estimation.[15] Some of the estimated $\Sigma(\sigma_m + \sigma_p)/2$ values are included in Table I in parentheses. The estimation is reliable to within a ±0.1-unit variation. The hydrogen-bonding interaction to the naphthalene ring appears to involve all ten π electrons since eq 2 holds regardless of the position of the substituents on the ring. This result again agrees with our earlier work.[2b]

The ν_{OH} spectra of phenol in solutions of N-alkylanilines (**50–57**) in carbon tetrachloride were not the expected triplet, but always a doublet. The lower frequency band of the doublet corresponds to the OH interacting with the π electron of the ring, because the $\Delta\nu_{OH}$ *vs.* $\Sigma(\sigma_m + \sigma_p)/2$ plot fell on the correlation line in Figure 2. The very weak and broad band at about 3400–3300 cm^{-1} owing to X–H···N interaction does not appear until phenols[3] or pyrrole[4] are dissolved in the neat liquid N,N-dimethylaniline. Evidently, the O–H···π type of interaction is much more favored than the O–H···N interaction in phenol-N-alkylaniline adducts, although the hydrogen bond shift is much larger for the latter than for the former. Steric inhibition of the n–π resonance in the anilines causes the O–H····n band to appear; a very weak and broad band centered at about 3200 cm^{-1} was observed when the proton accepting N,N-dialkylaniline has a methyl group in the *ortho* position (**54** and **58**). It is interesting to note that the protonation of N-alkylanilines in strong acid medium occurs also only on the nitrogen atom.[16]

The behavior of the oxygenated benzenes furnishes an interesting contrast with the N-alkylbenzenes; mono- and polyalkoxybenzenes (**25–33**) and thioalkoxybenzenes (**35–37**) act as bifunctional donors in hydrogen bonding, while in HSO_2F and $HF–BF_3$ they protonate exclusively on the ring carbon.[17] When the lone-pair electron on oxygen is hindered by two *t*-butyl groups in *ortho* position (**65** and **66**), the OH···O absorption band disappears and only the OH···π band was observed even if 0.5 *M* of the 2,6-di-*t*-butyl phenols were added to 0.016 *M* of phenol.[18]

Registry No.—**1**, 71-43-2; **2**, 108-88-3; **3**, 95-47-6; **4**, 108-38-3; **5**, 106-42-3; **6**, 95-63-6; **7**, 108-67-8; **8**, 95-93-2; **9**, 700-12-9; **10**, 87-85-4; **11**, 100-41-4; **12** (*o*), 135-01-3; **12** (*m*), 141-93-5; **12** (*p*), 105-05-5; **13**, 102-25-0; **15**, 604-88-6; **16**, 98-82-8; **17** (*m*), 99-62-7; **17** (*p*), 100-18-5; **18**, 99-82-1; **19**, 98-06-6; **20**, 98-51-1; **21**, 1012-72-2; **22**, 119-64-2; **23**, 827-52-1; **24**, 123-01-3; **25**, 100-66-3; **26**, 151-10-1; **27**, 150-78-7; **28**, 621-23-8; **29**, 104-93-8; **30**, 766-51-8; **31**, 623-12-1; **32**, 103-73-1; **33**, 122-95-2; **34**, 100-29-8; **35**, 100-68-5; **36**, 623-13-2; **37**, 123-09-1; **38**, 101-84-8; **39**, 103-50-4; **40**, 139-66-2; **41**, 3699-01-2; **42**, 13343-26-5; **43**, 92-52-4; **44**, 84-15-1; **45**, 92-06-8; **46**, 95-13-6; **47**, 103-29-7; **48**, 103-72-0; **49**, 103-71-9; **50**, 100-61-8; **51**, 121-69-7; **52**, 91-66-7; **53**, 613-29-6; **54**, 609-72-3; **55**, 121-72-2; **56**, 99-97-8; **57**, 91-67-8; **58**, 769-06-2; **59**, 103-33-3; **60**, 60-09-3; **61**, 2396-60-3; **62**, 588-04-5; **63**, 131-79-3; **64**, 538-51-2; **65**, 128-39-2; **66**, 128-37-0; **67**, 462-06-6; **68**, 108-90-7; **69**, 108-86-1; **70**, 591-50-4; **71**, 91-20-3; **72**, 90-12-0; **73**, 91-57-6; **74**, 581-40-8; **75**, 581-42-0; **76**, 208-96-8; **77**, 83-32-9; **78**, 1732-13-4; **79**, 90-13-1; **80**, 323-09-1; **81**, 2216-69-5; **82**, 93-04-9; phenol, 108-95-2.

Acknowledgment.—We thank Dr. Paul Jones for helpful advice on linguistic problems.

[15] Effect of the steric crowding appears itself in the equilibrium constant. The *K* for the phenol–hexamethylbenzene adduct is anomalously low.[2b] Hexaethylbenzene is a well-quoted example of sterically hindered π donor in CT complex: T. W. Nakagawa, L. J. Andrews, and R. M. Keefer, *J. Am. Chem. Soc.*, **82**, 269 (1960).

[16] W. Koch, private communication; also *cf.* T. Isobe, T. Ikenoue, and G. Hazato, *J. Chem. Phys.*, **30**, 1371 (1959).

