outlet to a trap containing a concentrated solution of sodium hydroxide for absorption of gaseous HCl. Charged to the flask were 40.9 g. (0.25 mole) of ethyltrichlorosilane, 48.1 g. (0.25 mole) of ethyltriethoxysilane and 500 ml. of reagent-grade benzene. The reactants were cooled to 5° in an ice-bath. Water (27.0 ml.) was added during 17 minutes at 3.5-11°, with continuous stirring. The reaction mixture was then heated slowly to facilitate the removal of hydrogen chloride. During 85 minutes, the boiling point rose from 44 to 68°. A Dean-Stark trap now replaced the addition tube. The aqueous layer which was separated also contained ethanol, benzene, and some HCl; total volume, 62.3 ml. The gain in weight of the caustic absorber approached the theoretical value. The solvents were distilled (480 ml., b.p. to 86°). The residue (74.4 g.) was filtered from a small amount of gel and distilled using the Claisen-type head previously described. Three fractions were taken: (1) 6.7 g., b.p. 138-149°, 7.0% $-OC_2H_5$; (2) 2.6 g., b.p. 149-161°, 7.1%. $-OC_2H_5$; (3) 3.7 g., b.p. 161-176°, 6.2% $-OC_2H_5$. The residue, a stiff, balsam-like material, weighed 26.5 g. and contained 5.3% $-OC_2H_5$.

Hydrolysis in Ethanol Solution.—One-half mole (96.2 g.) of ethyltriethoxysilane and 500 ml. of absolute ethyl alcohol were charged to the reaction flask. The water (27.0 ml. containing 2.5 ml. of 0.5 *N* HCl) was added in 12 minutes at 27-33°. Heat was applied slowly; then the reaction mixture was maintained at the boiling point (78°) for 3 hours. A still-head was attached, and alcohol was distilled until the liquid temperature reached 93°. Vacuum distillation followed immediately, giving: 7.5 g., b.p. 143-154° at 0.5 mm., 20.1% $-OC_2H_5$; 3.5 g., b.p. 166-180° at 0.5 mm., 15.5% $-OC_2H_5$; 34.4 g. residue, 14.0 $-OC_2H_5$.

Alkaline hydrolysis in ethanol was carried out similarly, the HCl being replaced by an equivalent volume of 0.5 *N* sodium hydroxide. There was some gel present after the heating period. The mixture was cooled and blown with CO_2 for 1.5 hours to remove alkali. The carbonate formed and the gel present were removed by filtering through a bed of Dicalite. After ethanol was distilled, a second filtration produced 1-2 g. more of gel. The concentrate was washed several times with water. On vacuum distillation, only an inconsequential yield of liquid was obtained. The gelled residue weighed 22 to 32 g. on several trials. Using less than three molar equivalents of water, however, distillable reaction products were obtained, as described previously.

Acknowledgment.—The distillations involving the spinning-band columns were carried out by E. M. Hadsell and Mrs. Dorothea Ladd. The ultimate analyses and molecular-weight determinations were carried out by various members of the Analytical Chemistry Unit of this Laboratory. C. A. Hirt is responsible for the infrared spectrograms. We wish to thank all these individuals for their assistance.

Schenectady, N. Y.

[Contribution from the Department of Chemistry, The Mount Sinai Hospital]

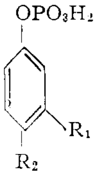
The Mechanism of the Hydrolysis of Organic Phosphates. III. Aromatic Phosphates[1]

By J. D. Chanley and Edward Feageson

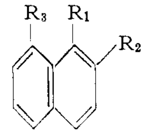
Received February 3, 1955

The rates of the hydrolysis, over the *p*H range 1-10, of the following six compounds: phenyl (I), *m*-carboxyphenyl(II), *p*-carboxyphenyl(III), α-naphthyl (IV), β-naphthyl (V) and 8-carboxy-α-naphthyl (VI) phosphates have been determined. First-order kinetics were observed in each instance. All six compounds exhibited a maximum rate of hydrolysis in an intermediate *p*H range, were quite stable at *p*H of 1, and completely stable at *p*H of 8 and above. An explanation for the observed *p*H dependency is offered and the influence of the carboxyl group is discussed. The *p*H *vs.* hydrolysis rate curve for compound VI differs fundamentally from that observed with the other compounds, but resembles that of *o*-carboxy-substituted aromatic phosphoric acid esters. This observation, in conjunction with other evidence, supports the view that the hydrolysis of compound VI proceeds, in contradistinction to compounds I through V, by a "participation" mechanism which involves the attack of the carboxylate anion on the phosphorus with formation of a seven-membered ring "transition state." The various ionization constants of compounds I through VI have been determined and the entropies and heats of activation evaluated.

