APPLICATION OF THE H_0 ACIDITY FUNCTION TO KINETICS AND MECHANISMS OF ACID CATALYSIS[1]

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I. INTRODUCTION

One of the ideas underlying the original development of the H_0 indicator acidity scale by Hammett and Deyrup (116) was its possible bearing on acid catalysis. In the subsequent years there have been many applications of this function to the kinetics of acid-catalyzed reactions, and a number of correlations between

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reaction rates and indicator acidity have been discovered. A point of special interest has been the possibility of using such correlations in attacking the difficult problem of reaction mechanisms.

The H_0 scale is defined in terms of ionization equilibria of a particular class of indicators, those functioning as uncharged bases:

$$B + H^+ \rightleftharpoons BH^+ \tag{1}$$

It is defined by the equation:

$$H_0 \equiv -\log \frac{C_{BH^+}}{C_B} + pK_{BH^+} \tag{2}$$

where C_{BH^+}/C_B is the ratio of the concentrations of the indicator in its acid and basic forms, directly measurable for a given solution by means of a spectrophotometer or a colorimeter, and K_{BH^+} is the thermodynamic ionization constant of the conjugate acid, BH^+. This definition is equivalent to:

$$H_0 = -\log \frac{a_{H^+} f_B}{f_{BH^+}} \tag{3}$$

where a_{H^+} represents hydrogen-ion activity and f_B and f_{BH^+} are molar-concentration activity coefficients. By convention, f_B and f_{BH^+} are taken to be unity in ideal dilute aqueous solutions, while a_{H^+} under this condition is identified with conventional hydrogen-ion concentration (115b, 193). It is convenient for some purposes to define also a function h_0, related to H_0 by the equation:

$$H_0 \equiv -\log h_0 \tag{4}$$

It follows that

$$h_0 = a_{H^+} \frac{f_B}{f_{BH^+}} \tag{5}$$

so that in the limiting case of the ideal dilute aqueous solution, h_0 becomes equal to hydrogen-ion concentration while H_0 becomes equal to pH.

Hammett and Deyrup succeeded in establishing that the values obtained for H_0 were reasonably independent of the particular indicator, at least for solutions of high dielectric constant. This means that for a given medium (the concentration of the indicator itself always being low) the activity coefficient ratios in equations 3 and 5 for different uncharged basic indicators, B and C, have approximately a common value:

$$\frac{f_B}{f_{BH^+}} = \frac{f_C}{f_{CH^+}} \tag{6}$$

The generality of this relationship has been subjected to many subsequent investigations which have been reviewed previously (193). It apparently holds quite accurately for a number of aromatic amines, azo compounds, and oxygen

TABLE 1

Comparison of values of indicator acidity with molar concentration for aqueous solutions

C_{HA}	Value of h_0			
	$HClO_4$	HCl	HNO_3	H_3PO_4
moles/liter				
0.1	0.11	0.11	0.11	0.045
1.0	1.6	1.6	1.6	0.23
3.0	17.0	11.2	10.5	1.2
6.0	690.	132.	62.	11.
10.0	620,000	4800	—	390.

bases in aqueous solutions of the strong acids (concentrated sulfuric acid, for example) and probably also in other media of high dielectric constant. In media of low dielectric constant there is evidence of greater specificity on the part of the indicators (111, 113); the interpretation of indicator and other measures of acidity in such media appears moreover to be complicated by extensive ion-pair formation (63, 136).

A characteristic feature of the H_0 acidity scale for aqueous solutions of the strong acids is that with increasing acid concentration h_0 grows increasingly larger than C_{H^+}.[2] For different acids, furthermore, the h_0 values at a given stoichiometric concentration show significant differences when the concentration exceeds 1 *M*. These points are illustrated in table 1, which compares h_0 and molarity values for aqueous solutions of several acids.[3] An opportunity is thus afforded to test whether certain acid-catalyzed reactions whose specific rates are known to increase much faster than C_{H^+} at high acid concentrations are in fact more closely correlated with the acidity function h_0.

An early demonstration of such a correlation was given by Hammett and Paul (118) for the hydrolysis of sucrose in aqueous solutions of the strong mineral acids. Figure 1 shows their plot of log k_1 against $-H_0$.[4] The rate coefficient k_1 of this classic first-order reaction increases in proportion to C_{H^+} at low acid concentrations but increases much more rapidly than C_{H^+} as the acid concentration increases beyond 1 *M*; the broken line in figure 1 shows, for example, the predicted variation of rate with acidity in the case of perchloric acid if the rate increased in direct proportion to the acid concentration. One sees in figure 1 that log k_1 actually increases linearly with $-H_0$ for all the strong acids included and that the slope of the observed straight line is close to unity. The only significant dis-

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[2] The symbol C_{H^+} denotes total concentration of solvated hydrogen ions. For a dilute or moderately concentrated aqueous solution of a strong monobasic acid such as perchloric, this is the same as the stoichiometric concentration of the acid. For a weaker acid such as phosphoric, its value will be related to the stoichiometric concentration through the familiar equilibrium law involving a thermodynamic ionization constant.

[3] The numerical values of h_0 in table 1, and of h_0 and H_0 in other parts of this article, are on a scale based on $pK_{BH^+} = 0.99$ for *p*-nitroaniline (193).

[4] Wherever determinate numerical values are given for rate data in this review the time unit is the *second* and the concentration unit is *mole liter*$^{-1}$.

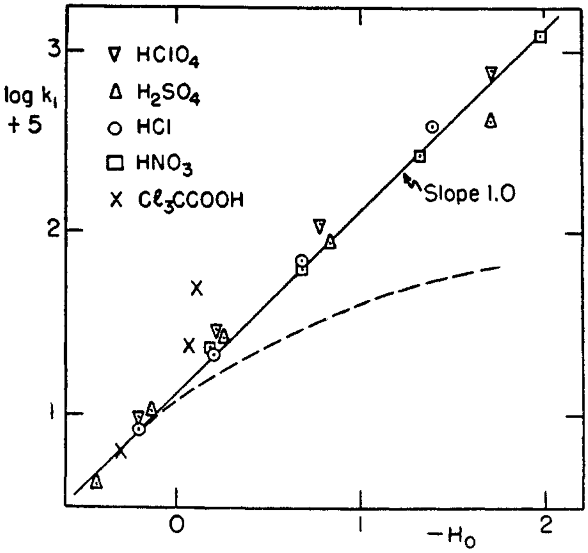

FIG. 1. Correlation between H_0 and first-order rate coefficient for the hydrolysis of sucrose by aqueous acids at 25°C. (118, 120). The dotted line gives the expected rate coefficient for solutions of perchloric acid if the rate were actually proportional to C_{H^+}.

crepancy is that shown by the relatively weaker acid, trichloroacetic, for which log k_1 increases considerably faster than does $-H_0$.

As Hammett (114, 115b) has pointed out, this correlation is to be expected if the hydrolysis mechanism involves a first-order rate-determining reaction of the conjugate acid of sucrose:

$$\left.\begin{array}{ll} S + H^+ \rightleftharpoons SH^+ & \text{Equilibrium} \\ SH^+ \rightarrow X^+ & \text{Rate determining} \\ X^+ + H_2O \rightarrow \text{products} + H^+ & \text{Fast} \end{array}\right\} \quad (\text{A-1})$$

where S in this case is sucrose and X^+ is an unspecified kinetic intermediate. Using Ingold's terminology (64, 127c), the notation A-1 denotes an acid reaction characterized by an essentially unimolecular rate step, regardless of the overall kinetics. It is obvious that the water molecule in this case can be replaced by any other nucleophile without affecting the rate equation. Applying the Brönsted equation for the effects of changes in the medium to the rate-determining step:

$$\text{Rate} \equiv -\frac{dC_S}{dt} = k'C_{SH^+}\frac{f_{SH^+}}{f_\ddagger} = \frac{k'}{K_{SH^+}}\,C_S\,\frac{a_{H^+}f_S}{f_\ddagger}$$

where k' is the rate coefficient for the rate-determining step, $f_\ddagger$ is the activity coefficient of the transition state, and K_{SH^+} is the acid ionization constant of SH^+. We shall assume that C_S^{total} is small in comparison with the concentration of catalyzing acid present. If, furthermore, S is such a weak base that it is almost entirely in the uncharged basic form over the range of acidities investigated so that C_S is practically the same as the overall stoichiometric concentration C_S^{total}, then the first-order rate coefficient k_1 satisfies the equation:[5]

$$k_1 \equiv -\frac{1}{C_S^{\text{total}}}\frac{dC_S^{\text{total}}}{dt} = \frac{k'}{K_{SH^+}}\frac{a_{H^+}f_S}{f_\ddagger} \tag{7}$$

Substituting for a_{H^+} from equation 5,

$$k_1 = \frac{k'}{K_{SH^+}}h_0\frac{f_{BH^+}f_S}{f_Bf_\ddagger} \qquad (C_{SH^+} \ll C_S) \tag{8}$$

Taking logarithms:

$$\log k_1 = -H_0 + \log\frac{f_{BH^+}f_S}{f_Bf_\ddagger} + \text{constant} \tag{9}$$

The observed linear correlation between log k_1 and $-H_0$ follows if the activity coefficient ratio in the second term on the right of equation 9 stays constant with changing medium, i.e., if

$$\frac{f_S}{f_\ddagger} = \frac{f_B}{f_{BH^+}} \tag{10}$$

This is quite plausible (see equation 6) if $f_\ddagger$ can be assumed to vary with changes in the medium in essentially the same way as f_{SH^+}, the activity coefficient of the

[5] More generally, when significant concentrations of both S and SH$^+$ are present, the expression for k_1 assumes the form:

$$k_1 = \frac{k'}{K_{SH^+}}\frac{C_S}{C_S + C_{SH^+}}\frac{a_{H^+}f_S}{f_\ddagger} = \frac{k'}{K_{SH^+}}\frac{1}{1 + \dfrac{a_{H^+}f_S}{K_{SH^+}f_{SH^+}}}\frac{a_{H^+}f_S}{f_\ddagger} \tag{7a}$$

Upon substitution for a_{H^+} from equation 5,

$$k_1 = \frac{k'}{K_{SH^+}}\frac{h_0\dfrac{f_{BH^+}f_S}{f_Bf_\ddagger}}{1 + \dfrac{h_0}{K_{SH^+}}\dfrac{f_{BH^+}f_S}{f_Bf_{SH^+}}} \tag{8a}$$

which reduces to equation 8 when $h_0 \ll K_{SH^+}$. If one can assume that the activity coefficient ratios in equation 8a do not depart significantly from unity, then

$$\log k_1 = -H_0 - \log\left(1 + \frac{h_0}{K_{SH^+}}\right) + \text{constant} \tag{9a}$$

This equation is equivalent to one derived by Schubert and Latourette (216) for their study of the deacylation of aromatic ketones. When the acidity is sufficiently high, equation 8a reduces to

$$k_1 = k'\frac{f_{SH^+}}{f_\ddagger} \qquad (h_0 \gg K_{SH^+}) \tag{9b}$$

so that if $f_\ddagger$ remains equal to f_{SH^+}, the rate coefficient approaches a limiting value independent of acidity.

conjugate acid of S. Such an assumption is *a priori* reasonable, since the transition state differs from SH^+ only in displacement along the reaction coördinate. In other words, equation 10 for an A-1 reaction of an uncharged molecule S should be almost as general as equation 6, which applies to the indicators used in the establishment of the H_0 acidity scale.

An alternative mechanism to the A-1 is the following:

$$\left.\begin{array}{ll} S + H^+ \rightleftharpoons SH^+ & \text{Equilibrium} \\ SH^+ + Y \rightarrow \text{products} + H^+ & \text{Rate determining} \end{array}\right\} \quad \text{(A-2)}$$

The rate-determining step here is characteristically bimolecular and hence the mechanism is designated A-2 (64, 127c). The rate should satisfy the equation:

$$\text{Rate} \equiv -\frac{dC_S}{dt} = k''C_{SH^+}C_Y\frac{f_{SH^+}f_Y}{f_\ddagger} = \frac{k''}{K_{SH^+}}C_SC_YC_{H^+}\frac{f_Sf_Yf_{H^+}}{f_\ddagger} \quad (11)$$

Since the transition state contains the reactant Y in addition to SH^+, one cannot expect equation 10 to apply, even for the important case of a hydrolysis reaction where Y is a water molecule.

If Y is a water molecule and if C_S^{total} is small in comparison with the concentration of catalyzing acid, then in aqueous solutions the rate-determining reaction will show first-order kinetics as will the overall reaction at constant acidity. In fact, in dilute aqueous solutions the overall reaction will be kinetically indistinguishable from one conforming with the A-1 mechanism. For the ordinary case where C_S is practically equal to C_S^{total}, the rate coefficient k_1 will satisfy the equation:[6]

$$k_1 \equiv -\frac{1}{C_S^{\text{total}}}\frac{dC_S^{\text{total}}}{dt} = \frac{k''}{K_{SH^+}}C_{H^+}\frac{f_Sf_{H^+}a_{H_2O}}{f_\ddagger} \quad (12)$$

or, taking logarithms:

$$\log k_1 = \log C_{H^+} + \log\frac{f_Sf_{H^+}a_{H_2O}}{f_\ddagger} + \text{constant} \quad (13)$$

Now Zucker and Hammett (252) found that for the acid-catalyzed iodination of acetophenone in aqueous perchloric acid solutions ranging up to 3.6 M, log k_1 was closely linear with unit slope in log C_{H^+} itself rather than in $-H_0$ (see figure 2). There is independent evidence in this case that a water molecule or some equivalent base is essential in the rate-determining conversion of the oxonium cation to the enol, i.e., that the reaction does proceed according to an A-2 mechanism (115a). To account for the observed relationship between log k_1 and log

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[6] More generally, at acidities so high that significant concentrations of SH^+ as well as S are present,

$$k_1 = \frac{k''}{K_{SH^+}}\frac{C_S}{C_S + C_{SH^+}}C_{H^+}\frac{f_Sf_{H^+}a_{H_2O}}{f_\ddagger} \quad (12a)$$

See equation 7a.

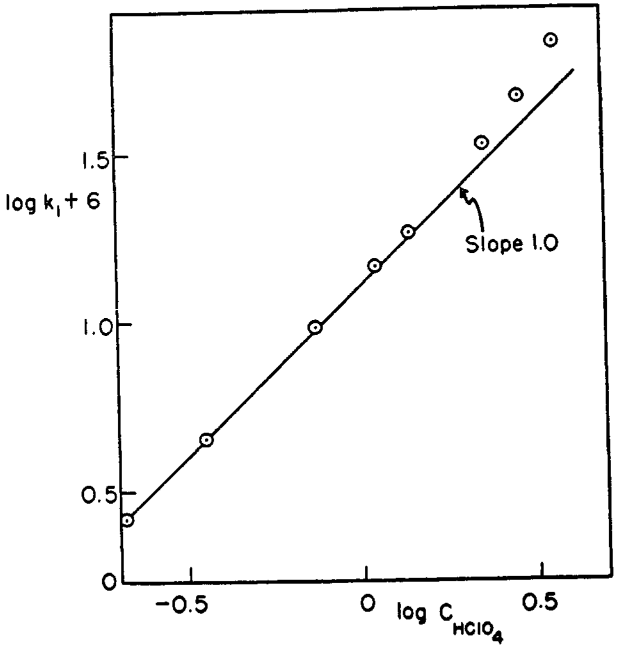

FIG. 2. Log k_1 vs. log C_{HClO_4} for the iodination of acetophenone in aqueous perchloric acid at 25°C. (252).

C_{H^+} it follows that the term $f_S f_{H^+} a_{H_2O}/f_{\ddagger}$ in equation 13 must remain practically unity with changing acid concentration, i.e.,

$$f_{\ddagger} = f_S f_{H^+} a_{H_2O} \tag{14}$$

If this empirical conclusion is generally valid for A-2 hydrolysis reactions, then, as Zucker and Hammett have suggested, one should be able to distinguish between A-2 and A-1 mechanisms for uncharged reactants according to whether log k_1 increases linearly with log C_{H^+} or with $-H_0$.[7] The hypothesis that an A-1 mechanism, i.e., one which does not call for a water or other additional reactant

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[7] The mechanism here designated A-2 embraces actually two distinct classes of nucleophilic displacements. In one, the nucleophilic agent Y (H_2O for example) abstracts from SH^+ a proton other than the one added on by S, i.e., Y functions as a base. This is presumably what happens in the acid-catalyzed enolization reactions of ketones, such as the iodination of acetophenone (figure 2). An attendant feature of such a reaction is that it should show general acid catalysis, for the product $C_Y C_{SH^+}$ on which the rate then depends is ideally equal to $C_S C_{YH^+} K_{YH^+}/K_{SH^+}$, where K_{YH^+} is the dissociation constant of the particular conjugate acid, YH^+; other acids besides YH^+ should show characteristic catalytic effects. The other class of reaction is an ordinary nucleophilic displacement in which Y does not specifically function as a base. The acid-catalyzed hydrolysis of many ordinary esters such as ethyl acetate is an example of this class (see Section II,A). Such a reaction should show only specific hydrogen-ion catalysis, as in the case of A-1 reactions. The evidence on medium effects so far available suggests that for either class of A-2 reaction with solvent water serving as Y, the first-order specific rate is proportional to hydrogen-ion concentration rather than to h_0.

molecule in the transition state, should lead to a linear relationship between log k_1 and $-H_0$ is clearly consistent with equations 9 and 10, since it is wholly plausible that a transition state containing only S and H^+ will behave as the conjugate acid of S. It is much less obvious that the presence of a water molecule in the transition state should necessarily lead to a linear relationship between log k_1 and log C_{H^+}, i.e., that an equation like 14 should hold.[8] In fact, there is no particular reason why there should not be cases intermediate between proportionality of rate with h_0 and with C_{H^+}. It is even possible that reactions which actually go by an A-2 mechanism will under certain conditions show a good correlation between log k_1 and $-H_0$. This will be the case whenever $-H_0$ happens to vary in the same way as log C_{H^+} with changes in the medium, as in the trivial example of aqueous solutions of the strong mineral acids below 1 *M* concentration. It may be the case also if all activity coefficients happen to remain individually constant over wide variations in the medium and hence in the acidity.

In this review the authors propose to treat the Zucker and Hammett suggestion as an explicit hypothesis, the most extreme statement of which is:

- (*a*) All A-1 reactions for uncharged reactants will follow H_0 in the sense that log k_1 will be linear in $-H_0$ with an essentially unit slope.
- (*b*) All A-2 solvolytic reactions for uncharged reactants will show linearity between log k_1 and log C_{H^+}, again with an essentially unit slope.

The previous discussion suggests that part (*a*) of this hypothesis is quite reasonable but that (*b*) is decidedly more uncertain. Clearly the ultimate test of the Zucker–Hammett hypothesis will be experimental and one of the major purposes of this review is to assess its present status.

Both of the foregoing A-1 and A-2 mechanisms presuppose a rapid equilibrium between the reactant S and its conjugate acid SH^+. For the particular case of catalysis by a strong acid, evidence for such an equilibrium is afforded by an increase in the reaction rate when D_2O is substituted for H_2O as the reaction medium (9c, 158, 244); the increase is attributed to the lower basicity of D_2O as compared with H_2O and should be quite general, provided of course that the subsequent reaction of the acid cation does not itself involve an appreciable isotope effect. Still another type of acid-catalysis mechanism comes to mind, however, in which the initial acid-base reaction is itself rate determining:

$$\left.\begin{array}{ll} S + H^+ \rightarrow SH^+ & \text{Rate determining} \\ SH^+ + Y \rightarrow \text{products} + H^+ & \text{Fast} \end{array}\right\} \quad (\text{A-S}_\text{E}2)$$

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[8] The proposed difference in behavior between A-1 and A-2 reactions is in no sense to be attributed simply to the formal presence of the term a_{H_2O} in equations 12 and 13 and its absence from equations 7 and 8. The situation is rather that the A-1 mechanism leads to a transition state closely similar in configuration to the conjugate acid of the reactant, whereas the A-2 solvolysis mechanism involves a transition state that results from a bimolecular reaction between the conjugate acid and a solvent water molecule. The A-2 transition state is therefore expected to be *structurally* quite different from the conjugate acid and hence may respond differently to changes in the medium. The numerical variation in the value of a_{H_2O} is in fact not particularly large for moderate changes in the acid concentration; for perchloric acid between 1 and 6 *M* concentrations, for example, a_{H_2O} changes by a factor of only 2, while the ratio of h_0 to C_{H^+} changes by a factor of 70 (table 1).

The proposed designation A-S_E2 suggests that this is a typical electrophilic substitution reaction. The symbol H^+ here as in the A-1 and A-2 mechanisms previously described represents by convention the solvated proton in the medium (water) in question. One would expect other acids to be possible sources of the proton, so that this is potentially a case of general acid catalysis. The rate equation will have the form:

$$\text{Rate} \equiv -\frac{dC_S}{dt} = k_2 C_S C_{H^+} \frac{f_S f_{H^+}}{f_\ddagger}$$

where k_2 is the rate coefficient for the proton transfer. The value of k_2 would of course be different for catalysis by some other acid than the solvated proton. However, for catalysis by fairly concentrated solutions of strong acids one can assume that the only significant term in the rate law will be that given above. This leads to:

$$k_1 \equiv -\frac{1}{C_S}\frac{dC_S}{dt} = k_2 a_{H^+} \frac{f_S}{f_\ddagger} = k_2 h_0 \frac{f_{BH^+}}{f_B}\frac{f_S}{f_\ddagger} \tag{15}$$

$$\log k_1 = -H_0 + \log \frac{f_{BH^+} f_S}{f_B f_\ddagger} + \text{constant} \tag{16}$$

No direct evidence is available concerning how the activity coefficient ratio appearing in equations 15 and 16 will behave with changing medium. Since the transition state in this case is a singly charged cation similar in size and configuration to the conjugate acid of S, there is certainly a good possibility that $f_S/f_\ddagger$ will vary in a similar manner as f_B/f_{BH^+}. In other words an A-S_E2 reaction may well show a linear correlation between $\log k_1$ and $-H_0$ similar to that found for the A-1 mechanism.[9]

It seems likely that where the reactant S functions as a nitrogen, sulfur, or oxygen base, its protonation will usually be so rapid as not to be rate determining. If the proton transfer takes place directly to a carbon atom, however, the acid-base reaction may well be slow. A definite distinction between A-1 and A-S_E2 may not be easy, but evidence from such studies as inversion of configuration and isotope exchange should be helpful. The A-S_E2 mechanism implies general acid catalysis but at the high acidities which are appropriate for investigating H_0 correlations, no clear experimental procedure exists for distinguishing this from specific hydrogen-ion catalysis. The concentration of hydronium ions is so large that one cannot hope to add a comparable concentration of some other acid without introducing changes in the medium which would com-

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[9] In the absence of definite experimental evidence this suggestion is speculative. In fact the argument has informally been advanced that if the reacting acid species is actually H_3O^+ the transition state will contain a water molecule in addition to S and H^+; one might accordingly expect the rate in aqueous solutions of strong acids to be proportional to C_{H^+}, as for A-2 hydrolysis reactions, rather than to h_0. Such a line of reasoning seems to the authors of this review to be questionable, depending as it does on attributing a specific structural role to what is in fact a solvation molecule. It does, however, emphasize the need for an experimental study of catalysis by strong acids in the case of a reaction for which proton transfer has been established as the rate-determining step.

plicate the effect sought. Nor can one always go to sufficiently low hydrogen-ion concentrations to study the general acid effect without retarding the rate excessively. In any event the absence of positive evidence for general acid catalysis can always be explained in terms of an exponent α close to unity in Brönsted's catalysis relationship (9b), i.e., hydronium ion may simply be a much more effective catalyst for such reactions than other weaker acids. Examples of reactions that appear favorable for the A-S_E2 type of mechanism will be noted later.

A rather different indicator measure of acidity is J_0, derived from the ionization of uncharged secondary bases such as 4,4′,4″-trinitrotriphenylcarbinol (71, 99, 193):

$$\mathrm{ROH} + \mathrm{H}^+ = \mathrm{R}^+ + \mathrm{H_2O}$$

$$J_0 \equiv -\mathrm{p}K_{\mathrm{ROH}} - \log \frac{C_{\mathrm{R}^+}}{C_{\mathrm{ROH}}} = -\log \frac{a_{\mathrm{H}^+} f_{\mathrm{ROH}}}{a_{\mathrm{H_2O}} f_{\mathrm{R}^+}} \tag{17}$$

With increasing concentration of sulfuric acid in water, this function has been observed to deviate in the negative direction from H_0 by increasingly larger amounts (71).[10] Some acid-catalyzed reactions may involve a similar preliminary equilibrium, i.e., may take place through a rate-determining reaction of an ion analogous to R^+ rather than to $\mathrm{ROH_2}^+$. Such a reaction may be expected under a condition corresponding to equation 10 to show rate correlation with J_0 rather than with H_0. This idea was in fact first suggested (241) in connection with aromatic nitration, on the supposition that nitronium ion is produced by the reaction:

$$\mathrm{HNO_3} + \mathrm{H}^+ = \mathrm{NO_2}^+ + \mathrm{H_2O}$$

Several applications of J_0 to mechanistic questions will be considered in the sections which follow.

These classes of mechanisms by no means exhaust the possibilities of acid catalysis. They represent rather some situations sufficiently simple to be analyzed with the aid of indicator and other related equilibrium data. Needless to say, it is entirely legitimate to investigate a possible correlation between H_0 (or any other acidity function) and the observed rate of any reaction whatever. However, the situations in which the significance of a correlation with H_0 can be readily interpreted will normally be restricted to a particular class of acid-catalyzed reactions, those in which the initial step consists in reaction of a single uncharged reactant molecule with a single acid species. For more complicated situations, such as those involving charged reactants or acid-catalyzed reactions of higher order, correlations with H_0 may still be empirically observed but their interpretation will ordinarily be more difficult. Caution must be observed also in interpreting studies made in nonaqueous or mixed solvents, where in general the variation of activity coefficients with changes in the medium is less well understood.

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[10] In reference 71 this function is called C_0.

It is worth emphasizing that the application of acidity functions to the problem of reaction mechanisms is a somewhat temporary expedient. The ultimate hope is to have enough information on activity coefficients of molecules and ions, including transition states, to permit complete and precise prediction of the medium effect for any mechanism and in fact for any reaction. Studies on activity coefficients of organic molecules and ions are in progress in several laboratories and knowledge of medium effects on them is gradually accumulating.[11] However, there is a long way to go before general and quantitative predictions of kinetic medium effects are possible. In the meantime there is a place for approximate predictions. The question to be examined in this review is whether acidity functions can perform a useful role in making such approximate predictions for certain mechanisms of acid catalysis.

Until very recently, all the available H_0 data (reviewed in reference 193) referred to a temperature of or close to 25°C. The rate data of interest have not been subject to this restriction and significant correlations between rate and H_0 have in fact been reported with rate temperatures ranging from 0° to 140°C. Some idea of the effect of comparing rate data at one temperature with indicator data at another can be derived from the precise study made by Leininger and Kilpatrick (151) on the hydrolysis of sucrose catalyzed by hydrochloric acid (0.6 to 6 M) at various temperatures. If one plots their log k_1 values against $-H_0$ for the same acid concentrations by volume at 25°C., the curve for each temperature is quite linear but with the following slopes:

t	Slope $\frac{d(\log k_1)_t}{d(-H_0)_{25°}}$	t	Slope $\frac{d(\log k_1)_t}{d(-H_0)_{25°}}$
°C.		°C.	
0	1.29	25	1.08
10	1.20	30	1.04
15	1.14	35	1.00
20	1.11	40	0.98

A similar trend has been found by Adams (1) for the acid-catalyzed dehydration of 1,1,2,2-tetraphenylethanol in the quite different medium, acetic acid–water mixtures containing 10^{-3} M perchloric acid (with rate coefficients corrected for solvent expansion):

t	Slope $\frac{d(\log k_1)_t}{d(-H_0)_{25°}}$	t	Slope $\frac{d(\log k_1)_t}{d(-H_0)_{25°}}$
°C.		°C.	
30	0.99	50	0.89
40	0.94	60	0.84

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[11] An interesting way to obtain general formulae for the prediction of medium effects due to solvent changes has recently been proposed by Grunwald and Berkowitz (111). If this type of procedure proves generally applicable, the semiquantitative calculation of useful activity coefficient ratios for organic species will be very greatly eased.