[17] T. Birchall, A. N. Bourns, R. J. Gillespie, and P. J. Smith, *Can. J. Chem.*, **42**, 1433 (1964). In aqueous H_2SO_4 and $HClO_4$, O protonation was observed to occur to a small extent: A. J. Kresge and L. E. Hakka, *J. Am. Chem. Soc.*, **88**, 3868 (1966).

[18] Note that di-*t*-butyl ether forms a hydrogen bond with phenol under similar conditions: R. West, D. L. Powell, M. K. T. Lee, and L. S. Whatley, *ibid.*, **86**, 3227 (1964).

The Hydrolysis of Some Monophenyl Phosphates[1]

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There is a linear free-energy relation between log k_ψ for hydrolysis of monoanions of monoalkyl or -aryl phosphates and p*K* of the alcohol or phenol, with a slope of approximately 0.3. Bulky *ortho* substituents hinder hydrolysis slightly. Acid-catalyzed hydrolyses are observed only with the nitrophenyl phosphates, with rate maxima at approximately 5 *M* acid. Hydrolyses of the undissociated nitrophenyl phosphates are important, especially at low temperatures with the *ortho* and *para* isomers.

The hydrolysis of a simple aryl phosphate involves phosphorus–oxygen bond fission and the most important reactive species is the monoanion $ArOPO_3H^-$.[3]

Acids catalyze the hydrolyses of *p*-nitro- and *p*-acetylphenyl phosphates in water, with a maximum reaction rate at approximately 5 *M* acid.[3–5] One aim of the present work was to find out whether the presence of a *m*-nitro group would lead to a similar rate maximum in acid. There is also some rate increase at high pH, probably caused by a reaction between hydroxide ion and the dianion $ArOPO_3^{2-}$.[6] This reaction becomes

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[1] This work was presented in part at the Symposium on Bio-Organic Reactions, Western Regional Meeting of the American Chemical Society, Los Angeles, Nov 19, 1965, and is abstracted in part from the theses of E. J. Fendler and K.-U. Yang, submitted in partial fulfillment of the respective requirements of the degrees of Doctor of Philosophy and Master of Arts of the University of California at Santa Barbara. It was supported by grants from the National Science Foundation and the National Institute of Arthritis and Metabolic Diseases. This support is gratefully acknowledged.

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[3] P. W. C. Barnard, C. A. Bunton, D. Kellerman, M. M. Mhala, B. Silver, C. A. Vernon, and V. A. Welch, *J. Chem. Soc., Sect. B*, 227 (1966).

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very rapid with dinitrophenyl phosphates,[7] whose dianions can also undergo spontaneous hydrolysis.[7,8]

The decomposition of the monoanion has generally been considered to occur with elimination of the unstable metaphosphate ion, which was rapidly captured by the solvent (eq A).[9] Some evidence has been con-

$$\mathrm{ArOPO_3H^-} \xrightarrow{\text{slow}} \mathrm{ArOH} + \mathrm{PO_3^-} \xrightarrow[\text{fast}]{\text{HOS}} \mathrm{SOPO_3H^-} \qquad \text{(A)}$$

sidered to support nucleophilic attack by solvent upon the monoanion;[10] therefore, we have examined the hydrolysis of substituted monophenyl phosphates, some of which contained bulky *ortho* substituents, because the steric and electronic effects of substituents should give evidence on the mechanism of hydrolysis of the monoanion.

Experimental Section

Materials.—*p*-Nitrophenyl phosphate, as its sodium salt, was a commercial sample. The other aryl phosphates were prepared by the standard method of reaction between the phenol and phosphorus oxychloride to give the phenyl phosphoryl dichloride, which was then hydrolyzed in dilute aqueous barium hydroxide and isolated as the barium salt by precipitation with either alcohol or acetone.[11] Some of the phenyl phosphoryl dichlorides were prepared by reaction in pyridine,[11] but in general we find it better to use an excess of phosphorus oxychloride, with no pyridine, and to remove the excess phosphorus oxychloride *in vacuo.*

The purity of the barium salts of the phenyl phosphates was checked by colorimetric determination of inorganic phosphate, after complete hydrolysis, using the Fiske–Subba Row method,[12] or for the nitrophenyl phosphates by the spectrophotometric determination of nitrophenol as phenoxide ion, at λ_{max} 4100 A for *o*-nitro-, 3800 A for *m*-nitro-, and 4030 A for *p*-nitrophenol. The following were the molecular weights, calculated for $\mathrm{ROPO_3Ba}$: R = *o*-Cl, 341 (calcd 344); *p*-Cl, 348 (calcd 344); *o-t*-Bu, 365 (calcd 368); 2,6-$\mathrm{Me_2}$, 334 (calcd 337); 2,6-*t*-$\mathrm{Bu_2}$, 4-Me, 431 (calcd 435); *o*-$\mathrm{NO_2}$, 352, 352 (nitrophenoxide analysis) (calcd 354); *m*-$\mathrm{NO_2}$, 358 (calcd 354) (nitrophenoxide analysis).

