The Hydrolysis of *p*-Nitrophenyl Diphenyl Phosphate[1]

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There are rate maxima in the acid-catalyzed hydrolyses of *p*-nitrophenyl diphenyl phosphate in water–dioxane (95:5 v/v) which are not caused by complete protonation of the substrate. The maximum values of the rate constants and the acid concentrations at which they are observed increase in the sequence $HClO_4$, H_2SO_4, HCl. The negative electrolyte effects of the acids are overcoming the catalysis by protons and the activation energy is small and the activation entropy very negative for the acid hydrolysis, suggesting that the transition state is strongly hydrated. Specific effects of univalent cations are observed on the reaction between hydroxide ion and the substrate.

The reactions of trialkyl and -aryl phosphates with nucleophiles have been studied widely,[2,3] but little work has been done on the acid-catalyzed hydrolyses, and trialkyl phosphates are not particularly sensitive to strong acids.[2,4,5] However, perchloric acid catalyzes the hydrolysis of triphenyl phosphate in aqueous dioxane at 100°, and there is a rate maximum at *ca.* 1.5 *M* acid, which is not caused by complete protonation of the substrate.[6]

Study of this acid hydrolysis is complicated by subsequent hydrolysis of diphenyl phosphate, and because the solvent contained large amounts (60–75 volume %) of dioxane the rate maximum might be associated with the relatively low water content of the solvent. Therefore, *p*-nitrophenyl diphenyl phosphate was used as a substrate, and its hydrolysis to *p*-nitrophenol was followed spectrophotometrically, in water–dioxane (95:5 v/v). The alkaline hydrolysis was also examined, and both hydrolyses were compared with those of triphenyl phosphate.

Experimental Section

Materials.—*p*-Nitrophenyl diphenyl phosphate was prepared by the reaction between diphenyl phosphochloridate and *p*-nitrophenol in pyridine, and recrystallized from hexane. It was then dissolved in a benzene–hexane mixture and swirled rapidly with acid-washed alumina to remove traces of *p*-nitrophenol, and again recrystallized from hexane, mp 49–50°, lit.[7] mp 49–51°. *p*-Nitrophenoxide (by hydrolysis) was obtained in 37.5% yield; the calculated yield was 37.2%.

The mixed aqueous–dioxane solvents were made up by weight from water and purified dioxane,[8] to give the quoted compositions by volume at 25°.

Kinetics.—The alkaline hydrolysis was followed directly at 4030 A using a Gilford recording spectrophotometer with a thermostatted cell compartment. A perforated plunger was used to insure rapid mixing.

The acid hydrolyses were followed using sealed tubes. The contents were added to excess Tris or sodium tetraborate buffer,[9] and the absorbance was measured at 4030 Å.

The first-order rate constants, k_ψ, were calculated graphically using the integrated form of the first-order rate equation.

Products.—The amount of *p*-nitrophenol, determined spectrophotometrically after complete hydrolysis in either acid or alkali, was in good agreement with that calculated theoretically. The formation of diphenyl phosphate as the other reaction product was shown by extracting the reaction mixture with ether, drying the ether ($MgSO_4$), and then evaporating it, and identifying diphenyl phosphate by thin layer chromatography using silica gel G chromatoplates, with *n*-butyl alcohol–acetic acid–water (3:1:1) as developing solvent. The spots for the reaction product and authentic material were developed by spraying with an iodine–ethanol solution.[10]

Activity Coefficients.—The effect of acids upon the distribution of *p*-nitrophenyl diphenyl phosphate between water and carbon tetrachloride at 25° was examined. A stock solution, usually 1 ml, of the phosphate, (0.01 *M*), in carbon tetrachloride, was shaken for 1 min at 25° in a jacketed separatory funnel with the aqueous acid, usually 10 ml. The organic layer, which contained the bulk of the ester, was run off, and the aqueous layer was centrifuged to remove any carbon tetrachloride. One portion of the aqueous layer was then neutralized with sodium phosphate, and the absorbance quickly measured at 4030 Å, using a PE-Hitachi spectrophotometer. The remainder was then treated with excess sodium hydroxide to hydrolyze the ester, and its absorbance measured at 4030 Å. Both measurements were made using as a blank a solution of the appropriately neutralized acid. The difference between the two absorbances measured the relative molar concentration of ester. The molar activity coefficients, *f*, were then calculated relative to water as the standard state[11] (Table I).