This trend is in the direction predicted by recent studies on the variation of H_0 itself with temperature (91, 92). These studies indicate that with sulfuric acid, for example, between 10 and 80 per cent concentration by weight the quantity $\mathrm{d}(H_0)_{80^\circ}/\mathrm{d}(H_0)_{20^\circ}$ remains approximately constant with a mean value of 0.93; if the H_0 values are compared for changing acid concentration by volume (uncorrected for solvent expansion) instead of by weight, then between 1 and 14 M the value of $\mathrm{d}(H_0)_{80^\circ}/\mathrm{d}(H_0)_{20^\circ}$ is 0.95. This indicates that for sulfuric acid solutions the slope of log $(k_1)_{80^\circ}$ vs. $(-H_0)_{20^\circ}$ for a reaction showing correlation between rate and H_0 will be smaller by a factor of order 0.95 than the ideal slope (unity) expected if log $(k_1)_{80^\circ}$ were plotted against $(-H_0)_{80^\circ}$. Other factors that may cause the slope of a log k_1 vs. $-H_0$ correlation to deviate from unity will be discussed in detail later (Section II,B,6).

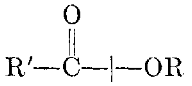
II. Acid Catalysis in Aqueous Solutions

From several standpoints aqueous solutions constitute the most favorable case for investigation of correlations between rate and H_0. Water is without doubt the best studied of all solvents. Certainly more information about activity coefficients of solutes is available for water than for any other solvent. The large majority of studies of acid catalysis have been made in water. Finally the H_0 function is better established, both experimentally and theoretically, for water than for any other solvent. The sections which follow consider several cases of correlations between rate and H_0 and several cases where such a correlation is not observed. In every instance consideration is given to evidence for other mechanisms and normally the data are discussed from the standpoint of the applicability of the Zucker–Hammett hypothesis.

A. ESTERS AND LACTONES

1. Hydrolysis of carboxylic esters

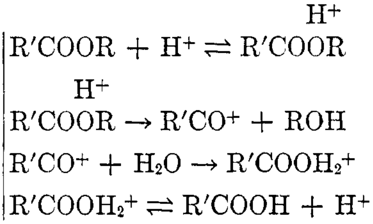
In an extensive discussion of the mechanisms of ester hydrolysis, Day and Ingold (64, 127c) noted that there are some eight possible mechanisms depending on whether the reaction is acid catalyzed or base catalyzed, whether alkyl–oxygen or acyl–oxygen bond fission occurs, and whether the rate-determining step is a unimolecular split or a bimolecular attack by water or hydroxide ion. With ordinary esters acyl–oxygen bond fission normally occurs:



$$\mathrm{R'{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}|{-}OR}$$

as has been shown by hydrolysis studies in O^{18}-labeled water (62, 160, 198). Hence for the acid-catalyzed hydrolysis the two likely mechanisms are those called by Ingold $A_{Ac}1$ and $A_{Ac}2$ (127c):

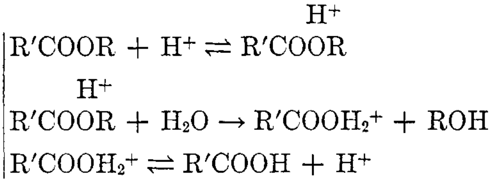
$A_{Ac}1$



$$\begin{array}{l|ll} & R'COOR + H^+ \rightleftharpoons \overset{H^+}{R'COOR} & \text{Equilibrium} \\ A_{Ac}1 & \overset{H^+}{R'COOR} \rightarrow R'CO^+ + ROH & \text{Slow} \\ & R'CO^+ + H_2O \rightarrow R'COOH_2^+ & \text{Fast} \\ & R'COOH_2^+ \rightleftharpoons R'COOH + H^+ & \text{Equilibrium} \end{array}$$

and

$A_{Ac}2$



$$\begin{array}{l|ll} & R'COOR + H^+ \rightleftharpoons \overset{H^+}{R'COOR} & \text{Equilibrium} \\ A_{Ac}2 & \overset{H^+}{R'COOR} + H_2O \rightarrow R'COOH_2^+ + ROH & \text{Slow} \\ & R'COOH_2^+ \rightleftharpoons R'COOH + H^+ & \text{Equilibrium} \end{array}$$

The proposed mechanisms for ester formation are simply the reverse of these.

As Ingold notes, the evidence clearly indicates that ordinary esters hydrolyze in dilute aqueous solutions of acids by the $A_{Ac}2$ mechanism. The large steric hindrance from ortho or alpha carbon substituents in the acid moiety and the small polar effects of other substituents are the expected results. When water is the solvent both the $A_{Ac}1$ and the $A_{Ac}2$ mechanisms lead to second-order kinetics (first order in ester and first order in concentration of catalyzing acid), but with "wet" acetone as the solvent it has been found that the rate of hydrolysis of methyl acetate is additionally proportional to concentration of water (88). The proposed equilibrium formation of the conjugate acid of the ester which is common to both mechanisms is supported by the observation that the hydrolysis is faster in solvent D_2O than in H_2O (244). Finally, in aqueous solutions only specific hydrogen-ion catalysis is observed (9a), and this is the expected result for the A-2 mechanism.

Even though the $A_{Ac}1$ mechanism is not common, it is clearly a possibility for special situations. It should characteristically show absence of steric hindrance, marked acceleration by electron-releasing groups in the acid moiety, and enhanced rate in solvents of high ionizing power such as sulfuric acid (127c). In fact, studies on the cryoscopic behavior of mesitoic acid in sulfuric acid constitute fairly good evidence that the $A_{Ac}1$ mechanism may enter for this reactant and solvent (177, 239). Recent studies on the kinetics of solvolysis of methyl benzoate in solutions of nearly anhydrous sulfuric acid show definitely that the rate is independent of the concentration of water and this strongly implies that the mechanism is A-1 (153); the reaction probably goes through an acylium ion, $R'CO^+$, similar to that formed from mesitoic acid.

Further evidence for these mechanisms should be available from application of the Zucker–Hammett hypothesis. The $A_{Ac}1$ mechanism leads to an activated complex which does *not* contain the water molecule; hence the prediction is that rate should be proportional to h_0. For the $A_{Ac}2$ mechanism, on the other hand, one would expect rate to vary in approximate proportion to C_{H^+}.

TABLE 2

Hydrolysis of methyl formate at 25°C.

C_{HCl}	10^4k_1	H_0	$\log \frac{k_1}{C_{HCl}}$	$\log k_1 + H_0$
moles/liter				
2.67	106	−0.79	−2.40	−2.76
3.58	153	−1.11	−2.37	−2.93
4.48	223	−1.40	−2.30	−3.05
5.30	291	−1.72	−2.26	−3.26
6.41	450	−2.11	−2.16	−3.46

Several studies show that in concentrated solutions of strong acids, rates of hydrolysis of ordinary esters quite generally follow C_{H^+} rather than h_0. Duboux and de Sousa (80) studied the hydrolysis of methyl acetate in aqueous solutions of hydrochloric acid with acid concentrations ranging up to 3.65 *M*. A plot of $\log k_1$ vs. $\log C_{H^+}$ for these data is almost linear with a slope of unity but shows a slight upward curvature at the highest concentrations of acid. In other words the data closely parallel concentration of acid but show a small positive salt effect. Recent studies by Bell, Dowding, and Noble (12) and by Chmiel and Long (55) show similar results. The former find that the first-order rate coefficients for the hydrolysis of methyl formate in solutions of hydrochloric acid are not precisely proportional to either C_{H^+} or h_0 but that the former variable fits the data much better (table 2). These same investigators have studied the hydrolysis of ethyl acetate in hydrochloric acid solutions ranging up to 10 *M* and in sulfuric acid solutions up to 6.75 *M* and again conclude that the data are much more nearly linear in C_{H^+} than in h_0. Chmiel and Long (55) have studied the hydrolysis of methyl benzoate and of monoglyceryl esters of benzoic and anisic acids in aqueous solutions of sulfuric acid and perchloric acid with concentrations ranging up to 8 *M*. For all three esters the rates are quite closely proportional to C_{H^+} and hence not at all proportional to h_0.

Since the A-2 mechanism is quite firmly established for the hydrolysis of all these esters in dilute aqueous solutions, the observed proportionality between rate and C_{H^+} lends strong support to the validity of the Zucker–Hammett hypothesis.

As implied earlier, one may hope to obtain ester hydrolysis by the $A_{Ac}1$ mechanism if the normal "bimolecular" mechanism is slowed down by steric hindrance and if the acid component of the ester is characterized by strong electron release. This possibility was investigated by hydrolyzing methyl mesitoate in aqueous solutions of perchloric and sulfuric acids, with the results shown in figure 3. Clearly in this case the rate is not at all proportional to C_{H^+} and instead is closely proportional to h_0. Actually the slope of the lines of figure 3 is 1.2, indicating that the rate increases slightly *faster* than expected from exact proportionality to h_0. The difference in behavior between this ester and those previously discussed is striking and it seems reasonable to conclude that the mechanism has changed to $A_{Ac}1$. In view of the strong steric hindrance involved, this change is surely not surprising.

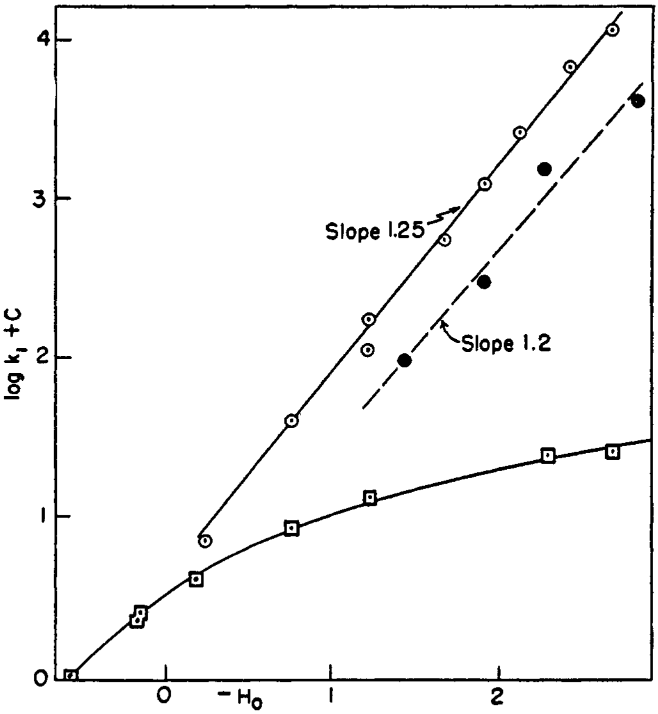
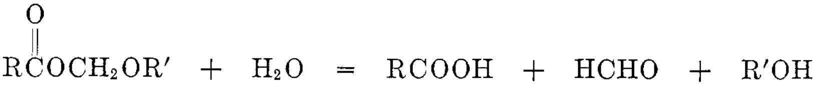


FIG. 3. Hydrolysis of esters in aqueous acids at 90°C. (55). Methyl mesitoate: ⊙, log k_1 + 7 for perchloric acid; ●, log k_1 + 7 for sulfuric acid. Glyceryl benzoate: ⊡, log k_1 + 4.5 for perchloric acid.

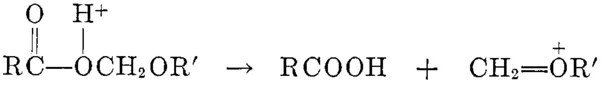
An example of $A_{Al}1$ ester hydrolysis is reported by Salomaa (211b) for alkoxymethyl esters of acetic and formic acids. These hydrolyze according to the overall equation:



$$R\overset{\overset{O}{\|}}{C}OCH_2OR' + H_2O = RCOOH + HCHO + R'OH$$

In 0.1–5.0 M aqueous hydrochloric acid and 0.7–3.3 M aqueous sulfuric acid at 25°C. the rate of hydrolysis for methoxymethyl acetate follows H_0 with a log k_1 vs. $-H_0$ slope of 1.15. Similar results were obtained for ethoxymethyl acetate and methoxymethyl formate studied over a more restricted range of acidities (0.1–2.5 M hydrochloric acid). Systematic deviations from H_0 were observed, however, with mixtures of sodium perchlorate and perchloric acid.

The investigator proposes as the rate-determining step:



$$R\overset{\overset{O}{\|}}{C}—\overset{\overset{H^+}{|}}{O}CH_2OR' \rightarrow RCOOH + CH_2{=}\overset{+}{O}R'$$

Independent evidence for such a mechanism comes from his studies with mixed solvents containing methanol or ethanol in addition to water. Here the $A_{Al}1$

reaction may be in competition with ordinary $A_{Ac}2$ fission:

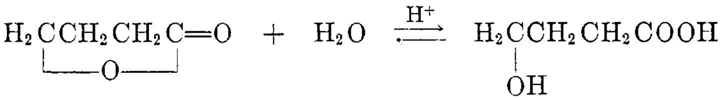
$$R\overset{\overset{O}{\|}}{C}-\overset{\overset{H^+}{|}}{O}CH_2OR' + H_2O \rightarrow R\overset{\overset{O}{\|}}{C}OH_2^+ + HOCH_2OR'$$

Hydrolysis of the hemiacetal produced by the latter reaction would be expected to yield exclusively formaldehyde as product (in addition to RCOOH and R′OH). The former reaction, however, in the presence of high alcohol concentration yields an acetal by reaction of the intermediate $CH_2{=}\overset{+}{O}R'$ ion. By actual analysis of the reaction mixtures, methylal was found among the solvolysis products of both methoxymethyl formate and methoxymethyl acetate in 30–65 mole per cent methanol–water containing 0.12 M hydrochloric acid; similarly, ethylal was found in the solvolysis of ethoxymethyl acetate by 35–80 mole per cent ethanol–water containing 0.1 M hydrochloric acid. Separation of the overall rate into a unimolecular ($A_{Al}1$) and a bimolecular ($A_{Ac}2$) component on the basis of such analyses permitted the conclusion to be drawn that the unimolecular rate followed h_0 reasonably closely with changing proportion of alcohol to water, whereas the bimolecular rate at fixed acid concentration was independent of the solvent composition. This is of course in agreement with the Zucker–Hammett hypothesis. Furthermore, the actual magnitudes of the relative rates indicated that in aqueous hydrochloric acid only the $A_{Al}1$ mechanism would be significant for methoxymethyl and ethoxymethyl acetates, whereas for methoxymethyl formate in the more dilute solutions, the $A_{Ac}2$ mechanism would also contribute. This indication was supported by the fact that the hydrolysis of methoxymethyl formate, unlike that of the others, showed deviation from the Arrhenius equation in 0.025 M and 0.1 M aqueous hydrochloric acid between 0° and 60°C., confirming the actual presence of two independent reaction paths with different activation energies.

Bell and Lukianenko (14) have recently reported on the acid-catalyzed reactions of the ester-like molecule, ethylidene acetate. In the aprotic solvent chlorobenzene, this molecule decomposes into acetic anhydride and acetaldehyde; the reaction is catalyzed both by trichloroacetic acid and by the Lewis acid, stannic chloride. In aqueous hydrochloric acid up to 9 M concentration there is a hydrolysis to acetic acid and acetaldehyde, the rate of which is much more closely proportional to hydrogen-ion concentration than to h_0. The course of the reaction is in fact very similar to that of ethyl acetate in the same medium. The investigators conclude that the mechanism is probably similar to the usual A-2. Salomaa (211c) has drawn the same conclusion from a similar study of this hydrolysis and also that of the closely related compound methylene diacetate.

2. Hydrolysis and formation of lactones

Lactones are simply inner esters of hydroxy acids and for the unstrained five-membered γ-lactones one would expect hydrolysis by the normal $A_{Ac}2$ mechanism. This in turn leads to the prediction that the first-order rate coefficient for the hydrolysis should be proportional to C_{H^+}, not to h_0. Long, Dunkle, and McDevit (159, 162) investigated this for γ-butyrolactone by studying its hydrolysis in aqueous solutions of perchloric and hydrochloric acids of from 0.4 to 4 M concentration. The reaction involved,



$$\underbrace{\mathrm{H_2CCH_2CH_2C{=}O}}_{\mathrm{O}} + \mathrm{H_2O} \overset{\mathrm{H^+}}{\rightleftharpoons} \underset{\mathrm{OH}}{\mathrm{H_2C}}\mathrm{CH_2CH_2COOH}$$

is reversible, but simultaneous study of rates and equilibria permits evaluation of the first-order rate coefficients k_1 for the hydrolysis reaction and k_r for its reverse, the reaction of lactone formation. Figure 4 gives the plots of log k_1 vs. log C_{H^+} for hydrolysis by perchloric and hydrochloric acids. For both cases the rates are closely proportional to C_{H^+} (the slopes of the straight lines are 1.1 for hydrochloric and 1.0 for perchloric acid) and depart widely from proportionality with h_0. This is support for the expected $A_{Ac}2$ mechanism and it may be concluded that γ-lactones behave like ordinary esters.

An interesting aspect of the γ-lactone reaction is that for the reverse reaction no water molecule is involved and hence the transition state is structurally equivalent to the conjugate acid of the reactant. The Zucker–Hammett hypothesis would therefore predict proportionality between k_r and h_0. Figure 5 is a plot of log k_r vs. $-H_0$, and it can be seen that indeed there is an almost linear dependence. The slopes of the straight lines in figure 5 are 0.9 rather than unity, but the data fit h_0 far better than they do C_{H^+}. This is clearly the expected

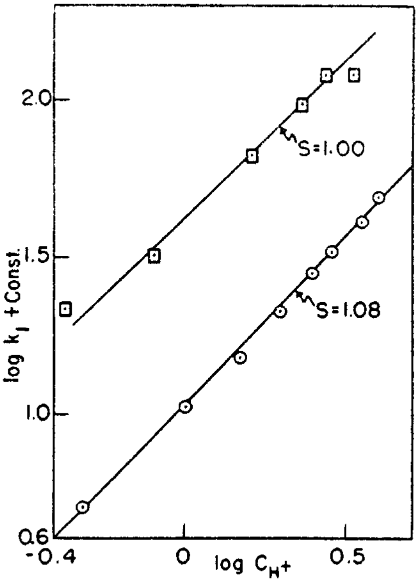


FIG. 4. Hydrolysis of γ-butyrolactone in aqueous solutions of acids: ⊡, perchloric acid at 5°C.; ⊙, hydrochloric acid at 0°C. (159, 162).

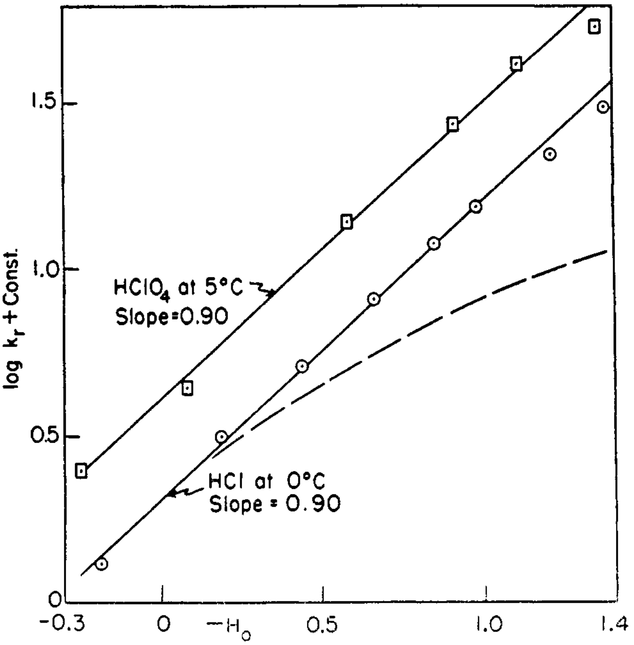


FIG. 5. Rate of formation of γ-butyrolactone. The dotted line gives the predicted behavior of log k_r for rate proportional to C_{HCl}.

result for the reverse of the $A_{Ac}2$ mechanism as applied to lactone formation and constitutes strong support for the Zucker–Hammett hypothesis.

Results of a very different character are obtained with the strained, four-membered β-lactones. The hydrolysis of these goes to completion, and kinetic studies by Johansson (131), Olson and Miller (187), and Long and Purchase (166) show that there are three distinct hydrolysis paths—acid, basic, and neutral—very similar to those found for epoxides (Section II,B,4; a further similarity is that β-lactones have a strong tendency to react with nucleophilic reagents just as do epoxides (7)). Olson and Hyde (186) have made studies with O^{18}-labeled water and find that the "neutral" hydrolysis involves alkyl–oxygen fission but that both the basic and the acid hydrolysis involve the more usual acyl–oxygen fission.

Long and Purchase (166) have studied the acid hydrolysis of β-propiolactone in concentrated solutions of sulfuric, nitric, and perchloric acids. Since there is also a pH-independent reaction the rate law can be written

$$-\frac{1}{C_L}\frac{dC_L}{dt} = k_1 + k_w$$

where k_1 is a function of acidity and k_w is not. The value of k_w can be determined in solutions of low acidity and then k_1 can be calculated by subtracting k_w from the observed first-order rate coefficient. Figure 6 gives a plot of log k_1 vs. $-H_0$.

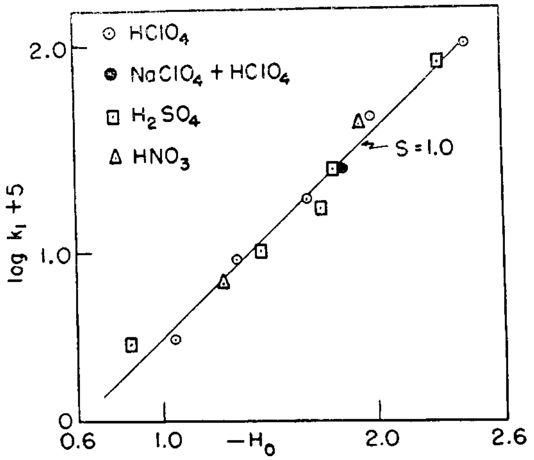


Fig. 6. Hydrolysis of β-propiolactone at 25°C. (166)

The straight line in the figure is drawn with a slope of unity and clearly fits the data very well.

Since the Zucker–Hammett hypothesis appears to be quite well established by other studies with esters and lactones, it seems safe to conclude from the H_0 correlation that a water molecule does not enter into the activated complex for β-lactones. This in turn strongly suggests that the hydrolysis goes through a "unimolecular" $A_{Ac}1$ mechanism, in contrast to the results for γ-lactones where the $A_{Ac}2$ mechanism operates.

3. Esterification by sulfuric acid

The clear implication of the $A_{Ac}2$ mechanism for ester hydrolysis outlined in the preceding sections is that the reverse acid-catalyzed esterification of an alcohol by a carboxylic acid is a third-order process. As a result the question of possible correlation of rate and h_0 is a complex one. A somewhat simpler case is presented by esterification with sulfuric acid,

$$ROH + H_2SO_4 = ROSO_3H + H_2O$$

a reaction which has recently been studied in aqueous solutions of from 65 to 93 per cent sulfuric acid (247) with low concentrations of 2,4-dinitrobenzyl alcohol. The rate of esterification is faster in D_2O–D_2SO_4 mixtures than in corresponding mixtures of H_2O and H_2SO_4, implying a preliminary equilibrium proton transfer. Rates increase markedly with acidity and are closely proportional to h_0. The investigators conclude that the reaction is probably of the "unimolecular" type. However, as they also point out, for these concentrated solutions of sulfuric acid it is not easy to distinguish a unimolecular rate step from a bimolecular one.

The same reaction was earlier studied by Deno and Newman (72), who interpreted their data by means of a bimolecular rate-determining step. However, they employed much larger concentrations of alcohol; a typical solution contained water, 2-butanol, and sulfuric acid in initial molar proportion of 0.860:1:1. They estimated H_0 for these solutions by assuming that the alcohol had the same effect as an equal number of moles of additional water. On this basis they concluded that the second-order rate coefficient for the esterification by sulfuric acid was proportional to h_0. In view of recent studies showing that isopropyl alcohol decreases $-H_0$ for sulfuric acid–water mixtures much more than does the same number of moles of water (6), the proposed correlation is rather uncertain.

4. Hydrolysis of amides

Since amides are closely related to esters, it is reasonable to expect their acid-catalyzed hydrolysis also to proceed by an A-2 mechanism (127c), as follows:

$$RCONH_2 + H^+ \rightleftharpoons RCONH_3^+ \qquad \text{Equilibrium}$$

$$RCONH_3^+ + H_2O \rightarrow RCOOH_2^+ + NH_3 \qquad \text{Slow}$$

$$RCOOH_2^+ + NH_3 \rightarrow RCOOH + NH_4^+ \qquad \text{Fast}$$

One might expect to obtain evidence for this by showing that k_1 for the reaction is proportional to C_{H^+} rather than to h_0 and in at least one favorable case, that of the hydrolysis of formamide in aqueous hydrochloric acid at concentrations up to 4 M, the rate does appear to be linear in C_{H^+} (142). However for most uncharged amides, such a comparison is seriously complicated by the fact that the hydrolysis rate reaches a maximum value at strong acid concentrations of from 4 to 6 M (17, 87, 202, 205, 238).

The most reasonable explanation of the leveling off of rate is that the reactant amides are sufficiently strong bases so that at these high acidities they are converted largely to their conjugate acid forms. From the above mechanism (for the usual case where $C_{H^+} \gg C_S^{\text{total}}$), one can write

$$\text{Rate} = k_2 C_{SH^+} = \frac{k_2}{K_{SH^+}} C_S C_{H^+}$$

$$= \frac{k_2 C_S^{\text{total}} C_{H^+}}{K_{SH^+} + C_{H^+}}$$

where K_{SH^+} is the ionization constant of the conjugate acid of the amide SH^+, C_S is the concentration of uncharged amide, and C_S^{total} is the total concentration of amide, i.e., the sum of C_S and C_{SH^+}. This rate law predicts that if the reactant is a relatively strong base (K_{SH^+} small), C_{H^+} can become large relative to K_{SH^+}, leading eventually to a rate which is independent of acid concentration. This appears to be the case for aliphatic amides. For example, the rate data for the hydrolysis of acetamide in aqueous hydrochloric acid are in reasonable agreement with the final form of the above rate equation using the known value of $K_{SH^+} = 3$ (87).

A more precise treatment (85a, 211a) with consideration of the activity coefficients of the reacting species leads to the equation (see equation 12a):

$$\text{Rate} = \frac{k_2^0 C_S^{\text{total}} C_{H^+}}{K_{SH^+} + \dfrac{a_{H^+} f_S}{f_{SH^+}}} \; \frac{f_S f_{H^+} a_{H_2O}}{f_\ddagger}$$

$$k_1 = \frac{k_2^0 C_{H^+}}{K_{SH^+} + h_0 \dfrac{f_{BH^+} f_S}{f_B f_{SH^+}}} \; \frac{f_S f_{H^+} a_{H_2O}}{f_\ddagger}$$

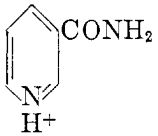
In view of equation 6 the activity coefficients in the denominator of this expression may be expected to cancel out with changing acid concentration, so that:

$$k_1 = \frac{k_2^0 C_{H^+}}{K_{SH^+} + h_0} \; \frac{f_S f_{H^+} a_{H_2O}}{f_\ddagger} \qquad (18)$$

With increasing acid concentration h_0 may become large compared with K_{SH^+} and since it also increases more rapidly than C_{H^+}, the specific rate k_1 may actually pass through a maximum consistently with the Zucker–Hammett hypothesis, i.e., with the activity coefficient factor in equation 18 canceling out as suggested by equation 14 for the A-2 hydrolysis mechanism. Taylor and Rosenthal (237) have shown that the maxima in the hydrolysis rates of acetamide and thioacetamide with changing acid concentration are in this sense in agreement with the A-2 mechanism.

