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Kinetics and Mechanism in the Acid-catalyzed Hydrolysis of Orthoesters

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The rates of hydrolysis of a series of *p*-substituted methyl orthobenzoates have been determined and catalytic constants for the reaction in the presence of lyonium ion and a series of weakly dissolved carboxylic acids have been computed. Adherence to the Brönsted catalysis law has been demonstrated for catalytic acids of similar structure and charge type. A good Hammett $\sigma-\rho$ relationship has been shown to exist for lyonium ion catalysis, but the catalytic coefficients for chloroacetic acid catalysis of the various *p*-substituted orthobenzoate hydrolyses fall on a smooth curve. A possible explanation of these observations has been considered briefly. The response of the rate to solvent composition in lyonium ion catalyzed hydrolysis of the *p*-nitroorthobenzoate has been interpreted with the aid of a sensitive acidity function. All these results have been applied in an attempt to elucidate the structure of the reaction transition state.

Introduction

Orthoesters in aqueous acid media are rapidly converted to carboxylic esters. This reaction was examined as early as 1877 by Gabriel.[2] Quantitative studies on the hydrolysis reactions of orthoesters have been reported by a number of investigators.[3] Brönsted and Wynne-Jones[3c] determined that many orthoesters undergo general acid catalysis. More recently, DeWolfe and Roberts[4] have determined a catalytic term for the hydrolysis of ethyl orthoformate in aqueous dioxane due to undissociated acid; in pure water the hydrolysis of this compound previously had been found to show only specific hydronium catalysis.[5] We are reporting here the results of our studies on the solvolyses of variously substituted ortho-benzoates that were undertaken with the objective of clarifying some aspects of the nature of general acid catalysis and, in particular, to elucidate mechanistic details of the acid-catalyzed cleavage of ether bonds.

Experimental

Materials.—Methanol and ethanol were dried by the method of Lund and Bjerrum[6] and distilled under an inert atmosphere. Karl Fischer analyses showed less than 0.05% water in these dried solvents.

Orthoester preparations were conducted according to the general method of Pinner[7a] and Reitter and Hess[7b] or the general procedure of McElvain and Venerable.[8]

Methyl ortho-*p*-methoxybenzoate, methyl ortho-*p*-toluate and methyl ortho-*p*-nitrobenzoate were prepared by analogy to the method of Pinner[7] and Reitter and Hess.[7b]

The proper nitrile was dissolved in anhydrous methanol in the case of *p*-OCH_3 and *p*-CH_3 derivatives and in nitrobenzene in the case of the *p*-NO_2 derivative. An equivalent amount of anhydrous HCl was bubbled into the solution. The flask then was stoppered and permitted to stand under refrigeration for several days. Crystals of the iminoether hydrochloride which formed were filtered, repeatedly washed with ether and dehydrated *in vacuo* in the presence of P_2O_5 and anhydrous KOH pellets. About 10 days elapsed before a small amount of the crystals, when dissolved in alcohol, showed a negative test toward congo red paper indicating a satisfactory removal of residual HCl.

The iminoether hydrochloride next was dissolved in anhydrous methanol and permitted to stand at room temperature for about 10 days; NH_4Cl crystals which formed were filtered off and the filtrate was separated into methanol, carboxylic ester and orthoester fractions by distillation. Because of the high boiling character of the *p*-NO_2 derivative, this orthoester was separated from the carboxylic ester by taking advantage of the normal resistance to alkaline hydrolysis of the former. After alkaline treatment, (addition of 10% volume of 1% aqueous NaOH solution) the unreacted orthoester repeatedly was ether-extracted from the solution. The residue after ether and methanol distillation was assayed for orthoester content and used as such in the kinetic studies.

Methyl orthobenzoate and methyl ortho-*p*-chlorobenzoate were prepared by the procedure of McElvain and Venerable.[8] The starting materials for these preparations were obtained from commercial sources (*p*-chlorobenzotrichloride was obtained from the Heyden Chemical Co., benzotrichloride from Distillation Products Industries). Physical property data for the orthoesters prepared are listed in Table I.

TABLE I

PERTINENT PROPERTIES OF ORTHOBENZOATE AND BENZOATE ESTERS USED IN KINETIC EXPERIMENTS

p-$ZC_6H_4C(OCH_3)_3$, Z =	Temp. collected		$p\text{-ZC}_6\text{H}_4\overset{\text{O}}{\overset{\Vert}{\text{C}}}\text{OCH}_3$	
	B.p., °C.	Mm.	λ_{max}, mμ	log max.
-H	114–115	25	228[a]	4.08
-Cl	83–85	2	241	4.37
$-CH_3$	102–104	10	241	4.16
$-OCH_3$	114–115	5	256	4.24
$-NO_2$	88–90[b]		262	4.02

[a] A maximinum exists at 273 mμ for methyl orthobenzoate. Because of expected interferences at the lower wave length value the kinetic study was conducted at 273 mμ in spite of the lower log ϵ value, 296. [b] M.p.

Kinetic Procedure.—The rate of hydrolysis was followed spectrophotometrically by measuring the increase in optical density of the solution as the carboxylic ester formed at the absorption maximum of the carboxylic ester. A Process and Instruments RS3 recording spectrophotometer[9] was used, and the variation in absorbance continuously charted on a modified Leeds and Northrup Speedomax recorder. A two-sectioned absorption cell (with quartz windows) was used for all measurements.[10] The catalyst solution

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[1] Part of the material for this article has been taken from the thesis of M. B. Price, submitted in partial fulfillment of the requirements for the Ph.D. degree of the University of Delaware.