TABLE I

EFFECTS OF ACIDS UPON THE MOLAR ACTIVITY COEFFICIENTS OF *p*-NITROPHENYL DIPHENYL PHOSPHATE[a]

Acid	C_{acid}, *M*	*f*
$HClO_4$	1.00	0.74
$HClO_4$	1.48	0.54
$HClO_4$	2.95	0.45
$HClO_4$	4.45	0.26
$HClO_4$	4.45	0.21
$HClO_4$	6.02	0.11
$HClO_4$	6.02	0.10
$HClO_4$	7.77	0.04
H_2SO_4	1.00	0.61
H_2SO_4	2.00	0.64
H_2SO_4	3.06	0.64
HCl	1.41	0.67
HCl	2.82	0.59
HCl	3.87	0.69
HCl	5.66	0.66
HCl	5.66	0.66
HCl	6.65	0.37
HCl	7.76	0.11

[a] In aqueous solution at 25°.

The plot of log *f* against acid concentration in Figure 1 shows that mineral acids salt in the triaryl phosphate, with perchloric acid being the most effective. There is considerable scatter in the experimental values especially at low acid concentrations

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(1) This work was supported by the National Science Foundation and Institute of Arthritis and Metabolic Diseases of the U. S. Public Health Service. This support is gratefully acknowledged.

(2) J. R. Cox and O. B. Ramsay, *Chem. Rev.*, **64**, 343 (1964).

(3) R. F. Hudson and D. C. Harper, *J. Chem. Soc.*, 1356 (1958).

(4) E. M. Thain, *ibid.*, 4694 (1957).

(5) P. W. C. Barnard, C. A. Bunton, D. R. Llewellyn, C. A. Vernon, and V. A. Welch, *ibid.*, 2670 (1961).

(6) P. W. C. Barnard, C. A. Bunton, D. Kellerman, M. M. Mhala, B. Silver, C. A. Vernon, and V. A. Welch, *ibid., Sect. B*, 227 (1966).

(7) W. M. Gulick and D. H. Geske, *J. Am. Chem. Soc.*, **88**, 2928 (1966).

(8) A. I. Vogel, "Textbook of Practical Organic Chemistry," Longmans, Green and Co., Ltd., London, 1949, p 177.

(9) C. A. Bunton, E. J. Fendler, and J. H. Fendler, *J. Am. Chem. Soc.*, **89**, 1221 (1967); C. A. Bunton, E. J. Fendler, E. Humeres, K. U. Yang, *J. Org. Chem.*, **32**, 2806 (1967).

(10) C. W. Stanley, *J. Chromatog.*, **16**, 467 (1964).

(11) F. A. Long and W. F. McDevit, *Chem. Rev.*, **51**, 119 (1952).

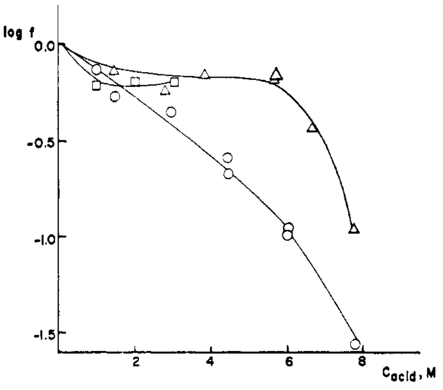

Figure 1.—Effects of acids upon the molar activity coefficient, *f*, of *p*-nitrophenyl diphenyl phosphate. Symbols are ○ for $HClO_4$, □ for H_2SO_4, and △ for HCl.

where the solubilities are similar to that in water, but there appears to be no simple relation between log *f* and electrolyte concentration.

Results

Acid Hydrolysis.—There are well-defined maxima in plots of k_ψ against C_{H^+} for hydrolyses in aqueous perchloric, and sulfuric and hydrochloric acids (Table II and Figure 2). However, if the ionic strength is kept constant by use of mixtures of lithium and hydrogen chloride there is a linear relation between k_ψ and C_{H^+} (Table II and Figure 2). There is a very small deuterium solvent isotope effect on both sides of the rate maximum (Table II and Figure 2), and the entropies of activation are large and negative, and the energies low (Table III).