Various other studies on amide hydrolysis are in conformity with the above $A_{Ac}2$ mechanism. Thus, as with the acid-catalyzed hydrolysis of esters, substitution in the meta and para positions of benzamide has only a small effect on the rate, regardless of polarity (204); in contrast, ortho substituents markedly retard the rate. Reitz (205, 206) has studied the relative rates of the hydrolysis of acetamide in D_2O and H_2O and finds that for reaction in dilute acid solutions the value of k_D/k_H is greater than unity, as expected for a reaction involving a preliminary acid-base equilibrium. However, for reaction in 4 M hydrochloric acid the value of k_D/k_H is only 0.86. The probable explanation is that at this high acidity most of the acetamide is converted to the conjugate acid both in H_2O and in D_2O; as a result the determining factor is not concentration of conjugate acid but relative rates of reaction of SH^+ and SD^+. For this situation the expected result is $k_D/k_H < 1$.

Jellinek, Gordon, and Urwin (129, 130) have found that the hydrolyses of the heterocyclic amides nicotinamide, isonicotinamide, and picolinamide in aqueous hydrochloric acid all show an almost linear increase in rate with concentration of acid up to 8.5 M. The absence of any leveling off in rate implies that these reactants function as much weaker bases than acetamide and similar uncharged amides. This is quite plausible, since the ring nitrogen will react with very low concentrations of acid; the actual reactant for the hydrolysis reaction will therefore be a charged species of the type:



The amide group in this case should be a much weaker base than in the more usual uncharged amides. Hence the reaction doubtless goes by the A-2 mechanism given previously with only the modification that because the R group in this case is charged, the preliminary acid-base equilibrium is not shifted far to the right even by 8.5 *M* acid.

B. ETHERS AND RELATED COMPOUNDS

1. Hydrolysis of sucrose

More recent kinetic studies of the hydrolysis of sucrose at high acid concentrations are in agreement with the previously noted correlation between rate and h_0. Krieble (141, 143) has conducted rate measurements at 20°C. with hydrochloric acid up to 10 molal concentration and with sulfuric acid up to 6.5 molal concentration. Duboux (79) has investigated aqueous hydrochloric acid up to 7 molal concentration at 0°C. and 25°C. and has also studied the effects of adding salts (81). Leininger and Kilpatrick (151) have investigated hydrochloric acid very precisely at concentrations up to 6 *M* over the range 0–35°C. and have shown that the relationship between rate coefficient and acid concentration varies slightly but systematically with temperature (see page 945). Figure 7 shows log k_1 vs. $-H_0$ from rate measurements by these various investigators; the straight lines have been drawn in with unit slopes, and one sees that the correlation is good up to at least $H_0 = -2.0$ (about 6 *M* acid). Krieble's data at higher acid concentrations show a trend away from the linear correlation, though there is some difficulty in interpretation because of the relatively large concentration of sucrose used (50 g. per liter of solution).

This reaction is generally regarded as showing specific hydrogen-ion catalysis rather than general acid catalysis (9a). Evidence for the establishment of an acid-base type of equilibrium prior to the rate-determining step is the fact that the reaction goes faster in D_2O than in H_2O (9c, 244). The rate in solutions of hydrochloric acid is markedly increased by addition of the salts lithium chloride, sodium chloride, potassium chloride, barium chloride, sodium bromide, or aluminum nitrate (112, 194). The precise effect is specific to the particular salt and is probably attributable to a general salting-out effect of the electrolytes on sucrose, i.e., to increases with electrolyte concentration in the activity coefficient of sucrose, f_S, which appears in equation 7. (Salt effects on reactions following the A-1 mechanism will be discussed more particularly in Section II,B,6). The rate has been measured also in mixed solvents containing 0.1 *M* hydrochloric acid

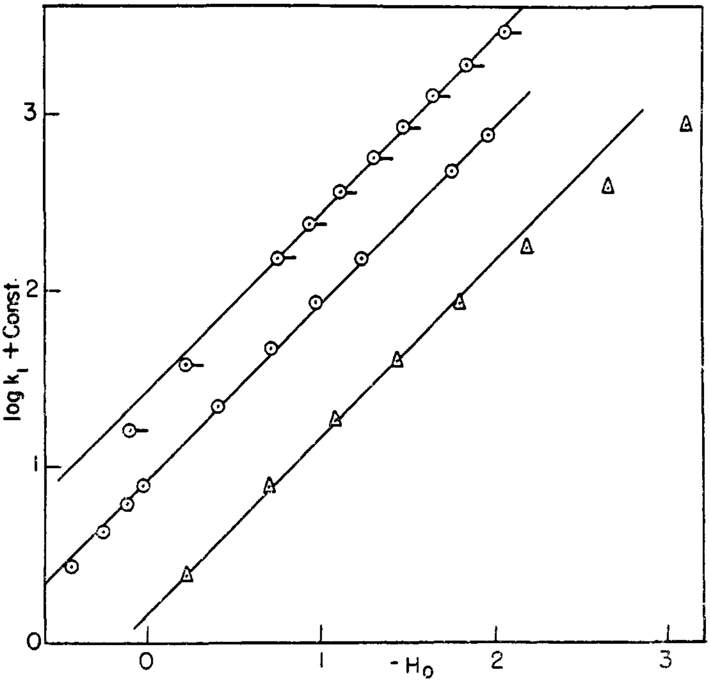


FIG. 7. Hydrolysis of sucrose in aqueous hydrochloric acid: ⊙–, 0.6–5.8 M acid at −0.01°C. (151); ⊙, 0.1–5.6 M acid at 25°C. (79); △, 1.0–8.3 M acid at 20°C. (141, 143). The straight lines are drawn with slopes of unity.

(2); it shows a slight decrease with increasing concentration of ethanol in water and an increase with increasing concentration of dioxane in water.

Various suggestions have been made to explain the lack of correlation noted in figure 1 between log k_1 and $-H_0$ for solutions of trichloroacetic acid. One suggestion is that esterification of one of the sucrose hydroxyls occurs, giving a more easily hydrolyzable compound (115b). Another possible explanation is general acid catalysis. Actually a very similar behavior will be noted in Section II,B,2 for the decomposition of paraldehyde; the explanation suggested there is that the H_0 scale is basically unsatisfactory for aqueous solutions of weak organic acids and that, as a result, log k_1 vs. H_0 correlations are not to be expected for studies with these acids.

The structure of sucrose is sufficiently complex so that the location of the proton which adds on to form the postulated conjugate acid SH^+ is not certainly known; there is therefore no reliable basis for surmising the precise nature of the rearrangement serving as the rate-controlling step in the hydrolysis. The overall reaction must in fact be quite complicated, involving mutarotation of both products and rearrangement of fructose from the furanose to the pyranose configuration (151). In other words, there is no independent evidence aside from the Zucker–Hammett hypothesis itself that the reaction goes according to an A-1 rather than an A-2 mechanism.

2. Depolymerization of trioxane and paraldehyde

A somewhat simpler picture is presented by the acid-catalyzed depolymerization of trioxane and paraldehyde. The former is a cyclic trimer of formaldehyde and the latter is the corresponding cyclic trimer of acetaldehyde. Each decomposes in aqueous acid solutions to the respective monomer at a rate which is first order in the polymer concentration. At the comparatively low trimer concentrations which are suitable for rate studies, the reactions appear to be uncomplicated and irreversible. Both decompositions have been investigated also as thermal gas reactions (51). The thermal decompositions proceed at ordinary pressures as first-order homogeneous gas reactions (270–345°C.) and trioxane in particular shows a decrease in rate coefficient with decreasing pressure below 15 mm. of mercury, in accordance with Lindemann's hypothesis; paraldehyde does not show this effect over the range of pressures investigated.

The depolymerization of trioxane in aqueous solutions of mineral acids has been studied by several investigators (10, 190, 240). The rate coefficient correlates closely with H_0 over a wide range of acidities (189). This is shown for the older data in figure 8 and is confirmed in more recent studies by Bell, Bascombe, and McCoubrey (10); for their more precise data, however, these investigators report a log k_1 vs. $-H_0$ slope of 1.2 rather than unity. For hydrofluoric acid (figure 2 of reference 10), the rate increases considerably more rapidly than h_0 at acid concentrations exceeding 8 M. The rate in perchloric acid solutions is markedly increased by the addition of sodium perchlorate but still remains in close correlation with H_0 (190).

The depolymerization of paraldehyde was studied by Bell and Brown (11), who found that for aqueous solutions of the strong mineral acids sulfuric, perchloric, nitric, and hydrochloric, log k_1 was linear in $-H_0$ with slope of 1.16

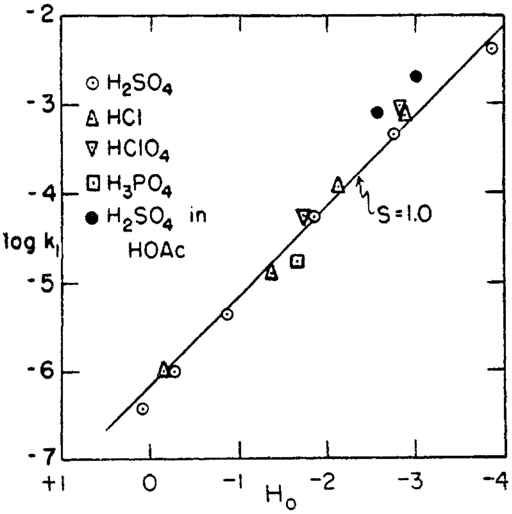


FIG. 8. Depolymerization of trioxane in aqueous solutions of acids at 40°C.; however, the solid points are for solutions of sulfuric acid in glacial acetic acid (189, 240).

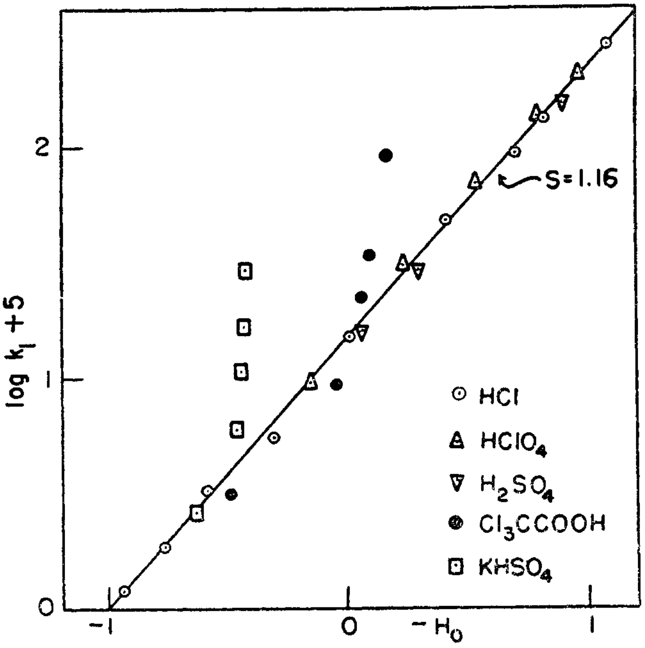


FIG. 9. Depolymerization of paraldehyde in aqueous acids at 25°C. (11)

(figure 9). For the weaker acids potassium acid sulfate, trichloroacetic acid, and dichloroacetic acid, however, the value of log k_1 increases with acid concentration much more rapidly than does $-H_0$, a situation found also for trichloroacetic acid in the inversion of sucrose (figure 1).[12] For these "weak" acids, H_0 actually levels off and shows a plateau of practically constant value at concentrations above 1 M (see figure 9 of reference 193). The failure of log k_1 to follow $-H_0$ therefore results from the rate continuing to increase with increasing acid concentration while $-H_0$ stays constant. A plausible explanation (193) of the leveling of H_0 in these cases is a "salting-in" effect by the relatively large acid molecules and their ions on the uncharged indicator molecule B, i.e., a decrease in the activity coefficient f_B appearing in equations 3 and 5. This decrease must compensate for the increase in the factor, a_{H^+}/f_{BH^+}, most of which results from the increase in C_{H^+} itself with increasing acid concentration. In such circumstances it is not surprising that the condition of equation 9 for k_1 to be propor-

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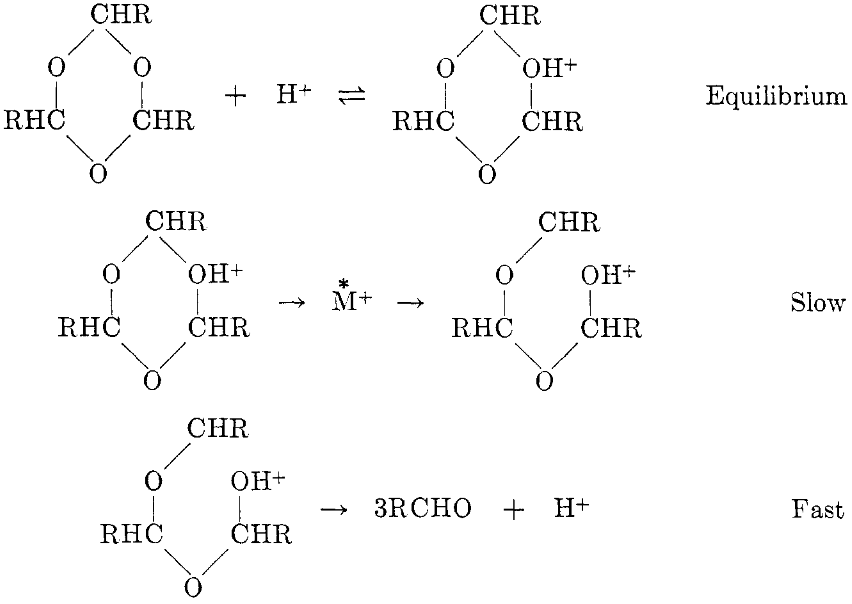
[12] The H_0 values in figure 9 for potassium acid sulfate were established from indicator measurements by Bell and Brown. The H_0 values for trichloroacetic acid have been recalculated (193) from recent indicator studies of Randles and Tedder (203) and have been used in preference to the older and less complete values of Hammett and Paul (117). Actually, the Hammett and Paul data lead to log k_1 vs. H_0 points which fall almost on top of those for the acid sulfate (see figure 2 of reference 11) and from this standpoint appear to be somewhat more plausible than those of Randles and Tedder. This uncertainty about trichloroacetic acid serves to emphasize the need for another H_0 study of its solutions in order to remove the present discrepancy.

tional to h_0 may not be satisfied; we should in fact expect to find that "salting-in" effects will be quite specific to the uncharged molecule B or S and will of course vary with the particular weak acid involved. These effects will be discussed more particularly in Section II,B,6. Bell and Brown, on the other hand, suggest the possibility that the departure of log k_1 from $-H_0$ may indicate general acid catalysis by the unionized acid molecules, but one then has to assume that the effect is proportional to a higher power than the first in the concentration. The decomposition of paraldehyde has been investigated also in nonaqueous solutions of both proton acids and Lewis acids (13, 15), but no H_0 data exist for these solutions.

The mechanism of acid catalysis for these reactions may be conceived as follows:



A rapid acid-base equilibrium is followed by a slow rearrangement resulting in rupture of a carbon–oxygen bond. The presence of a proton on the oxygen atom presumably lowers the activation energy of this step; it is noteworthy that the activation energy for the acid-catalyzed aqueous decomposition of trioxane is about 26 kcal. (240) as compared with 47.4 kcal. for the uncatalyzed thermal gas reaction (51). As suggested by Bell and Brown, the decomposition of the intermediate linear polymer in solutions of the strong acids probably takes place through a series of successive stages, each involving the separation of one of the monomeric units. While the monomeric product is undoubtedly extensively hydrated in aqueous solutions, no solvent molecule is actually needed for the decomposition, which may be effected simply through an electronic rearrangement. From this standpoint an A-1 mechanism is *a priori* plausible. The rate of decomposition of paraldehyde in aqueous solutions is about 5000 times more rapid than that of trioxane under similar conditions. This is consistent with the greater electron release afforded by the presence of the methyl groups on the ring carbon atoms.

One may conclude that there is substantial independent evidence in these cases for an A-1 mechanism. The fact that the rates actually correlate well with H_0 therefore provides support for the Zucker–Hammett hypothesis.

3. Hydrolysis of ordinary ethers

Available kinetic studies show that the hydrolysis of ordinary ethers is acid catalyzed. However, for the linear aliphatic ethers (and for unstrained cyclic ethers) the rate of hydrolysis is exceedingly slow even in concentrated solutions of acids (52, 221). As a result there are no data which permit a comparison between rate and h_0. Mechanisms for the acid-catalyzed hydrolysis have been reviewed by Burwell (52), who notes that relatively little firm evidence is available. He concludes that an A-2 mechanism is probable for primary ethers, that an A-1 mechanism involving formation of a carbonium ion is probable for tertiary ethers, and that for secondary ethers the picture is uncertain. This is evidently the sort of situation where kinetic studies which would permit application of the Zucker–Hammett hypothesis would be quite useful.

One minor piece of evidence which suggests that the acid-catalyzed hydrolysis of both primary and secondary ethers is by way of an A-1 mechanism is that the entropies of activation (231) have positive values of from 5 to 20 e.u. (rate coefficients in liters mole^{-1} sec.$^{-1}$). In a recent compilation (165) it appears that A-1 hydrolysis reactions in aqueous solutions generally have entropies of activation between 0 and +20 e.u., whereas A-2 reactions have values between −25 and −15 e.u.

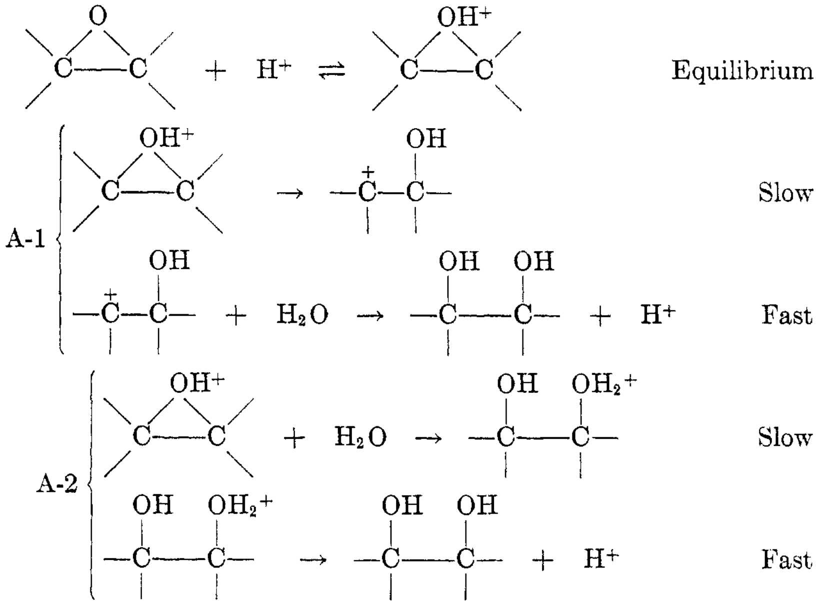
4. Hydrolysis of epoxides

In aqueous solutions epoxides are hydrolyzed to 1,2-glycols by at least three distinct mechanisms. There is a base-catalyzed reaction, an acid-catalyzed reaction, and a pH-independent water reaction (37, 156). Thus the complete rate law for hydrolysis is:

$$-\frac{1}{C_{\text{ox}}}\frac{\mathrm{d}C_{\text{ox}}}{\mathrm{d}t} = k_1C_{\text{H}^+} + k_2C_{\text{OH}^-} + k_wC_{\text{H}_2\text{O}}$$

In addition, both the oxide and its conjugate acid will react with a large number of nucleophilic reagents, such as halide ions (37). As a result, when an acid like hydrochloric acid is present, substitution to give a chlorohydrin will compete with hydrolysis. If it is desired to study the uncomplicated hydrolysis reaction, it is necessary to use an acid like perchloric acid whose anion is unreactive.

The early studies of Brönsted, Kilpatrick, and Kilpatrick (37) led to the conclusion that the hydrolysis of epoxides and their other reactions with nucleophiles exhibit only specific hydrogen-ion catalysis. This has recently been questioned by Swain (230), but his experimental studies are at such high concentrations, 4 M acetic acid and 1 M sodium acetate, that the observed rate increase may well be due to specific effects of the medium rather than to general acid catalysis. Pritchard and Long (200) find that the rate of hydrolysis is faster in solvent D_2O than in solvent H_2O and conclude that there is a rapid preliminary equilibrium between the epoxide and its conjugate acid. It thus appears that the most likely mechanism for the acid-catalyzed hydrolysis is either A-1 or A-2:



This is obviously a situation where the Zucker–Hammett hypothesis should permit a decision. The hydrolysis of ten simple epoxides has been studied in aqueous solutions of perchloric acid at 0°C. (199). For seven of the oxides the rates are slow enough to permit the study at acid concentrations above 1 *M*, where a significant difference exists between h_0 and C_{H^+}. Figure 10 shows the kinetic studies for several of the oxides and table 3 summarizes all of the results. Slopes of log k_1 vs. $-H_0$ are somewhat less than unity for epoxides with polar substituents and are generally slightly greater than unity for oxides of hydrocarbons. These small differences are probably due to specific effects of the type to be discussed in Section II,B,6. The important conclusion is that for all cases the rates are closely proportional to h_0. The predicted curve for proportionality between rate and C_{H^+} is shown for one of the epoxides in figure 10, and it is evident that at the higher concentrations the rate does not follow this measure of acidity. These results suggest that the activated complex does not contain a water molecule and hence support an A-1 carbonium-ion mechanism.

Several other facts also indicate a carbonium-ion mechanism. As table 3 shows, the rate increases strongly with substitution of electron-releasing groups. In fact, the rate data for monosubstituted ethylene oxides are well fitted by the Taft (232, 234) $\rho^*\sigma^*$ relation with a ρ^* value of -1.95 (199). This indicates little or no steric hindrance as well as a strong acceleration by electron-releasing

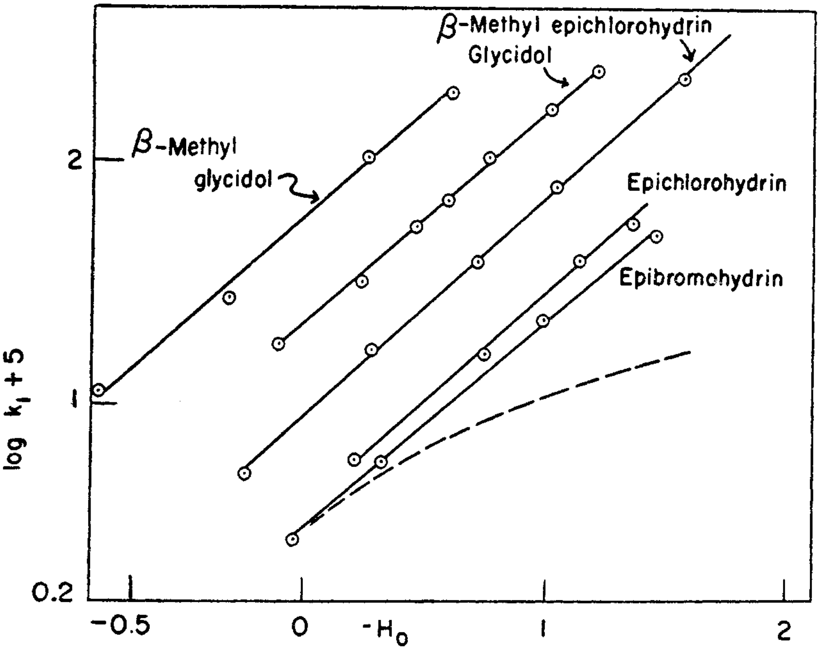


FIG. 10. Hydrolysis of epoxides in aqueous solutions of perchloric acid at 0°C. (199). The dotted line gives the predicted curve for epibromohydrin if the rate were proportional to C_{H^+}.

TABLE 3

Hydrolysis rates of epoxides in aqueous solutions of perchloric acid at 0°C.

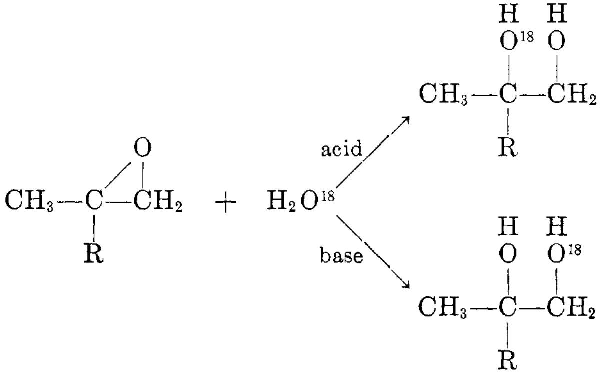
Epoxide	Concentration Range of $HClO_4$	$10^5 k_1$, sec.$^{-1}$ at $H_0 = 0.12$	Slope log k_1 vs. $-H_0$
	moles/liter		
Epibromohydrin	0.2–3.5	3.8	0.86
Epichlorohydrin	1.0–3.3	4.8	0.87
β-Methylepichlorohydrin	0.4–2.6	11.5	0.89
Glycidol	0.6–3.0	26.6	0.89
β-Methylglycidol	0.1–1.6	75.	0.89
Ethylene oxide	0.5–2.2	63.	1.06
Propylene oxide	0.8–2.5	350.	1.06
trans-2,3-Epoxybutane	0.01–0.5	770.*	1.01†
cis-2,3-Epoxybutane	3×10^{-3}–0.1	1480.*	0.95†
Isobutylene oxide	5×10^{-5}–2×10^{-3}	33000.*	0.98†

* Extrapolated value.

† Slope of plot of log k_1 vs. log C_{H^+}.

groups, both in accord with a carbonium-ion mechanism. Data are also available on the hydrolysis of asymmetrical epoxides in O^{18}-labeled water (164). With both propylene oxide and isobutylene oxide, hydrolysis in basic solution leads to entrance of the O^{18} at the primary carbon, whereas after acid hydrolysis the O^{18}

is found on the branched carbon:



These results are in accord with a nucleophilic attack by hydroxide ion for the basic hydrolysis and formation of a carbonium ion for the acid reaction. Since a comparison of rate and h_0 also points to an A-1 mechanism, it appears that the Zucker–Hammett hypothesis is valid for this reaction and gives added evidence for the mechanism.

Even though several lines of evidence thus point to a carbonium-ion mechanism, at least one important problem remains. This is that the stereochemical results (248) indicate essentially complete inversion accompanying the hydrolysis even for acid solutions. The epoxide system is a favorable case for "shielding" which would force the major reaction of a carbonium ion to occur at the side opposite to the displaced group. However, complete inversion is somewhat unexpected. Further study of this system, particularly of its stereochemical behavior, is clearly desirable.

5. Hydrolysis of acetic anhydride

The rate of hydrolysis of acetic anhydride has been investigated by Gold and Hilton (100, 101) in aqueous solutions of hydrochloric, perchloric, sulfuric, and phosphoric acids at 0°C. The first-order rate coefficient is approximately proportional to h_0 for all of these acids over a wide range of concentrations (figure 11). Deviations from exact proportionality are found with the different acids and are possibly attributable to variations in the activity coefficient ratio appearing in equation 9. The exact interpretation of these specific effects is uncertain, but in spite of them the correlation of log k_1 with $-H_0$ is far better than with log C_{H^+}.

The mechanism proposed by Gold and Hilton is as follows:

$$\mathrm{Ac_2O} + \mathrm{H}^+ \rightleftharpoons \mathrm{Ac_2OH}^+ \qquad \text{Equilibrium}$$

$$\mathrm{Ac_2OH}^+ \rightarrow \overset{*}{\mathrm{M}}{}^+ \rightarrow \mathrm{Ac}^+ + \mathrm{AcOH} \qquad \text{Slow}$$

$$\mathrm{Ac}^+ + \mathrm{H_2O} \rightarrow \mathrm{AcOH} + \mathrm{H}^+ \qquad \text{Fast}$$

where $\overset{*}{\mathrm{M}}{}^+$ represents the transition state for the rate-controlling step. There is no independent evidence that this reaction goes by the A-1 mechanism; hence it is desirable to obtain further kinetic data for other acid anhydrides.