Kinetics.—The hydrolysis of the nitrophenyl phosphates was followed spectrophotometrically by adding portions of the reaction mixture to dilute sodium carbonate and measuring the optical density of the nitrophenoxide ion with a Gilford 220 or PE-Hitachi 139 spectrophotometer.[3,7] Beer's law was obeyed by these nitrophenoxide ion solutions. For reactions in moderately concentrated acid, portions of the reaction mixture were added to excess Tris or sodium tetraborate.

The hydrolysis of the other aryl phosphates was followed by the colorimetric determination of inorganic phosphate.[12] Either a Bausch and Lomb Spectronic 20 colorimeter or a PE-Hitachi spectrophotometer was used. Some of the hydrolyses of the nitrophenyl phosphates were also followed by phosphate determination. Stoppered flasks were used for the experiments at 25° and sealed tubes at higher temperatures. Substrate concentrations were in the range 10^{-5} to 5×10^{-4} *M*. When the phosphates were used as their barium salts, the barium ions were removed by passing an aqueous solution through a column of Dowex 50W-X8 in its acid form. Examples of the kinetic runs are shown in Figure 1.

Buffer Solutions.—Potassium hydrogen phthalate (0.01 *M*) was used at pH 3–6.5 and sodium borate (0.015 *M*) was used at pH 8–10. When the evolution of nitrophenol was followed, the buffers were generally potassium dihydrogen phosphate (0.01 *M*) at pH 6–8 and disodium hydrogen phosphate (0.01 *M*) at pH 10–12. The reaction solutions were made up with the substrate present, at 25°, so that the pH value was that required at the reaction temperature, using the temperature corrections obtained by interpolation from values in the literature.[13] Mineral acid was used at low pH and sodium hydroxide at high pH. No temperature correction was applied to the pH when it was controlled by strong acid or base.

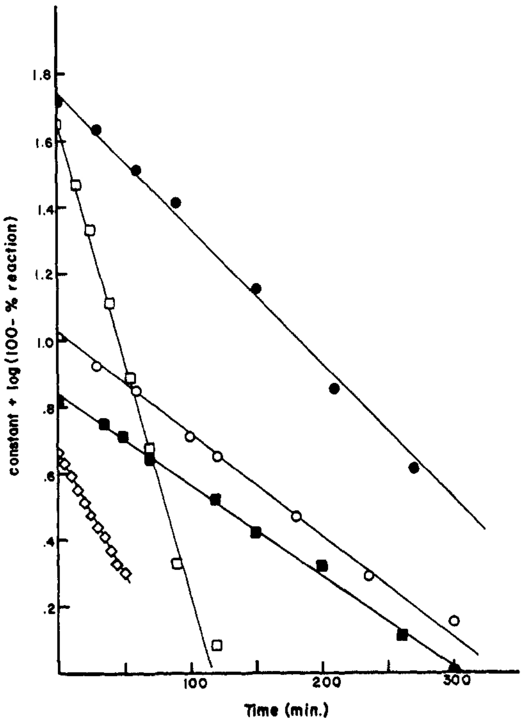

Figure 1.—Typical kinetic runs for hydrolyses at 100°: ■, *o*-chlorophenyl phosphate, pH 6.1; □, *m*-nitrophenyl phosphate, pH 4.0; ●, 2,6-dimethylphenyl phosphate, pH 4.1; O, *o*-nitrophenyl phosphate, pH 8.7; ◇, *m*-nitrophenyl phosphate, in 5.0 *M* perchloric acid.

Dissociation Constants.—The values of pK_2 of *o*- and *m*-nitrophenyl phosphates were determined using the usual equation pH = p*K* + log ([anion]/[acid]). The pH was measured with a Deltamatic expanded scale pH meter and the concentration of aryl phosphate was 0.01 *M*. The values of pK_1 were obtained by determining the pH of 0.01 *M* solutions of the phosphates, then diluting these solutions and remeasuring the pH. This process was repeated several times. For a concentration of aryl phosphate of *C* and a degree of dissociation of α, $\mathrm{pH} = {}^1/_2 pK_1 - {}^1/_2 \log C - \log(1 - \alpha)$ and the values of pK_1 and α can be obtained by the method of successive approximations. In the dilute solutions used in these experiments, $1 - \alpha$ is small and changes little with changes in concentration of the nitrophenyl phosphate.

The following p*K* values were obtained—for *o*-nitrophenyl phosphate: pK_1, 1.01 at 22°, 1.05 at 50°; pK_2, 5.6 at 32°; for *m*-nitrophenyl phosphate: pK_1, 1.05 at 22°, 1.11 at 50°; pK_2, 5.5 at 32°. In calculating the proportion of aryl phosphate present as monoanion,[14] we used the following values—for *o*-nitrophenyl phosphate: pK_1, 1.0 at 25°, 1.1 at 73°; pK_2, 5.6; for *m*-nitrophenyl phosphate: pK_1, 1.1 at 25°, 1.2 at 73°, 1.2 at 100°; pK_2, 5.5—on the assumption that the variation of pK_1 with temperature would be similar to that for other phosphate esters.[3-5,14] (No temperature correction was applied to pK_2, because we did not examine the hydrolyses of *o*- and *m*-nitrophenyl phosphate beyond pH 6 and into the region where the dianion is an important species.)