The spontaneous hydrolysis is slow, as for the hydrolysis of triphenyl phosphate.[5,6]

The hydrolyses were also followed in dioxane–water (60:40 v/v) containing perchloric acid to allow rate comparisons with triphenyl phosphate (Table IV). The reaction rate is decreased by increasing the dioxane content of the solvent.

Alkaline Hydrolysis.—The reaction between hydroxide ion and *p*-nitrophenyl diphenyl phosphate was examined with several hydroxides (Table V); a few experiments were also done in dioxane–water (60:40 v/v) to allow comparison with triphenyl phosphate (Table VI).

Products.—*p*-Nitrophenyl diphenyl phosphate is more reactive than triphenyl phosphate in both acid and alkali, and in both reactions it is the *p*-nitrophenyl residue which is lost.

Discussion

Acid Hydrolysis.—The dominant feature of the acid hydrolysis of *p*-nitrophenyl diphenyl phosphate is the rate maximum at acid concentrations of 2–6 *M*, depending upon the nature of the catalyzing acid (Figure 2). Rate maxima are often observed with acid hydrolyses of moderately basic substrates, *e.g.*, amides, which can be fully protonated in moderately concentrated acid.[12] However, in the present case, as for acid hydrolyses of other aryl phosphates, the substrate is not fully protonated in the region of the rate maximum.[6,9] The pK_a of triphenyl phosphate is −2.8 and that of *p*-nitrophenyl diphenyl phosphate should be even more negative, because of electron withdrawal by the nitro group. Also the deuterium

Table II

Acid Hydrolysis of *p*-Nitrophenyl Diphenyl Phosphate[a]

Reagent	C_{Acid}, *M*	10^4k_ψ, sec^{-1}
$HClO_4$	0.75	5.10
	0.91	1.32[b]
	1.00	6.04
	1.93	7.41
	1.98	7.72
	1.98	2.15[b]
	2.98	6.90
	3.70	5.95
	3.70	1.24[b]
	4.00	5.82
	6.00	4.54
	7.30	2.35
	7.30	0.433[b]
	7.30	0.101[c]
	8.00	1.80
H_2SO_4	0.60	5.76
	0.98	7.91
	1.96	10.40
	3.95	8.73
	5.93	7.02
	7.82	3.70
D_2SO_4	0.50	5.11
	2.00	9.98
	3.32	9.33
HCl	1.00	3.83
	2.00	5.07
	3.97	8.06
	6.00	9.10
	7.94	7.95
	7.94	3.61[d]
	7.94	1.37[e]
	8.00	7.53
	9.93	5.95
	10.00	5.52
HCl + LiCl[f]	0.10	0.40
	2.00	2.29
	4.00	4.17
	6.00	5.70
	6.00	5.76
	6.00	2.39[d]
	6.00	1.11[e]
	8.00	7.53
HCl + LiCl[g]	2.00	1.23
	4.00	2.57
	6.00	3.53
	8.10	4.66
	10.00	5.52

[a] In water–dioxane (95:5 v/v) at 100.0° unless specified. [b] At 80.0°. [c] At 60.0°. [d] At 85.0°. [e] At 70.0°. [f] I = 8.0. [g] I = 10.0.

Table III

Arrhenius Parameters for the Hydrolysis of *p*-Nitrophenyl Diphenyl Phosphate[a]

Reagent	*E*, kcal/mole	Log *A*	ΔS^*,[b] eu
7.30 *M* $HClO_4$	19	7.4	−30
7.94 *M* HCl	16	6.2	−36
6.00 *M* HCl[c]	14.8	5.4	−39
0.1 *M* NaOH	10.5	6.3	−28

[a] In water–dioxane (95:5 v/v). [b] Calcd for 1 *M* reagents at 25° as standard state. [c] I = 8.0 with added LiCl.

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[12] D. Rosenthal and T. I. Taylor, *J. Am. Chem. Soc.*, **79**, 2684 (1957); S. Marburg and W. P. Jencks, *ibid.*, **84**, 232 (1962); J. T. Edward and S. C. R. Meacock, *J. Chem. Soc.*, 2000 (1957).