In continuation of our studies[2a,b] on the hydrolysis of aromatic phosphoric esters, we wish to report on the hydrolysis of the following six compounds: phenyl (I), *m*-carboxyphenyl (II), *p*-carboxyphenyl (III), α-naphthyl (IV), β-naphthyl (V) and 8-carboxy-α-naphthyl (VI) phosphate to the parent phenol or naphthol and phosphoric acid. Compounds I, II and III were chosen for study, since they form—in conjunction with the previously investigated *o*-carboxyphenyl phosphate (salicyl phosphate)—a series, which lends itself particularly well to a study of the effect exerted on the hydrolysis by the intact carboxyl group and carboxylate anion. Compounds IV and V are related to *o*-carboxynaphthyl phosphates previously studied, while with compound VI the carboxyl group, albeit in the other ring, is so close to the phosphate grouping as to suggest "a priori" the possibility of behavior analogous to the *ortho* position.



I, $R_1 = H$; $R_2 = H$
II, $R_1 = COOH$; $R_2 = H$
III, $R_1 = H$; $R_2 = COOH$



IV, $R_1 = OPO_3H_2$;
$R_2 = H$; $R_3 = H$
V, $R_1 = H$;
$R_2 = OPO_3OH$; $R_3 = H$
VI, $R_1 = OPO_3H$;
$R_2 = H$; $R_3 = COOH$

***p*H Dependency and Rates.**—The rates of hydrolysis of compounds I through VI were determined at 80° over the *p*H range 1-10 in buffered medium of ionic strength $\mu = 0.1$ by analysis for liberated phosphoric acid. In each instance first-order kinetics obtained throughout the course of the reaction. All six compounds exhibited a maximum rate of hydrolysis in an intermediate *p*H region, were quite stable at *p*H *ca.* 1, and completely stable at *p*H of 8 and above (see Figs. 1

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[1] This work was supported in part by a grant from the National Science Foundation. The material was presented in part at the Annual Meeting of the American Chemical Society in New York City, Division of Organic Chemistry, on September 16, 1954. For the preceding papers in this series see reference 2a,b.

[2] (a) J. D. Chanley, E. M. Gindler and H. Sobotka, This Journal, **74**, 4347 (1952); (b) J. D. Chanley and E. M. Gindler, *ibid.*, **75**, 4035 (1953).

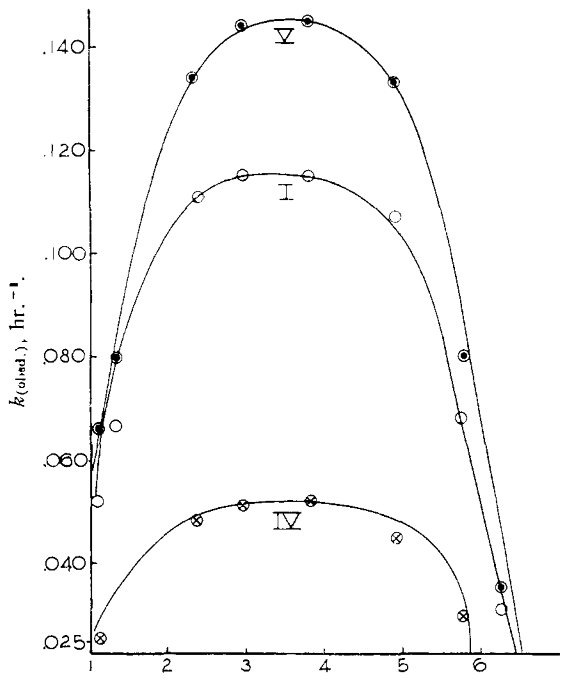


Fig. 1.—Observed rates of hydrolysis in hours^{-1} at 80° for compounds I, IV and V at various pH values are indicated by ○, ⊗, ⊙, respectively. The solid curve is the theoretical one.

and 2). The same reasoning as before[2a,b] was employed in the elucidation of the pH dependency for the hydrolysis of these compounds. The rate equation, deduced to describe the observed rate of hydrolysis at any pH for compounds I, IV and V is

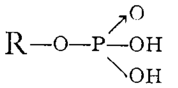
$$k_{\text{obsd.}} = k_1M_1 \qquad \text{(a)}$$

and for compounds II, III and VI

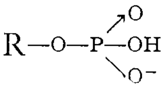
$$k_{\text{obsd.}} = k_1M_1 + k_2M_2 \qquad \text{(b)}$$

where in both equations k_1 is the specific rate constant for the hydrolysis of the monoionic form, while M_1 is the mole fraction of this form at the particular pH; k_2 (referring only to the carboxy substituted compounds) is the specific rate constant associated with the diionic form and M_2 the mole fraction of this form at the particular pH.