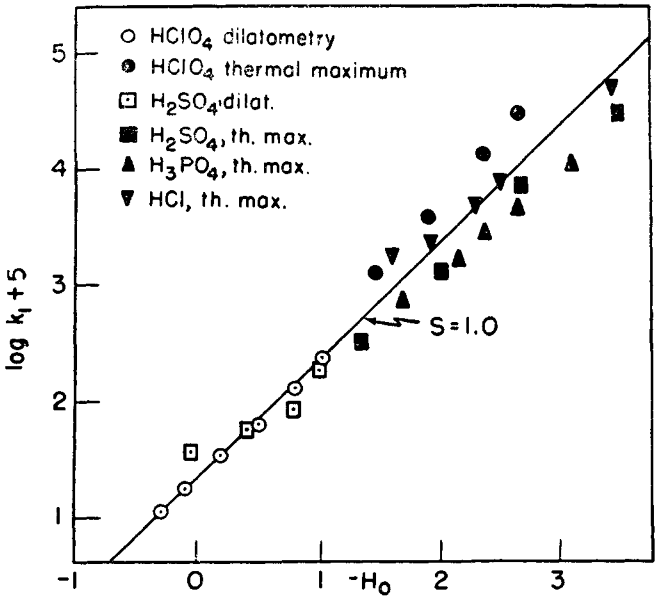


FIG. 11. Hydrolysis of acetic anhydride at 0°C. (100, 101)

6. *Hydrolysis of acetals, ketals, and glucosides*

(a) Aqueous solutions of strong acids

Various lines of evidence indicate that the acid-catalyzed hydrolysis of acetals goes through an A-1 mechanism (127b):

$$R'OCH_2OR + H^+ \rightleftharpoons R'OCH_2\overset{H^+}{O}R \qquad \text{Equilibrium}$$

$$R'OCH_2OH^+R \rightarrow R'OCH_2^+ + ROH \qquad \text{Slow}$$

$$R'OCH_2^+ + H_2O \rightarrow R'OCH_2OH + H^+ \qquad \text{Fast}$$

$$R'OCH_2OH \rightarrow R'OH + HCHO \qquad \text{Fast}$$

The hydrolysis in aqueous solutions shows specific hydrogen-ion catalysis (36, 38), a result which is consistent with this mechanism. The hydrolysis is faster for solutions in D_2O than for solutions in H_2O (244), and this is evidence for the proposed equilibrium formation of the conjugate acid. From studies of the hydrolysis of optically active *sec*-octyl acetal, O'Gorman and Lucas (185) concluded that the reaction does not go through an alkyl carbonium ion and hence that the above mechanism is correct. A similar conclusion follows from a recent study of the hydrolysis in O^{18}-labeled water (224). As Ingold has emphasized, the very large increases in rate which accompany increasing substitution of alkyl groups for hydrogens (220, 221) are the expected result for an A-1 mechanism. A recent study by Kreevoy and Taft (139, 140) has shown that the rates of hydrolysis of saturated aliphatic acetals and ketals of the general formula $RR'C(OC_2H_5)_2$ in 50 per cent dioxane–water satisfy the relationship

$$\log \frac{k}{k_0} = (\Sigma\sigma^*)\rho^* + (\Delta n)h$$

where ρ^* is a reaction constant, $(\Sigma\sigma^*)$ is the sum of Taft substituent constants σ^* for R and R′ (232, 234), and $(\Delta n)h$ is a hyperconjugation term proportional to the difference Δn between the number of α-hydrogen atoms in R and R′ and in the standard of comparison (acetonal). The fact that this simple relationship fits the data indicates that there is little or no steric hindrance for the addition of water to an acetal, and this is consistent with the proposed mechanism. Finally, the observed large negative value of ρ^*, −3.60, is consistent with formation of an "onium" ion in the rate step.

A kinetic study of the hydrolysis of methylal was carried out by McIntyre and Long (175) in aqueous solutions of three strong acids with concentrations ranging up to 4.3 M. In addition a few experiments were made with aqueous mixtures of sodium perchlorate and perchloric acid. Values of H_0 for these latter solutions are known from the work of Harbottle (121). Figure 12 is a plot of $\log k_1$ against H_0. Data for the solutions of the acids and of the salt–acid mixtures all fall fairly well on the same straight line. It is quite evident that the rate is

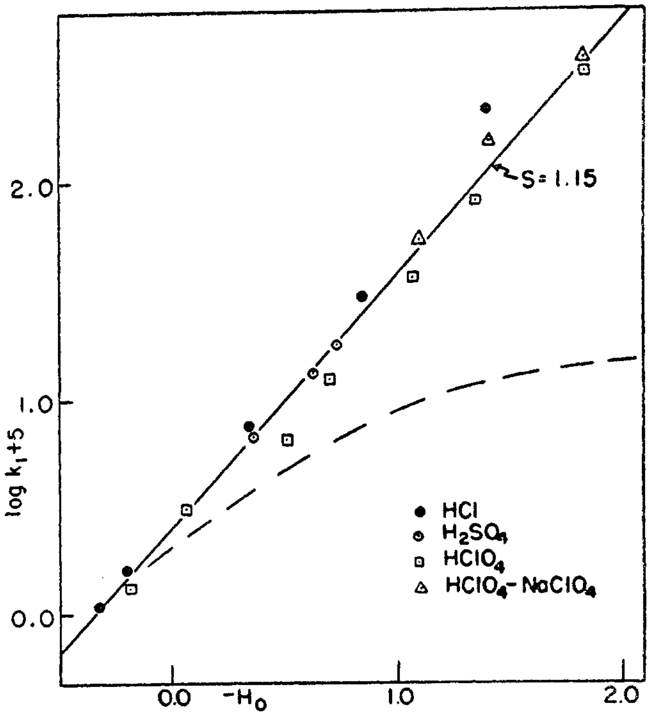


FIG. 12. Hydrolysis of methylal at 25°C. (175). The dotted line is predicted for the rate proportional to C_{H^+}.

proportional to h_0 and decidedly not proportional to concentration of acid. In terms of the Zucker–Hammett hypothesis this suggests that the activated complex does not contain a water molecule. Put another way, if the unimolecular mechanism can be assumed to be established from other evidence, the kinetic results are support for the Zucker–Hammett hypothesis.

The agreement between rate and h_0 for the data of figure 12 is not exact in that the slope of the straight line of the figure is 1.15, slightly greater than unity. Furthermore there is a small dependence of slope on the particular strong acid employed, "best" slopes of log k_1 vs. $-H_0$ for the individual acids being 1.25 for hydrochloric, 1.15 for sulfuric, and 1.08 for perchloric. Similar non-unit slopes have been noted for many other systems (see figures 4, 5, and 7) and it seems likely that the explanation for methylal given in the following paragraphs has general utility.

Given that the hydrolysis of methylal goes by an A-1 mechanism, the rate is expected to vary with H_0 by an equation of the form of equation 9. For log k_1 to be linear in $-H_0$ with a unit slope there must be a constant value of the activity-coefficient ratio $f_A f_{BH^+}/f_{\overset{*}{M}^+} f_B$, where A refers to methylal, B to an indicator, and $\overset{*}{M}^+$ to the transition state. Since all of the individual activity coefficients are unity in dilute aqueous solution by choice of standard state, the constant value must be unity. Hence for unit slope,

$$\frac{f_A}{f_{\overset{*}{M}^+}} = \frac{f_B}{f_{BH^+}}$$

The fact that the observed slopes are somewhat greater than unity means that the term $f_A/f_{\overset{*}{M}^+}$ increases relatively more with increasing concentration of acid than does the term f_B/f_{BH^+}. Furthermore, the magnitude of the increase varies with the different strong acids in that the observed slopes are from 1.08 to 1.25. Now, given the difference in structure between methylal and a typical Hammett indicator base, for example *p*-nitroaniline, one would surely expect a difference in the influence of electrolytes on their respective activity coefficients. Put another way, the ratio f_A/f_B would normally be expected to vary both with electrolyte concentration and with particular choice of electrolyte (161). Hence only if the activity coefficient ratio for the two ions, $f_{\overset{*}{M}^+}/f_{BH^+}$, varies with concentration and species of electrolyte in precisely the same way as does f_A/f_B will a unit slope for log k_1 vs. $-H_0$ be obtained. Since exact parallelism of these activity coefficient ratios is not to be expected, small departures of slope from unity can be assumed to be the normal behavior.

Actually a similar lack of precision is characteristic of the H_0 scale itself. The establishment and measurement of the H_0 scale involve assumptions of the type

$$\frac{f_B}{f_{BH^+}} = \frac{f_C}{f_{CH^+}}$$

where B and C are different indicators. Arguments similar to those above would lead one to believe that quite generally these ratios are not exactly equal but only approximately so, and this is indeed borne out by the indicator studies themselves (193). To this extent the H_0 scale is inexact and an at least comparable lack of exactness is to be expected for correlations of rate and H_0. Probably the most important reason why correlations of rate with H_0 may sometimes be even less satisfactory is that the reactant species for a rate study is occasionally very different indeed from a typical Hammett indicator, whereas for establishment of the H_0 scale itself the indicators were of fairly similar size and structure (115b, 116).

Two other studies are available on the rates of hydrolysis of acetals in concentrated solutions of strong acids. One is that of Leininger and Kilpatrick (152) on the hydrolysis of ethylal in solutions of hydrochloric acid at 0° and 10°C. A plot of log k_1 vs. $-H_0$ for these data gives straight lines but the slope is about 1.4, decidedly different from unity (see figure 2 of reference 175). McIntyre and Long (175) conclude that this larger slope, relative to that of 1.25 for methylal, is reasonable, since ethylal is a larger molecule and would be expected to show a larger salting-out effect (161). That is, the value of the ratio f_A/f_B would be larger for ethylal than for methylal and hence would lead to a larger slope of log k_1 vs. $-H_0$. The other study is by Kreevoy and Taft (139) on the acid-catalyzed hydrolysis of chloroacetal in solutions containing perchloric, sulfuric, and hydrochloric acids. The solvent is actually 4 per cent dioxane in water, but it seems reasonable to assume that behavior in this solvent will be very similar to that in water. The slope of log k_1 vs. $-H_0$ is close to unity for perchloric acid but is distinctly higher (about 1.5) for hydrochloric acid. The explanation for this is probably the same as that discussed above.

(b) Aqueous salt solutions

An explicit discussion of the relation between "salt effects" for acetal hydrolysis and dependence of rate on H_0 is given by Long and McIntyre (163), who studied the effects of several salts on the specific rate k_1 of the acid-catalyzed hydrolysis reaction, on the activity coefficient f_A of methylal, and on the activity coefficient f_B of the Hammett indicator *p*-nitroaniline. These various sets of data were compared with those of Paul (191) for the influence of the same salts on H_0 for solutions of 0.1 *M* hydrochloric acid as measured with the same indicator, *p*-nitroaniline. It was found that while all the salts increased the rate of hydrolysis, some of them caused an increase in the indicator acidity $-H_0$ while others caused a decrease. There was no apparent correlation between the two effects.

Since log k_1, log f_A, and log f_B are all approximately linear in salt concentration C_S, as is the change in $-H_0$, it is convenient to compare the various salt effects by giving the slopes of the respective plots, and this is done in table 4. The second column shows the kinetic salt effects for the hydrolysis of methylal in 0.37 *M* hydrochloric acid; the third column gives salt effects on $-H_0$ for 0.1 *M* hydrochloric acid with *p*-nitroaniline as indicator (these effects are not sensitive to the precise concentration of acid), while the fourth and fifth columns give the salting out parameters (slopes of log f_i vs. C_S) for the two nonelectrolytes methylal

TABLE 4

Comparison of salt effects

Salt	Slope b $\log k_1$ vs. C_s	Slope a $-\Delta H_0$ vs. C_s	Slope k_A $\log f_A$ vs. C_s	Slope k_B $\log f_B$ vs. C_s
NaBr	0.49	0.205	0.158	0.040
LiCl	0.42	0.245	0.145	0.082
NaCl	0.36	0.205	0.225	0.072
KCl	0.33	0.145	0.150	0.030
$(CH_3)_4NBr$	0.33	−0.12	0.127	−0.272
$(C_2H_5)_4NBr$	0.26	−0.41	0.075	−0.44
$C_7H_7SO_3Na$	0.11	−0.06	0.034	−0.51
$NaClO_4$	0.29	0.180		−0.082
HCl			0.00	0.10 (estimated)
$HClO_4$				0.18 (estimated)

and *p*-nitroaniline. The specific character of the salt effects is apparent, as is the lack of correlation between salt effects on $\log k_1$ and on $-H_0$.

One will note that there is a qualitative agreement between salt effects on $-H_0$ and on $\log f_B$, in that salts of small ions, e.g., sodium chloride, tend both to increase the indicator acidity and to salt out the indicator, while salts of large ions, e.g., tetraethylammonium bromide, tend both to decrease the indicator acidity and to salt in the indicator. Now from the definition of H_0 (see equation 3), the increase in acidity caused by the salt is given by

$$-\Delta H_0 \equiv (H_0)_{0.1M\,\mathrm{HCl}} - (H_0)_{\substack{0.1M\,\mathrm{HCl}\\+\mathrm{salt}}} = \log \frac{f_{\mathrm{H}^+} f_{\mathrm{B}}}{f_{\mathrm{BH}^+}}$$

where in this case the standard state for the activity coefficients is a salt-free solution of 0.1 M hydrochloric acid. The observed similar behavior of $-\Delta H_0$ and $\log f_B$ suggests that a major part of the influence of added salts on H_0 comes from the term f_B, i.e., from salt effects on the activity coefficient of the uncharged indicator molecule.

There is a similar qualitative agreement between the kinetic salt effects and the salt effects on $\log f_A$. All the salts increase the rate coefficient and salt out the reactant methylal. Analysis of the kinetic salt effect at constant acid concentration leads to the equation:

$$\log k_1 = -H_0 + \log \frac{f_{\mathrm{A}} f_{\mathrm{BH}^+}}{f_{\overset{*}{\mathrm{M}}{}^+} f_{\mathrm{B}}} + \text{constant} \tag{19}$$

which differs from equation 9 only in that the standard state is a salt-free acid solution of constant concentration instead of pure water. A correlation between $\log k_1$ and $-H_0$ would thus require that

$$\frac{f_{\mathrm{A}}}{f_{\mathrm{B}}} = \frac{f_{\overset{*}{\mathrm{M}}{}^+}}{f_{\mathrm{BH}^+}}$$

Table 4 shows that the ratio f_A/f_B varies considerably both with concentration and with species of electrolyte. The experimental fact that log k_1 does not parallel $-H_0$ for salt additions means that the term $f_{\overset{*}{M}^+}/f_{BH^+}$ does not change in the same way as f_A/f_B.

While $f_{\overset{*}{M}^+}/f_{BH^+}$ is of course not directly measurable, its value may be computed by difference from equation 19 and the data of table 4 for the particular reactant and indicator under consideration. For most of the salts its value remains close to unity (163). It follows that the lack of correlation between rate and H_0 for the salt solutions arises mainly from non-unit values of the ratio f_A/f_B. It follows also that the good correlation observed for solutions of the strong acids themselves reflects the fact that these electrolytes have comparatively small and nearly equal salt effects on different nonelectrolytes (161); the differences show up in log k_1 vs. $-H_0$ slopes differing slightly from unity, as exemplified in figure 12 and discussed previously.

Deno and Perizzolo (73a) have actually determined activity coefficients for a variety of compounds in sulfuric acid solutions from solubility measurements (e.g., benzene, diphenylmethane, acrylonitrile, acetophenone, triphenylcarbinol, etc.) and have shown that quite generally the slope of log f_A vs. acid concentration stays almost constant and close to zero up to at least 60 per cent acid. Similar results were noted in perchloric acid solutions (70). It is very reasonable therefore to conclude that a factor of the form f_A/f_B will stay nearly constant for these solutions. It follows that where rate correlations of A-1 reactions with H_0 are observed in aqueous solutions of the strong acids, the quantity $f_{BH^+}/f_{\overset{*}{M}^+}$ must likewise cancel out.[13] In sulfuric acid solutions beyond 60 per cent concentration, however, many aromatic compounds with polar substituents (e.g., nitrobenzene, benzoic acid) show a rapid decrease in log f_A and the magnitude of this effect is specific to the particular compound.

(c) Hydrolysis of glucosides

A combined isotopic-tracer and acidity-function study of the mechanism of the acid-catalyzed hydrolysis of several glucopyranosides has recently been reported (47). The compounds were methyl α-, methyl β-, phenyl α-, and phenyl

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[13] By comparing H_0 with the acidity function J_0 (see equation 17),

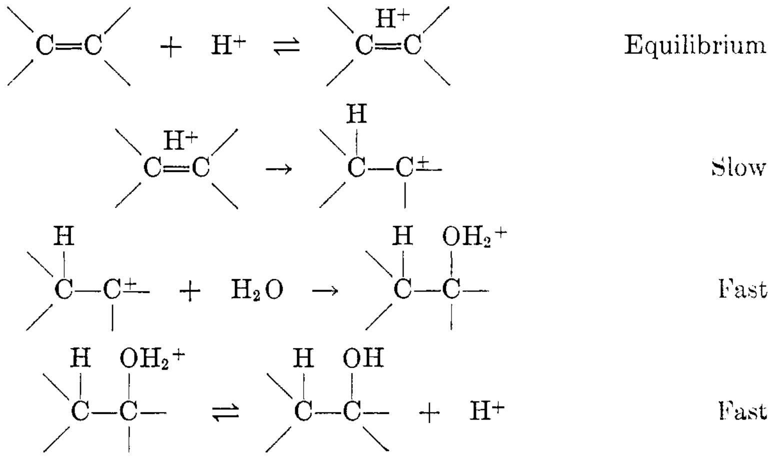
$$J_0 - H_0 = \log a_{H_2O} - \log \frac{f_{BH^+}f_{ROH}}{f_B f_{R^+}}$$

Deno and Perizzolo (73a) show that an activity coefficient ratio of the form of f_{BH^+}/f_{R^+} (where BH^+ is the cation of a typical Hammett indicator and R^+ is a tertiary carbonium ion) does *not* stay constant but increases rapidly with increasing sulfuric acid concentration. They suggest the possibility that for acid-catalyzed reactions of tertiary alcohols, correlations of rate with acidity intermediate between H_0 and J_0 may be found, depending on the extent to which the carbon–oxygen bond is extended in the transition state (i.e., whether $\overset{*}{M}^+$ is closer in structure to $R—OH_2^+$ or to R^+. Since $-J_0$ increases about twice as rapidly as $-H_0$ in aqueous sulfuric acid solutions of intermediate compositions (71), the distinction between the two extreme situations is certainly feasible for observation.

β-D-glucopyranoside. Hydrolysis in H_2O^{18} showed that in all cases fission of the hexose–oxygen bond was involved. Kinetic studies in aqueous perchloric and sulfuric acids up to 3.7 *M* concentration showed that in all cases the rates were closely proportional to h_0. Slopes of log k_1 vs. $-H_0$ for rate studies at temperatures of from 57° to 73°C. varied from 0.89 to 0.95. On the basis of these results the investigators concluded that an A-1 mechanism is involved. They noted, however, that two alternatives are available for the slow step. In one the conjugate acid loses methanol or phenol to give a "glucose" carbonium ion; in the other the conjugate acid undergoes an initial ring opening.

C. HYDRATION OF OLEFINS

It has been known for some time that the hydration of olefins is an acid-catalyzed reaction (168, 169) and that the hydrolysis shows only specific hydrogen-ion catalysis (56). This latter fact suggests (but does not demand) a preliminary proton transfer to the olefin. Taft (233) found that the rate of hydration of isobutene in aqueous nitric acid followed H_0 and from the Zucker–Hammett hypothesis concluded that the mechanism is as follows:

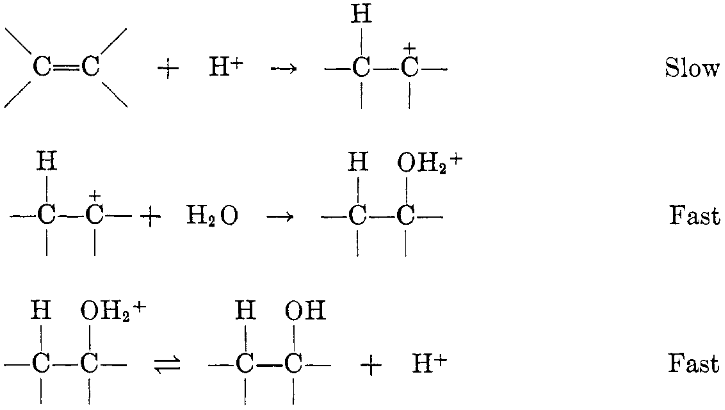


The proposed rate-determining step involves the transformation of a π-complex to a carbonium ion.

Several sorts of evidence have been adduced in favor of this mechanism (236). The fact that the hydrations of 2-methyl-1-butene and of 2-methyl-2-butene lead to the same product, *t*-amyl alcohol (169), but without any isomerization of the reactants (154) eliminates the possibility that a simple carbonium ion is formed in a preliminary acid-base equilibrium. This leads to only two alternatives. One is a rate-determining proton transfer with a Brönsted α close to unity so that only specific hydrogen-ion catalysis is observed. The other is a preliminary proton transfer to give a conjugate acid which on reversal loses the same proton it added. Purlee and Taft (201) conclude from the effect of D_2O as solvent on the rate of hydration that a preliminary equilibrium proton transfer does occur. As additional support for an A-1 mechanism (233, 236) it has been noted that the entropies of activation are close to zero, even though the entropy changes for the overall hydration are in the order of -20 e.u. This is in marked contrast to the strongly negative entropy of activation for the hydration of α,β-unsaturated aldehydes, which are probably hydrolyzed by an A-2 type of mechanism since their rates vary with concentration of strong acid, not with h_0 (249).

This mechanism for olefin hydration still presents some difficulties and, perhaps as a result, alternative explanations have been proposed (69). One difficulty is that the ratio of rate constants for hydration in D_2O versus H_2O is actually very close to unity for the two reactions so far studied (201), whereas for most A-1 reactions with a preliminary proton transfer this ratio is from two to three (200). As a result, the only real evidence for the equilibrium proton transfer is semiquantitative agreement with the Nelson–Butler (176) theory and unfortunately this is not a very sensitive test when k_{D_2O}/k_{H_2O} is close to unity.

At present it does not seem easy to exclude the possibility that the olefin hydration involves a slow proton transfer as the rate-determining step. For example,



Assuming a Brönsted α close to unity, only specific hydrogen-ion catalysis would be observed. As noted earlier, proportionality of rate and h_0 is plausible for this A-S_E2 mechanism. Finally, the observed small change in rate for reaction in D_2O vs. H_2O would be quite reasonable.

For the dehydration of an alcohol, which is the reverse of this reaction, both of the above mechanisms predict reaction through a carbonium ion. One might thus expect the dehydration rate to vary with the J_0 acidity function (equation 17). Although no direct rate studies appear to have been made for the simpler aliphatic alcohols, it has been reported that the concentration equilibrium constant for the reaction is almost independent of acid concentration (235). This implies that the rate of dehydration also increases with H_0 acidity and hence not with J_0, since even at low acid concentrations these two acidity functions differ appreciably (71). For the somewhat complex case of ring-substituted β-phenyl-β-hydroxypropionic acids, Noyce (180) has found that the dehydration rates in 5–10 M sulfuric acid increase more rapidly than h_0 and in fact show good correlation with J_0.

D. HYDROGEN ISOTOPE EXCHANGE OF AROMATIC COMPOUNDS

The kinetics of hydrogen isotope exchange reactions for aromatic compounds in aqueous acids have been investigated by Geib (90), by Gold and Long (102), and by Gold and Satchell (103–108, 212). The compounds investigated were resorcinol-d_5, pyrogallol, 9-deuteroanthracene, monodeuterobenzene, *o*-, *m*-, and *p*-deuterotoluene, and *o*-deutero derivatives of anisole, *p*-cresol, *p*-chlorophenol, and *p*-nitrophenol. The anthracene studies were complicated by the limited solubility of the organic substrate and the necessity of working with a two-phase system. The other compounds were studied under single-phase conditions and the results are subject to much more definite interpretation.

In aqueous sulfuric acid ranging from 9 to 85 per cent by weight, log k_1 for the homogeneous isotope exchange reactions was found to be linear in $-H_0$ with slope close to unity. Figure 13 gives data for three *o*-deutero-substituted phenols and illustrates the correlation of rate and H_0. The departure from proportionality which occurs for *p*-nitrophenol at the highest acidities is probably due to formation of the ordinary conjugate acid, $ArOH_2^+$, which is assumed by Gold and Satchell (104) to be unreactive. For hydrochloric acid in the case of *p*-cresol and for phosphoric acid in the case of *p*-chlorophenol, similar linear correlations between log k_1 and $-H_0$ were observed though the slopes were not identical with those obtained for sulfuric acid. The divergences were considered, however, to fall within a range accountable in terms of different specific salt effects of the acids on the uncharged substrate molecules as described in Section II,B,6.

These results suggest that a possible rate-determining step for the exchange reaction is an intramolecular rearrangement of a protonated form of the aromatic compound. Since the mechanism should apply to the exchange of benzene itself, a problem is presented as to how the entering proton is differentiated in the equilibrium stage, prior to the rearrangement, from those already bonded to the aromatic nucleus.

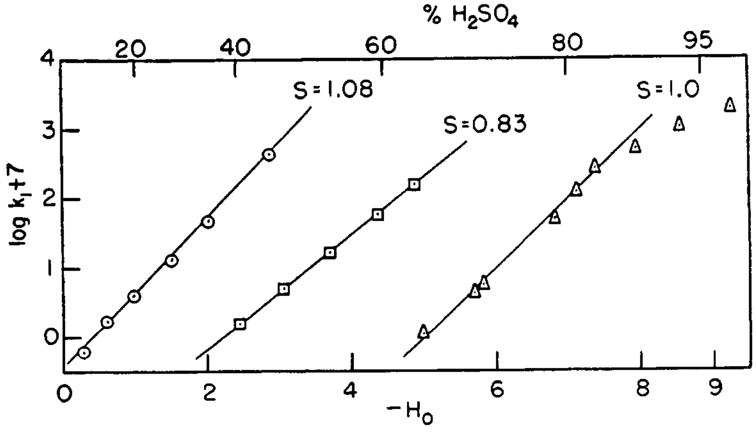
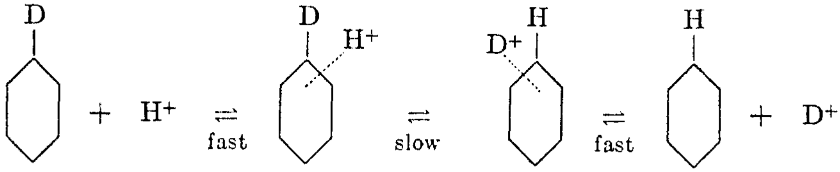


FIG. 13. Hydrogen isotope exchange in aqueous sulfuric acid at 25°C. (104): ⊙, *p*-cresol; ⊡, *p*-chlorophenol; △, *p*-nitrophenol.

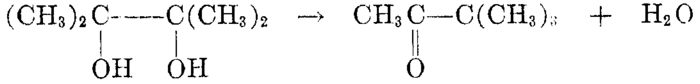
Gold and Satchell (104) propose a solution similar to that proposed by Taft (236) for the analogous problem in the case of olefin hydration discussed in the preceding section. They postulate that the entering proton is attached to the aromatic nucleus as an "outer complex," in which it is bonded less firmly (perhaps by some form of π bond) than the deuterium atom to be replaced. The rearrangement then consists of an exchange of bonding between the nonequivalent proton and the deuteron:



This is evidently an A-1 mechanism, since it involves an equilibrium proton transfer with a subsequent unimolecular rate step. On the basis of the evidence so far available, however, the possibility cannot be ruled out that these reactions may be examples of the A-S_E2 mechanism in which the rate is controlled by the initial reaction of the aromatic compound with the hydrogen ion. There is in fact a modicum of support for this mechanism in that Geib (90) found a slightly larger rate for the hydrogen isotope exchange of resorcinol-d_5 in H_2O, catalyzed by H^+, than for the exchange of normal resorcinol in D_2O, catalyzed by D^+. The expectation for an A-1 mechanism is a larger rate in D_2O.