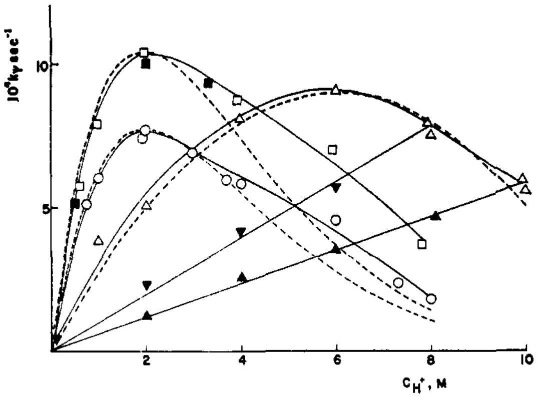

Figure 2.—Effects of acids upon the hydrolysis of *p*-nitrophenyl diphenyl phosphate at 100°. Broken lines are calculated. Symbols are ○ for $HClO_4$, □ for H_2SO_4, ■ for D_2SO_4, △ for HCl, ▼ for HCl + LiCl, I = 8.0, and ▲ for HCl + LiCl, I = 10.0.

TABLE IV

ACID HYDROLYSIS OF *p*-NITROPHENYL DIPHENYL PHOSPHATE AND TRIPHENYL PHOSPHATE[a]

C_{HClO_4}, M	*p*-Nitrophenyl diphenyl phosphate	Triphenyl phosphate[b]
0.50	16.1	6.13
1.0	25.7	9.73
1.52	40.7	11.2
2.01	45.3	9.93
2.43	53.8	8.27
2.43	54.9	

[a] Values of 10^6k_ψ, sec^{-1} in dioxane–water (60:40 v/v) at 100°. [b] Interpolated from values given in ref 6.

solvent isotope effect is the same on both sides of the rate maximum, whereas in amide hydrolysis k_{H_2O}/k_{D_2O} is less than 1 in dilute acid and greater than 1 in more concentrated acid in which the amide is fully protonated.[13]

Bunnett and Olsen have shown that for many acid hydrolyses plots of log k_ψ and H_0 against log $C_{H^+} + H_0$ are linear, and they suggest that the slopes ϕ are characteristic of the mechanism.[14] Their treatment was tested on reactions in water, but where the dioxane content of our solutions is low it seemed to be reasonable to apply it to our results. There is a linear relation between log $k_\psi + H_0$ and log $C_{H^+} + H_0$, for the three acids, and, for $HClO_4$, $\phi = 1.25$; for H_2SO_4, $\phi = 1.48$; and for HCl, $\phi = 1.09$ (calculated using a least-square treatment).

These values are similar to those found for the acid hydrolyses of mononitrophenyl phosphates,[6] ϕ = 1–1.4, and dinitrophenyl phosphates,[9] ϕ = *ca.* 1.2. It has been suggested that ϕ values in these ranges are evidence for slow proton transfers in the rate-determining step of reaction.

An attempt was made to fit the result to Bunnett's earlier equations relating to protonating power and water activity.[15] However, plots of log $k_\psi + H_0$ against log a_{H_2O} were curved for hydrolyses in both sulfuric and perchloric acids, with slopes, *w*, of *ca.* 15 at low acid concentrations, decreasing to *ca.* 6 at high.

TABLE V

HYDROLYSIS OF *p*-NITROPHENYL DIPHENYL PHOSPHATE AT HIGH pH[a]