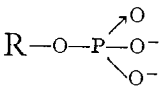
Ionic Species


$\mathrm{R{-}O{-}P(O)(OH){-}OH}$

Un-ionized (M_0)

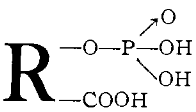

$\mathrm{R{-}O{-}P(O)(O^-){-}OH}$

Monoionic (M_1)

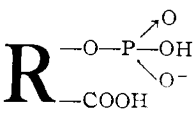

$\mathrm{R{-}O{-}P(O)(O^-){-}O^-}$

Diionic (M_2)

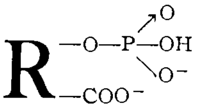
R = phenyl(I), α-naphthyl (IV), β-naphthyl (V)



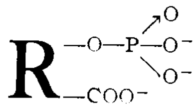
Un-ionized (M_0)



Monoionic (M_1)



Diionic (M_2)



Triionic (M_3)

R = phenyl (II, III), R = naphthyl (VI)

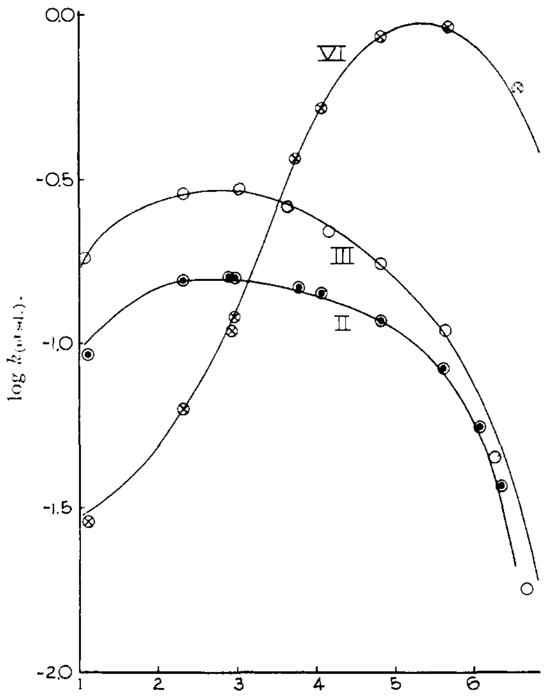


Fig. 2.—Logarithms of the observed rates of hydrolysis at 80° for compounds II, III and VI at various pH values are indicated by ⊙, ○ and ⊗, respectively. The solid curve is the theoretical one.

Only at pH 1 do we encounter a significant concentration of un-ionized material; at this pH, the rate of hydrolysis is substantially accounted for by the monoionic species present.

The specific rate constants k_1 and k_2 were obtained in the same manner as previously described.[2a,b] The determination of the various ionization constants (K_1, K_2, K_3) (*cf.* Table II) at ionic strength $\mu = 0.1$ makes possible the calculation of the mole fractions (M_1, M_2, etc.)[2a,b] at any pH. The specific rate constants k_1 of the unsubstituted phosphates were computed from the observed rate constants at pH 3.8. At this pH M_1 is *ca.* 99%. For the carboxy substituted phosphoric acid esters (II, III and VI) k_1 and k_2 were evaluated from the observed rate constants at pH 2.3 and 4.8. The observed rates of hydrolysis at a number of other pH's then were compared with the values calculated from equations a and b (*cf.* Table I, Figs. 1 and 2). The agreement between observed and calculated values is very satisfactory. In general the greater deviations occur at higher pH's since small changes in pH effect a considerable percentage change in the mole fraction of the reactive species. The various specific rate constants are given in Table II.

It should be mentioned at this point that this agreement was obtained for runs made at 80°, whereas the mole fractions were calculated from the pK's determined at 26 ± 1°. This is permissible if neither the pK's nor the pH's of the buffer change substantially with temperature or if the changes in the pK's with temperature are compensated for by concomitant changes in the pH of the buffer. The rates were much too slow to be accurately

TABLE I

HYDROLYSIS OF COMPOUNDS I–VI[a]