E. REARRANGEMENTS

A number of acid-catalyzed rearrangements probably occur through reaction of the protonated reactant species to form a carbonium ion (115c, 243). According to the Zucker–Hammett hypothesis, proportionality between rate and h_0 is therefore frequently to be expected. A classic example is the rearrangement of pinacol:

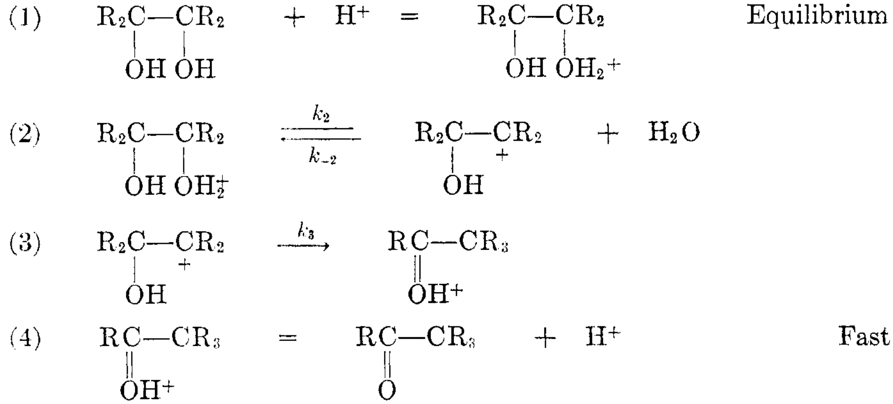


$$\underset{\text{OH}}{\overset{}{(CH_3)_2\underset{|}{C}}}\text{---}\underset{\text{OH}}{\underset{|}{C}}(CH_3)_2 \rightarrow CH_3\underset{\text{O}}{\underset{\|}{C}}\text{—}C(CH_3)_3 + H_2O$$

The rates of this and related reactions in aqueous solutions of strong acids have recently been studied in some detail (43, 82–84, 155).

The rearrangement of pinacol itself has been studied with sulfuric acid, 0.001 to 6.33 M, at temperatures from 72° to 154°C. (83) and with perchloric, hydrochloric, nitric, and p-toluenesulfonic acids, 0.01 to 1.4 M, at temperatures from 68° to 114°C. (82). The value of log k_1 at each temperature was found to be accurately linear in $-H_0$ (at 25°C.) with practically unit slope; for the lower acidities, $-H_0$ was of course indistinguishable from log C_{H^+}. Tests for catalysis by acids other than hydrogen ion gave negative results (84). The specific effects of sodium chloride mixed with hydrochloric acid at constant 0.1 M ionic strength and of potassium perchlorate mixed with perchloric acid at constant 0.05 M ionic strength were found to be negligible, the rates in both cases remaining proportional to the acid concentration. The investigators found no evidence for a secondary reaction mechanism by way of an intermediate epoxide, such as has been reported for the rearrangement of benzopinacol in nearly anhydrous acetic acid solutions (see reference 89 and also Section IV,A). They consider their results to be consistent with a simple A-1 mechanism whose rate-determining step is a rearrangement of the conjugate acid of pinacol. Rather similar conclusions were reached by Bunton and coworkers (43) and by Ley and Vernon (155) from studies of this and related rearrangements. The latter investigators also conducted O^{18} exchange studies on the reactants.

The mechanism for the pinacol rearrangement may be summarized as follows:



$$(1)\quad \begin{array}{c}R_2C{-}CR_2\\ |\quad\;\; |\\ OH\;OH\end{array} + H^+ = \begin{array}{c}R_2C{-}CR_2\\ |\quad\;\; |\\ OH\;OH_2^+\end{array} \qquad \text{Equilibrium}$$

$$(2)\quad \begin{array}{c}R_2C{-}CR_2\\ |\quad\;\; |\\ OH\;OH_2^+\end{array} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \begin{array}{c}R_2C{-}\overset{+}{C}R_2\\ |\quad\quad\\ OH\quad\end{array} + H_2O$$

$$(3)\quad \begin{array}{c}R_2C{-}\overset{+}{C}R_2\\ |\quad\quad\\ OH\quad\end{array} \xrightarrow{k_3} \begin{array}{c}RC{-}CR_3\\ \|\quad\quad\\ OH^+\quad\end{array}$$

$$(4)\quad \begin{array}{c}RC{-}CR_3\\ \|\quad\quad\\ OH^+\quad\end{array} = \begin{array}{c}RC{-}CR_3\\ \|\quad\quad\\ O\quad\end{array} + H^+ \qquad \text{Fast}$$

For an A-1 reaction the slow step would be 2. Actually, the rates of O^{18} exchange and of the rearrangement at relatively low acidities are about the same, implying that steps -2 and 3 are comparable in rate. With increasing acidity, i.e., as a_{H_2O} decreases, step -2 should become comparatively less important and there is some evidence that this is the case (40).

As a final item on this reaction, Deno (70) reports that in solutions of from 38 to 75 per cent sulfuric acid (for which the J_0 acidity function differs markedly from H_0), the rate of the pinacol rearrangement continues to be accurately proportional to h_0. Apparently even at these acidities step 3 does not become rate-determining.[14]

[14] *Note added in proof:* Duncan and Lynn (84a) have reported further isotope effects for this reaction. They found tritium exchange between both the hydroxyl hydrogens and tritiated water to be rapid at room temperature, exchange by the methyl hydrogens being relatively insignificant under these conditions. The rate of the rearrangement in 99.7 per cent D_2O at 100°C. was greater than in H_2O by a factor of 1.9, though unexpectedly a little smaller than in water containing 75 per cent D_2O. These facts are generally consistent with the hypothesis that the initial proton uptake (step 1) is rapid. With C^{14}-labeled pinacol and with aqueous hydrochloric acid at concentration of 0.01 and 0.2 *M* as catalyst, the rate of rearrangement at 100°C. was observed to be slower than for the normal compound by a factor of 0.47 when methyl carbon atoms were labeled and 0.75 when carbinol carbon atoms were labeled. These rather surprising isotope effects are reported to disappear at lower temperatures (60°C.). The investigators discuss the mechanistic implications of the isotope effects and reach the conclusion that different mechanisms must enter at high and at low temperature.

A comparison of rate with h_0 has shed light on another well-known rearrangement, that of benzidine. The rate of this reaction has previously been found to depend on the square of the hydrogen-ion concentration (53, 119) with some indication that the slow step might involve slow reaction of a monoprotonated species with a general acid (57). Studies of the rearrangement of hydrazobenzene in the solvent, 60 per cent by volume aqueous dioxane, have now shown that the reaction rate actually increases with the 2.5 power of the h_0 acidity (44). This strongly implies preëquilibrium formation of a diprotonated species, followed by a rate-determining rearrangement of this. Some confirmation is given by the fact that the k_D/k_H ratio for reaction in D_2O–dioxane as compared with reaction in H_2O–dioxane attains the high value of 4. Actually the reaction rate of a diprotonated molecule might be expected to depend on the product h_0h_+, but it is reasonable to suppose that the variation of h_+ with acid concentration is not very different from that of h_0 (20).

F. MISCELLANEOUS REACTIONS

There are several reactions where the question of parallelism between rate and h_0 can usefully be discussed but where, for one reason or another, conclusions are not entirely definite. This section considers examples.

A recent application of H_0 to mechanism is the study by Bunton, Konasiewicz, and Llewellyn (46) of oxygen exchange and racemization of *sec*-butyl alcohol in aqueous perchloric acid. The exchange reaction was studied at 100°C. both using O^{18}-enriched alcohol and using ordinary alcohol in acid solutions containing O^{18}-enriched water. The kinetic results are identical for the two procedures. The data show that the oxygen exchange is acid catalyzed and that the rate follows the acidity function H_0 rather than concentration of acid.[15] This result leads the investigators to propose a typical A-1 mechanism for the exchange:

$$\begin{array}{ll} ROH + H^+ \rightleftharpoons ROH_2^+ & \text{Equilibrium} \\ ROH_2^+ \rightarrow R^+ + H_2O & \text{Slow} \\ R^+ + H_2O^{18} \rightarrow RO^{18}H_2^+ & \text{Fast} \\ RO^{18}H_2^+ \rightleftharpoons RO^{18}H + H^+ & \text{Fast} \end{array}$$

Calculation of the entropy of activation for the racemization from the observed reaction rate and its temperature coefficient leads to an approximate value of +12 e.u. (with rate coefficients in liters mole^{-1} sec.^{-1}). This large value is consistent with the proposed A-1 mechanism (165).

The point of interest is that the racemization of optically active *sec*-butyl alcohol at 100°C. is also acid catalyzed and proceeds at a rate which is just

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[15] The original study extended only to perchloric acid concentrations of 0.9 M so that it was difficult to be sure that rates were indeed following H_0. However, in more recent work (49) the exchange rate has been shown to follow H_0 with a log k_1 vs. $-H_0$ slope close to unity up to values of H_0 equal to -1.3. Hence the conclusion that the rate of exchange follows H_0 seems well established.

twice that for O^{18} exchange. This implies that every act of substitution gives complete inversion of configuration. If the above mechanism is accepted this then means that the "carbonium ion" R^+ never becomes free and that instead the leaving water molecule so shields the point of reaction that the incoming water molecule always enters on the opposite side. Partial shielding would not be surprising, but the complete shielding implied by these results is unexpected. Since the observed relative rate of racemization is the expected result for an A-2 mechanism it is probably more than normally important to try to find additional evidence for the A-1 proposal.[16]

The second-order rate coefficient for the reaction between *t*-butyl alcohol and acrylonitrile to yield *N*-*t*-butylacrylamide has been found to be proportional to h_0 for aqueous sulfuric acid solutions containing 20–70 per cent acid (70a). The reaction was studied at 25°C. The investigators present evidence against a *t*-butyl carbonium ion and in favor of an S_N2 displacement reaction between acrylonitrile and the protonated alcohol. Since the rate of oxygen exchange between the alcohol and O^{18}-enriched water is the same within a factor of three, as is also the rate of reaction with propionitrile, they propose that the incoming molecule is so weakly bonded to the transition state that its nature has little effect on the rate. This would nevertheless imply that the water reaction takes place essentially through an A-2 mechanism and the observed correlation of its rate with H_0 would therefore be contrary to the Zucker–Hammett hypothesis. The investigators suggest that the reaction of *sec*-butyl alcohol with water may be similar. They studied also the rate of hydrolysis of acrylonitrile itself to acrylamide and found the first-order rate coefficient to be proportional to h_0 for sulfuric acid concentrations between 25 and 85 per cent; in this case no independent evidence is available for the mechanism.

Preliminary results are available for the aqueous hydrolysis of several phosphate esters in solutions of sufficient acidity that a diagnostic correlation of rate and H_0 can be sought (5). For most of the systems investigated, information is also available on whether phosphorus–oxygen or carbon–oxygen bond fission is involved (5, 19). It appears that with monomethyl phosphate there is an acid-catalyzed hydrolysis which involves the breaking of both phosphorus–oxygen and carbon–oxygen bonds and whose rate is proportional to C_{H^+}, not h_0. An A-2 mechanism with mixed bond fission is indicated. Monophenyl and *p*-tolyl phosphates, in contrast, show no acid-catalyzed hydrolysis in solutions as acid as 7 *M* perchloric acid. With a rather different type of compound, α-D-glucose 1-phosphate, the bond fission is exclusively carbon–oxygen and the rate is accurately proportional to h_0. This hydrolysis is very like that of the methyl and phenyl glucosides (Section II,B,6) and an A-1 mechanism is doubtless involved in both reactions. An acid-catalyzed hydrolysis also enters for 1- and 2-glyceryl

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[16] *Note added in proof:* Grunwald, Heller, and Klein (111a) have recently reported a similar study of 1-phenylethyl alcohol with 0.01–1 *M* aqueous perchloric acid at 30–65°C. They find that the rate of racemization is 1.22 times the rate of oxygen exchange, indicating partial shielding. Log k_1 for racemization is reported to increase with acid concentration more rapidly than $-H_0$ but less rapidly than $-J_0$.

phosphates but is complicated by an acid-catalyzed intramolecular rearrangement of the phosphate group between the 1- and the 2-positions. Isotopic tracer experiments show that both the hydrolysis and the rearrangement involve fission of phosphorus–oxygen bonds only.

Studies on the hydrolysis of other organophosphorus compounds suggest that comparison of rate with H_0 might give useful information on the mechanism of the acid-catalyzed reactions. Work on the hydrolysis of acetyl phosphate (137) and benzoyl phosphate (135) shows the existence of acid-catalyzed, base-catalyzed, and "water" mechanisms very similar to the results observed with epoxides and β-lactones. However, the acid-catalyzed reactions have so far not been carried to high enough acidity to distinguish between dependence of rate on C_{H^+} or on h_0. Dimethylamides of phosphoric acids show rather similar behavior (124) and in this case the hydrolysis has been studied to as high as 2.8 M hydrochloric acid. A steep rise in the rate with acidity is observed, suggesting parallelism of rate and h_0. In view of the contrast between this and the behavior of ordinary amides of carboxylic acids, further study would be most interesting.

One of the reactions whose rate was found originally by Hammett and Paul (118) to show correlation with H_0 is the hydrolysis of cyanamide to urea in aqueous solutions of nitric acid. The first-order rate coefficient, k_1, as determined by Grube, Motz, and Schmid (109, 110), was found to be accurately proportional to h_0 over the range 0.05 to 5 M nitric acid. This fact suggested as the rate-determining step a rearrangement of the conjugate acid of cyanamide, $HN{=}C{=}NH_2^+$, followed by rapid electrophilic addition of the water molecule (115d). More recent data by Sullivan and Kilpatrick (229) indicate that the reaction is rather complicated. Catalysis by halogen acids, in particular by hydrochloric and hydrobromic acids, is apparently hindered by the formation of a stable complex between the halide ion and either cyanamide itself or its conjugate acid. With trichloroacetic acid the specific rate, surprisingly, is higher than with nitric acid at the lower acid concentrations; the rate for nitric acid becomes faster only at concentrations above approximately 3 M. An additional complication is provided by the high base strengths of both cyanamide itself and the product urea, so that ionization appears to be extensive at the higher acid concentrations. Kilpatrick (134) has concluded that the rate-determining step in the hydrolysis is removal of a proton by general base catalysis (water itself serving as the base in nitric acid solutions) from an intermediate of the form, $HN{=}C(OH_2)^+{-}NH_2$, that is, a complex between a water molecule and the conjugate acid, to cyanamide. If this mechanism is accepted the observed correlation of rate and h_0 is fortuitous. However, the reaction is clearly complex and some further studies, for example of the hydrolysis in solutions of perchloric acid and in D_2O versus H_2O, might be desirable.

There are some acid-catalyzed reactions which, at acid concentrations sufficiently high for h_0 to be discriminated from C_{H^+}, proceed at rates too fast to be measured by ordinary techniques. An example is the solvolysis of diazoacetic ester, which has been studied only at acidities up to that of aqueous 0.1 M hydrochloric acid. A preliminary proton transfer appears here to be reliably established [enhanced rate in D_2O as compared with H_2O (9c) together with absence of general acid catalysis (9a)]. Further, good evidence has been offered that the actual structure for the conjugate acid cation is $N_2CH_2COOC_2H_5^+$, the two α-protons being equivalent (209). The decomposition of diazoacetone likewise shows specific hydrogen-ion catalysis in dilute aqueous acid solutions and fairly large salt effects (174). For the specific case of the solvolysis reactions of these species, there remains the question of whether the mechanism is A-1 or A-2, and the Zucker–Hammett hypothesis might usefully be applied if the reactions could be kinetically investigated at higher acid concentrations. Two possible courses are indicated: one could perhaps slow down the reactions without changing the mechanism by appropriate substitution of electron-withdrawal groups, or one could study the present reactions by the use of fast-reaction techniques.

An interesting example of an inverse application of h_0 to a reaction mechanism is the acid-inhibited oxidation of imidazole, $\underline{\mathrm{CH{=}CHN{=}CHNH}}$, by bromine (54). In aqueous acid solutions this molecule is present as the conjugate acid GH_2^+ so that the overall reaction is:

$$GH_2^+ + Br_2 = \text{products} + 2H^+ + 2Br^-$$

A plausible mechanism is:

$$GH_2^+ \rightleftharpoons GH + H^+ \qquad \text{Equilibrium}$$

$$GH + Br_2 \rightarrow \text{products} + H^+ + 2Br^- \qquad \text{Slow}$$

The equilibrium concentration of GH will vary inversely with h_0 acidity. Hence if the effect of the medium on the rate-determining step is small, that is, if $f_{GH}f_{Br_2} \cong f_M^*$, the observed rate should vary inversely with h_0. Experimentally a plot of $\log k_1$ vs. $-H_0$ for solutions of sulfuric acid up to 2.5 M is found to be linear with slope -0.9.

It is occasionally found that rates of acid-catalyzed reactions do not parallel either h_0 or C_{H^+}. In these cases the mechanism is likely to be complex and specific conclusions can be drawn only on the basis of further evidence. One such example is the cyclization of 3,3-dimethyl-5-ketohexenoic acid to dimedon in aqueous sulfuric acid (125). A plot of $\log k_1$ vs. $-H_0$ gave a somewhat curved line with a slope of only about 0.35. A plot of $\log k_1$ versus $\log C_{H_2SO_4}$ gave a more nearly straight line but with a slope of 4.6. From this the investigators concluded that the reaction probably does not conform to any simple mechanism.

The reaction between hydrogen peroxide and benzeneboronic acid to yield phenol and boric acid shows acid catalysis and has recently been studied for aqueous solutions of sulfuric, perchloric, and phosphoric acids up to 9 M concentrations (144). The reaction is first order in both reactants. For phosphoric acid the second-order rate coefficient is closely proportional to h_0. For sulfuric and perchloric acids, while the rate increases considerably faster than the acid concentration, it does not increase as fast as h_0. Log k_2 is reported to be linear with almost unit slope in the quantities $\log a_{H_2O}^{1/2} a_{H_2SO_4}^{3/2}$ and $\log a_{H_2O}a_{HClO_4}$, respectively, but since the data used for the acid activities are actually mean ionic activities, the significance of these relationships is doubtful.

The reaction between formaldehyde and polyvinyl alcohol to give a formal is acid catalyzed, the rate at constant acidity being first order in concentration of alcoholic hydroxyl groups as well as in concentration of formaldehyde (184). It has been reported that the rate changes with acidity in proportion to h_0 and from this the conclusion has been drawn that the reaction exhibits general acid catalysis. Unfortunately the highest acidity employed was only 0.75 *M* aqueous solutions of the mineral acids, and at this acidity h_0 is not significantly different from hydrogen-ion concentration.

III. Acid Catalysis in Concentrated Solutions of Sulfuric Acid

A. ACIDITY OF SULFURIC ACID SOLUTIONS

Values of H_0 have been determined for the complete range of sulfuric acid–water mixtures (116, 193). In fact the studies extend beyond the anhydrous acid to 107 per cent sulfuric acid, i.e., a solution of 32 per cent sulfur trioxide in H_2SO_4 (23, 27). The measured H_0 for this last solution is -12.9, a value which demonstrates that the sulfuric acid system alone furnishes an exceedingly wide range of acidity.

Considerable attention has been given to sulfuric acid as a solvent. The anhydrous acid has a dielectric constant higher than that of water (28, 29, 94) and dissolved salts satisfactorily obey an extended form of the Debye–Hückel equation (97). Water behaves as an almost strong 1:1 electrolyte (115b), ionizing according to the equation:

$$H_2O + H_2SO_4 = H_3O^+ + HSO_4^-$$

The equilibrium constant of this reaction has been estimated by Deno and Taft (74) to have a value of 50 at 25°C., so that in sulfuric acid containing less than 10 per cent water the reaction is more than 97 per cent complete. The acidity in this range is apparently determined by self-ionization of the solvent, just as in dilute aqueous solutions of bases; that is,

$$\frac{a_{H^+}\,a_{HSO_4^-}}{a_{H_2SO_4}} = K$$

where K is an equilibrium constant (115b). Brand (23) has shown that for concentrations of between 87 and 99.8 per cent sulfuric acid, H_0 satisfies an equation of the form

$$H_0 = \text{constant} + \log \frac{C_{HSO_4^-}}{C_{H_2SO_4}}$$

where $C_{HSO_4^-}$ and $C_{H_2SO_4}$ are computed on the simple assumption that the water ionization reaction goes to completion ($C_{HSO_4^-} = C^0_{H_2O}$ and $C_{H_2SO_4} = C^0_{H_2SO_4} - C^0_{H_2O}$, where $C^0_{H_2O}$ and $C^0_{H_2SO_4}$ are stoichiometric concentrations of water and sulfuric acid). This implies that activity coefficients of the various ionic and molecular species which are present stay constant over this range. The approximate constancy of the activity coefficients for these particular species should not, however, be taken to mean that *all* solutes behave ideally in almost anhydrous sulfuric acid. Brand (25) reports that 2,4-dinitrochlorobenzene, a compound known not to be ionized in anhydrous sulfuric acid, has an activity coefficient in 90 per cent sulfuric acid of 13 relative to a value of unity in the anhydrous solvent. Solubility data for other polynitro compounds imply comparable variations in activity coefficients (95, 126).

For solutions of from 87 to 100 per cent sulfuric acid, where the mole fraction of water is less than 0.5, one cannot expect to apply without modification all the concepts applicable to dilute aqueous solutions. The A-1 mechanism remains a plausible reaction path, and for this mechanism it seems reasonable to continue to expect proportionality of rate with h_0. In contrast, the status of the A-2 solvolysis reaction in highly concentrated solutions of sulfuric acid becomes less clear and the characteristics of such a reaction, if it occurs, are not known. As a consequence the mechanistic significance of a correlation between rate and H_0 is much less definite than in more dilute aqueous solutions. From a more empirical standpoint, H_0 is a practical measure of acidity which can be applied to sulfuric acid solutions containing small concentrations of water, and it is of the greatest interest to note that a number of reactions have been discovered whose rates do show correlation with H_0 in these media. As Hammett (115b) has pointed out, such correlations tend at least to establish acid catalysis, rather than "inhibition by water," as the effective mechanism. Of equal interest is the fact that the H_0 scale extends continuously into solutions of anhydrous sulfuric acid containing excess sulfur trioxide, thus affording a test for acid catalysis in this highly acid nonaqueous medium.

The J_0 acidity function is also well established for concentrated solutions of sulfuric acid and the acidity measured by $-J_0$ is known to increase much more rapidly with acid concentration than that measured by $-H_0$ (71). Hence it should be feasible to distinguish between reactions which proceed through the ordinary conjugate acid of the reacting molecule and those which proceed through a carbonium ion. Examples of reactions for which this possibility has been investigated are given in the following sections.

B. DECOMPOSITION OF CARBOXYLIC ACIDS

In their original paper on the acidity function, Hammett and Deyrup (116) discussed several correlations of rate and H_0 for studies with concentrated sulfuric acid. Among them were decompositions of carboxylic acids. A typical case is that of formic acid (75), which decomposes rapidly in pure sulfuric acid:

$$\mathrm{HCOOH} \rightarrow \mathrm{CO} + \mathrm{H_2O}$$

Figure 14 shows a plot of log k_1 vs. $-H_0$ for the reaction in 95–100 per cent sulfuric acid. The solid line is drawn with a slope of unity, and it is evident that the correlation of rate and H_0 is good. A similar but less precise correlation was found for the decomposition of malic acid (76, 78, 242). Cryoscopic studies have

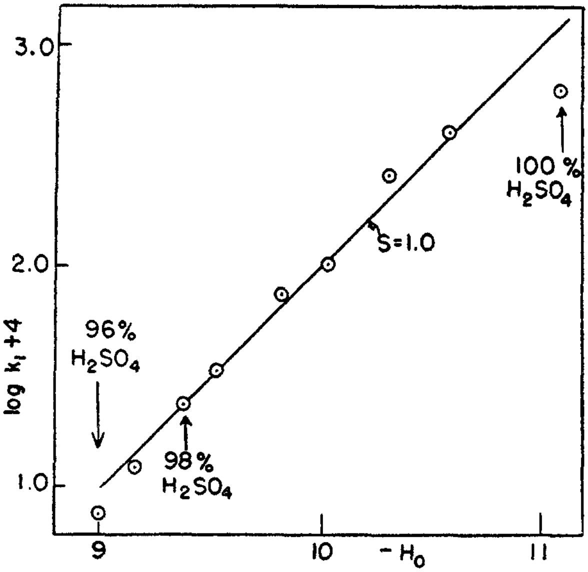


FIG. 14. Decomposition of formic acid in concentrated solutions of aqueous sulfuric acid at 15°C. (75, 116).

shown that a large number of aliphatic carboxylic acids behave in sulfuric acid as simple uncharged bases, undergoing ionization to the conjugate acid cation (95). There is no difficulty therefore in accepting this species as a reaction intermediate and in supposing that the observed correlation between rate and H_0 signifies an A-1 decomposition mechanism.

The formic acid reaction has recently been studied in 80–98 per cent aqueous sulfuric acid and in aqueous phosphoric acid containing 72–84 per cent phosphorus pentoxide (93). The results indicate a more complicated picture. Temperatures were from 20° to 100°C. and explicit account was taken of the variation of H_0 itself with temperature. For phosphoric acid at a given temperature, both the reaction rate and $-H_0$ were observed to pass through maximum values at a concentration of 79.7 per cent phosphorus pentoxide, which corresponds to the composition $H_4P_2O_7$. For both acids, however, with decreasing concentration log k_1 was found to decrease more rapidly than $-H_0$; the deviation was related to a change of activation energy with acid concentration. The investigators consider the possibility that a carbonium-ion intermediate, $O{=}\overset{+}{C}{-}H$, is involved, but this species appears improbable on structural grounds. Another feature of the results is that at a given value of H_0, log k_1 is considerably smaller for the sulfuric acid than for the phosphoric acid solutions.

For two other acids, oxalic (157, 246) and citric (245), plots of log k_1 vs. $-H_0$ show extended regions with slopes of 2 (114). More precisely, a plot of log k_1 vs. $-H_0$ for oxalic acid is curved but shows a slope of about unity for acid concentrations of from 90 to 96 per cent sulfuric acid and a slope of about 2 for acid concentrations of from 98 to 100 per cent sulfuric acid. With citric acid (figure

15) a similar slope of 2 has been interpreted (115b) as indicating a mechanism of the following type (where Cit is an abbreviation for citric acid):

$$\text{Cit} + 2\text{H}^+ \rightleftharpoons \text{Cit H}_2^{++} \qquad \text{Equilibrium}$$

$$\text{Cit H}_2^{++} \rightarrow \text{products} + 2\text{H}^+ \qquad \text{Slow}$$

In other words, formation of a diprotonated species is proposed. With citric acid there is a further complication in that the rate actually reaches a maximum value and then drops for higher acidities (see figure 15). There are several possible explanations of this latter behavior, but the most likely is that at the highest acidities the reactant is being converted into some species of much lower reactivity.

An extensive study has recently been made on the decarboxylation of benzoylformic acid (86). The rate of this reaction was followed in 94–98 per cent sulfuric acid and also in aqueous mixtures containing added potassium sulfate. Log k_1 vs. $-H_0$ for the former data gave a linear plot with a slope of 2.1. The investigators conclude that the reactant is the diacidium ion $C_6H_5COCO_2H_3^{++}$. Actually, for both this case and the previous examples, if two protons are added in the preliminary equilibrium the relevant acidity function is $H_+ + H_0$. The fact that the log k_1 vs. $-H_0$ slope is close to 2 then suggests that H_0 and H_+ are parallel functions of concentration for these sulfuric acid solutions (86). This is in agreement with actual indicator studies (20, 27).