Reagent	C_{OH^-}, M	10^4k_ψ, sec^{-1}	$10k_2$ sec^{-1} mole^{-1} l.
Borate, pH 8.0[b]		0.097	
Borate, pH 9.0[b]		0.42	
Borate, pH 10.0[b]		1.14	
Borate, pH 10.5[b]		2.64	
Phosphate, pH 11.0[c]		7.23	
Phosphate, pH 11.5[c]		11.1	
NaOH	0.01	33.6	3.30
NaOH	0.01	32.5	
NaOH	0.05	69.0	3.45
NaOH	0.10	368	3.73
NaOH	0.10	373	
NaOH	0.10	375	
NaOH	0.10	77.7[d]	0.78[d]
NaOH	0.30	263[d]	0.88[d]
KOH	0.0086	2.92	3.28
KOH	0.0086	2.70	
KOH	0.043	14.5	3.49
KOH	0.043	15.7	
KOH	0.086	31.4	3.62
KOH	0.086	30.8	
LiOH	0.01	33.2	3.38
LiOH	0.01	34.5	
LiOH	0.05	170	3.40
LiOH	0.10	355	3.52
LiOH	0.10	350	
$(CH_3)_4N \cdot OH$	0.01	29.5	2.95
$(CH_3)_4N \cdot OH$	0.05	175	3.50
$(CH_3)_4N \cdot OH$	0.10	364	3.80
$(CH_3)_4N \cdot OH$	0.10	398	
NaOH + NaCl[e]	0.10	155	1.55
NaOH + Na_2SO_4[e]	0.10	159	1.59
KOH + KCl[e]	0.086	134	1.55
LiOH + LiCl[e]	0.10	152	1.52
LiOH + $LiClO_4$[e]	0.10	147	1.47
$(CH_3)_4NOH + (CH_3)_4NCl$[e]	0.10	396	4.18
$(CH_3)_4NOH + (CH_3)_4NCl$[e]	0.10	440	
$(CH_3)_4NOH + (CH_3)_4NCl$[e]	0.10	435	

[a] In water–dioxane (95:5 v/v) at 25.0° unless specified. [b] 0.015 *M* buffer. [c] 0.05 *M* buffer. [d] At 0.65°. [e] I = 2.0.

TABLE VI

ALKALINE HYDROLYSIS OF *p*-NITROPHENYL DIPHENYL PHOSPHATE[a]

C_{NaOH}, M	$10k_2$ sec^{-1} mole^{-1} l.
0.015	2.15
0.060	1.67
0.149	1.43

[a] In dioxane–water (60:40 v/v) at 25°; in these conditions 10^2k_2 = 1.06 sec^{-1} mole^{-1} l. for the hydrolysis of triphenyl phosphate.[5]

For hydrolysis in hydrochloric acid a reasonably good linear plot was obtained with *w ca.* 6.

Bunnett had earlier commented on the failure of these relations when the activity coefficients of the substrate varied markedly with acid concentration,[15] and our partitioning experiments suggest that these variations may be partly responsible for the large changes in the *w* values, because the salting-in of the ester is less for hydrochloric than for perchloric acid (Table I).

Other empirical treatments can be applied to these phosphate hydrolyses which show rate maxima in acid. The Brønsted–Bjerrum equation for a A-2 reaction

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[13] R. P. Bell, "Acid-Base Catalysis," Oxford University Press, London, 1941, p 143; K. B. Wiberg, *Chem. Rev.*, **55**, 713 (1955).

[14] J. F. Bunnett and F. P. Olsen, *Can. J. Chem.*, **44**, 1917 (1966).

[15] J. F. Bunnett, *J. Am. Chem. Soc.*, **83**, 4956 (1961), and accompanying papers.

$$\mathrm{S} + \mathrm{H_3O^+} \rightleftharpoons \mathrm{HS^+} + \mathrm{H_2O} \rightleftharpoons (\mathrm{X^*}) \longrightarrow \text{products}$$

can be written formally as eq 1 (where f_s, $f_{\mathrm{H_2O}}$, $f_{\mathrm{H^+}}$, and

$$k_\psi = k_0 C_{\mathrm{H^+}} C_{\mathrm{H_2O}} \frac{f_s f_{\mathrm{H_2O}} f_{\mathrm{H^+}}}{f_{\mathrm{X}}^*} \qquad (1)$$

f_{X}^* are, respectively, the molar activity coefficients of the substrate, water, the hydrogen ion, and the transition state). In this formulation we assume that only one water molecule is forming a new covalent bond in the transition state,[16] and the interactions between the other water molecules and the reacting species are taken into account by the activity coefficients.

If we assume that each proton is bonded to four water molecules, and that the logarithm of the activity coefficient term varies linearly with electrolyte concentration, eq 1 can be written as eq 2 (where a = 1.14, 1.16, and

$$\log k_\psi = \log k_0 + \log C_{\mathrm{H^+}} + \log 52.8\,(1\text{–}0.072\,aC_{\mathrm{H^+}}) - bC_{\mathrm{H^+}} \qquad (2)$$

1.15 for perchloric, sulfuric, and hydrochloric acid, respectively, in water–dioxane, 95:5 v/v).