pH	M_0	M_1	M_2	M_3	$k_{\text{obsd.}}$ hr.$^{-1}$ × 1000	$k_{\text{calcd.}}$ hr.$^{-1}$ × 1000	M_0	M_1	M_2	M_3	$k_{\text{obsd.}}$ hr.$^{-1}$ × 1000	$k_{\text{calcd.}}$ hr.$^{-1}$ × 1000	pH	M_0	M_1	M_2	M_3	$k_{\text{obsd.}}$ hr.$^{-1}$ × 1000	$k_{\text{calcd.}}$ hr.$^{-1}$ × 1000
	Phenyl phosphate (I)						α-Naphthyl phosphate (IV)							β-Naphthyl phosphate (V)					
1.10	0.44	0.56	..		52.3	65.1	0.43	0.57	..		25.3	29.6		0.59	0.41	..		68.5	60.3
1.31	.33	.67	..		66.5	78.3	..	..	..		...	...		..	..	..		...	...
2.37	.64	.96	..		111	111	.05	.95	..		48.3	49.8		.12	.88	..		134	134
2.96	.01	.99	..		115	115	.10	.99	..		51.4	51.6		.03	.97	..		144	143
3.83	..	.99	0.01		115	(115)	..	.99	0.01		52.0	(52.0)		..	.99	0.01		145	(145)
4.90	..	.81	.09		107	105	..	.93	.07		45.0	48.6		..	.91	.09		133	134
5.74	..	.58	.42		68.2	67.4	..	.61	.36		29.9	33.5		..	.60	.40		80.1	87.6
6.26[b]	..	.29	.71		31.1	34.2	..	..	..		...	...		..	.31	.69		35.4	46.0
	3-Carboxyphenyl phosphate (II)						4-Carboxyphenyl phosphate (III)							8-Carboxy-α-naphthyl phosphate (VI)					
1.11	0.36	0.64	..	..	92.3	103	0.36	0.64	..	..	181	196	1.11	0.22	0.58	..	..	28.7	30.8
2.34	.02	.95	0.03	..	157	(157)	.06	.93	0.01	..	286	(286)	2.34	.04	.94	0.02	..	66.4	(66.4)
2.91[b]	..	.91	.09	..	159	157	..	..	..	..	...	...	2.93[b]	.01	.93	.06	..	109	114
2.97	..	.89	.10	..	157	156	.01	.93	.05	..	295	291	2.97	.01	.92	.07	..	121	120
3.64	..	..	..	..	...	...	..	.78	.21	..	259	268	3.73	..	.70	.30	..	363	347
3.77	..	.58	.42	..	147	143	..	..	..	..	...	...	4.06[b]	..	.52	.48	..	518	521
4.07[b]	..	.40	.59	0.01	142	136	..	..	..	..	...	...	4.80	..	.16	.83	0.01	857	(857)
4.16	..	..	..	..	...	...	..	.52	.47	0.01	218	227	5.67	..	.02	.87	.11	903	894
4.82	..	.10	.83	.07	116	(116)	..	.18	.77	.15	167	(167)	6.55[b]	..	..	.51	.49	591	527
5.62	..	.10	.65	.34	83.8	80.8	..	.03	.69	.28	107	110							
6.05[b]	..	..	.41	.58	55.3	50.0	..	..	..	..	...	...							
6.26[b]	..	..	..	..	...	...	..	..	.36	.64	41.9	53.8							
6.34[b]	..	..	.27	.73	36.8	31.9	..	..	..	..	...	...							
6.67[b]	..	..	..	..	...	...	..	..	.17	.83	17.8	25.7							

[a] Temperature 80.0 ± 0.05° except for β-naphthyl phosphate (V) where it is 80.6 ± 0.05°. [b] Self-buffered medium (see Experimental); pH *ca.* 1 obtained with 0.1 N HCl. Computations based on figures in parentheses.

TABLE II

REACTION RATES, DISSOCIATION CONSTANTS,[a] HEATS AND ENTROPIES OF ACTIVATION

Cmpd.	Dissociation constants			pH of reacn.	Calcd. specific rate constants of hydrolysis, hr.$^{-1}$ × 1000				ΔH‡,– kcal./mole	ΔS‡,– e.u.
					80.0°[b]		70.0°			
	pK_1	pK_2	pK_3		k_1	k_2	k_1	k_2		
I	1.00	5.88	..	3.83	116	..	34.7	...	28.4	+ 0.9
II	0.85	3.91	5.90	2.36	161	..	50.3	...	27.3	− 1.4
				4.82	....	120	..	37.8	27.1	− 2.6
III	.88	4.20	5.90	2.31	307	..	94.5	...	27.7	+ 0.9
				4.84	....	147	..	46.7	26.8	− 3.1
IV	.97	5.85	..	3.82	52.4	..	14.6	...	30.0	+ 4.1
V	1.28	5.83	6.57	3.85	147[c]	..	39.7	...	28.9	+ 5.5
VI	0.97	4.08	6.57	2.34	52.0	..	14.3	...	30.4	+ 5.0
				4.80	....	1027	..	284	30.3	+10.6

[a] Dissociation constants were determined at 26 ± 1° (see Experimental). [b] Temperature variation ±0.05°. [c] This value was obtained at 80.6 ± 0.050.

evaluated at *ca.* 30°. However, a qualitative determination of the rates of hydrolysis of these compounds at various pH's at 37° showed the same pH *vs.* hydrolysis rate relationship as observed at 80°. This we take as confirming our view that, although the curves in actuality may be shifted along the pH axis, the concentrations of the various ionic species (mole fractions) evaluated at 26° substantially reflect those which would be calculated from ionization constants and pH measurements of the buffer at 80°.

With the unsubstituted esters, where only the monoionic species need be considered, the three curves have the same general shape, since their ionization constants are so much alike (*cf.* Table II). The broadness of the maximum results from the wide separation of pK_1 and pK_2. Compounds II, III and VI are discussed below.