The mechanisms of these acid-catalyzed decompositions in concentrated sulfuric acid have not been established, but an A-1 type seems highly plausible

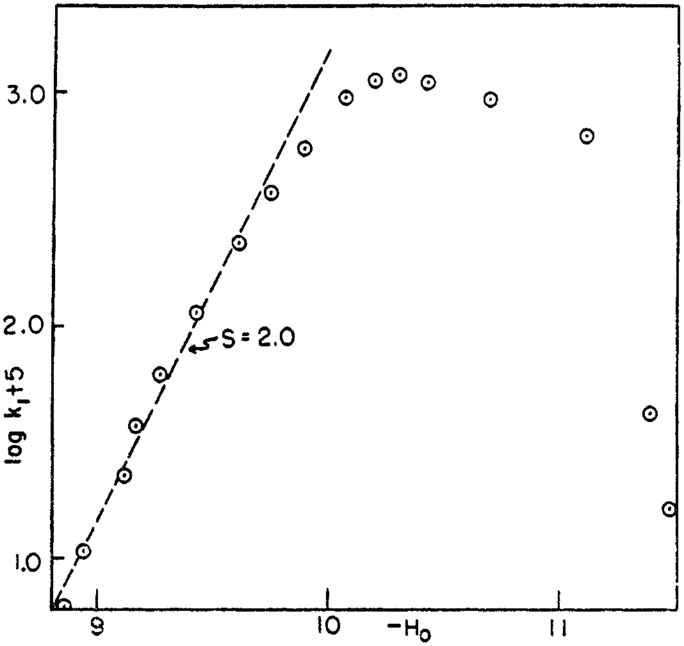


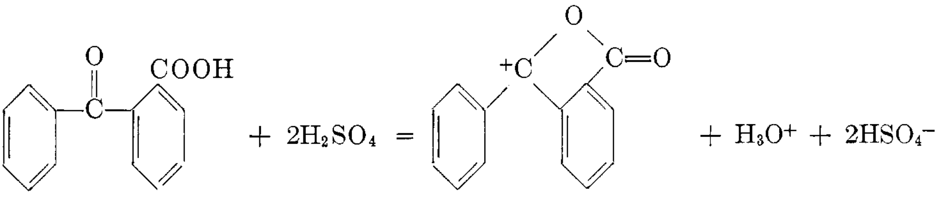
FIG. 15. Decomposition of citric acid in concentrated solutions of sulfuric acid at 25°C. (114, 245).

(115b). Elliot and Hammick (86) point out that the mechanism for the decarboxylation of triphenylacetic acid (77, 78) may be different from that for the others both because of the nonintegral slope of 2.6 in the log k_1 vs. $-H_0$ relationship and because it is the only acid showing a slope much greater than unity which does not have a number of base centers equal to the presumed number of protons added. This reaction has also been considered by Deno and Taft (74), who note that log k_1 closely parallels the J_0 acidity function rather than H_0. They conclude that the mechanism is different and that the ionization probably goes to the oxycarbonium ion, $(C_6H_5)_3CCO^+$, rather than to a conjugate acid or diacidium ion.

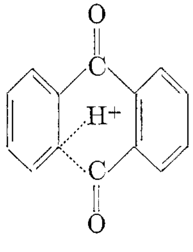
C. REARRANGEMENTS

Hammett and Deyrup (116) noted a good correlation between log k_1 and $-H_0$ for the Beckmann rearrangement of acetophenone oxime (68, 195, 222). The mechanism of this reaction is closely related to A-1, since a unimolecular rearrangement of a positive ion is quite probably involved (115c).

An approximate correlation of rate and H_0 was early reported (114, 116) for the condensation of *o*-benzoylbenzoic acid to anthraquinone (98). Later experimental work by Deane and Huffman (65–67) extended the kinetic studies into fuming sulfuric acid. Actually, the correlation of rate and h_0 is not very good even at the lower acidities. At the highest acidities the rate becomes approximately constant, independent of acidity. The probable explanation of these results is to be found in the studies of Newman and coworkers on this system (178, 179). One item is that the cryoscopically determined "*i*" factor for *o*-benzoylbenzoic acid in pure sulfuric acid is 4, indicating complete ionization in this medium to an acylium ion. The investigators presented evidence for the formation of a cyclic acylium ion:



although this is not essential to explain the cryoscopic results. Newman also suggests that the rearrangement to anthraquinone goes through reaction of the ordinary acylium ion (formed from the above cyclic one) with a transition state of the structure:



The important point is that for reaction via an acylium ion the rate at low acidities should vary with the J_0 acidity function rather than with H_0. The observed approximate correlation of log k_1 and $-H_0$ for solutions of from 85 to 90 per cent sulfuric acid is then perhaps to be explained by the proposal that a sizeable amount of the reactant is already transformed to the acylium ion. Further study at lower acidities should be illuminating.

Deno and Newman (73) have found that *d*-*sec*-butyl hydrogen sulfate and *d*-pinacolyl hydrogen sulfate (present initially as the lithium and barium salts, respectively) are racemized at measurable rates in solutions containing 45–65 per cent of sulfuric acid. The concentrations, which on a molarity scale are only from 5 to 9 *M* in sulfuric acid, are almost certainly low enough that the Zucker–Hammett hypothesis can be validly applied. For the butyl hydrogen sulfate log k_1 is linear in H_0, as shown by the following table:

H_2SO_4	H_0	log $k_1 + 6$	log $k_1 + H_0 + 6$
per cent			
45	−2.84	0.46	−2.38
55	−3.91	1.48	−2.43
57.74	−4.24	1.81	−2.43
65	−5.04	2.66	−2.38

The investigators conclude that the reactant is the negative ion, RSO_4^-, and that the slow step is formation of a carbonium ion.

$$\begin{array}{lcccccl} d\text{-}RSO_4^- & + & H^+ & \rightleftharpoons & d\text{-}RSO_4H & & \text{Equilibrium} \\ d\text{-}RSO_4H & \rightarrow & R^+ & + & HSO_4^- & & \text{Slow} \\ & & & & \upharpoonleft\downharpoonright & & \\ & & & & dl\text{-}RSO_4H & & \end{array}$$

Correlation of the rate of a negatively charged reactant with H_0 would be quite interesting, since it implies equality of the following type for the relevant activity coefficients:

$$\frac{f_{\mathrm{B}}}{f_{\mathrm{BH^+}}} = \frac{f_{\mathrm{S^-}}}{f_{\overset{*}{\mathrm{M}}}}$$

However, in this particular case it seems entirely possible that in 45 per cent sulfuric acid the alkyl sulfate is present primarily in the unionized form and that the mechanism for reaction is:

$$\begin{array}{ll} RHSO_4 + H^+ \rightleftharpoons RH_2SO_4^+ & \text{Equilibrium} \\ RH_2SO_4^+ \rightarrow R^+ + H_2SO_4 & \text{Slow} \end{array}$$

In fact, the observed correlation of rate and H_0 might conceivably have been adduced as evidence for this.

D. AROMATIC SULFONATION AND ITS REVERSE

Sulfonation of aromatic compounds is normally carried out in concentrated or fuming sulfuric acid. Several discussions of possible mechanisms are available

(107, 127a, 128, 147, 148), but the reaction is evidently in a somewhat uncertain state compared, for example, to the analogous nitration reaction. However, it appears that application of H_0 to the rate of reaction can be of considerable use.

Sulfonation is reversible with an equilibrium which depends strongly on the medium. The reaction can be written

$$RH + SO_3 \rightleftharpoons RSO_3H$$

indicating that the sulfonated product will be favored in concentrated solutions of sulfuric acid but that desulfonation may well occur in less concentrated solutions. The desulfonation reaction is actually well known and its kinetics have been studied for several situations.

Crafts made extensive kinetic studies of the desulfonation, i.e., the hydrolysis, of a variety of substituted benzenesulfonic acids (60, 61). The experiments were at temperatures of from 80° to 200°C. and involved aqueous solutions of such acids as hydrochloric, hydrobromic, and sulfuric. The most obvious characteristic of the data is a strong dependence of rate on acidity. Figures 16 and 17 give Crafts' results for typical compounds, and it is evident that the rate of the hydrolysis varies approximately in proportion to the h_0 acidity of the solutions (107). Lantz's studies of the hydrolysis of α-naphthalenesulfonic acid in aqueous sulfuric acid (147, 148) also show an approximate dependence of rate on h_0. Pinnow (196 197) has studied the rates of both the sulfonation and the desulfonation of hydro

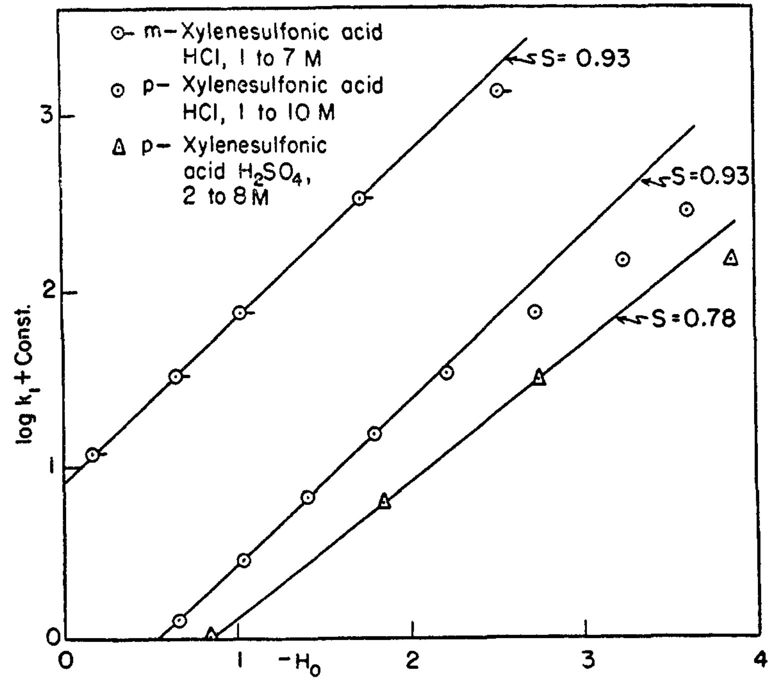


FIG. 16. Hydrolysis of sulfonic acids at 140°C. (61)

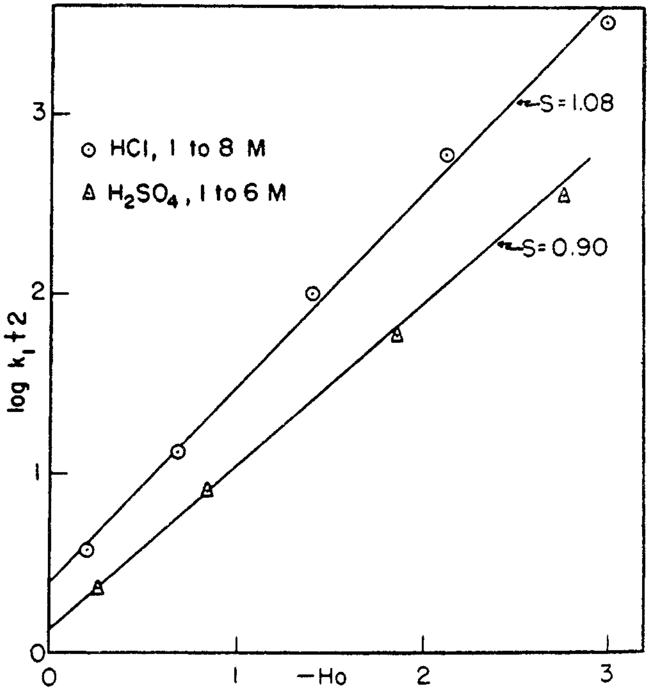


FIG. 17. Hydrolysis of mesitylenesulfonic acid at 100°C. (61)

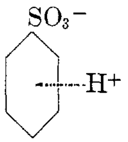
quinone in sulfuric acid. The data clearly show a dependence of desulfonation rate on acidity but the proportionality with h_0 is not very good; log k_1 vs. $-H_0$ plots are reasonably linear but the slopes are only about 0.6 instead of unity. It has recently been suggested (107) that a possible reason for some variations in the dependence of rate on acidity is that sizeable amounts of the reactant may actually be converted to the conjugate acid, i.e., that an equation such as 7a or 9a should really be applied. In view of the high acidities involved this is certainly possible. Still another possible reason for log k_1 vs. $-H_0$ slopes of less than unity is the large differences in temperature between the rate and indicator measurements; the desulfonation studies are usually at temperatures of at least 100°C. and, as noted in Section I, a decrease of slope with increasing temperature of the rate measurements is to be expected.

Brand and Horning (24, 26) have studied the kinetics of sulfonation in fuming sulfuric acid and find that for several reactions the rates are satisfactorily given by the expression

$$\log k = -H_0 + \log p_{SO_3} + \text{constant} \qquad (20)$$

where p_{SO_3} is the measured partial vapor pressure of sulfur trioxide (30). Studies of sulfonation in aqueous sulfuric acid also give evidence of a rate dependence that is qualitatively like the above. Pinnow (196, 197) has shown that the rate of sulfonation of hydroquinone increases much more rapidly with concentration of acid than does the desulfonation, and in fact slopes of log k_1 vs. $-H_0$ for his data on sulfonation are found to be about 1.2, i.e., almost double the slopes for desulfonation. Lantz's sulfonation data show a similar dependence on acidity (145–150). Cowdrey and Davies (59), in a discussion of their data for the sulfonation of *p*-nitrotoluene in concentrated sulfuric acid, do not consider the acidity explicitly but do note that in fuming sulfuric acid the rate frequently increases faster than the sulfur trioxide concentration. Similarly, the observed marked drop in rate for additions of either water or bisulfate ion is in qualitative agreement. with a dependence of rate on acidity as well as on concentration of sulfur trioxide. The sulfonation rate of benzene at 25°C. in sulfuric acid solutions of from 77 to 87 per cent likewise increases very rapidly with acidity (107); a plot of log k_1 vs. $-H_0$ is linear with a slope of 2.3.

As Gold and Satchell note (107), the data for desulfonation clearly imply acid catalysis. These authors consider that (at least at the lower acidities) there is equilibrium formation of an "outer-sphere" complex of the type previously proposed for the hydrogen isotope exchange (see Section II,D).



However, this is not essential to the kinetics and another obvious possibility is an A-1 reaction of the unionized sulfonic acid:

$$ArSO_3H + H^+ \rightleftharpoons ArSO_3H_2^+ \qquad \text{Equilibrium}$$

$$ArSO_3H_2^+ \rightleftharpoons ArH + SO_3 + H^+ \qquad \text{Slow}$$

This latter mechanism is in accord with the observed acid catalysis and is also consistent with the acid catalysis observed for sulfonation. It fits nicely therefore with equation 20, given by Brand and Horning for the rate of sulfonation. Still another possible mechanism for desulfonation consistent with these observations is the A-S_E2, in which the transfer of the proton to the unionized sulfonic acid molecule would be rate determining. At present the evidence available on the mechanism is inconclusive and indicates the need for further study of this important reaction.

E. ELIMINATION REACTIONS OF STERICALLY HINDERED SYSTEMS

An extensive study has been made by Schubert and collaborators of elimination reactions for such systems as mesitoic acid (213, 215), mesitaldehyde (214, 217, 218), and 2,4,6-trimethoxybenzoic acid (219). The entities eliminated are CO_2 for the acids, CO for the aldehydes, and acyl groups for the ketones (216); the other product for all cases is the hydrocarbon. Most of the studies have been made at sulfuric acid concentrations between 75 and 100 per cent, and at these concentrations the rates do not generally show much variation with acidity.

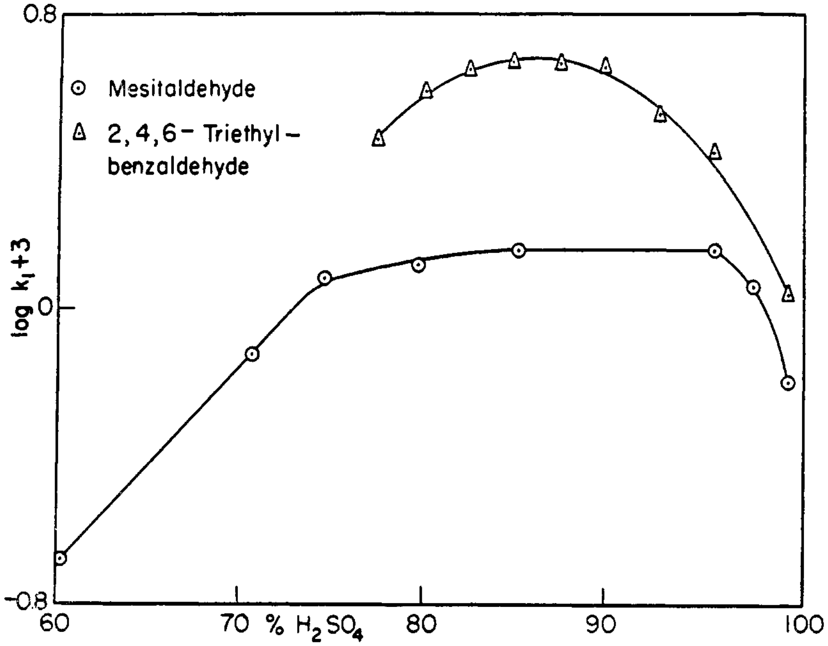


FIG. 18. Decarbonylation of substituted benzaldehydes in concentrated solutions of sulfuric acid at 100°C. (218, 219).

Typical results for two of the decarbonylation reactions (218) are shown in figure 18. The striking feature is the broad maximum with sizeably smaller rates at both lower and higher acid concentrations. Also of note is the fact that the reaction still takes place at a moderate rate in anhydrous sulfuric acid. At a given temperature the rate for the triethyl compound is roughly threefold faster than for the trimethyl; for triisopropylbenzaldehyde the rate is faster than for triethyl by another factor of 3. Changes in substituents at the meta and para positions also cause large changes in rates. For example, 2,4,6-trimethylacetophenone is deacylated about 70 times more rapidly than the 2,6-dimethyl compound (216). A similar dependence of rate on acid concentration and on substituents is found for the decarboxylations, though in this case the reaction is complicated at the highest acidities by ionization to acylium ions, RCO^+.

The decarboxylation of mesitoic acid has recently been studied at lower acidities (167); the results at 90°C. are given in figure 19, which includes also one determination of Schubert's (213) and one result for aqueous phosphoric acid (18). The maximum at the higher acidities is quite similar to that reported by Schubert for measurements at 80°C. (213). At the lower acidities the rate quite evidently is proportional to h_0, and it is of interest that on an h_0 basis the results for phosphoric and perchloric acids agree well with those for sulfuric acid.

After a detailed consideration of mechanisms, including the A-1 mechanism, Schubert and coworkers conclude that the only mechanism which will explain all of the data is a somewhat unusual sort of general acid catalysis. Written for

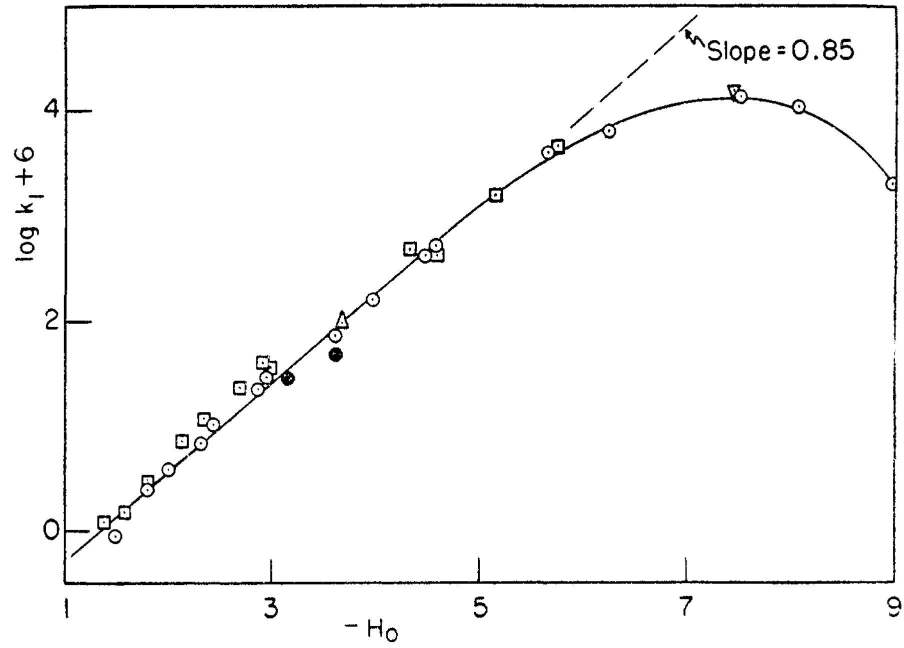
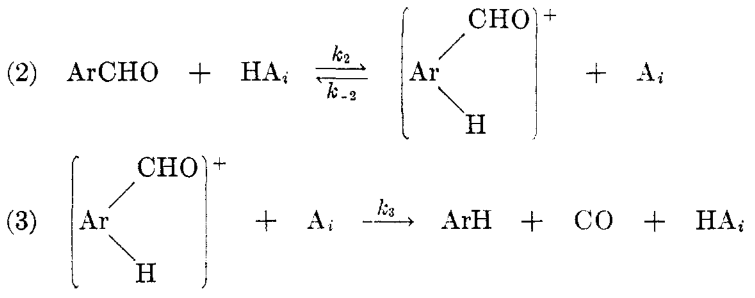


FIG. 19. Log k_1 versus $-H_0$ for decarboxylation of mesitoic acid in aqueous solutions of acids at 90°C. (167): ⊙ and ◬ (213), sulfuric acid; ⊡, perchloric acid; ●, hydrochloric acid; △, phosphoric acid (18).

the decarboxylation reaction, with charges on the solvent acids and bases left unspecified, it is as follows:

(1) $\mathrm{ArCHO} + \mathrm{H}^+ = \mathrm{ArCHOH}^+$ Equilibrium



$$(2)\quad \mathrm{ArCHO} + \mathrm{HA}_i \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \left[\mathrm{Ar}\begin{matrix}\mathrm{CHO}\\ \mathrm{H}\end{matrix}\right]^+ + \mathrm{A}_i$$

$$(3)\quad \left[\mathrm{Ar}\begin{matrix}\mathrm{CHO}\\ \mathrm{H}\end{matrix}\right]^+ + \mathrm{A}_i \xrightarrow{k_3} \mathrm{ArH} + \mathrm{CO} + \mathrm{HA}_i$$

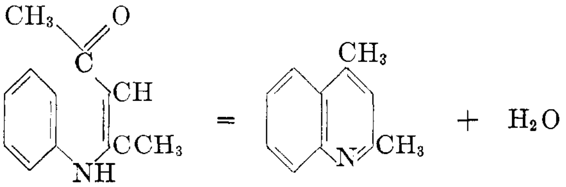
Formation of the ordinary conjugate acid ArCHOH^+ (with the proton attached to the oxygen atom) occurs in step 1 but is postulated to be just a disturbing side reaction, since only steps 2 and 3 lead to reaction. Schubert and Burkett (214) conclude that this mechanism will explain both the kinetic data and the results for a deuterium study of the mesitaldehyde reaction, provided (*a*) that step 3 is rate controlling at low acidities but that at high acidities (over 85 per cent sulfuric acid) steps 2 and 3 are of comparable velocity, and (*b*) that the rate coefficients for the various acid catalysts are assumed to be of the approximate size to lead to the observed decrease in rate at the highest acidities. The leveling off in rate which usually occurs at H_0 values of about -7 is attributed to extensive formation of the ordinary unreactive conjugate acid by step 1; in agreement with this, pK_{BH^+} values for several of the conjugate acids have been measured and found to be of the order of -7 to -8. Finally, the explanation of the commonly observed decrease in rate at the highest acidities is that catalysis by other acid species is entering (for example, catalysis by H_2SO_4 replaces that by H_3O^+).

In spite of the fit which may be obtained with this mechanism, there appear to be some difficulties (167). One is that general acid catalysis is being used to explain a decrease in rate as the acidity increases and this seems somewhat unlikely. A second is that the actual operational meaning of general acid catalysis for these concentrated acid solvents is not at all well defined. It is worth noting also that a quite similar decrease in rates occurs for aromatic nitrations in concentrated sulfuric acid and has been attributed to general medium effects (96).

F. MISCELLANEOUS REACTIONS

One example of a reaction in concentrated sulfuric acid where the rate appears not to depend on the acidity function is the cleavage of a carbon–silicon bond in trimethylsilyl groups to produce methane. The kinetics of this reaction have been studied in the concentration range of from 87 to 97 per cent acid (223). The reaction is homogeneous and first order in the substrate. The rate increases moderately with increasing concentration of acid but much less than does the h_0 acidity. The investigators show that the rate is very close to first order in unionized H_2SO_4 and postulate a slow reaction of this entity with the substrate to give methane and a siliconium ion, $R(CH_3)_2Si^+$. This correlation of rate with concentration of sulfuric acid is even better if the value of the latter is calculated by the procedure of Deno and Taft (74). Another study of carbon–silicon bond fission is described in Section IV,B.

As noted previously (71, 193), for concentrated solutions of sulfuric acid the J_0 acidity function (equation 17) deviates considerably from the H_0 function and as a result one may hope to distinguish between certain reaction mechanisms by determining which acidity function appears to govern the rate. This type of test has been made by Bonner, Thorne, and Wilkins (21, 22) for acid-catalyzed cyclodehydration reactions of the type:



The kinetics of two of these reactions were determined at 25°C. for aqueous sulfuric acid solutions containing 84–97 per cent H_2SO_4. The relation, log k_1 +

H_0 = constant, was found to hold with good precision. In contrast, the sum, $\log k_1 + \log (C_{\mathrm{ROH}}/C_{\mathrm{R}^+})$, where ROH represents a J_0 indicator of the triphenylmethylcarbinol type, varied by more than one logarithmic unit over the acidity range studied. It was concluded that this reaction involves a preliminary ionization to the conjugate acid of the reactant rather than to a carbonium ion. Actually it seems likely that at the acidities involved, the nitrogen base center of the molecule is completely protonated, i.e., the reactant is a positively charged ion rather than a neutral molecule. If so, the relevant acidity functions would be H_+ and J_+ rather than H_0 and J_0. The diagnostic argument is probably still valid however, since H_+ is known to parallel H_0 at acidities close to these (20, 27) and J_+ will probably also parallel J_0.

IV. ACID CATALYSIS IN MIXED AND NONAQUEOUS SOLVENTS

This group of solvents clearly encompasses a wide range of possible behavior. For a solvent like 1:1 ethanol–water one can probably expect similar behavior to water itself, i.e., the dielectric constant of the medium is high and the ionization and dissociation behavior of electrolytes should not be very different from that in water. Thus one might expect the H_0 acidity scale to show about the same generality and utility as for water. However, for a solvent with low dielectric constant such as anhydrous dioxane or acetic acid one can expect extensive ion-pair formation and frequent examples of specific behavior. It is fairly certain that the H_0 scale will be less general for anhydrous dioxane solutions than for water and in fact its generality may be so restricted as to make the function useless (113, 173). Actually, the available data do not permit a firm conclusion on this even for dioxane, let alone the many mixed solvent possibilities. Consequently many of the discussions of correlations between rate and H_0 for these solvents are bound to have a somewhat tentative air.

It is worth noting that studies with mixed solvents permit two rather different sorts of variation of H_0 and as a result two rather different kinds of correlation of rate with acidity. One type of variation is that given by changes in the solvent for fixed concentration of acid solute. The data of Braude and Stern (32, 34) on H_0 for solutions of 0.1 *M* hydrochloric acid in water–ethanol, water–dioxane, and water–acetone mixtures constitute a good example. This kind of variation will usually involve large changes in the properties of the medium (in addition to changes in indicator acidity). As a result it should not be surprising that correlations between rate and H_0 are sometimes poor, particularly for the solvents of lowest dielectric constant.

Another type of variation of acidity for mixed or nonaqueous solvents is that obtained by changing the concentration of a strong acid in a solvent of fixed composition. The data of Bunton and associates (48) for solutions of 0.25–4.5 *M* perchloric acid in solvents consisting of 40 and 60 per cent by volume of dioxane in water are an example. This type of variation minimizes the changes in the properties of the medium other than acidity. Consequently such solutions should be particularly favorable for investigating mechanistic implications of correlations of rate with H_0.