[2] S. Gabriel, *Ber.*, **10**, 185 (1877).

[3] (a) J. A. Smythe, *Proc. Univ. Durham Phil. Soc.*, **4**, 75 (1911); (b) A. Skrabal and O. Ringer, *Monatsh.*, **42**, 9 (1921); (c) J. N. Brönsted and W. F. K. Wynne-Jones, *Trans. Faraday Soc.*, **25**, 59 (1929).

[4] R. H. DeWolfe and R. M. Roberts, THIS JOURNAL, **76**, 4379 (1954).

[5] See ref. 3b and 3c as well as J. C. Hornel and J. A. V. Butler, *J. Chem. Soc.*, 1361 (1936); F. Brescia and V. K. LaMer, THIS JOURNAL, **60**, 1962 (1938); **62**, 612 (1940); H. S. Harned and N. T. Samaras, *ibid.*, **54**, 1 (1932).

[6] H. Lund and J. Bjerrum, *Ber.*, **64**, 210 (1931).

[7] (a) A. Pinner, *ibid.*, **16**, 356, 1644 (1883); (b) H. Reitter and E. Hess, *ibid.*, **40**, 3020 (1907).

[8] S. M. McElvain and J. T. Venerable, THIS JOURNAL, **72**, 1661 (1950).

[9] Manufactured by Process and Instruments, 15 Stone Ave., Brooklyn 33, N. Y. This instrument, ideal for kinetic studies, is essentially of double beam construction and possesses a fully thermostated cell compartment. The stability of the zero and 100% absorption lines was so unwavering that a reaction could be charted continuously for many hours without the necessity of checking for base line drift or any other calibrations (including wave length).

[10] For a description of this, see H. Kwart and M. M. Baevsky, THIS JOURNAL, **80**, 580 (1958).

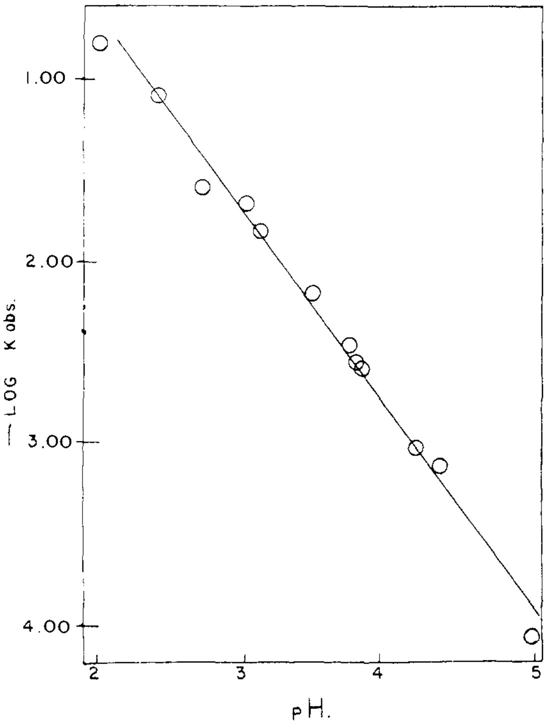

Fig. 1.—Dependence of methyl orthobenzoate hydrolysis rate on pH in a 70% methanol-30% water solution at 30.0°.

and the substrate solution were thus thermostatted in the same cell. The solutions were thoroughly mixed just prior to placing the cell in the spectrophotometer by uniting the content of both chambers and replacing sufficient of the reacting mixture in the optical absorption chamber. The recorder paper time chart was started simultaneously with the admixing of the two phases. Using this technique all but the initial 10–15 seconds of the reaction was monitored. Microburet quantities of reactants and solvents were placed in the two chambers of the cell, the catalyst and substrate being kept apart in each case.

Under these conditions it was established that the rate was pseudo first order and the application of the Guggenheim method of computing the rate constants was consequently permitted.[11]

pH Measurements.—All pH measurements were made using a standardized glass electrode Beckman model H-a pH meter. In every case the electrodes were standardized against known buffers of pH value less than two units removed from the value obtained.

Preparation of the Buffer Solutions.—Several different acids in buffered solutions were used in the course of the investigation. The preparation in detail of one of these will be described.

A 70% methanol (v./v.) solution containing $ClCH_2COOH$ and $ClCH_2COONa$ in a molar ratio of 3 to 1 at an ionic strength (determined by the molar concentration of $ClCH_2COONa$) of 0.01 μ has a (determined) pH value of 3.90. Except for the ionic strength effect on the dissociation equilibrium of chloroacetic acid, a solution of a reasonable dilution of this acid and its salt in 3:1 molar ratio would have a pH of 3.90. The effect of this ionic strength on the equilibrium was eliminated by the addition of KCl in such quantities that the total ionic strength of all of the solutions involved was 0.01 μ. Table II illustrates these points over a fivefold variation in buffer concentration.

In all systems the acid solution was made by dissolving analytically weighed freshly distilled acid in water. The molarity was checked by titration against standardized NaOH. The KCl was reagent grade recrystallized from water-methanol solution.