Discussion.—From this and our previous investigations,[2a,b] we note the following common features in the hydrolysis of aromatic phosphoric acid esters. The reactions are neither hydrogen ion nor hydroxyl ion catalyzed over the pH region 1–10; a maximum rate is observed where the phosphoric acid moiety exists in the single charge form $(\text{–OPO}_3\text{H})^-$, while the fully ionized species $(\text{–OPO}_3)^=$ is completely stable and the un-ionized form $(\text{–OPO}_3\text{H}_2)$ is relatively stable toward hydrolysis. A similar observation has been made by Desjobert[3] in his investigations of a few aliphatic phosphoric acid esters. The complete stability of simple phosphates in alkaline medium and the difficulty of hydrolysis in acid (pH *ca.* 1) has been observed by numerous investigators.[4a,b,c] The carboxyl group on the aromatic nucleus in no way alters the above generalizations. The following is offered as a possible explanation for these differences. If we dismiss, as unlikely, the supposition that the rate of the reaction is governed by simple dissociation of the phosphate group, the mechanism of the hydrolysis may be described as the attack

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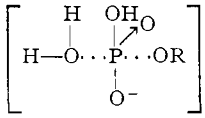
(3) A. Desjobert, *Compt. rend.*, **224**, 575 (1945); *Bull. soc. chim.*, 809 (1947).

(4) (a) G. M. Kosolapoff, "Organic Phosphorus Compounds," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 233; (b) E. A. Peterson and H. A. Sober, THIS JOURNAL, **76**, 169 (1954); (c) E. Cherbuliez and J. P. Lieber, *Helv. Chim. Acta*, **35**, 2589 (1952).

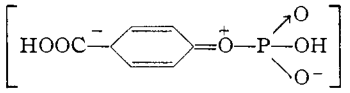
of a nucleophilic reagent on the phosphorus and the breakdown of the "transition state"



to the parent phenol and phosphoric acid.[5]

The effective nucleophilic agent in the case of compounds I through V is water.[6] The supposition that the oxygen of the water dipole is repelled by the high negative charge of the completely ionized phosphate grouping is sufficient reason to explain the stability of this group and suggests that the ease of approach of the water molecule would decrease from the un-ionized to the monoionic to the fully ionized form. However, the assumption that the ease of approach of the nucleophilic reagent and the formation of the new O–P bond is the only factor governing the hydrolysis leads to the erroneous prediction that the un-ionized ester would hydrolyze fastest. Obviously, another parameter whose effect is opposite to the one just discussed must come into play. In the formation of the "transition state" a stretching, prior to cleavage of the oxygen to phosphorus bond, takes place. It is presumed that the ease of stretching will be a function of the strength of this bond in the various ionic forms under discussion and that the greater the negative charge on the phosphate grouping, the stronger will be the repulsive force acting on the oxygen attached to both aromatic nucleus and the phosphorus, and thus the weaker will be the bond. In passing from the doubly charged to the singly charged to the un-ionized form the strength of the O–P bond will increase, while the ease of stretching will decrease. Whereas in the fully ionized form the resistance of the O–P bond to rupture is governed primarily by the repulsion of the water dipole, the relatively high resistance to cleavage in the case of the un-ionized form is due to the greater "intrinsic" strength of this O–P bond. With the monoionic form neither of these two features assume such magnitude as to effectively impede the hydrolysis and, consequently, the fastest cleavage occurs with this form.

Effect of the Carboxyl Group.—In the hydrolysis of the carboxy-substituted phosphates, *p*-carboxyphenyl (II) and *m*-carboxyphenyl (III) phosphate, the attacking agent over the *p*H-range investigated is invariably the water molecule; the carboxyl group is present in this *p*H range as the undissociated form, as the carboxylate anion or as both; the only form of the phosphate grouping, subject to splitting, remains the same, namely, the singly charged group. We have then an excellent opportunity to evaluate the effect on the rate of hydrolysis of the intact carboxyl group as compared with the carboxylate anion, and to compare the magnitude of this effect, with reference to the position of the group on the aromatic nucleus. An examination of the specific rate constants of the hydrolysis of compounds I, II and III reveals the following situation: the specific rate constants of the diionic form (M_2) of both compound II (k_2 0.120 hr.$^{-1}$) and compound III (k_2 0.147 hr.$^{-1}$) show but a slight increase over the rate of phenyl phosphate (I) (k_1 0.116 hr.$^{-1}$) in the case of compound III. The specific rate constants for the monoionic forms (M_1) for both compounds II (k_1 0.161 hr.$^{-1}$) and III (k_1 0.307 hr.$^{-1}$) are larger than those observed with phenyl phosphate and with the related diionic forms. This result may be qualitatively accounted for by a consideration of an "inductive" effect. The greater tendency of a carboxyl group compared to a carboxylate anion to withdraw electrons from the ring facilitates the rupture of the O–P bond. The larger increase in k_1 for the *para* compound III (*ca.* 3 times over that of phenyl phosphate) as compared with the *meta* compound II may be associated with the former's greater enhancement of electron withdrawal in compound III through an increase of resonance of the oxygen, bound to both the phosphorus and the ring. This is a consequence of the closer proximity of the electron-attracting carboxyl group to the negative charge on the benzene nucleus when in *para* position