Equation 2 can be differentiated, and, at the rate maximum where $\mathrm{d}\ln k_\psi/\mathrm{d}C_{\mathrm{H^+}} = 0$, we have eq 3.

$$\frac{1}{C_{\mathrm{H^+}}} - \frac{0.072a}{1\text{–}0.072aC_{\mathrm{H^+}}} - 2.3b = 0 \qquad (3)$$

From the values of $C_{\mathrm{H^+}}$ at the rate maxima we calculate the following values for k_0 and b, at 100°: $\mathrm{HClO_4}$, $1.96 \times 10^{-5}(1.7 \times 10^{-5})$ sec^{-1}mole^{-2}l.^{2}, 0.175; $\mathrm{H_2SO_4}$, $2.68 \times 10^{-5}(2.4 \times 10^{-5})$ sec^{-1} mole^{-2}l.^{2}, 0.178; and HCl, $0.57 \times 10^{-5}(0.6 \times 10^{-5})$ sec^{-1} mole^{-2}l.^{2}; 0.001.

(The values of k_0 in parentheses were calculated from the initial slopes of plots of k_ψ against $C_{\mathrm{H^+}}$ (Figure 2). There is considerable uncertainty in the value of b for hydrochloric acid, because it is determined by a small numerical difference between two larger numbers.)

The broken lines in Figure 2 were plotted using the values of k_0 and b obtained from eq 3. The fit is good except at the higher acid concentrations where the assumptions about the number of water molecules attached to each proton break down.[17]

The b values are least for hydrochloric acid, which also salts-in the aryl phosphate less than does perchloric acid (Table I and Figure 1).

Although calculated and experimental values agree up to, and beyond the rate maxima, this does not prove that only one water molecule is interacting covalently with the phosphorus atom in the transition state. Following other workers we have not allowed for anion hydration,[17] and we cannot be sure that the parameters k_0 and b are independent variables, and also the logarithm of the activity coefficient of the substrate itself does not vary linearly with concentration as is assumed in eq 2. However the treatment does show how rate maxima can arise in acid hydrolyses, particularly those in which the substrate is "salted-in" strongly by acid, and the transition state is "salted-out" because of its strong demand for hydration.[18,19]

The solvent isotope effect $k_{\mathrm{H_2O}}/k_{\mathrm{D_2O}}$ is very close to unity, whereas generally for specific hydrogen ion-catalyzed reactions $k_{\mathrm{H_2O}}/k_{\mathrm{D_2O}} < 1$. This small kinetic isotope effect could arise because there is strong hydrogen bonding between the transition state and water, which would also lead to the high dependence of reaction rate upon water activity,[20] and the very negative values of the entropy of activation and the low energy of activation (Table III). However these results would also be understandable if the proton transfer was incomplete in the transition state, and it is quite possible that making and breaking of phosphorus oxygen bonds is concerted with protonation, as has been suggested for some hydrolyses of thiol sulfinates.[21] Indeed such a situation would not be unexpected for reaction of substrates as weakly basic as the triaryl phosphates.

Perchlorates generally "salt-in" organic nonelectrolytes, as compared with the effects of other anions of lower charge density,[11] and the relative ineffectiveness of perchloric acid as a catalyst may be caused largely by its ability to stabilize the initial state, as indicated by the larger value of b for perchloric than for hydrochloric acid in eq 2.

There are a number of acid hydrolyses of ester in which rate maxima are observed, but in which the substrate is not fully protonated.[6,9,22]

In all these reactions the substrates are very weakly basic, so that proton transfers to oxygen may not be very fast, but at the same time the transition states will contain hydroxyl groups which will be correspondingly acidic, and will therefore hydrogen bond strongly with water. The rate of these reactions should therefore be strongly affected by electrolytes which effectively remove the water, especially if they also "salt-in" the substrate.

