 3; A. Goel, A. S. N. Murthy, and C. N. R. Rao, *Indian J. Chem.*, **9**, 56 (1971); J. R. Hoyland and L. B. Kier, *Theor. Chim. Acta*, **15**, 1 (1969).

(26) (a) J. Emsley and D. Hall, "The Chemistry of Phosphorus", Wiley, New York, N.Y., 1976, p 106; (b) C. F. Callis, J. R. Van Wazer, J. N. Schoolery, and W. A. Anderson, *J. Am. Chem. Soc.*, **79**, 2719 (1957).

(27) W. J. Stec, J. R. Van Wazer, and N. Goddard, *J. Chem. Soc., Perkin Trans. 2*, 463 (1972).

(28) (a) A. L. McClellan, "Tables of Experimental Dipole Moments", Vol. 2, Rahara Enterprises, El Cerrito, Calif., 1974, p 464; (b) V. I. Minkin, O. A. Osipov, and Y. A. Zhdanov, "Dipole Moments in Organic Chemistry", W. E. Vaughan, Ed., Plenum Press, New York, N.Y., 1970, p 240.

(29) (a) M. Halmann, D. Vofsi, and S. Yanai, *J. Chem. Soc., Perkin Trans. 2*, 1210 (1976); (b) M. Gordon, V. A. Notaro, and C. E. Griffin, *J. Am. Chem. Soc.*, **86**, 1898 (1964); (c) G. M. Blackburn and M. J. Brown, *J. Am. Chem. Soc.*, **91**, 525 (1969).

(30) G. A. Olah and C. W. McFarland, *J. Org. Chem.*, **36**, 1374 (1971).

(31) J. A. Hirsch, "Concepts in Theoretical Organic Chemistry", Allyn and Bacon, Boston, Mass., 1975, pp 159–160.

(32) G. Binsch in "Dynamic Nuclear Magnetic Resonance Spectroscopy", L. A. Jackman and F. A. Cotton, Ed., Academic Press, New York, N.Y., 1975, Chapter 3.

Solid-Phase Cosolvents. Triphase Catalytic Hydrolysis of 1-Bromoadamantane[1]

Steven L. Regen,* Jacques J. Besse, and Jerome McLick

Contribution from the Department of Chemistry, Marquette University,
Milwaukee, Wisconsin 53233.

Received June 2, 1978

Abstract: The triphase catalytic hydrolysis of 1-bromoadamantane in a toluene-water system using 14 closely related insoluble graft copolymers has been studied. The enthalpies of activation computed from kinetic analysis of the first-order rate constants showed considerable variation accompanied by a compensating fluctuation in the entropy values. In addition, the free energy of activation for all systems investigated was energetically more favorable than that of the uncatalyzed biphase system. These results provide strong evidence for cosolvent behavior by the resins.

Introduction

We have recently reported preliminary data for the triphase hydrolysis of 1-bromoadamantane employing an insoluble graft copolymer as a catalyst (Scheme I).[2] In the absence of the polymer (biphase system), reaction occurred but at a much lower rate. The catalytic property of the resin was attributed

0002-7863/79/1501-0116$01.00/0