A truly complete correlation requires that the rate data for all acidities in all solvents should fall on a single plot of log k_1 vs. $-H_0$ characterized by a straight line with unit slope. No systematic study of any reaction along these lines, extending to mixed and nonaqueous solvents, appears to have been made. Scattered results are listed in subsequent sections; they indicate that for comparisons between different solvents the indicator acidity often gives an approximate but by no means precise correlation of the rates. Since the H_0 function itself has been shown to be not entirely independent of the indicator and since even for aqueous solutions the correlations between rate and H_0 are not exact, this lack of precision for other solvents is not unexpected. The important (and only partially answered) questions are: what, in a broad sense, are the limits of utility of the indicator acidity scale, and to what extent can rate correlations with H_0 for mixed and nonaqueous solvents be used as evidence for mechanisms?

A. ACETIC ACID

Several studies of kinetics have been reported with acetic acid as solvent. This medium has a low dielectric constant (6.2 at 25°C.) and while considerable indicator research has been done on it, the generality of the H_0 scale cannot be regarded as firmly established (193). In fact, there is evidence that equilibria between ions and ion pairs play a specific role in acid-base reactions taking place in this solvent (39, 136). The Zucker–Hammett hypothesis can therefore be applied only on an exploratory basis.

In figure 8 for the decomposition of trioxane, experimental points were shown for 0.5 *M* and 1 *M* solutions of sulfuric acid in anhydrous acetic acid. The rate data of Walker and Chadwick (240) are not especially precise because the reaction product, formaldehyde, tends to react slowly with the solvent acetic acid. Still, the correlation through H_0 with the rates in aqueous acid solutions is fairly good, considering that for 1 *M* sulfuric acid concentration the shift from aqueous to acetic acid solution increases the reaction rate by a factor of nearly 2000.

A detailed comparison of the acid-catalyzed hydrogen isotope exchange of anisoles (see Section II,D) has recently been made for water–sulfuric acid and acetic acid–sulfuric acid mixtures, with the results shown in table 5 (212). From these data it seems clear not only that the reaction follows H_0 in both solvents

TABLE 5

Comparison of behavior of deuterated anisoles for solutions of sulfuric acid in water and in acetic acid, 25°C.

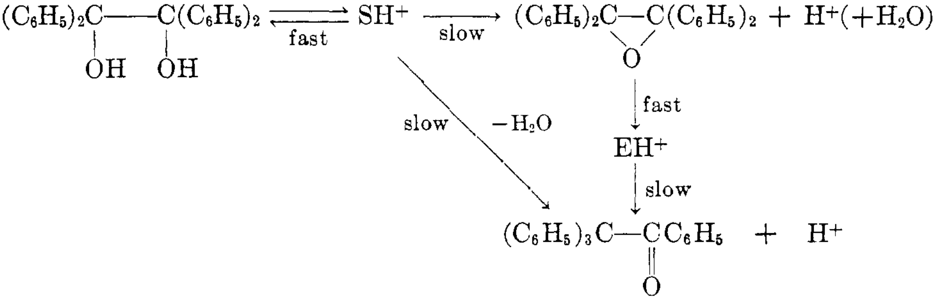
Reactant	H_2SO_4-H_2O		H_2SO_4-CH_3COOH	
	10^5k_1(sec.$^{-1}$) at $H_0 = -3.3$*	Slope log k_1 vs. $-H_0$	10^5k_1(sec.$^{-1}$) at $H_0 = -3.3$†	Slope log k_1 vs. $-H_0$
Anisole-*o*-*d*	1.2	1.18	1.3	1.18
Anisole-*p*-*d*	2.6	1.18	2.4	1.18

* 6.77 *M* H_2SO_4 in water.

† 1.75 *M* H_2SO_4 in acetic acid.

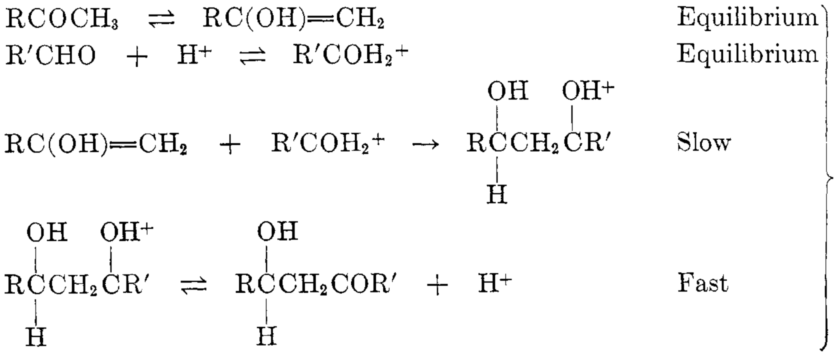
but that at a given H_0 value the absolute rates in the two solvents are much the same. The results certainly suggest that the mechanism of the reaction is the same in the two solvents. Of equal interest, the data give added evidence for the utility of the H_0 scale for mixtures of sulfuric and acetic acids.

The rearrangement of benzopinacol to the corresponding pinacolone has been studied by Gebhart and Adams (89) in acetic acid containing 7×10^{-5} to 5.5×10^{-3} M perchloric acid and also 0.03 to 3 per cent by weight of water (see also Section II,E). Two concurrent reactions take place, one a direct conversion to the pinacolone and the other an indirect conversion by way of the stable intermediate, tetraphenylethylene oxide:



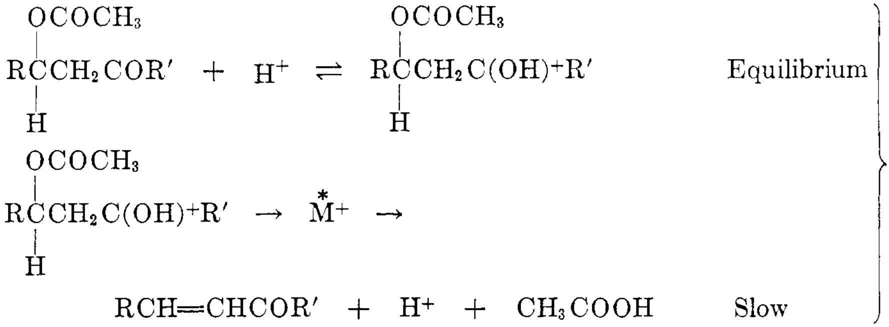
Both the direct conversion of the pinacol and the conversion of the intermediate epoxide were found to proceed at rates such that log k_1 was linear in $-H_0$ with slope of about 0.9. The authors conclude that A-1 mechanisms are involved. Since these rearrangements can be effected simply by intramolecular bond shifts, the proposed mechanism is certainly plausible. A similar correlation with H_0 in perchloric acid–water mixtures has been reported for the dehydration of 1,1,2-triphenylethanol (188).

Noyce and Pryor (181) have studied the kinetics of the acid-catalyzed aldol condensation of benzaldehyde with acetophenone in acetic acid containing 0.18–2.16 M sulfuric acid plus small quantities of water. They found the *second-order* rate coefficient to be proportional to h_0. They conclude that the rate-determining step is reaction between the enol form of the ketone and the conjugate acid of the aldehyde:



$$\left.\begin{aligned}
&RCOCH_3 \rightleftharpoons RC(OH){=}CH_2 && \text{Equilibrium}\\
&R'CHO + H^+ \rightleftharpoons R'COH_2^+ && \text{Equilibrium}\\
&RC(OH){=}CH_2 + R'COH_2^+ \rightarrow R\underset{H}{\overset{OH}{C}}CH_2\overset{OH^+}{C}R' && \text{Slow}\\
&R\underset{H}{\overset{OH}{C}}CH_2\overset{OH^+}{C}R' \rightleftharpoons R\underset{H}{\overset{OH}{C}}CH_2COR' + H^+ && \text{Fast}
\end{aligned}\right\} \text{(I)}$$

In anhydrous acetic acid the ketol thus formed apparently undergoes esterification and the ester then loses a molecule of acetic acid to form the ultimate product, *trans*-chalcone. This latter reaction is also acid catalyzed and in anhydrous acetic acid containing 0.4–1 *M* sulfuric acid, its rate is closely proportional to h_0 (182) (if a little water is present the reaction is complicated by partial reversion of the ketol back to benzaldehyde and acetophenone). There is no difficulty in accepting A-1 as a plausible mechanism for reaction II:



$$\left.\begin{aligned}
&\mathrm{R\overset{\overset{\textstyle OCOCH_3}{|}}{\underset{\underset{\textstyle H}{|}}{C}}CH_2COR' + H^+ \rightleftharpoons R\overset{\overset{\textstyle OCOCH_3}{|}}{\underset{\underset{\textstyle H}{|}}{C}}CH_2C(OH)^+R'} && \text{Equilibrium}\\
&\mathrm{R\overset{\overset{\textstyle OCOCH_3}{|}}{\underset{\underset{\textstyle H}{|}}{C}}CH_2C(OH)^+R' \rightarrow \overset{*}{M}^+ \rightarrow}\\
&\qquad\mathrm{RCH{=}CHCOR' + H^+ + CH_3COOH} && \text{Slow}
\end{aligned}\right\}\ \text{(II)}$$

Since the mechanism proposed for reaction I however is A-2 (though it does not specifically involve a molecule of the solvent), the significance of the observed correlation with h_0 is not at all obvious.

The rate of oxidation of methylcyclohexane by chromic acid has been studied (211) with solutions of sulfuric, perchloric, and phosphoric acids in acetic acid containing low concentrations of water (between 0 and 15 per cent). The rate determined at temperatures between 20° and 50°C. is first order in both reactants and the logarithm of the second-order rate coefficient is reported to be linear in $-H_0$ as determined with the indicator 4-chloro-2-nitroaniline (210). The slope is close to unity for nearly anhydrous sulfuric acid–acetic solutions, but it increases with water concentration, having a value of 1.58 for a solvent containing 15 per cent water. The precise significance of these correlations as regards the reaction mechanism is difficult to establish, since the order of the reaction is high and effects of the medium on the various reactants may be quite specific.

The chloromethylation of mesitylene:

$$\mathrm{ArH + CH_2O + HCl = ArCH_2Cl + H_2O}$$

has been studied at 60°C. for hydrochloric acid concentrations between 0.2 and 1.0 *M* in acetic acid containing 10 per cent by volume of water (183). Values of H_0 were obtained at 20°C. with the indicator *o*-nitroaniline for the actual reaction mixtures and also for solutions simply of hydrochloric acid and of sulfuric acid in the same solvent. The reaction is first order in both mesitylene and formaldehyde, and log k_2 for the second-order rate coefficient was found to be linear in $-H_0$ with slope 0.96. From this the investigators draw the conclusion that the rate-determining step is a bimolecular reaction between the hydrocarbon and the conjugate acid of formaldehyde. It is difficult to see how this conclusion follows from the observations reported.

The decarboxylation of several substituted cinnamic acids has been studied by Johnson and Heinz (132) in acetic acid–water mixtures containing 1.3–4.5 M hydrogen bromide. The rates increase much faster than the stoichiometric concentration of catalyzing acid. No H_0 data for these solutions are available, but the nature of the reaction suggests that an A-1 mechanism may well be involved. Further investigation would be desirable.

The Thiele acetylation of benzoquinone and of toluquinone was investigated by Mackenzie and Winter (171, 172) in acetic acid–acetic anhydride mixtures containing 0.0778 M perchloric acid. They attempted also to measure an indicator acidity (170) but their indicator, 2,6-dimethoxyquinone, ionized in a complex way; their acidity scale is therefore not comparable to H_0. At fixed perchloric acid concentration, both the reaction rates and the indicator acidity increased in approximate proportion with increase in the ratio of acetic anhydride to acetic acid. No definite conclusions can be drawn, however, concerning the reaction mechanism in view of the theoretical difficulties in interpreting the indicator measurements.

The bromination of *m*-nitroacetophenone is an example of a reaction which does *not* follow H_0 in acetic acid solutions. This reaction was studied by Paul and Hammett (192) in solutions containing 0.02–1.6 molal sulfuric acid. While $\log k_1$ was approximately linear in $-H_0$, the slope was about 1.6, showing that k_1 increases much more rapidly than h_0. From evidence for the similar iodination reaction of acetophenone in aqueous acid solutions (250–252), the reaction probably follows an A-2 mechanism, complicated in the case of sulfuric acid by bisulfate-ion catalysis. No significant correlation would therefore be expected between rate and H_0. It would be desirable in this case to establish the rate law for catalysis by perchloric or other acids whose anions show no specific catalytic effect.

B. ALCOHOLS, DIOXANE, AND THEIR MIXTURES WITH WATER

From the standpoint of a study of reaction mechanisms, there are two reasons for desiring an H_0 acidity scale for mixed or anhydrous organic solvents. One is the enhanced solubilities of organic materials, permitting studies of reactants which are insoluble in water. Another is the possibility that the acidity measures h_0 and C_{H^+} may diverge from each other significantly at lower acidities than for water, thus extending the range of usefulness of the Zucker–Hammett hypothesis. For both of these reasons the recent H_0 data for solutions of perchloric acid in 40–60 volume per cent aqueous dioxane (48) are of considerable interest. These studies were made with three indicators, so that the generality of the H_0 scale seems reasonably well established. Furthermore, enough kinetic studies have been made with the solvents to suggest that the Zucker–Hammett hypothesis applies in much the same sense as with water.

For solutions of perchloric acid in 60 per cent dioxane up to 2.3 M concentration, the rate of hydrolysis of ethyl acetate is closely proportional to C_{H^+} and departs widely from proportionality with h_0 (48). This is the same result as is found for water solutions (12) and is of course the expected result for an A-2 mechanism. As a further point it was found that the value of the bimolecular rate

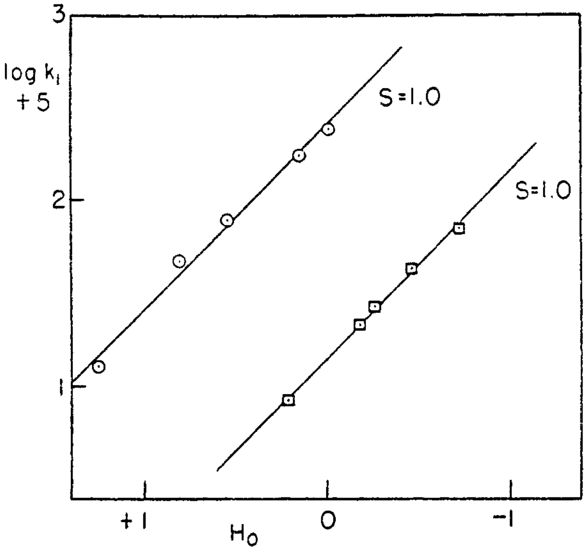


FIG. 20. Hydrolysis of sucrose at 25°C.: ⊡, aqueous hydrochloric acid (151) ⊙, perchloric acid in 60 per cent by volume aqueous dioxane (48).

coefficient k_2 (where rate $= k_2 C_{\text{ester}} C_{H^+}$) was almost identical with the value for water solutions at the same temperature.

The results for the hydrolysis of sucrose in the same solvent are shown in figure 20 along with those for a study in aqueous hydrochloric acid (151). The rates in the dioxane solutions increase much faster than in proportion to the acid concentration and in fact show excellent correlation with H_0. In this sense the results are similar to those obtained for water solutions and are as expected for an A-1 mechanism. On an absolute basis, however, the agreement between the two sets of data is less satisfactory. At $H_0 = 0$, for example, the rate in the solvent containing dioxane is 13 times faster than in water.

As an example of a mechanism study with one of these solvents, Bunton and Hadwick (42) find that the rate of hydrolysis of *p*-methoxybenzohydryl acetate in solutions of perchloric acid in 60 per cent aqueous dioxane is proportional to h_0, not to C_{H^+}. Studies with O^{18} show that alkyl–oxygen bond fission takes place and the conclusion is drawn that, in agreement with the results for other similar molecules (41, 45, 50, 226), an $A_{Al}1$ mechanism is involved. Further evidence is that during hydrolysis of an optically active sample of ester there is complete racemization, showing that the carbonium ion from the alcohol is effectively free during the reaction. (For another example see the discussion of the benzidine rearrangement in Section II,E.)

Studies with a similar solvent have been made by Kreevoy (138), who finds that for 50 per cent by volume aqueous dioxane containing 0.06–4.7 *M* perchloric acid, the hydrolysis rates for several acetals and ketals show close proportionality with h_0. Since the A-1 mechanism seems well established for these hydrolyses, this is the expected result.

A series of indicator acidity measurements for the solvents ethanol, acetone, dioxane, and their mixtures with water has been reported by Braude and Stern (32, 34). Using the indicators *p*-nitroaniline and *m*-nitroaniline at fixed concentrations of hydrochloric acid, they found that $-H_0$ went through a rather deep minimum of acidity (about 1.5 logarithmic units below the value for water in the case of 0.1 *M* hydrochloric acid) at approximately 1:1 molar proportion of organic solvent to water (see figure 21 and see also figure 13 of reference 193). For 0.1 *M* hydrochloric acid in pure ethanol the value of $-H_0$ was about 0.4 unit higher, and in pure acetone 0.7 unit higher, than in water, while in pure dioxane the value was lower (less acid) than in water. Other acidity measures such as electrometric pH and H_- (from ionization of uncharged acid indicators) do not show this effect (8). An opportunity is thus afforded to test whether the rates of acid-catalyzed reactions agree or disagree with the behavior of H_0 in these solvents.

As noted previously there is some reason to question the utility of these data for studies of mechanism, particularly for the solutions of lowest dielectric constant. In fact, Braude's results have been criticized by Gutbezahl and Grunwald (113), who have shown that the H_0 concept loses some of its generality as one

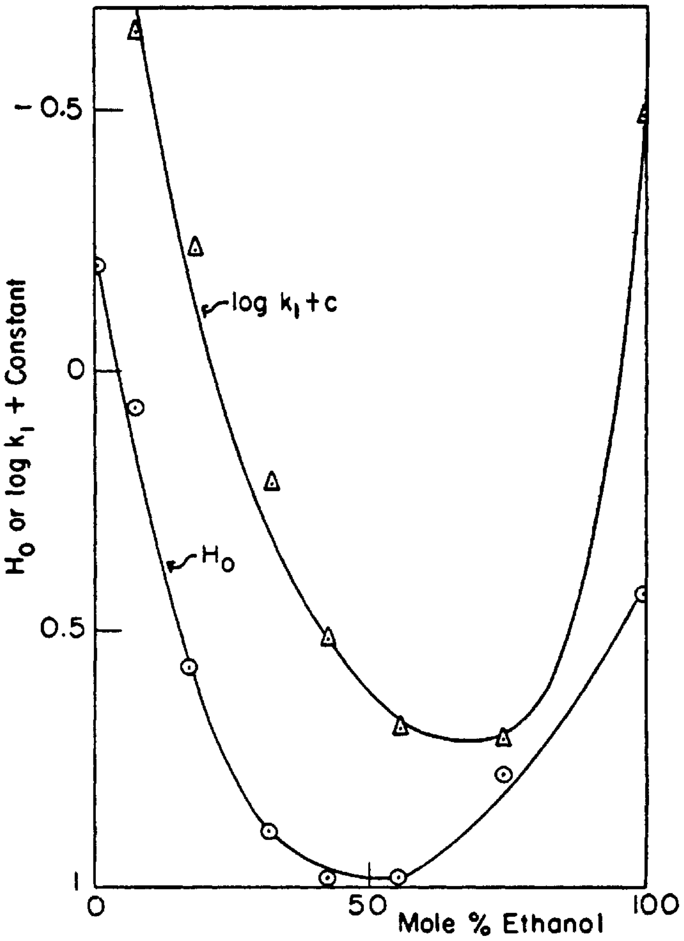


FIG. 21. Rearrangement of ethynylpropenylcarbinol in solutions of 1 *M* hydrochloric acid in aqueous ethanol at 30°C. (31, 33, 35).

passes from aqueous solutions to media of lower dielectric constant. Specifically, the displacements in $pK^{S}_{BH^+}$ values (at infinite dilution in the solvent S) from pK_{BH^+} (at infinite dilution in water) vary to some extent with the particular base B and are not precisely determined simply by the nature of S, as equation 6 would imply. From this standpoint it is unfortunate that Braude's data refer to but two indicators so closely similar in structure. One is therefore unable to assess how general his conclusions may be. Nevertheless several interesting correlations with reaction rates have been reported.

Braude and Jones (31, 33) found originally that the rearrangement of ethynylpropenylcarbinol:

$$CH_3CH{=}CHCHOHC{\equiv}CH \rightarrow CH_3CHOHCH{=}CHC{\equiv}CH$$

took place in hydrochloric acid (0.02–4 *M*) and sulfuric acid (0.02–2 *M*) containing a fixed proportion of ethanol (20 per cent by volume) at rates such that log k_1 was linear with slope 1.09 in $-H_0$ as measured for the corresponding aqueous solutions (without ethanol). A positive salt effect was observed for potassium chloride and several other inorganic salts when added to hydrochloric acid, while the absence of general acid catalysis was indicated by experiments with buffer mixtures. All of this evidence is consistent with an A-1 type of mechanism. Braude and Stern (35) then found that the rate for 1 *M* hydrochloric acid with changing proportion of ethanol to water went through a minimum following quite closely the corresponding change in h_0 (see figure 21). Similar results were obtained for this reaction with acetone–water and dioxane–water mixtures, and also for the analogous rearrangement of phenylpropenylcarbinol,

$$C_6H_5CHOHCH{=}CHCH_3 \rightarrow C_6H_5CH{=}CHCHOHCH_3$$

in 0.1 *M* hydrochloric acid (table 6).

TABLE 6

Rate versus H_0 for rearrangement of phenylpropenylcarbinol by 0.1 M hydrochloric acid in aqueous mixed solvents

Rates at 30°C.; time in seconds

Organic Solvent	Dioxane			Ethanol			Acetone		
	log k_1	H_0	log $k_1 + H_0$	log k_1	H_0	log $k_1 + H_0$	log k_1	H_0	log $k_1 + H_0$
volume per cent									
0	—	0.97	—	—	0.97	—	—	0.97	—
20	−1.46	1.23	−0.23	—	1.14	—	—	1.29	—
40	−1.90	1.63	−0.27	−1.84	1.48	−0.36	−1.75	1.63	−0.12
60	−2.46	2.19	−0.27	−2.40	1.99	−0.41	−2.24	2.13	−0.11
70	−2.69	2.28	−0.41	−2.65	2.13	−0.52	−2.46	2.31	−0.15
80	−2.94	2.35	−0.59	−2.83	2.21	−0.62	−2.55	2.39	−0.16
90	−2.99	2.05	−0.94	−2.91	2.19	−0.72	−2.65	2.35	−0.30
100	−2.02	1.31	−0.71	−1.38	0.57	−0.81	−1.16	0.23	−0.93

The proportionality between k_1 and h_0 for these rearrangements is not exact and is in fact rather poor for the nearly anhydrous solvents (note for example the large change in log $k_1 + H_0$ for the higher acetone concentrations in the last column of table 6). Even so, the results are of considerable interest in view of the fact that no other reported measure of acidity for these mixed solvents reproduces the characteristic minimum shown by both k_1 and h_0.

Somewhat similar results have been obtained by Kaeding and Andrews (3, 133) for the hydrolysis of benzophenone diethylketal and its *p*-nitro derivative. The rate of the latter for 0.1 *M* hydrochloric acid goes through a minimum with changing ethanol concentration at about 80 mole per cent ethanol, but it increases much less rapidly than h_0 with increase in the ethanol concentration beyond that point. The investigators report that the quantities log (k_1/C_{H_2O}) and log (k_1/a_{H_2O}) are practically linear in $-H_0$ and conclude that the rate-determining step is $SH^+ + H_2O$, where S represents the ketal. This of course would be an A-2 mechanism and one would have no *a priori* reason to expect correlation with H_0. However, as Kreevoy and Taft (139) have pointed out, the data are also nicely consistent with an A-1 mechanism (which as noted in Section II,B,6 holds for ketal hydrolysis in aqueous solutions) if it be supposed that the conjugate acid reacts about as readily with ethanol as with water.

Salomaa (211d) has in fact used such an explanation to account for the continuous decrease observed in the rate of hydrolysis of ethylal with increasing proportion of ethanol to water in a solvent containing hydrochloric acid at fixed 0.1 *M* concentration. The reaction was studied at 25°C. and the ethanol concentration was varied from 0 to 78 mole per cent. The postulated A-1 mechanism for this reaction has as the rate-controlling step:

$$\overset{H^+}{C_2H_5OCH_2OC_2H_5} \rightarrow C_2H_5\overset{+}{O}{=}CH_2 + C_2H_5OH$$

followed in aqueous solution by rapid hydrolysis of the ethoxymethyl cation to ethanol and formaldehyde. In an alcoholic solvent this latter step is assumed to be in competition with the reaction:

$$C_2H_5\overset{+}{O}{=}CH_2 + C_2H_5OH \rightleftharpoons \overset{H^+}{C_2H_5OCH_2OC_2H_5}$$

leading back to ethylal. The relative rates of the rapid hydrolysis and alcoholysis reactions of the ethoxymethyl cation are deduced by Salomaa from the proportion of formaldehyde to ethylal found in the solvolysis of ethoxymethyl chloride, $C_2H_5OCH_2Cl$, in a solvent of the same composition, for this compound presumably gives rise to the same intermediate. When the true rate coefficient k_1 for the hydrolysis of ethylal is computed by this procedure from the observed overall or apparent rate, it turns out to follow Braude and Stern's h_0 values reasonably closely, going through a minimum at about 50 mole per cent ethanol. A gradual increase now observed in log $k_1 + H_0$ with increasing alcohol concentration is attributed by the investigator to a shift in the value of log $(f_{BH^+}/f^{*}_{M^+})$ with dielectric constant of the medium (see equation 9) and is shown to be linear in $1/D$, in agreement with theoretical analysis. Work by the same investigator

(211a) on the solvolysis of alkoxymethyl esters in methanol–water and ethanol–water solvents containing a fixed concentration of hydrochloric acid has been described previously (Section II,A,1).

The hydrolysis of several *t*-butyl and diphenylmethyl esters of carboxylic acids has been studied in aqueous ethanol and aqueous acetone solutions with hydrochloric acid, 0.005–0.04 *M*, as catalyst (122, 123, 225–228). The *t*-butyl ester of 2,4,6-trimethylbenzoic acid was chosen for the initial studies since from other evidence it seemed fairly certain that its hydrolysis and alcoholysis go by an $A_{Al}1$ path, with alkyl–oxygen bond fission, rather than by the more usual A-2 mechanism (41, 58). Recent studies with O^{18} in fact confirm the alkyl–oxygen fission and make it fairly certain that the mechanism is $A_{Al}1$ (40). The hydrolysis turned out to be much faster than that of the methyl or ethyl esters of substituted benzoic acids; the value of the activation energy E_A was high, of the order of 30 kcal., but this was more than compensated for by the large value of log A; in fact the entropy of activation was of order +10 e.u. (rate coefficients in liters mole^{-1}sec.$^{-1}$). All these items are in accord with the proposed $A_{Al}1$ mechanism. Similar behavior was shown by *t*-butyl benzoate and by the corresponding esters of diphenylmethanol, suggesting similar mechanisms. However, the hydrolysis behavior of the formates was quite different, and Stimson suggests that for these molecules the mechanism has reverted back to $A_{Ac}2$ (122, 227). Diphenylmethyl acetate shows an intermediate type of behavior, suggesting that for this ester both mechanisms are simultaneously in operation (122).

In the case of *t*-butyl 2,4,6-trimethylbenzoate, Stimson (225) extrapolated to obtain k_1 values for solutions of 0.1 *M* hydrochloric acid and then compared these with Braude's H_0 data for hydrochloric acid dissolved in aqueous ethanol and in aqueous acetone. The sum, log $k_1 + H_0$, was found to be approximately constant for solutions containing from 60 to 90 per cent ethanol or acetone. However, for ethanol between 90 and 100 per cent concentrations, log k_1 increased much less rapidly than $-H_0$, while for acetone solutions between 90 and 100 per cent, log k_1 actually decreased whereas $-H_0$ increased by about two logarithmic units. Since there is good reason to believe that the A-1 mechanism holds for reaction in all of these solutions, this is formally an indication of a failure of the Zucker–Hammett hypothesis. Actually this failure is quite similar to that noted for the lower water concentrations in table 6 and is probably only an indication of the lack of generality and utility of the Braude H_0 scale for these solutions.