Determination of "I" Values of Various Methanol–Water Ratios in Acid Solution.—These determinations were made in the manner of Braude and Stern.[12] The optical density values of the brom cresol green indicator solutions of the various solvent–acid compositions involved were made with a Beckman DU spectrophotometer. The "I"-values were computed from the relationship

TABLE II

Relative number of moles			pH of soln. prepared by adding 3.00 ml. of aqueous soln. to 7.00 ml. of anhyd. methanol
Chloroacetic acid	Sodium chloroacetate	Potassium chloride	
0.100	0.0333	....	3.90
.0800	.0267	0.0066	3.89
.0600	.0200	.0133	3.89
.0400	.0133	.0200	3.91
.0200	.0067	.0266	3.88

$$I = C_{BH^+}/C_B = (\epsilon_N - \epsilon_A)/\epsilon_A$$

where the symbols used have their usual significance.[12]

Results and Discussion

Rate and Kinetic Order.—The reaction was determined to be first order with respect to hydronium ion concentration, $k_{obs} = k_{H^+}(H^+)$, over the range pH 2 to 5 that could be studied conveniently with our instrumentation in 30% aqueous methanol. The linear relationship between log k_{obs} and pH which demonstrates this is shown in Fig. 1.

The rate variation with water concentration (in methanol at constant concentration of HCl) is, however, not linear. The observed paraboloid relationship can be constructed from the data given in Table III. It has been widely noted[13] that the variation of the rate of some acid-catalyzed reactions in alcohol solution may exhibit a minimum with the addition of water. A more detailed discussion of this point will be presented in a later section.

TABLE III

DEPENDENCE OF THE RATE OF METHYL ORTHOBENZOATE HYDROLYSIS ON SOLVENT COMPOSITION IN WATER–METHANOL MIXTURES AT 30.0° AND 0.001 M HCl

Volume % methanol	$k_{obs} \times 10^{-3}$, sec. $^{-1}$	Volume % methanol	$k_{obs} \times 10^{-3}$, sec. $^{-1}$
20.0	8.25	80.0	1.08
40.0	4.77	90.0	0.75
60.0	2.41	95.0	1.00
70.0	2.02	97.5	1.10

General Acid Catalysis.—It readily was ascertained by the classical procedure of Brönsted and Pederson[14] that methyl orthobenzoate hydrolysis is catalyzed both by lyonium ion and undissociated acid. Thus, the rate of reaction at constant pH in buffers of weak acid was shown to depend on the buffer concentration and, therefore, on the concentration of undissociated acid. The usual straight line plot of the k_{obs} *versus* the concentration of undissociated buffer acid was obtained, as is characteristic of reactions exhibiting general acid catalysis, where the positive slope of this line is a measure of the catalytic constant, k_a, of the undissociated acid catalyst according to the general rate equation

$$k_{obs} = k_{H^+}(H^+) + k_a(HA)$$

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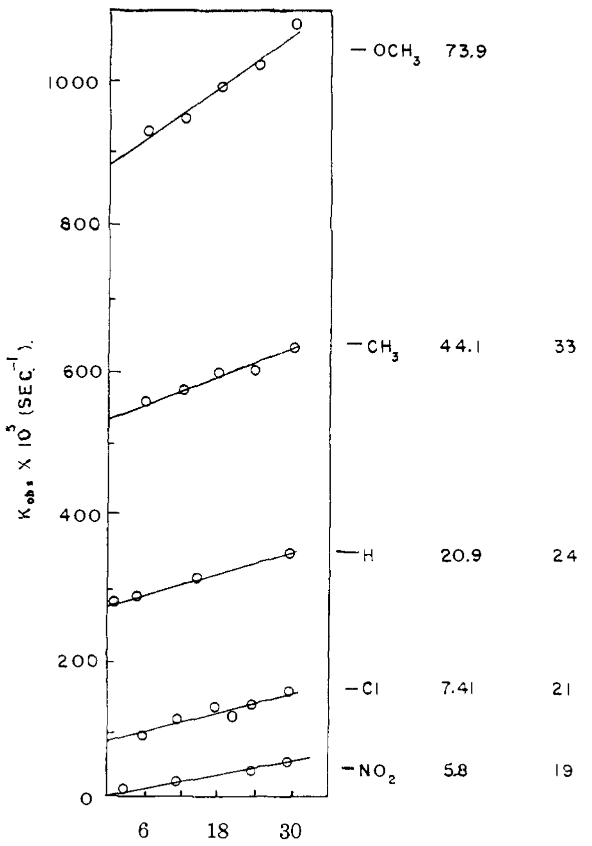
(11) E. A. Guggenheim, *Phil. Mag.*, **2**, 538 (1926).

(12) E. A. Braude and E. S. Stern, *J. Chem. Soc.*, 1982 (1948).

(13) See for examples, (a) E. A. Braude and E. R. H. Jones, *J. Chem. Soc.*, 442 (1944); (b) J. D. Roberts and W. Watanabe, THIS JOURNAL, **72**, 4869 (1950).

(14) J. N. Brönsted and K. J. Pederson, *Z. physik. Chem.*, **A108**, 185 (1923).



($ClCH_2COOH$) × 10³.

p-Subst. $K_{H_3O^+}$ $K_{ClCH_2COOH} \times 10^3$

Fig. 2.—Substituent effect on acid catalysis.

With a chloroacetic acid–sodium chloroacetate buffer the k_a value of methyl orthobenzoate and four other p-substituted orthobenzoates were determined. From Fig. 2, the relationship between the k_a value for the reaction and the electronic nature of the p-substituent involved can be perceived.