Results

The values of the first-order rate constants are given in Tables I–VII. Acid-catalyzed hydrolyses were observed only with the nitrophenyl phosphates. The

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[8] A. J. Kirby and A. G. Varvoglis, *ibid.*, **88**, 1823 (1966); **89**, 415 (1967).

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[13] S. Stene, *Rec. Trav. Chim.*, **49**, 1133 (1930); R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," Butterworth and Co. Ltd., London, 1959, Appendix 12.3.

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TABLE I

HYDROLYSIS OF ALKYL- AND CHLORO-SUBSTITUTED PHENYL PHOSPHATES^a

Substituent, pH	H^b	p-CH$_3$^{b}	o-t-Bu	p-t-Bu	2,6-Me$_2$^{b}	2,6-t-Bu$_2$, 4-Me	o-Cl^d	p-Cl
0.00	5	3.1	0.49	...	...	0.87	8.92	...
1.15	..	8.5	1.26	...	4.48	1.15	...	...
1.80	..	14.0	2.73	...	10.3	2.40	17.2	24.3
3.10	27	22.0	3.75	...	15.0	2.98	...	...
3.40	..	...	3.91	...	16.1	...	...	...
3.50	27	...	...	17.3	...	...	...	30.4
3.60	..	...	...	...	...	3.29	23.0	...
3.80	..	...	4.00	...	16.2	...	...	...
4.10	27	23.0	4.00	17.8	16.1	3.35	23.0	30.2
4.60	..	...	3.97	18.0	...	3.36	...	28.5
5.10	..	...	3.84	...	14.5	3.11	22.2	...
5.60	23	19	3.12	...	...	...	...	18.5
5.90	..	...	...	12.1	...	...	...	...
6.10	..	...	2.78	...	12.1	2.00	10.8	...
6.50	11	3	1.67	...	...	...	...	...
8.00	..	...	0.60	3.00	2.10	0.48	0.80	0.83

[a] 10^5k_ψ, sec^{-1}, at 100° unless specified. [b] Values interpolated from data in ref 3. [c] At 73.0° $10^5k_\psi = 0.70$ sec^{-1} at pH 4. [d] At 73.0° $10^5k_\psi = 1.33$ sec^{-1} at pH 4.1.

TABLE II

HYDROLYSIS OF p-NITROPHENYL PHOSPHATE

pH	10^5k_ψ, sec^{-1} 25.0°	73.0°
0.00	0.0974	8.60^a
0.50	0.0167	...
1.00	0.0139	3.83^a
1.50	0.0119	3.33^a
2.00	0.0111	4.20^a
3.30	0.0115	6.60^a
3.70	0.0121	6.92^a
4.00	0.0116	6.30^a
4.50	0.0106	...
9.00	...	6.16^b
12.00	...	4.85^b
13.00	...	5.16^b
14.00	...	0.27^c

[a] See ref 3. [b] At 100°. [c] $k_\psi = 8.55 \times 10^{-5}$ sec^{-1} at 100°.

TABLE III

HYDROLYSIS OF o-NITROPHENYL PHOSPHATE

pH	10^5k_ψ, sec^{-1} 25.0°	73.0°	100.0°
1.00	0.0128	5.44	...
1.00	0.0119	...	...
2.00	0.0108	6.38	...
2.50	0.0109	...	...
3.30	0.0096	7.09	...
3.70	0.0100	7.46	...
4.00	0.0099	6.71	...
4.50	0.0093	6.26	...
5.70	...	3.38	66.8
8.70	...	0.27	11.8
11.70	...	0.31	11.6
13.00	...	0.29	13.7
14.20	...	1.15	...
14.50	...	...	34.9

TABLE IV

HYDROLYSIS OF m-NITROPHENYL PHOSPHATE

pH	10^5k_ψ, sec^{-1} 25.0°	73.0°	100.0°
1.00	0.0171	2.52	32.6
2.00	0.0121	3.03	46.9
3.30	0.0155	3.18	54.2
3.70	...	3.27	56.5
4.00	0.0160	3.20	57.3
4.50	0.0147	3.17	49.0
6.30	...	...	7.07
9.00	...	...	0.40
11.70	...	...	0.26
13.00	...	...	0.23
14.20	...	...	1.86

TABLE V

HYDROLYSIS OF ALKYL- AND CHLORO-SUBSTITUTED PHENYL PHOSPHATES IN AQUEOUS HYDROCHLORIC ACID^a

Substituent C_{H^+}, M	H^b	o-t-Bu	2,6-Me$_2$	2,6-t-Bu$_2$, 4-Me	o-Cl	p-Cl
1.00	...	0.49	...	0.87	8.92	...
2.00	3.7	...	...	...	...	8.40
2.65	...	0.80	0.93	0.98	14.0	...
3.00	3.6	...	...	...	...	...
4.60	...	1.00	1.00	1.10	...	...
5.20	...	...	...	...	13.4	...
6.00	...	...	...	...	...	10.0
7.05	3.0	1.12	1.25	1.03	...	...
8.00	...	...	...	...	18.0	9.10

[a] 10^5k_ψ, sec^{-1} at 100°. [b] Values interpolated from data for hydrolysis in perchloric acid.[3]

TABLE VI

ACID HYDROLYSIS OF o-NITROPHENYL PHOSPHATE

C_{HClO_4}, M	10^5k_ψ, sec^{-1} 25.0°	73.0°
0.10	0.012	5.44
1.04	0.072	10.3
3.00	...	19.9
4.00	0.235	24.0
6.00	0.251	23.6
8.00	0.184	18.0

hydrolysis at high pH was not examined extensively because of attack of alkali upon the glass, although there is some enhancement of rate at high pH for the nitrophenyl phosphates.[6] The relation between reaction rate and acidity is shown in Figures 2–4.