The activity coefficient terms of the Brønsted–Bjerrum rate equation can be kept constant by maintaining the electrolyte concentration with lithium chloride, as shown by the linear relation between rate constant and hydrogen ion concentration for mixtures of hydrogen and lithium chloride of constant ionic strength (Figure 2 and Table II). Lithium and hydrogen chloride have similar effects upon water activity,[23] but they could also have similar effects on the activity coefficient of the triaryl phosphate. In accord with the preceding discussion of the dependence of rate on water activity, we note that the rate of the acid hydrolysis of p-nitrophenyl diphenyl phosphate increases *ca.* twofold in going from water–dioxane, 40:60 v/v to 95:5 v/v (Tables II and IV).

Alkaline Hydrolysis.—p-Nitrophenyldiphenyl phosphate is approximately 20 times as reactive as triphenyl phosphate toward hydroxide ion (Table VI) as is generally found for other phenolic esters.[24] The reac-

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(16) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1954, Chapter VII.

(17) K. N. Bascombe and R. P. Bell, *Discussions Faraday Soc.*, **24**, 158 (1957); P. A. H. Wyatt, *ibid.*, **24**, 162 (1957). *Cf.* D. Rosenthal and J. S. Dwyer, *Can. J. Chem.*, **41**, 80 (1963).

(18) One of the referees suggested that the effect of electrolytes on the reorganization of the solvent in going from the initial to the transition state[19] could also be responsible for the rate maxima in aqueous acid. Robertson's views on the reorganization of water as an important factor in determining kinetic parameters have been developed for hydrolyses of alkyl halides and sulfonates, and we would expect strong hydrogen bonding interactions to be less important in these reactions than in those involving strong acids.[15,17] However, insofar as hydrogen bonding plays a major role in determining the structure of water,[19] these two explanations have much in common.

(19) R. E. Robertson, *Prog. Phys. Org. Chem.*, **4**, 213 (1967).

(20) C. A. Bunton and V. J. Shiner, *J. Am. Chem. Soc.*, **83**, 3207 (1961).

(21) J. Kice and G. Guaraldi, *ibid.*, **89**, 4113 (1967).

(22) C. A. Bunton and T. Hadwick, *J. Chem. Soc.*, 3248 (1958); 943 (1961). J. G. Tillett, *ibid.*, 5138 (1960). C. A. Bunton and G. Schwerin, *J. Org. Chem.*, **31**, 842 (1966).

(23) R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," Butterworth and Co. (Publishers) Ltd., London, 1959, Appendix 8.

(24) K. N. Wiberg, "Physical Organic Chemistry," John Wiley and Sons, New York, N. Y., 1964, p 404.

tion can be written either as a synchronous displacement on phosphorus, or as a prior addition followed by elimination; however, inversion has been observed in nucleophilic displacements on phosphorus.[25] There is an electrolyte effect upon this reaction (Table V), and tetramethyl ammonium hydroxide is a more effective reagent than the alkali metal hydroxides. These observations suggest that cations of low charge density assist this reaction in which the initial state, a neutral substrate, and the hydroxide ion, which has a high charge density, go to an anionic transition state of low charge density. A similar salt order has been observed for reactions between alkoxide ions and chloronitrobenzenes, generally in solvents which favor ion pairing.[26]

However, the attack of lyate ions upon 2,4-dinitrochlorobenzene in water or aqueous methanol is assisted by tetraalkyl ammonium ions, and hindered by lithium, sodium, and potassium ions, as is the reaction between thiosulfate ion and *n*-pentyl bromide in aqueous ethanol,[27] suggesting that these specific electrolyte effects may be general for these classes of nucleophilic displacements.

The reaction with hydroxide is approximately twice as fast in dioxane–water, 5:95 v/v, than in dioxane–water, 60:40 v/v, although one might have expected the hydroxide ion to be more nucleophilic in the less aqueous solvent,[28] and the results do not fit the qualitative Hughes–Ingold solvent theory.[16] These observations suggest that the transition state for the alkaline as well as the acid hydrolysis is strongly hydrated, consistent with the low activation energy and very negative activation entropy for the alkaline hydrolysis of these triaryl phosphates, and a similar solvent effect is observed with triphenyl phosphate in going from dioxane–water, 60:40 v/v to 75:25 v/v.[5]

Strong interactions between water and the transition states for both the acid and alkaline hydrolyses of these phosphate triesters are to be expected in terms of the preferred model for bimolecular substitution at a phosphoryl phosphorus atom,[2,29] because any factor which increases the electrophilicity of the phosphoryl phosphorus atom, and hence lowers the activation energy for substitution, will also increase the polarity of the transition state and hence increase its solvation. The net effect will therefore be a further lowering of the activation energy for substitution, at the cost of very negative entropy of activation arising from the ordering of the solvent about the transition state.