Determination of the Brönsted Catalytic Relationship.—In the study of the ability of various weak acids to catalyze the hydrolysis of methyl orthobenzoate, a linear relationship was established between the log of the dissociation constant in water of the particular acid involved (log K_A) and the log of its acid catalytic constant (log k_a). These data are presented in Table IV and Fig. 3. The magnitude of the slope (from the original Brönsted[14] catalysis law: $G_AK_A\alpha = k_A$, $\alpha = -0.74$) demonstrates that a considerable relationship exists between the catalytic ability and the (aqueous) ionization characteristic of the catalyzing acid.

The existence of this Brönsted linear free energy relationship[14,15] indicates also that small structural changes in the carboxylic acid catalysts do not cause any major alteration in the reaction species. Thus, the strengths of the acids chosen is their most significant, distinguishing characteristic. (The acids cnosen were similar. This was partly necessitated by the analytical procedure involved in the rate studies. The presence of aromatic acids, in sizable concentrations compared to the substrate, would obscure the ultraviolet absorption phenomenon on which pursuit of the reaction was based; see Experimental.) However, the oxonium ion included in the study (value obtained from the slope of the line plotted in Fig. 1), represents a distinct alteration of charge type of the acid catalyst. It can be seen in Fig. 3 that the value for H_3O^+ deviates considerably more from the line than any other point. The log K_A values used were the available constants measured for these acids in pure water. It is reasonable that in the actual solvent in which the rates were taken the deviation of the charged acid H_3O^+ from the straight line developed by the uncharged acids would be even greater.[16a] The $k_{H_3O^+}$ would be less influenced by solvent polarity than k_{HA}, since in the dissociation of uncharged, weak acids oppositely charged ions are formed. Therefore, since the K_A values in Fig. 3 are the values in water, the $k_{H_3O^+}$ value may

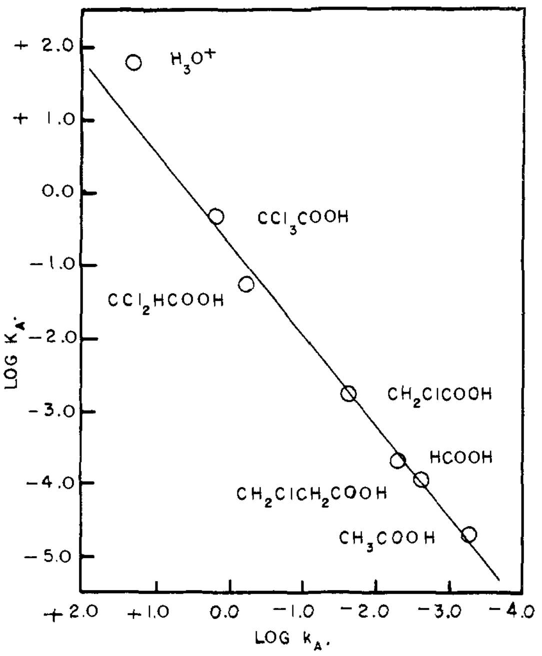


Fig. 3.—Brönsted catalytic plot: undissociated acid catalysis of hydrolysis of methyl orthobenzoate in 70% methanol–30% water at 30.0°.

TABLE IV

BRØNSTED CATALYSIS DATA

Catalytic acid	k_A, sec.$^{-1}$ moles^{-1}	log k_A	log K_A (H_2O, 25°)
CH_3COOH	65×10^{-3}	−3.28	−4.75
$ClCH_2CH_2COOH$	2.33×10^{-3}	−2.63	−3.98
$HCOOH$	5.15×10^{-3}	−2.29	−3.75
$CH_2ClCOOH$	2.43×10^{-2}	−1.62	−2.82
$CHCl_2COOH$	0.77	−0.21	−1.31
CCl_3COOH	1.50	+0.176	−0.36
H_3O^+	20.9	1.36	+1.74

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[15] (a) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 222 ff.

[16] (a) I. M. Kolthoff and L. S. Guss, THIS JOURNAL, **61**, 330 (1939); (b) see for example L. Zucker and L. P. Hammett, *ibid.*, **61**, 2785 (1939), and ref. 16, p. 237 ff.

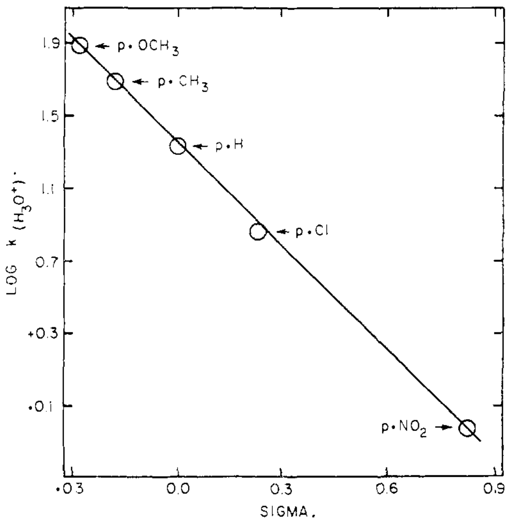


Fig. 4.—Variation of $k_{H_3O^+}$ with σ: hydrolysis of *p*-substituted methyl orthobenzoates in 70% methanol-30% water at 30.0°.

be expected to depart still further from the line in which the K_A values in the actual solvents had been plotted.