With the carboxylate anion no such effect would be anticipated, and the *meta* and *para* positions thus become practically equivalent in the diionic forms. In line with this postulation it may be noted that the second ionization constant of compound II (pK_2 3.91) is larger than that observed with the *para*-substituted derivative (compound III) (pK_2 4.20); while the third ionization constants of the two compounds are the same. Of interest in this connection is the case of *m*- and *p*-carboxybenzenephosphonic acids. In these instances, where π-electron interaction of the phosphorus and the benzene ring are, if not altogether non-existent, negligible,[7] the *pK* of the *p*-carboxy- (3.95) is slightly smaller than that of the *m*-carboxy (4.03) benzenephosphonic acid. The greater speed of hydrolysis of *p*-carboxyphenyl sulfate over that of *m*-carboxyphenyl sulfate has been reported.[8]

8-Carboxy-α-naphthyl Phosphate.—In contrast to compounds II and III, compound VI shows a maximum in the rate *vs.* *p*H curve at that *p*H where it exists predominantly in the diionic form (M_2) ($k_2 >> k_1$). To postulate the same mechanism for the hydrolysis of compounds I, II or III, and

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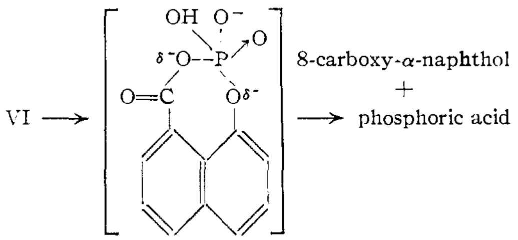
[5] S. S. Stein and D. E. Koshland, Jr., *Arch. Biochem. Biophys.*, **39**, 229 (1952). We do not necessarily imply a true pentacovalent intermediate for our "transition state."

[6] The two other nucleophilic agents, present in the reaction mixture, are the hydroxyl ions and the anions of the buffers employed. These are relatively unimportant, since changes in type of buffer or buffer concentration do not change the rate significantly, while the $(OH)^-$ ion, although a more powerful nucleophilic reagent than water, attains a significant concentration only at those *p*H's where the phosphate exists in the stable fully ionized form. Presumably, the high negative charge surrounding the phosphorus in the fully ionized form repels the attack of the hydroxyl ion.

[7] H. H. Jaffe, L. D. Freedman and G. O. Doak, THIS JOURNAL, **75**, 2209 (1953).

[8] G. N. Burckhardt, W. G. K. Ford and E. Singleton, *J. Chem. Soc.*, 17 (1936); G. N. Burckhardt, C. Horrax and D. J. Jenkins, *ibid.*, 1649, 1654 (1936). In this connection it may be noted that the hydrolysis rate of β-naphthyl > phenyl > α-naphthyl sulfate, determined by these authors, parallels that observed in the phosphate series.

VI is obviously inconsistent. In fact, the shape of the hydrolysis rate *vs.* *p*H curve of VI is the same as that encountered with *o*-carboxy-substituted aromatic phosphoric acid esters.[2a,b] In the latter instances, to account for both the speed and the *p*H dependency, a participation mechanism for the hydrolysis was presented. With compound VI, the absolute rate of hydrolysis is considerably smaller than that observed with the related 2-carboxy-α-naphthyl phosphate, but the quotient k_2/k_1 falls in line with the fast splitting *o*-carboxy phosphates. This we take as good evidence that a "participation" mechanism obtains also in the *peri* isomer. In line with this reasoning we observe that the specific rate constant associated with the hydrolysis of the monoionic form (M_1) of compound VI is the same as that obtained for α-naphthyl phosphate, thus eliminating the possibility that a simple steric effect of the carboxyl group in 8-position is the driving force of the reaction. The fact that the relative increase in rate occurs in that *p*H region where the di-ion prevails emphasizes the active involvement of the carboxylate anion in the mechanism of the hydrolysis. Furthermore, the hydrolysis of the diionic form of all *o*-carboxy substituted aromatic phosphates is considerably increased in the presence of dioxane and formamide,[9] whereas compounds I through V do not show this effect. Compound VI again gives the same relative increase in rate with dioxane and formamide. The relative slowness of the hydrolysis of compound VI could be ascribed to the intrinsic difficulty in forming the required seven-membered "transition state."