Discussion

Monoanion Hydrolysis.—For most of these aryl phosphates, only hydrolysis of the monoanion makes any significant contribution to the over-all reaction. If the monoanion is the only reactive species, the first-

TABLE VII

ACID HYDROLYSIS OF *m*-NITROPHENYL PHOSPHATE

	10^4k_ψ, sec^{-1}				
	25.0°	73.0°			100.0°
C_{H^+}, *M*	$HClO_4$	$HClO_4$	H_2SO_4	HCl	$HClO_4$
0.10	0.0171	2.52	...	...	...
1.00	0.0297	3.65	...	...	...
1.30	...	...	...	3.71	...
1.44	...	...	4.20	...	...
2.00	...	...	...	...	29.3
2.60	...	...	...	5.38	...
2.74	...	...	...	5.61	...
3.00	0.0391	4.50	...	...	31.5
4.00	0.0384	4.30	5.70	6.10	30.0
5.00	...	...	...	...	28.3
5.48	...	...	...	5.97	...
6.00	0.0367	4.03	...	...	19.7
8.00	0.0211	2.32	3.32	5.08	...

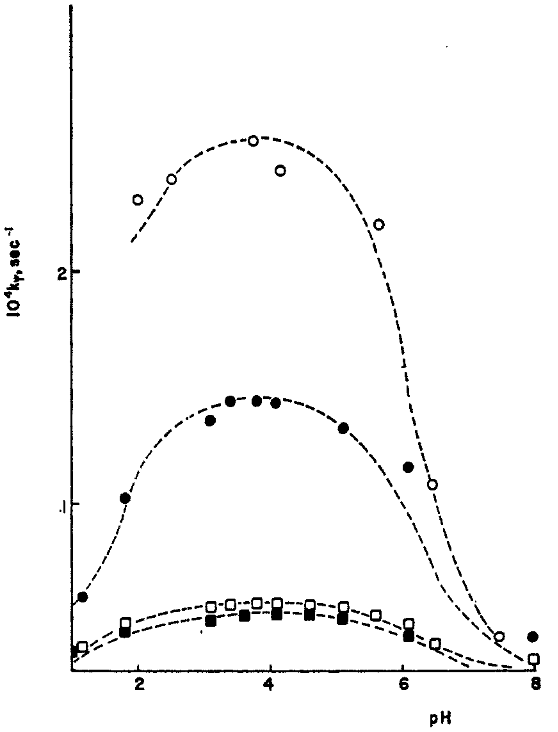

Figure 2.—Plot of k_ψ against pH at 100° (broken lines are calculated): ○, phenyl;[3] ●, 2,6-dimethylphenyl; □, *o*-*t*-butylphenyl; ■, 2,6-di-*t*-butyl-4-methylphenyl phosphate.

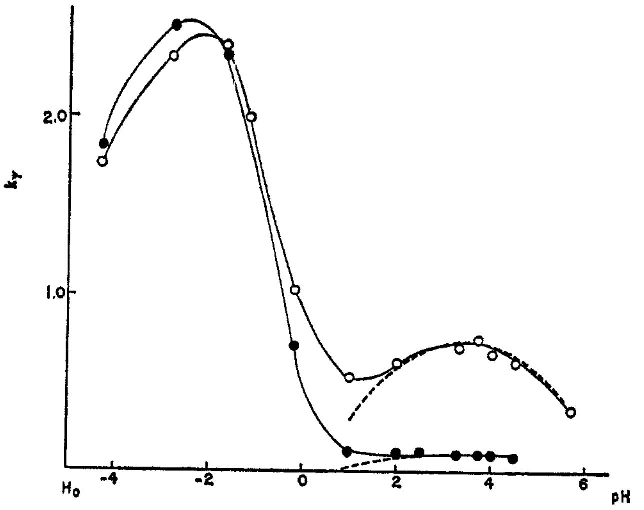

Figure 3.—Variation of k_ψ with acidity for the hydrolysis of *o*-nitrophenyl phosphate (broken lines are calculated): ● at 25.0°, 10^6k_ψ, sec^{-1}; ○ at 73.0°, 10^4k_ψ, sec^{-1}.