Many earlier results argue[16b] strongly against a rate-determining proton transfer to oxygen as a mechanistic feature. Since adherence to the Brönsted catalysis law must be taken to indicate that the proton is only partially bonded[17] to an ether oxygen of the substrate in the activation step, it is entirely understandable that the residual structure of the acid in the transition state will manifest a non-linear influence as we institute large changes in the acid type. In this reaction, clearly, a systematic effect of charge density in the conjugate base present in the transition state gives rise to this restriction in the permissible variation of catalyst structure over which the linear free-energy relation holds.[18] The manner and extent to which the conjugate base of the catalyst exercises its influence will be discussed at greater length in the next section of this article.

The Hammett Relationship.[19]—A large negative ρ-value is exhibited by the lyonium-catalyzed hydrolysis of the methyl orthobenzoates. By varying the acid concentration we observed the expected variation in the rate for the methyl orthobenzoates; that is, at each of several different acid concentrations a new linear relation of log k_A and σ was found. The ρ-values obtained for each individual *p*H series were virtually identical; see Table V and Fig. 4 which illustrates one of the several linear plots which can be realized for these data.

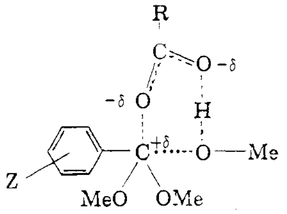
The magnitude of $\rho = -2.02$ would seem to suggest that, at least for lyonium ion-catalyzed reaction, a considerable amount of carbon–oxygen bond breaking has occurred in the transition state and the carbon seat of reaction bears a sizable positive charge density. This charge is very poorly tolerated with *p*-nitro-substitution and enhanced by *p*-methoxyl substitution and the linear free energy relationship is observed only because the polar effect of the substituent is independent of the acid, lyonium ion, in the activation step. In other words, the complete independence of σ and ρ may be assumed in this reaction,[20] when we confine our studies to the series of (only) *p*-substituted reagents.

TABLE V

VARIATION OF LYONIUM ION-CATALYZED HYDROLYSIS RATE CONSTANT WITH *p*H AND SUBSTITUENT EFFECTS, IN 70% MeOH–30% H_2O AT 30.0°

Substituent	Value[20]	*p*H 2.99 log k_{obs}	*p*H 3.14 log k_{obs}	*p*H 3.90 log k_{obs}	log $k_{(H_3O^+)}$
p-OCH_3	−0.268	−1.223	−1.666	−2.054	1.869
p-CH_3	− .170	−1.587	−1.479	−2.276	1.644
p-H	.000	−1.695	−1.840	−2.564	1.320
p-Cl	.227	−2.163	−2.755	−3.056	0.870
p-NO_2	.778	−3.322	−3.404	−4.222	−0.237

In the preceding section and in Fig. 3 it was shown (for the unsubstituted orthobenzoate) that lyonium ion stands somewhat above the Brönsted catalysis line for uncharged acids, indicating a higher α-constant. This may be interpreted to indicate the proton is more fully imparted to the substrate by the (strong) cationic acid than is the case for the remaining weakly dissociated, neutral carboxylic acids tested. Alternatively, this may be taken to mean that the carboxylic acids are more tightly complexed with the substrate in the activation step, the extent of complexing varying with the polar effect of the substituent. The complexation may be visualized as occurring between the anionic conjugate of the carboxylic acid and the seat of reaction developing positive charge in the transition state as is illustrated in



This picture predicts that in the instance of catalysis by weak, undissociated acids the substituent effect would be twofold. A substituent Z on the aromatic ring could influence the degree of complexing between the substrate (ether) oxygen and the undissociated acid, as well as supplement or retard through its polar effect the activity of an anionic center of the acid in solvating and in dispersing the positive charge developing at the carbon center of reaction in the transition state. An electron-withdrawing substituent would both reduce the basicity of the ether oxygen as well as retard the bond breaking and, thus, would exercise considerably greater inhibition of the solvolysis rate than in the lyonium ion-catalyzed reaction. A strongly electron-releasing substituent would be

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[17] For a more complete discussion of this point, see A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 214.

[18] For a case where charge type changes of this nature is a permissible structure variation see F. H. Westheimer, *J. Org. Chem.*, **2**, 431 (1937).

[19] See ref. 16, chapter VII.

[20] An extensive discussion of this point is presented by C. G. Swain and W. P. Langsdorf, THIS JOURNAL, **73**, 2813 (1951).

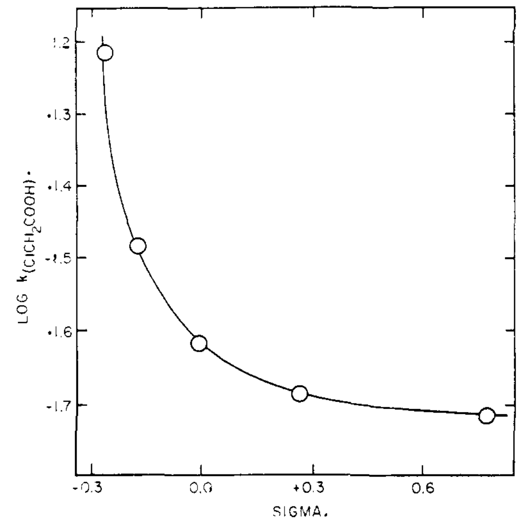

Fig. 5.—Dependence of undissociated acid catalysis on substrate substitution.

expected to have a compound effect on the rate of exactly opposite character.