Energies and Entropies of Activation.—The rates of hydrolysis for all six compounds were determined at 70° at the same *p*H chosen for the evaluation of the specific rate constant at 80°. The heat and entropy of activation for both the monoionic and diionic forms were calculated from the Eyring equation.[10] Of significant interest is the high positive entropy (+10 e.u.) associated with the hydrolysis of the diionic form of compound VI. We previously have noted in the series of *o*-carboxynaphthyl phosphates, where the "participation" mechanism is operative, the highest positive entropy of activation was exhibited by 1-carboxy-β-naphthyl phosphate, which in turn hydrolyzed most slowly. The latter phenomenon has been correlated with the restriction in rotation of the carboxylate group.[2b] The same situation exists in compound VI. In general the enormous increase in the speed of hydrolysis observed with *o*-carboxy substituted aromatic phosphates over that of the corresponding non-substituted and *m*- or *p*-carboxy-substituted phosphate is associated primarily with a large decrease in the energy of activation accompanying the change in the mechanism of the hydrolysis.

Experimental

Phenyl Phosphate.—A mixture of phenyl phosphorodichloridate (46.6 g., 0.222 mole), b.p. 122° at 13 mm., chloroform (170 ml.) and water (8.0 g., 0.44 mole) was stirred at room temperature for 2–3 days until a homogeneous solution was obtained. The solution was concentrated to 100 ml. and allowed to stand overnight in the cold. The crystalline phenyl phosphate was collected and recrystallized from chloroform; yield 20 g., m.p. 100–101°, reported 97–98°[11]; neut. equiv.: calcd. 87.1, found 86.9.

α-Naphthyl phosphate (IV) was prepared according to Friedman[12] and recrystallized several times by adding 20 parts of boiling benzene to a hot solution of one part acid and 1.2 parts of acetone; m.p. 157–158°, reported 155–157°.

β-Naphthyl phosphate (V) was prepared according to the latter authors[11] and recrystallized several times by addition of 2.5 volumes of hot chloroform to a hot solution of 1 part of acid in 1.3 parts of acetone; m.p. 177–178°, reported 176–177°.

***p*-Carboxyphenyl Phosphate (III).**—The trichloride COCl-4-C_6H_4-1-$OPOCl_2$ (10.1 g., 0.0372 mole), b.p. 145–146° at 2.5 mm. (prepared essentially according to Anschuetz and Moore[13] and rigorously purified by several fractionations) was dissolved in benzene (17 ml.) and acetone (15 ml.); water (2.0 ml., 0.11 mole) was added dropwise with vigorous stirring and the mixture, after stirring overnight, was allowed to stand another day. The crystalline precipitate was removed by filtration, washed thoroughly with benzene, air-dried, then washed with dry ether, and dried in high vacuum over P_2O_5 and KOH; yield 7.2 g., 90%, m.p. 193° dec., reported 201°.[13] The product was found to be analytically pure.

Anal. Calcd. for $C_7H_7O_6P$: C, 38.54; H, 3.24; P, 14.20; neut. equiv., 72.7. Found: C, 38.78; H, 3.75; P, 14.19; neut. equiv., 71.6.

***m*-Carboxyphenyl phosphate (II)** was prepared in 90% yield from the trichloride COCl-3-C_6H_4-1-$OPOCl_2$ of b.p. 142° at 1.5 mm. in an analogous fashion to the previous preparation, except that the acetone was omitted and the mixture stirred for 3 days; m.p. 193.5° dec. reported 200°.[13]

Anal. Calcd. for $C_7H_7O_6P$: C, 38.54; H, 3.24; neut. equiv., 72.7. Found: C, 38.43; H, 3.36; neut. equiv., 71.6.

8-Carboxy-α-naphthyl Phosphate (VI).—Naphthostyril, prepared from α-naphthylimide according to the direction of Ullmann and Cassirer,[14] was hydrolyzed and diazotized and the resulting diazonium salt decomposed by boiling water to 8-carboxy-α-naphthol according to Ekstrand[15]; m.p. 173°, reported 169°; neut. equiv.: calcd. 188. Found 186. A mixture of the hydroxy acid (7.5 g., 0.041 mole) and PCl_5 (13 g., 0.062 mole), protected by a calcium chloride tube, was heated on the water-bath at 70–75° for half an hour after the initial vigorous reaction had subsided. Dry benzene (25 ml.) was added to the cooled reaction mixture and unreacted PCl_5 was filtered off. Acetone (10 ml.) was added to the filtrate, followed by the careful addition of water (3.75 ml.) with manual shaking. The mixture was allowed to stand overnight at room temperature and 2 days in the cold. The highly crystalline precipitate, which usually appeared in the interface of the two phases (benzene/acetone-water) was removed by filtration and dried overnight in a vacuum desiccator over KOH; yield 5.5 g., m.p. 173–176°. The mother liquor was extracted 4 times with 100-ml. portions of ether. The ether solution decolorized with Norite and evaporated to dryness. The residue was dissolved in 20 ml. of wet acetone and after benzene had been added (10 ml.), the mixture, on standing in the cold overnight, furnished 0.8 g. of the same material.

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(9) Unpublished observation to be reported on separately.