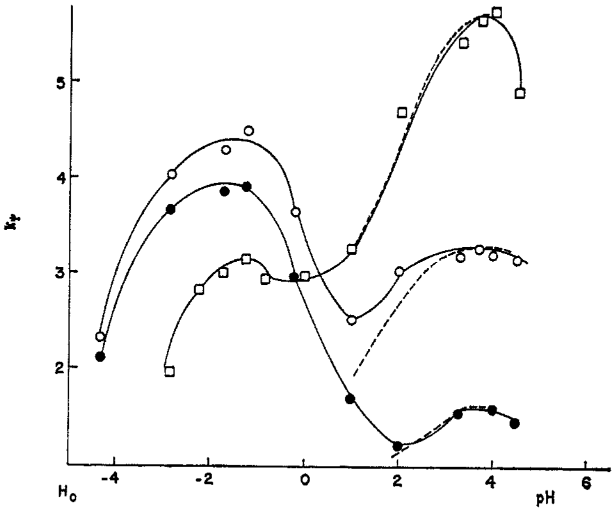

Figure 4.—Variation of k_ψ with acidity for the hydrolysis of *m*-nitrophenyl phosphate (broken lines are calculated): ● at 25.0°, 10^7k_ψ, sec^{-1}; ○ at 73.0°, 10^5k_ψ, sec^{-1}; □ at 100°, 10^4k_ψ, sec^{-1}.

order rate constant is given by eq 1, where k_1 is the first-order rate constant for decomposition of the monoanion and C_1 and C are the concentrations of monoanion and total phosphate.

$$k_\psi = k_1(C_1/C) \qquad (1)$$

Equation 1 fits the experimental results well, as shown in Figure 2, where we plot k_ψ against the pH, taking the value of k_1 as that of the maximum value of k_ψ at pH ≈ 4 (where the aryl phosphate is present almost wholly as the monoanion). The broken line is calculated using eq 1 and the values of C_1/C at varous pH. (We assume for the dissociation constants of the alkyl phenyl phosphates $pK_1 = 1.45$ and $pK_2 = 6.12$, using the known values for phenyl phosphate.[15] These values should be little affected by alkyl substituents; in any event the calculation is not very sensitive to the actual p*K* values used.) As shown in Figure 2 the agreement between experimental and calculated values is satisfactory for hydrolyses of these aryl phosphates, confirming that the monoanion is the predominant reactive species, as has been found for hydrolyses of other aryl phosphates.[3,9] At pH 8 the observed rate for some compounds is a little higher than that calculated (Figure 2), suggesting that there is a small amount of reaction arising from a spontaneous hydrolysis of the dianion or attack of hydroxide ion. These reactions at high pH are more important with the nitrophenyl phosphates.[6-8]

A nitro substituent increases the reactivity of monophenyl phosphate considerably (Tables II–IV), but again the monoanion is the most reactive species at pH 2–6, except at 25° (Figures 3 and 4). The value of k_ψ is generally greater than that predicted from eq 1 (broken line in the figures) because at low pH spontaneous and acid-catalyzed hydrolyses become important.

Substituent Effects upon Reaction of the Monoanion.—Our work confirms the previous observations that the hydrolysis of an aryl phosphate monoanion is assisted by electron-attracting substituents and slightly retarded by electron-donating substituents.[3,9] Bulky *ortho* substituents retard the reaction and 1-naphthyl

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[15] J. O. Chanley and E. Feageson, *J. Am. Chem. Soc.*, **77**, 4002 (1955); cf. A. Desjobert, *Bull. Soc. Chim. France*, 683 (1963).