It would, therefore, be predicted by this interpretation that the Hammett plot for an uncharged carboxylic acid catalyst would have a non-linear characteristic. Here the steepest slope and, therefore, the maximum ρ value would be greater than the ρ of the linear lyonium ion-catalyzed reaction and would occur in the region of the strongest electron-releasing substituents (the largest negative σ values). This expectation is nicely borne out by the data plotted in Fig. 5. The rate shows a maximum change in the region of the *p*-methoxy case (ρ approaches minus infinity), and tapers toward zero as the curve approaches the *p*-nitro point.

It is still conceivable that the mechanism of the lyonium ion-catalyzed reaction is similar. This is to say that the mechanism is A-2 in character[21] and the water molecules[22] associated with the positively charged seat of reaction are constant in number. Here, unlike the case of undissociated acid catalysis above, the activity of the water molecules in the transition state, assisting the bond breaking step by dispersing positive charge, is constant and independent of the substituent effect and thus permits a simple linear relationship between log $k_{H_3O^+}$ and σ. We have presently in progress an experimental study of this possibility.

The Effect of Variation in Solvent Composition.—Lyonium ion-catalyzed reactions, in which a fast pre-equilibrium proton transfer to the substrate occurs with formation of the conjugate acid, have been classified[21] into two groups depending on whether the conjugate acid decomposed unimolecularly (A-1) or bimolecularly with solvent molecules being covalently bound in the transition state (A-2). It has been demonstrated recently by Whalley and co-workers[23] that the proportionality of rate and Hammett acidity function, h_0, cannot be applied with confidence as a criterion of the A-1 mechanism. These workers also have developed a more reliable index for distinguishing the A-1 and A-2 solvolytic mechanisms in the use of the *pressure effect* on the rate and the estimation thereby of the volume of activation of hydrolysis reactions.

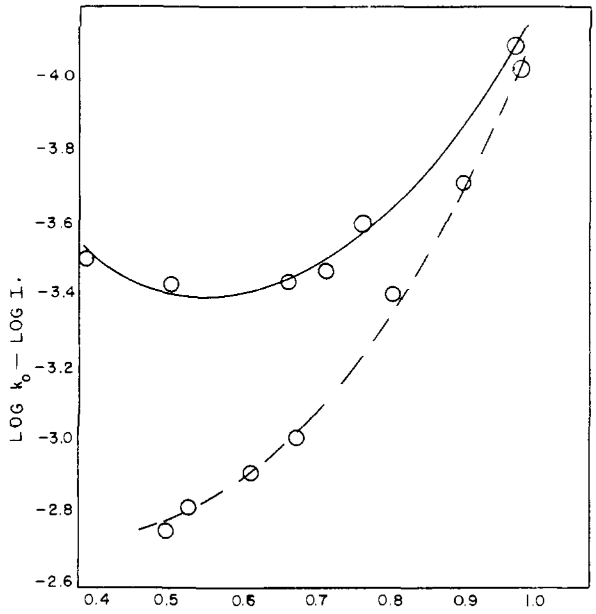

Fig. 6.—Comparison of *p*-nitrodiethyl ketal hydrolysis (- - - -) and methyl ortho-*p*-nitrobenzoate hydrolysis (———) by solvent composition–acidity function criterion.

In these laboratories it has been shown[24] that a satisfactory measure is available for distinguishing the occurrence of A-1 and A-2 mechanisms in partially aqueous media by applying a correlation between rate, acidity and an empirical function of the solvent composition developed by Grunwald and co-workers.[25] This measure is somewhat more easily attained experimentally and, thus far, has afforded results which parallel those obtained by measurement of the *pressure effect*[23b] on the rates of similar reactions.[26]

The report by Koskikallio and Whalley[23b] that the hydrolysis of formals, acetals and orthoformates proceed by an A-1 mechanism in aqueous oxonium ion solutions is pertinent. Also of interest is a report by Kaeding and Andrews[17] who studied the rates of hydrolysis of *p*-nitrobenzophenone diethyl ketal in aqueous ethanol solutions of HCl. They concluded that a ketal lyonium ion reacted with water in the rate-determining step in view of their failure to obtain the usual h_0 dependence of the rate that was accepted as the criterion of sol-

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[21] For a discussion of the basis of these classifications see C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953.

[22] J. F. Bunnett, THIS JOURNAL, **82**, 499 (1960).

[23] (a) E. Whalley, *Trans. Faraday Soc.*, **55**, 798 (1959); (b) J. Koskikallio and E. Whalley, *ibid.*, **55**, 809 (1959); (c) **55**, 815 (1959); (d) *Can. J. Chem.*, **37**, 783 (1959); (e) **37**, 788 (1959); (f) J. Koskikallio, D. Pouli and E. Whalley, *ibid.*, **37**, 1360 (1959).

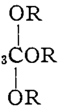
[24] (a) H. Kwart and L. B. Weisfeld, THIS JOURNAL, **80**, 4670 (1958); (b) H. Kwart and A. Goodman, *ibid.*, **82**, 1947 (1960).

[25] (a) E. Grunwald and B. J. Berkowitz, *ibid.*, **73**, 4939 (1951); (b) B. Gutbezahl and E. Grunwald, *ibid.*, **75**, 559, 565 (1953).

[26] Compare for example the conclusions reached in ref. 23c and 24b.

[27] W. W. Kaeding and L. J. Andrews, THIS JOURNAL, **74**, 6189 (1952).