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The crude product (5.0 g.) was suspended in 30 ml. of dry acetone containing 0.5 ml. of water and the mixture was heated under reflux until practically complete solution was effected. Norite was added and 70 ml. of hot benzene was added to the clear filtrate. On standing overnight in the cold, the compound (3.0 g.) crystallized in cubes as the trihydrate, m.p. 176–179°. This compound is insoluble in dry acetone and was recrystallized twice more for analysis.

Anal. Calcd. for $C_{11}H_9O_6P \cdot 3H_2O$: P, 9.63; neut. equiv., 107.3. Found: P, 9.66; neut. equiv., 108.0.

When 0.4080 g. of the trihydrate was heated *in vacuo* over P_2O_5 for 4 hours at 60° and then at 80° constant weight was obtained in *ca.* 15 hours. The anhydrous material melted at 177–179°; calcd. for loss of 3 moles of water: 0.0674 g., found 0.0667 ± 0.0004.

Anal. Calcd. for $C_{11}H_9O_6P$: C, 49.27; H, 3.38; P, 11.55; neut. equiv., 89.3. Found: C, 49.67; H, 3.48; P, 11.63; neut. equiv., 89.6.

Determination of Ionization Constants.—The determination of the second and third ionization constant were performed, as previously described[2a,b] on solutions which were 0.01 *M* in acid, and to which sufficient KCl was added to bring the ionic strength to $\mu = 0.1$; the first ionization constants were obtained on solutions 0.1 *M* in acid. Since β-naphthyl phosphate was not soluble enough at the latter concentration, the determinations were made in solution containing 10% dioxane. Since both phenyl and α-naphthyl phosphate show an increase of 0.1 *p*H unit on determination of the first ionization constant in 10% dioxane over water, this correction was subtracted from the value in dioxane in the case of the β-compound.

Buffers and Mole Fractions.—The buffer solutions were the same as those used in our previous report.[2a,b] However, at *p*H values of 6 and above, the observed rates showed marked drifts. This effect we attribute to the ineffectiveness of the veronal buffer at 80°. Therefore, these *p*H values were achieved by adding the requisite amount of NaOH to the acid, and under these conditions the observed rate constants showed but small drifts during the progress of the reaction. We term these solutions self-buffered; they are indicated by superscript b in the tables. As a further check, the specific rate constants also were determined with self-buffered solutions at those *p*H values where phthalate buffers were used and the two derived rates checked within experimental error. The mole fractions, M_1, M_2, etc., present at any *p*H were evaluated as previously described, employing the semi-classical ionization constants determined in this work.

Determinations of Rates of Hydrolysis.—The rates of hydrolysis were determined essentially by the method already described,[2a,b] and the specific rate constants (k_1 and k_2) were evaluated from an average of at least 4 runs, at the *p*H's discussed and noted in Table II. The method was modified only to the extent that aliquots of stock solutions containing the acid (1.291×10^{-3} mole per liter) and the requisite amount of buffer and KCl to bring the ionic strength to $\mu = 0.1$ and the desired *p*H were placed in well stoppered tubes and heated in a constant temperature bath for at least 15 minutes to ensure thermal equilibrium. These aliquots then were removed at appropriate intervals and plunged into an ice-bath. Samples were removed and the liberated phosphate determined as previously described. Blanks and solutions containing known amounts of inorganic phosphate were run under identical conditions in parallel experiments, to eliminate any day to day variations in the colored development with the molybdate reagent. The deviation in any particular run was no greater than 3% and the results in repeated runs were the same within experimental error.

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NEW YORK, N. Y.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF KANSAS]

Relative Rates of Migration of Aryl Groups in the Schmidt Reaction of Benzhydrols[1]

BY RAYMOND F. TIETZ[2] AND WILLIAM E. MCEWEN

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A series of five *m*- and *p*-substituted benzhydrols has been prepared and subjected to the Schmidt rearrangement. Product ratios have been determined and relative participation aptitudes assigned to the various aryl groups. These results have been correlated by a suitable adaptation of the Hammett equation.

Introduction

In recent years, mechanism studies have been carried out on Schmidt rearrangements of carboxylic acids,[3] ketones,[4] aldehydes[5] and olefins.[6] Relatively little is known concerning the Schmidt rearrangement of reactive alcohols, however, such reactions having been attempted only with menthol,[7] borneol,[7] benzhydrol,[7,8] fluoren-9-ol,[8] *p*-methylbenzhydrol,[9] triethylcarbinol,[10] and methyldiphenylcarbinol.[6b] Partly to extend the scope of such reactions, but principally for theoretical reasons to be discussed in the following paragraphs, the Schmidt rearrangement of several unsymmetrically substituted benzhydrols has now been investigated.

Experimental[11]

Preparation of Benzhydrols.—*m*-Chlorobenzhydrol, m.p. 38.4–39.6°, was prepared by reduction of *m*-chlorobenzophenone by aluminum isopropoxide (60% yield); reported

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(2) Du Pont Fellow, 1953–1954.

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