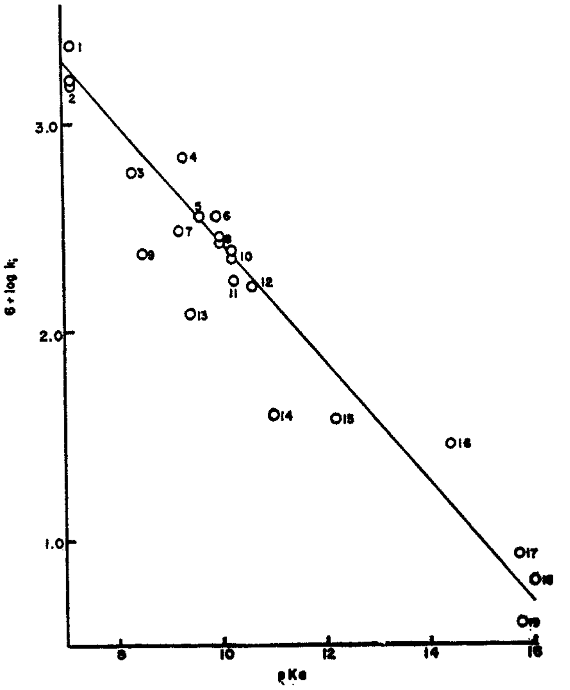

Figure 5.—Plot of the logarithm of the first-order rate constant for hydrolysis of the monoanions of monoalkyl and aryl phosphates against pK_a of the alcohol or phenol at 25°: 1, *o*-nitrophenyl; 2, *p*-nitrophenyl; 3, *m*-nitrophenyl; 4, *p*-carboxyphenyl; 5, 2-naphthyl; 6, *m*-carboxyphenyl; 7, *p*-chlorophenyl; 8, phenyl; 9, *o*-chlorophenyl; 10, *p*-tolyl; 11, *p*-*t*-butylphenyl; 12, 2,6-dimethylphenyl; 13, 1-naphthyl; 14, *o*-*t*-butylphenyl; 15, 2,6-di-*t*-butyl-4-methylphenyl; 16, 2-glyceryl; 17, methyl; 18, ethyl phosphate; 19, phosphoric acid (oxygen exchange). The rate constants were taken from this work or from ref 3 and 9. The values of pK_a were taken from "The Handbook of Chemistry and Physics," R. C. West, Ed., 45th ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1964; G. B. Barlin and D. D. Perrin, *Quart. Rev.* (London), **20**, 75 (1966); P. Deinerseman, J. P. Lechartier, R. Reynand, A. Cheutin, R. Royer, and P. Rumpf, *Bull. Soc. Chim. France*, 2559 (1963); G. Kortum, W. Vogel, and K. Andrussow, "Dissociation Constants of Organic Acids in Aqueous Solution," Butterworths and Co. Ltd., London, 1961; L. A. Cohen and W. M. Jones, *J. Am. Chem. Soc.*, **85**, 3397 (1963); P. Ballinger and F. A. Long, *ibid.*, **82**, 795 (1960).

is less reactive than 2-naphthyl phosphate,[9] but the effect is not large, as it would have been had the reaction involved a bimolecular substitution on phosphorus. There is a linear free-energy relation between the hydrolysis of the monoanion and the dissociation constant of the corresponding phenols or alcohol, as shown in Figure 5, where we plot log k_1 against pK_a. The slope of the straight line is -0.32 and the fit is satisfactory for the hydrolyses of a large number of monoalkyl and aryl phosphates and even for the oxygen exchange of phosphoric acid.[16]

Our observations are consistent with a mechanism of hydrolysis in which phenol rather than phenoxide ion is eliminated and the preferred mechanism involves proton transfer to the phenolic oxygen atom and elimination of metaphosphate ion. This proton transfer could take place directly or more probably through a water molecule.[9] (For the hydrolysis of the dianions of the dinitrophenyl phosphate, where a phenoxide is eliminated rather than a phenol, the rate is much more sensitive to electronic effects than in the present system; *e.g.*, for hydrolyses of the 2,4-, 2,5-, and 2,6-dinitrophenyl phosphate dianions, a plot of log k against $-\mathrm{p}K_A$ of the phenol has a slope of ~1.7.)[7]

The linear free-energy relation between reaction rate and acid strength of the phenol is obeyed reasonably well even by *ortho*-substituted phenyl phosphates, suggesting that bulky *ortho* substituents affect both phosphate hydrolysis and acid dissociation of the phenol or alcohol similarly. They decrease base strength by hindering solvation of the anion[17] and therefore we suppose that in hydrolysis of the monoanion they hinder the hydrogen bonding to the phenolic oxygen atom. Breaking of the phosphorus oxygen bond is not the only requirement for hydrolysis; if it were we should expect to observe large substituent effects upon reaction rate and steric acceleration by bulky *ortho* substituents.

The Arrhenius parameters of the monoanion hydrolyses (Table VIII), like the reaction rates, are relatively insensitive to substituent effects although the activation energy is decreased by the substitution of electron-attracting groups. The energies of activation are close to 30 kcal mole^{-1} and the entropies of activation are approximately zero.

TABLE VIII

ARRHENIUS PARAMETERS FOR HYDROLYSIS OF MONOARYL PHOSPHATES

Reaction	Substrate	*E*, kcal mole^{-1}	$\Delta S^{\ddagger}$, eu
Monoanion	*o*-Nitro	28	+5
Monoanion	*m*-Nitro	31	+4
Monoanion	*p*-Nitro	27	−1
Monoanion	*o*-Chloro	27	−4.5
Monoanion	2,6-Dimethyl	30	+2.5
Acid[a]	*o*-Nitro	20	−23
Acid[a]	*m*-Nitro	20	−25

[a] Calculated at the rate maximum.

Acid Hydrolysis.—Our results confirm the earlier conclusion that the hydrolysis of a monoaryl phosphate is catalyzed by aqueous acids only when the aryl group contains a powerful electron-attracting substituent, *e.g.*, nitro or acetyl.[3–5] In the earlier work, only *para* substituents were used, but the present results show that hydrolysis is also acid catalyzed when an *o*- or *m*-nitro group is present. Plots of k_ψ against acid concentration have maxima, which for the monoaryl phosphates occur at 3–5 *M* acid (Figures 3 and 4). The positions of the rate maxima and the maximum values of k_ψ depend upon the catalyzing acid and, as in other systems, we find the effectiveness of acids to be HCl > H_2SO_4 > $HClO_4$.[3,7] The observation of an acid hydrolysis of *m*-nitrophenyl phosphate shows that conjugation between the strongly electron-attracting group and the phenolic oxygen atom is not essential for acid catalysis in a monoaryl phosphate in water, although the contribution of the acid hydrolysis is much less important for *m*-nitrophenyl phosphate than for *o*- and *p*-nitrophenyl and the dinitrophenyl phosphates.[3,7] The acid hydrolysis of *m*-nitrophenyl phosphate makes a much smaller contribution to the over-all reaction at 100° than at lower temperatures (Figures 3 and 4 and Table VII) and the activation energies of the acid hydrolyses are lower than those of the monoanions. The activa-

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(16) C. A. Bunton, D. R. Llewellyn, C. A. Vernon, and V. A. Welch, *J. Chem. Soc.*, 2670 (1961).