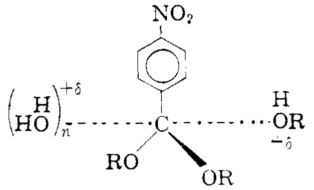
TABLE VI

SUMMARY OF GROUP SUBSTITUTION EFFECTS ON RATE AND MECHANISM OF ACID-CATALYZED SOLVOLYSIS OF  $\mathrm{CH_3C(OR)_3}$ (AN A-1 MECH.)

Effect of substitution of ⟶ on	($-CH_3$ by C_6H_5-)	($-CH_3$ by $NO_2C_6H_5-$)	($-OR$ by C_6H_5-)	($-CH_3$ by H)	$-CH_3$ by C_6H_5 and $-OR$ by $NO_2C_6H_5-$
Magnitude of k_{HA}	Increased	Decreased from 1	..	Eliminated[30]	..
Magnitude of k_{H3O^+}	Increased	Decreased from 1	..	Decreased	..
General mechanism	?	A-2	A-1	A-1	A-2
Reference	This work	This work	28	30	27

volytic mechanism. It seems likely that the nitro substitution on the benzophenone ketal is responsible for effecting the transition from the A-1 (reported by Koskikallio and Whalley for analogous compounds)[23b] to the A-2 mechanism of hydrolysis. We have assumed an A-1 mechanism for the unsubstituted benzophenone ketal hydrolysis, also, from the analogous case of 2,2-diphenyl-1,3-dioxalane[28] where the mechanism has been established to be A-1 in ethanol–water lyonium ion solutions by the application of the mechanistic criterion discussed by Kwart and Weisfeld.[24a]

For purposes of discussion let us tentatively accept the assumption that the observed linear Hammett free energy relationship signifies a common mechanism of lyonium ion-catalyzed solvolysis for all the substituted cases falling on the plot in Fig. 4.[29] On this basis we have applied the solvent composition–acidity function[24] to the ortho-*p*-nitrobenzoate solvolysis where the reaction rates are still readily measurable at the higher acid concentrations required for sensitivity of this mechanistic criterion. In Fig. 6 are displayed plots which permit a comparison of the *p*-nitro substitution effect in benzophenone diethyl ketal and methyl orthobenzoate. It will be noted that nitro-substitution in the orthobenzoate produces an even greater departure from the linear relationship that identifies[24] an A-1 mechanism of solvolysis. This perhaps establishes that a considerable extent of covalent solvent involvement in the transition state has occurred which may indeed be greatest for *p*-nitro substitution. Such circumstances may be represented by the transition state



Furthermore, if our assumption is correct of an identity of mechanism in all of the cases correlated by the linear plot of Fig. 4, then the data of Fig. 6 would seem to support the A-2 mechanism tentatively suggested above in a explanation of the general case of lyonium ion-catalyzed solvolysis of orthobenzoates.

Some Aspects of the Mechanism of Solvolysis of Orthoesters, Acetals and Ketals.—Reference to Table VI permits a crude but useful comparison of general effects in the solvolysis of each of these classes of ethers. It is, perhaps, not unexpected that electron-releasing groups substituted at the seat of reaction will drive the solvolytic mechanism in the direction of A-1 by affording greater stability to the carbonium ion. Conversely, it is seen from columns 2 and 5 that substitution of groups which are electron withdrawing introduce the requirement for nucleophilic assistance from solvent in the transition state and tend to shift the character of the reaction toward A-2.

It is of great interest, also, to realize that substitution by electron-withdrawing groups depresses the magnitudes of both the general acid and specific oxonium ion catalytic coefficients, as noted from column 2, and from column 4 where k_{HA} is almost[4] eliminated by replacing methyl with hydrogen. The significance of this may perhaps be correlated with a previously noted conclusion. The electron-withdrawing groups not only destabilize the carbonium ion but also exert their influence at very short range in the transition state by decreasing the extent to which the proton is imparted to substrate by HA. In this fashion it depresses the catalytic effect by reducing the development of positive charge in the neighborhood of the seat of reaction. Expressed another way, the electron-attracting substituent has reduced the basicity of the substrate and thereby the ability to coördinate a proton from any source, particularly from a weak acid with a threshold ability to impart the proton. The transitions from general acid to specific lyonium ion catalysis and from A-1 to A-2 are clearly not discontinuous. On the contrary, both the nature and magnitudes of these catalytic effects change with all factors which can influence the substrate basicity, substitution being one of the most important.

In general, it has been noted by Koskikallio and Whalley,[23b] comparing $k_{H_3O^+}$ for dimethoxymethane, diethoxymethane and dimethoxyethane, and by Ingold,[31] that alkyl substitution on acetals, ketals and orthoesters increases the magnitude of $k_{H_3O^+}$ but evidently does not alter the A-1 mechanism of solvolysis. It is conceivable that we are

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(28) Unpublished results from these laboratories by E. C. Braak.

(29) However, it is possible that the straight line character of the Hammett plot does not reflect an (activation) isentropic relationship of the rates but rather one in which the enthalpy of activation varies linearly with activation entropy. Many cases where this seems to occur have been discussed, although such occurrences have not been previously correlated with a change in mechanism; see for examples and discussion, J. E. Leffler, *J. Org. Chem.*, **20**, 1202 (1955).

(30) See ref. 3c and 23b as well as pertinent articles cited in ref. 5; (b) see, however, ref. 4.