Registry No.—*p*-Nitrophenyl diphenyl phosphate, 10359-36-1; $HClO_4$, 7601-90-3; H_2SO_4, 7664-93-9; HCl, 7647-01-0; NaOH, 1310-73-2; KOH, 1310-58-3; LiOH, 1310-65-2; $(CH_3)_4N \cdot OH$, 75-59-2.

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(25) R. F. Hudson and M. Green, *Angew. Chem. Intern. Ed. Engl.*, **2**, 11 (1963).

(26) J. D. Reinheimer, W. F. Kieffer, S. W. Frey, J. C. Cochran, and E. W. Barr, *J. Am. Chem. Soc.*, **80**, 164 (1958); J. D. Reinheimer, J. T. Gerig, and J. C. Cochran, *ibid.*, **83**, 2873 (1961).

(27) L. Robinson, unpublished results.

(28) J. Miller and A. J. Parker, *J. Am. Chem. Soc.*, **83**, 117 (1961); A. J. Parker, *J. Chem. Soc.*, 1328 (1961).

(29) G. Aksnes, *Acta Chem. Scand.*, **14**, 1515 (1960).

The Reactions of Some Alicyclic 1,2-Dihalopolyfluoro Olefins with Ethanolic Potassium Hydroxide. The Effect of Ring Size on Product Distribution

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A series of 1,2-dihalotetrafluorocyclobutenes and corresponding cyclopentenes was synthesized, and their reactions with alkoxide ion are reported and these results interpreted on the basis of carbanion formation.

Nucleophilic substitution reactions of fluoro olefins, particularly displacement of halogen by alkoxide ion, constitute one of the most thoroughly studied aspects of fluorocarbon chemistry. Mechanistic interpretations concerning these reactions have generally been based on the pioneering work of Miller[2] who first rationalized the base-catalyzed addition of alcohols to chlorotrifluoroethylene on the basis of a rate-determining carbanion formation. Alicyclic polyfluorinated olefins (I) were subsequently found to yield unsaturated products of structure II, and the mechanism illustrated in Scheme I has been advanced as a compromise between a concerted displacement[3] of vinylic halide and an addition–elimination of hydrogen halide, the differentiation between which cannot be made on the basis of presently available data.

The continuing program concerned with the synthesis of new polyhalo olefins in this laboratory has given rise to a new series of 1,2-dihaloperfluorocyclobutenes and -pentenes which serve as convenient systems to evaluate nucleophilic attack on alicyclic olefins with respect to two points: initial attack to form a monoether and direction of the subsequent attack.

A series of 1,2-dihalotetrafluorocyclobutenes and 1,2-dihalohexafluorocyclopentenes was prepared in which the vinylic halogens were the three possible combinations of chlorine, bromine, and iodine. The addition of an equivalent amount of ethanolic potassium

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(1) This paper represents parts of Ph.D. Theses submitted to the Graduate School, University of Colorado, Boulder, Colo., by R. J. McMurtry, 1965, and by R. Sullivan, 1964.

(2) W. T. Miller, E. W. Fager, and P. H. Griswold, *J. Am. Chem. Soc.*, **70**, 431 (1948).

(3) It is generally recognized that the transition states for reactions at unsaturated centers of low electron density such as carbonyl[4a] and phosphoryl[4b] resemble the corresponding addition intermediates. Thus, although a discrete carbanion may not be involved, as implied above, the transition state leading to a concerted displacement of halide would presumably possess considerable bond formation between the attacking nucleophile and the relatively slight bond cleavage between the carbon and the leaving halogen.

(4) (a) M. L. Bender, *Chem. Rev.*, **60**, 53 (1960); (b) R. F. Hudson, *Advan. Inorg. Radiochem.*, **5**, 362 (1963).