(17) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, p 233.

tion entropies for the acid hydrolyses are more negative than for the monoanion hydrolyses. No acid hydrolysis has been observed in water with monophenyl phosphates which do not contain nitro or acetyl groups, but it might be possible to observe acid hydrolysis even with these compounds by working at low temperatures, which would favor reactions having low activation energies. However, the hydrolyses would then be inordinately slow. Acid catalysis has been observed in hydrolyses of aryl phosphates in aqueous dioxane.[4]

There is a linear free-energy relation between the rates of the acid hydrolysis and the acid dissociation constants of the nitrophenols and a plot of pK of the nitrophenyl against log k_ψ (at the rate maximum) has a slope of 0.5, showing that electronic effects upon the acid hydrolysis are greater than those upon the hydrolysis of the monoanion.[7]

For the mononitrophenyl phosphate, the activation energies of the acid hydrolyses are lower than for those of the monoanions and the activation entropies are much more negative (Table VIII), as expected for acid hydrolyses in which the transition state is heavily hydrated.[3,7] Bunnett and Olsen have recently suggested that the kinetic dependence of an acid hydrolysis upon acidity can usefully be characterized by the value of φ, which is the slope of a plot of log $k_\psi + H_0$ against $H_0 + \log C_{\mathrm{H}^+}$.[18] The values of φ are o-nitrophenyl phosphate in perchloric acid, $\varphi = 1.15$ at 25° and 1.03 at 73°; m-nitrophenyl phosphate in perchloric acid, $\varphi = 1.28$ at 25 and 73°, and in HCl, $\varphi = 1.38$ at 73°. They are very similar to those for p- and the dinitrophenyl phosphates[3,7] and, like the values of the Arrhenius parameters, indicate that the transition state is much more hydrated than the initial state.

Reaction of the Undissociated Aryl Phosphate.—Plots of k_ψ against pH for the hydrolyses of o-, m-, and p-nitrophenyl phosphate at 73° show well-defined minima at pH 1–2. However, Desjobert found no minimum in a plot of k_ψ against pH for the hydrolysis of p-nitrophenyl phosphate at 37°.[5] He assumed, we believe incorrectly, that it arose from incursion of a carbonium ion mechanism, as in the hydrolyses of glucose 1- and t-butyl phosphates.[19] We find similar behavior for o- and p-nitrophenyl phosphate at 25° (Figure 3 and Tables II and III). However, there are minima in plots of k_ψ *vs.* pH for hydrolysis of m-nitrophenyl phosphates even at this temperature (Figure 4).

Although the predominant reactions of monoalkyl phosphates are the spontaneous hydrolysis of the monoanion and an acid-catalyzed hydrolysis, a spontaneous hydrolysis of the undissociated alkyl phosphate is generally sandwiched in between them and, occasionally, it may be more important than hydrolysis of the monoanion. (In most of these special cases, a carbonium ion is generated.)[19]

The spontaneous hydrolyses of o- and p-nitrophenyl phosphate must have lower activation energies than have the monoanion hydrolyses and probably involve nucleophilic attack by a water molecule upon the undissociated aryl phosphate and should be assisted more by an *ortho* and *para* than a *meta* substituent. It is not possible to evaluate the contribution of this spontaneous hydrolysis, because although we can allow for the contribution of the monoanion hydrolysis, we do not know the exact form of the dependence of the rate of the acid hydrolysis upon acid concentration at low acid concentrations. The observation of a spontaneous hydrolysis only with o- and p-nitrophenyl phosphates and not with the *meta* isomer shows that this reaction must be more sensitive to mesomerically electron-attracting substituents than either the acid-catalyzed or monoanion hydrolyses.

Registry No.—Phenyl phosphate, 701-64-4; p-methylphenyl phosphate, 6729-45-9; o-t-butylphenyl phosphate, 13388-85-7; p-t-butylphenyl phosphate, 13421-39-1; 2,6-dimethylphenyl phosphate, 13388-86-8; 2,6-di-t-butyl-4-methylphenyl phosphate, 13388-87-9; o-chlorophenyl phosphate, 13428-19-8; p-chlorophenyl phosphate, 13388-88-0; p-nitrophenyl phosphate 330-13-2; o-nitrophenyl phosphate, 6064-84-2; m-nitrophenyl phosphate, 13388-91-5.

Acknowledgments.—We thank Dr. J. H. Fendler for assistance in measuring the rates of some of these hydrolyses.

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

[19] C. A. Bunton, D. R. Llewellyn, K. G. Oldham, and C. A. Vernon, *J. Chem. Soc.*, 3588 (1958); A. Lapidot, D. Samuel, and M. Wiess-Broday, *ibid.*, 637 (1964); F. Cramer, *Angew. Chem.*, **73**, 344 (1961).