(31) See ref. 22, p. 334, *et seq.*

witnessing here the operation of a steric acceleration effect.[32] This factor also may be involved in interpreting many of the effects of substitution, but it does not appear to vitiate any of the conclusions we have reached above regarding polar influences in these acid-catalyzed solvolysis reactions.

[32] See for other examples, H. C. Brown and R. S. Fletcher, THIS JOURNAL, **71**, 1845 (1949); H. C. Brown and A. Stern, *ibid.*, **72**, 5068 (1950); H. C. Brown and H. L. Berneis, *ibid.*, **75**, 10 (1953); F. Brown, T. D. Davis, I. Dostrovsky, O. J. Evans, and E. D. Hughes, *Nature*, **167**, 987 (1951), as well as ref. 22, *inter alia*.

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Specific Solvation in Binary Solvent Mixtures. Part I. Variations in Activation Energy of Reactions in Mixed Solvents

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Existing evidence for solvent sorting in the immediate vicinity of ionic solute species in binary solvent mixtures is reviewed briefly. A model is presented which considers the influence of such specific solvation on the activation energy of reactions in mixed solvents and is shown to account satisfactorily for data for solvolytic reactions. The effect of temperature dependence of bulk dielectric constant on activation energy is discussed and shown to be insufficient to account for the observed phenomena.

Introduction

In this paper, and subsequent papers of the series, the phenomenon of specific solvation, or solvent sorting in the immediate vicinity of solute species in binary solvent mixtures, will be considered in general. In particular, emphasis will be placed on the effect of this phenomenon as it is revealed in the activation parameters for kinetic processes in solution.

As early as 1927, Debye[2] attempted a quantitative treatment of the phenomenon, as it relates to systems of ions in binary solvent mixtures. Later Scatchard[2] considered the particular system of ions in ethanol–water mixtures and computed the magnitude of the differences between the solvent composition near the ion and in the bulk as a function of distance from the ion. Since these early attempts to treat the problem, several workers[3-5] have investigated the phenomenon both theoretically and experimentally and have established beyond doubt the reality of solvent sorting in a number of systems. Reference will be made at a later stage to many of these non-kinetic examples of the phenomenon, but paralleling these developments there has been an interest in specific solvation as a factor determining kinetic behavior.

Laidler and Eyring[6] and Scatchard[7] recognized the possible importance of specific solvation as a determining factor in the behavior of the rate constant. This apparently secondary effect on the rate constant, however, has been largely ignored in the many recent correlations of rate with structural and solvent properties.[8-10] The essentially linear nature of these rate correlations reflects the linear dependence of the free energy of activation, ΔF^*, on the correlation parameters. However, as has been amply demonstrated in the past, and most recently by Laidler,[11] the observed linear dependence of ΔF^* is due, in large part, to the compensatory behavior of the activation enthalpy and entropy.

$$\Delta F^* = \Delta H^* - T\Delta S^*$$

There are now many cases in the literature where the behavior of both the enthalpy and entropy of activation is far from linearly related to any property of a solvent medium which is being varied in composition. Many of these cases will be dealt with in detail in this and subsequent papers. The most striking of these deviations from linear behavior are to be found in the variations of the activation enthalpy or energy as a function of solvent composition and it is this parameter which will be emphasized in the treatment offered here.

Many workers[12-15] have attempted to account for the observed activation energy behavior in terms of the temperature dependence of the dielectric constant and have measured, or computed, "isodielectric" activation energies. It will be shown later, however, that this explanation can, at best, account for only part of the devious variations of the activation energy.

The suggestion that specific solvation or solvent sorting may play an important part in determining activation energy behavior has been made recently by several workers in the field.[16,17] The results of Tommila and co-workers are of particular sig-

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[2] P. Debye, *Z. physik. Chem.*, **130**, 56 (1927).

(2a) G. Scatchard, *J. Chem. Phys.*, **9**, 34 (1941).

[3] J. E. Ricci and G. J. Nesse, THIS JOURNAL, **64**, 2305 (1942).

[4] H. L. Clever and F. H. Verhoek, *J. Phys. Chem.*, **62**, 1061 (1958).

[5] E. Grunwald, private communication.

[6] K. J. Laidler and H. Eyring, *Ann. N. Y. Acad. Sci.*, **39**, 303 (1940).

[7] G. Scatchard, *ibid.*, **39**, 341 (1940).

[8] L. P. Hammett, *Chem. Revs.*, **17**, 125 (1935).

[9] S. Winstein, E. Grunwald and H. W. Jones, THIS JOURNAL, **73**, 2700 (1951).

[10] C. G. Swain and C. B. Scott, *ibid.*, **75**, 141 (1953).

[11] K. J. Laidler, to be published. The author is indebted to Prof. Laidler for a prepublication copy of the manuscript.

[12] W. J. Svirbely and J. C. Warner, THIS JOURNAL, **57**, 1883 (1935).

[13] J. C. Warner, *Ann. N. Y. Acad. Sci.*, **39**, 345 (1940).

[14] E. A. Moelwyn-Hughes, "Kinetics of Reactions in Solution," Oxford Univ. Press, 2nd Ed., 1947, pp. 120, 213.

[15] E. A. Braude, *J. Chem. Soc.*, 442 (1944).

[16] E. Tommila, A. Koivisto, J. P. Lyyra, K. Antell and S. Heimo, *Ann. Acad. Sci. Fenn.*, *A II*, **47**, 1 (1952).

[17] D. A. Brown and R. F. Hudson, *J. Chem. Soc.*, 3352 (1953).