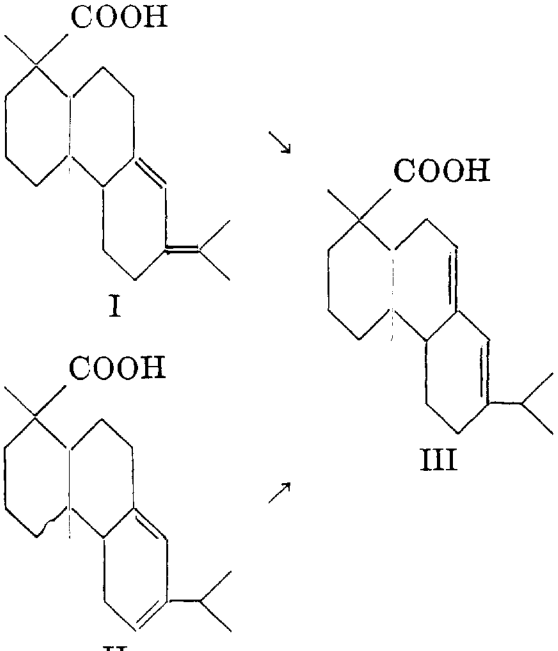
Eaborn (85) has reported a study of the acid-catalyzed cleavage of a silane derivative in methanol containing 9 per cent water by volume:

$$p\text{-}(CH_3)_3SiC_6H_4OCH_3 + ROH = (CH_3)_3SiOR + C_6H_5OCH_3$$

where ROH represents methanol or water. The silanol then rapidly undergoes condensation to hexamethyldisiloxane, the ultimate product of the reaction. He found that with hydrochloric acid or perchloric acid as catalyst, k_1 was accurately proportional to h_0. The same was true in a solvent containing 27 per cent water by volume, but the rates were relatively larger. A fairly close correlation with

H_0 was found also in water–dioxane mixtures of various proportions containing hydrochloric acid. Actually the concentration of acid was not particularly high in any of these studies (0.05–1.3 M) and only a single indicator (p-nitroaniline) was used for the measurements of H_0. More information is needed to establish the generality of the H_0 scale before firm conclusions can be drawn concerning its kinetic applications. Eaborn concludes, however, that the reaction probably follows an A-1 mechanism and this is certainly reasonable in view of the nature of the change involved (16). Further studies along these lines have been reported for the decompositions of other silane derivatives in 95 per cent aqueous ethanol containing dissolved hydrogen chloride (4). In Section III,F for a related example of carbon–silicon bond fission it was reported that the rate appears not to depend on the H_0 acidity. The experimental conditions, however, were quite different (concentrated sulfuric acid rather than water–dioxane as solvent) as was the fission studied (methyl–silicon rather than aryl–silicon). Consequently a different sort of dependence of rate on acidity is perhaps not surprising.

The rates of the acid-catalyzed isomerizations of neoabietic acid (I) and levopimaric acid (II) into abietic acid (III) have been measured by Ritchie and McBurney (207, 208) in anhydrous ethanol using hydrogen chloride, hydrogen bromide, and sulfonic acids as catalysts. The rate coefficients for neoabietic acid are about tenfold smaller than for levopimaric acid; this difference appears to arise from a difference in entropy of activation, since the energies of activation are reported to be identical. With hydrogen chloride in the concentration range of from 0.01 to 0.1 M the rate for the neoabietic acid reaction increases significantly more rapidly than does the concentration of the mineral acid. Addition of water to a solution containing 0.06 M hydrochloric acid in anhydrous ethanol causes a marked drop in the rates of both reactions. Although indicator data have



I

II

III

not been reported for these solutions, the observed behavior of the rate coefficients is qualitatively that to be expected for reactions showing correlation with H_0. The isomerizations are apparently of a simple nature and subject only to specific hydrogen-ion catalysis. Since water is not involved in the reaction, they may be especially suitable for a more extensive study of acid catalysis in nonaqueous solvents.

An excellent illustration of possible danger in the interpretation of results from studies in mixed solvents is given by a recent report on the kinetics of the acid-catalyzed iodination of acetone in a series of water–ethanol mixtures (212a). The ethanol content of the solvent was varied from 0 to 64 mole per cent, while the catalyst was hydrochloric acid at concentrations up to 3 M. In pure water the rate is accurately proportional to C_{H^+}, in agreement with the earlier results on iodination of acetophenone (252). As the concentration of ethanol in the solvent is increased, the rate tends to increase faster than in proportion to C_{H^+} and the departure is greater the higher the concentration of ethanol. At about 44 mole per cent ethanol the rate is in fact closely proportional to h_0. The mechanism of the aqueous reaction quite surely involves a rate-determining acid-base reaction of the conjugate acid with water and it is most unlikely that there is a change to an A-1 mechanism for the solvents containing more ethanol. Hence the observed departure from simple concentration dependence is probably a reflection of relatively large changes in activity coefficient ratios with the solvent. Whatever is the detailed explanation, the results do show the need for great caution in applying rate–acidity correlations from studies with mixed solvents to problems of reaction mechanisms.

V. SUMMARY

Among the simpler acid-catalyzed reactions of uncharged molecules, two mechanisms (A-1 and A-2) have been recognized on the basis of a variety of evidence. Both involve a preliminary acid-base equilibrium but the former, exemplified by the hydrolysis of acetals, postulates a unimolecular rate step on the part of the resulting conjugate acid cation while the latter, exemplified by the hydrolysis of ordinary esters, postulates a bimolecular rate step involving a second molecule.

The data summarized in this review support the idea that these different mechanisms correspond with widely different effects of the medium on the rates. Many reactions for which the A-1 mechanism appears to be well established show in aqueous solutions of strong acids an increasingly rapid rise in rate with increasing acid concentration, particularly evident beyond 1 M concentration; the increase in rate is closely proportional to a similar increase in the indicator acidity function h_0. Many reactions for which the A-2 mechanism has been established show a much smaller change of rate with acidity, the rate remaining more nearly proportional to acid concentration itself.

If detailed information were available for the activity coefficients of the reacting species, including reliable estimates for the transition states, one could expect to predict medium effects on the rate for a given reaction mechanism completely and precisely. In the absence of such information the acidity function H_0 (or h_0)

serves as a practical means of approximating the value of an activity coefficient ratio of a particular form, f_A/f_{M^*+}, which enters the theoretical rate equation for an A-1 reaction of the uncharged species A. In effect this ratio is equated to f_B/f_{BH^+}, where B represents an uncharged basic indicator. There are theoretical as well as empirical grounds for regarding this as a good approximation in aqueous solutions of the strong mineral acids and it is probably good also in other media of high dielectric constant. Where it is valid, one can expect close correlation between rate and H_0, provided the mechanism is in fact A-1; where it is invalid (as in the case of acid solutions containing added salts or in the case of large acid molecules such as trichloroacetic), there will be no such correlation.

If the mechanism is A-2, the theoretical basis for correlating rate simply with acid concentration is less well founded. Nevertheless there remains a significant empirical difference in strongly acid solutions between effects of the medium on this and on the A-1 type of reaction. The Zucker–Hammett hypothesis takes cognizance of this difference, though in the extreme form stated in Section I it is probably lacking in generality; that is, A-2 reactions for which log k_1 is accurately linear with unit slope in log C_{H^+} may be exceptional rather than the general rule.

It would be unsound to conclude that because an acid-catalyzed reaction follows H_0 it necessarily proceeds by an A-1 mechanism. Evidence so far available suggests the possibility that a proton-transfer rate step (the mechanism designated A-S_E2 in this review) may lead to a similar variation of rate with acidity. It should be possible to distinguish this mechanism from A-1 by means of hydrogen isotope and stereochemical effects. Acid-catalyzed reactions may be attended also by varying degrees of complexity, so that occasionally an H_0 correlation will be an accidental consequence of a complex actual mechanism.

Effects of the medium on activity coefficients in mixed and nonaqueous solvents are at present less well understood than in water, though progress is being made. Therefore any theoretical interpretation of reaction rates based on Brönsted's equation is more open to question in such media, particularly at low dielectric constant. Several correlations of rate with H_0 have been reported for presumed A-1 reactions in acetic acid, ethanol–water, dioxane–water, and other solvents. The most interesting of these involve mixtures of 40:60 or 60:40 volume proportion of water–dioxane in which the acidity is increased by the addition of perchloric acid. The indications are that the Zucker–Hammett hypothesis will be useful for these solvents. There is much more uncertainty about studies at constant concentration of strong acid when the acidity is varied by changing the composition of the solvent. The data presently available are insufficient to test the generality or modify the form of the Zucker–Hammett hypothesis as applied to these solvents. Until the generality of the H_0 scale itself has been more conclusively established for nonaqueous systems, one should exercise due restraint in interpreting correlations between rates and indicator acidities for such media.

VI. REFERENCES

(1) ADAMS, K. H.: Personal communication.
(2) AMIS, E. S., AND HOLMES, F. C.: J. Am. Chem. Soc. **63**, 2231 (1941).

(3) Andrews, L. J., and Kaeding, W. W.: J. Am. Chem. Soc. **73,** 1007 (1951).
(4) Baines, J. E., and Eaborn, C.: J. Chem. Soc. **1956,** 1436.
(5) Barnard, P. W. C., Bunton, C. A., Llewellyn, D. R., Oldham, K. G., Silver, B. L., and Vernon, C. A.: Chemistry & Industry **1955,** 760.
(6) Bartlett, P. D., and McCollum, J. D.: J. Am. Chem. Soc. **78,** 1441 (1956).
(7) Bartlett, P. D., and Small, G., Jr.: J. Am. Chem. Soc. **72,** 4867 (1950).
(8) Bates, R. G., and Schwarzenbach, G.: Helv. Chim. Acta **38,** 699 (1955).
(9) Bell, R. P.: *Acid-Base Catalysis.* Oxford University Press, London (1941): (a) Chap. IV; (b) Chap. V; (c) Chap VII.
(10) Bell, R. P., Bascombe, K. N., and McCoubrey, J. C.: J. Chem. Soc. **1956,** 1286.
(11) Bell, R. P., and Brown, A. H.: J. Chem. Soc. **1954,** 774.
(12) Bell, R. P., Dowding, A. L., and Noble, J. A.: J. Chem. Soc. **1955,** 3106.
(13) Bell, R. P., Lidwell, O. M., and Vaughan-Jackson, M. W.: J. Chem. Soc. **1936,** 1792.
(14) Bell, R. P., and Lukianenko, B.: J. Chem. Soc. **1957,** 1686.
(15) Bell, R. P., and Skinner, B. G.: J. Chem. Soc. **1952,** 2955.
(16) Benkeser, R. A., and Krysiak, H. R.: J. Am. Chem. Soc. **76,** 6353 (1954).
(17) Benrath, A.: Z. anorg. Chem. **151,** 53 (1926).
(18) Beringer, F. M., and Sands, S.: J. Am. Chem. Soc. **75,** 3319 (1953).
(19) Blumenthal, E., and Herbert, J. B. M.: Trans. Faraday Soc. **41,** 611 (1945).
(20) Bonner, T. G., and Lockhart, J. C.: J. Chem. Soc. **1957,** 364.
(21) Bonner, T. G., Thorne, M. P., and Wilkens, J. M.: J. Chem. Soc. **1955,** 2351.
(22) Bonner, T. G., and Wilkens, J. M.: J. Chem. Soc. **1955,** 2358.
(23) Brand, J. C. D.: J. Chem. Soc. **1950,** 997.
(24) Brand, J. C. D.: J. Chem. Soc. **1950,** 1004.
(25) Brand, J. C. D.: Personal communication.
(26) Brand, J. C. D., and Horning, W. C.: J. Chem. Soc. **1952,** 3922.
(27) Brand, J. C. D., Horning, W. C., and Thornley, M. B.: J. Chem. Soc. **1952,** 1374.
(28) Brand, J. C. D., James, J. C., and Rutherford, A.: J. Chem. Phys. **20,** 530 (1952).
(29) Brand, J. C. D., James, J. C., and Rutherford, A.: J. Chem. Soc. **1953,** 2447.
(30) Brand, J. C. D., and Rutherford, A.: J. Chem. Soc. **1952,** 3916.
(31) Braude, E. A.: J. Chem. Soc. **1948,** 794.
(32) Braude, E. A.: J. Chem. Soc. **1948,** 1971.
(33) Braude, E. A., and Jones, E. R. H.: J. Chem. Soc. **1944,** 436.
(34) Braude, E. A., and Stern, E. S.: J. Chem. Soc. **1948,** 1976.
(35) Braude, E. A., and Stern, E. S.: J. Chem. Soc. **1948,** 1982.
(36) Brönsted, J. N., and Grove, C.: J. Am. Chem. Soc. **52,** 1394 (1930).
(37) Bronsted, J. N., Kilpatrick, M., and Kilpatrick, M.: J. Am. Chem. Soc. **51,** 428 (1929).
(38) Bronsted, J. N., and Wynne-Jones, W. F. K.: Trans. Faraday Soc. **25,** 59 (1929).
(39) Bruckenstein, S., and Kolthoff, I. M.: J. Am. Chem. Soc. **78,** 10 (1956).
(40) Bunton, C. A.: Personal communication.
(41) Bunton, C. A., Comyns, A. E., Graham, J., and Quayle, J. R.: J. Chem. Soc. **1955,** 3817.
(42) Bunton, C. A., and Hadwick, T.: J. Chem. Soc., to be published.
(43) Bunton, C. A., Hadwick, T., Llewellyn, D. R., and Pocker, Y.: Chemistry & Industry **1956,** 547.
(44) Bunton, C. A., Ingold, C. K., and Mhala, M. M.: J. Chem. Soc. **1957,** 1906.
(45) Bunton, C. A., and Konasiewicz, A.: J. Chem. Soc. **1955,** 1354.
(46) Bunton, C. A., Konasiewicz, A., and Llewellyn, D. R.: J. Chem. Soc. **1955,** 604.
(47) Bunton, C. A., Lewis, T. A., Llewellyn, D. R., and Vernon, C. A.: J. Chem. Soc. **1955,** 4419.
(48) Bunton, C. A., Ley, J. B., Rhind-Tutt, A. J., and Vernon, C. A.: J. Chem. Soc. **1957,** 2327.

(49) Bunton, C. A., and Llewellyn, D. R.: J. Chem. Soc., to be published.
(50) Bunton, C. A., and Wood, J. L.: J. Chem. Soc. **1955,** 1522.
(51) Burnett, R. L., and Bell, R. P.: Trans. Faraday Soc. **34,** 420 (1938).
(52) Burwell, R. L., Jr.: Chem. Revs. **54,** 615 (1954).
(53) Carlin, R. B., Nelb, R. G., and Odioso, R. C.: J. Am. Chem. Soc. **73,** 1002 (1951).
(54) Charman, H. B., and Ridd, J. H.: Personal communication.
(55) Chmiel, C. T., and Long, F. A.: J. Am. Chem. Soc. **78,** 3326 (1956).
(56) Ciapetta, F. G., and Kilpatrick, M.: J. Am. Chem. Soc. **70,** 639 (1948).
(57) Cohen, M. D., and Hammond, G. S.: J. Am. Chem. Soc. **72,** 220 (1950).
(58) Cohen, S. G., and Schneider, A.: J. Am. Chem. Soc. **63,** 3382 (1941).
(59) Cowdrey, W. A., and Davies, D. S.: J. Chem. Soc. **1949,** 1871.
(60) Crafts, J. M.: Ber. **34,** 1350 (1901).
(61) Crafts, J. M.: Bull soc. chim. France [4] **1,** 917 (1907).
(62) Datta, S. C., Day, J. N. E., and Ingold, C. K.: J. Chem. Soc. **1939,** 838.
(63) Davis, M. M., and Schuhmann, P. J.: J. Research Natl. Bur. Standards **39,** 221 (1947).
(64) Day, J. N. E., and Ingold, C. K.: Trans. Faraday Soc. **37,** 686 (1941).
(65) Deane, C. W.: J. Am. Chem. Soc. **59,** 849 (1937).
(66) Deane, C. W.: J. Am. Chem. Soc. **67,** 329 (1945).
(67) Deane, C. W., with Huffman, J. R.: Ind. Eng. Chem. **35,** 684 (1943).
(68) de Bruyn, C. A. L., and Sluiter, C. H.: Proc. Koninkl. Akad. Wetenschap. Amsterdam **6,** 773 (1904).
(69) de la Mare, P. B. D., Hughes, E. D., Ingold, C. K., and Pocker, Y.: J. Chem. Soc. **1954,** 2930.
(70) Deno, N. C.: Unpublished data reported at the Sixth Reaction Mechanism Conference, Swarthmore College, September, 1956.
(70a) Deno, N. C., Edwards, T., and Perizzolo, C.: J. Am. Chem. Soc. **79,** 2108 (1957).
(71) Deno, N. C., Jaruzelski, J. J., and Schriesheim, A.: J. Am. Chem. Soc. **77,** 3044 (1955).
(72) Deno, N. C., and Newman, M. S.: J. Am. Chem. Soc. **72,** 3852 (1950).
(73) Deno, N. C., and Newman, M. S.: J. Am. Chem. Soc. **73,** 1920 (1951).
(73a) Deno, N. C., and Perizzolo, C.: J. Am. Chem. Soc. **79,** 1345 (1957).
(74) Deno, N. C., and Taft, R. W., Jr.: J. Am. Chem. Soc. **76,** 244 (1954).
(75) De Right, R. E.: J. Am. Chem. Soc. **55,** 4761 (1933).
(76) De Right, R. E.: J. Am. Chem. Soc. **56,** 618 (1934).
(77) Dittmar, H. R.: J. Phys. Chem. **33,** 533 (1929).
(78) Dittmar, H. R.: J. Am. Chem. Soc. **52,** 2746 (1930).
(79) Duboux, M.: Helv. Chim. Acta **21,** 236 (1938).
(80) Duboux, M., and de Sousa, A.: Helv. Chim. Acta **23,** 1381 (1940).
(81) Duboux, M., and Rochat, J.: Helv. Chim. Acta **22,** 563 (1939).
(82) Duncan, J. F., and Lynn, K. R.: J. Chem. Soc. **1956,** 3512.
(83) Duncan, J. F., and Lynn, K. R.: J. Chem. Soc. **1956,** 3519.
(84) Duncan, J. F., and Lynn, K. R.: J. Chem. Soc. **1956,** 3674.
(84a) Duncan, J. F., and Lynn, K. R.: Australian J. Chem. **10,** 1, 7 (1957).
(85) Eaborn, C.: J. Chem. Soc. **1953,** 3148.
(85a) Edward, J. T., and Meacock, S. C. R.: J. Chem. Soc. **1957,** 2000.
(86) Elliott, W. W., and Hammick, D. L.: J. Chem. Soc. **1951,** 3402.
(87) Euler, H. v., and Ölander, A.: Z. physik. Chem. **131,** 107 (1928).
(88) Friedman, H. B., and Elmore, G. V.: J. Am. Chem. Soc. **63,** 864 (1941).
(89) Gebhart, H. J., Jr., and Adams, K. H.: J. Am. Chem. Soc. **76,** 3925 (1954).
(90) Geib, K. H.: Z. physik. Chem. **A180,** 211 (1937).
(91) Gelbstein, A. I., Shcheglova, G. G., and Temkin, M. I.: Zhur. neorg. Khim. **1,** 282, 506 (1956).
(92) Gelbstein, A. I., Shcheglova, G. G., and Temkin, M. I.: Doklady Akad. Nauk S.S.S.R. **107,** 108 (1956).

(93) Gelbstein, A. I., Shcheglova, G. G., and Temkin, M. I.: Zhur. Fiz. Khim. **30,** 2267 (1956).
(94) Gillespie, R. J., and Cole, R. H.: Trans. Faraday Soc. **52,** 1325 (1956).
(95) Gillespie, R. J., and Leisten, J. A.: Quart. Revs. (London) **8,** 40 (1954).
(96) Gillespie, R. J., and Millen, D. J.: Quart. Revs. (London) **2,** 277 (1948).
(97) Gillespie, R. J., and Oubridge, J. V.: J. Chem. Soc. **1956,** 80.
(98) Gleason, A. H., and Dougherty, G.: J. Am. Chem. Soc. **51,** 310 (1929).
(99) Gold, V., and Hawes, B. W. V.: J. Chem. Soc. **1951,** 2102.
(100) Gold, V., and Hilton, J.: J. Chem. Soc. **1955,** 838.
(101) Gold, V., and Hilton, J.: J. Chem. Soc. **1955,** 843.
(102) Gold, V., and Long, F. A.: J. Am. Chem. Soc. **75,** 4543 (1953).
(103) Gold, V., and Satchell, D. P. N.: Nature **176,** 602 (1955).
(104) Gold, V., and Satchell, D. P. N.: J. Chem. Soc. **1955,** 3609.
(105) Gold, V., and Satchell, D. P. N.: J. Chem. Soc. **1955,** 3619.
(106) Gold, V., and Satchell, D. P. N.: J. Chem. Soc. **1955,** 3622.
(107) Gold, V., and Satchell, D. P. N.: J. Chem. Soc. **1956,** 1635.
(108) Gold, V., and Satchell, D. P. N.: J. Chem. Soc. **1956,** 2743.
(109) Grube, G., and Motz, G.: Z. physik. Chem. **118,** 145 (1925).
(110) Grube, G., and Schmid, G.: Z. physik. Chem. **119,** 19 (1926).
(111) Grunwald, E., and Berkowitz, B. J.: J. Am. Chem. Soc. **73,** 4939 (1951).
(111a) Grunwald, E., Heller, A., and Klein, F. S.: J. Chem. Soc. **1957,** 2604.
(112) Guggenheim, E. A., and Wiseman, L. A.: Proc. Roy. Soc. (London) **A203,** 17 (1950).
(113) Gutbezahl, B., and Grunwald, E.: J. Am. Chem. Soc. **75,** 559, 565 (1953).
(114) Hammett, L. P.: Chem. Revs. **16,** 67 (1935).
(115) Hammett, L. P.: *Physical Organic Chemistry*, McGraw-Hill Book Company, Inc., New York (1940): (a) Chap. VIII; (b) Chap. IX; (c) Chap. X; (d) Chap. XI.
(116) Hammett, L. P., and Deyrup, A. J.: J. Am. Chem. Soc. **54,** 2721 (1932).
(117) Hammett, L. P., and Paul, M. A.: J. Am. Chem. Soc. **56,** 827 (1934).
(118) Hammett, L. P., and Paul, M. A.: J. Am. Chem. Soc. **56,** 830 (1934).
(119) Hammond, G. S., and Shine, H. J.: J. Am. Chem. Soc. **72,** 220 (1950).
(120) Hantzsch, A., and Weissberger, A.: Z. physik. Chem. **125,** 251 (1927).
(121) Harbottle, G.: J. Am. Chem. Soc. **73,** 4024 (1951).
(122) Harvey, G. J., and Stimson, V. R.: J. Chem. Soc. **1956,** 3629.
(123) Hawke, J. G., and Stimson, V. R.: J. Chem. Soc. **1956,** 4676.
(124) Heath, D. F., and Casapieri, P.: Trans. Faraday Soc. **47,** 1093 (1951).
(125) Henshall, T., Silbermann, W. E., and Webster, J. G.: J. Am. Chem. Soc. **77,** 6656 (1955).
(126) Hough, A., Savage, W., and Van Marle, D. J.: Chem. Met. Eng. **23,** 666 (1920).
(127) Ingold, C. K.: *Structure and Mechanism in Organic Chemistry*, Cornell University Press, Ithaca, New York (1953): (a) Chap. VI; (b) Chap. VII; (c) Chap. XIV.
(128) Ioffe, I. S.: J. Gen. Chem. (U.S.S.R.) **3,** 437, 963 (1933).
(129) Jellinek, H. H. G., and Gordon, A.: J. Phys. & Colloid Chem. **53,** 996 (1949).
(130) Jellinek, H. H. G., and Urwin, J. R.: J. Phys Chem. **57,** 900 (1953)
(131) Johansson, H.: Chem. Zentr. [5] **20,** II, 557 (1916).
(132) Johnson, W. S., and Heinz, W. E.: J. Am. Chem. Soc. **71,** 2913 (1949).
(133) Kaeding, W. W., and Andrews, L. J.: J. Am. Chem. Soc. **74,** 6189 (1952).
(134) Kilpatrick, M. L.: J. Am. Chem. Soc. **69,** 40 (1947).
(135) Koefoed, J., and Jensen, A. H.: Acta Chem. Scand. **5,** 23 (1951).
(136) Kolthoff, I. M., and Bruckenstein, S.: J. Am. Chem. Soc. **78,** 1 (1956).
(137) Koshland, D. E., Jr.: J. Am. Chem. Soc. **74,** 2286 (1952).
(138) Kreevoy, M. M.: J. Am. Chem. Soc. **78,** 4236 (1956).
(139) Kreevoy, M. M., and Taft, R. W., Jr.: J. Am. Chem. Soc. **77,** 3146 (1955).
(140) Kreevoy, M. M., and Taft, R. W., Jr.: J. Am. Chem. Soc. **77,** 5590 (1955).
(141) Krieble, V. K.: J. Am. Chem. Soc. **57,** 15 (1935).

(142) Krieble, V. K., and Holst, K. A.: J. Am. Chem. Soc. **60,** 2976 (1938).

(143) Krieble, V. K., and Reinhart, F. M.: J. Am. Chem. Soc. **57,** 19 (1935).

(144) Kuivila, H. G.: J. Am. Chem. Soc. **77,** 4014 (1955).

(145) Lantz, R.: Bull. soc. chim. France [5] **2,** 2092 (1935).

(146) Lantz, R.: Bull. soc. chim. France [5] **6,** 302 (1939).

(147) Lantz, R.: Bull. soc. chim. France [5] **12,** 253 (1945).

(148) Lantz, R.: Bull. soc. chim. France [5] **12,** 1004 (1945).

(149) Lantz, R.: Bull. soc. chim. France [5] **14,** 95 (1947).

(150) Lantz, R.: Bull. soc. chim. France [5] **17,** 1253 (1950).

(151) Leininger, P. M., and Kilpatrick, M.: J. Am. Chem. Soc. **60,** 1268, 2891 (1938).

(152) Leininger, P. M., and Kilpatrick, M.: J. Am. Chem. Soc. **61,** 2510 (1939).

(153) Leisten, J. A.: J. Chem. Soc. **1956,** 1572.

(154) Levy, J. B., Taft, R. W., Jr., and Hammett, L. P.: J. Am. Chem. Soc. **75,** 1253 (1953).

(155) Ley, J. B., and Vernon, C. A.: Chemistry & Industry **1956,** 146.

(156) Lichtenstein, H. J., and Twigg, G. H.: Trans. Faraday Soc. **44,** 905 (1948).

(157) Lichty, D. M.: J. Phys. Chem. **11,** 225 (1907).

(158) Long, F. A.: To be published.

(159) Long, F. A., Dunkle, F. B., and McDevit, W. F.: J. Phys. & Colloid Chem. **55,** 829 (1951).

(160) Long, F. A., and Friedman, L.: J. Am. Chem. Soc. **72,** 3692 (1950).

(161) Long, F. A., and McDevit, W. F.: Chem. Revs. **51,** 119 (1952).

(162) Long, F. A., McDevit, W. F., and Dunkle, F. B.: J. Phys. & Colloid Chem. **55,** 813 (1951).

(163) Long, F. A., and McIntyre, D.: J. Am. Chem. Soc. **76,** 3243 (1954).

(164) Long, F. A., and Pritchard, J. G.: J. Am. Chem. Soc. **78,** 2663 (1956).

(165) Long, F. A., Pritchard, J. G., and Stafford, F. S.: J. Am. Chem. Soc. **79,** 2362 (1957).

(166) Long, F. A., and Purchase, M.: J. Am. Chem. Soc. **72,** 3267 (1950).

(167) Long, F. A., and Varker, A.: Unpublished work.

(168) Lucas, H. J., and Eberz, W. F.: J. Am. Chem. Soc. **56,** 460 (1934).

(169) Lucas, H. J., and Liu, Y.: J. Am. Chem. Soc. **56,** 2138 (1934).

(170) Mackenzie, H. A. E., and Winter, E. R. S.: Trans. Faraday Soc. **44,** 159 (1948).

(171) Mackenzie, H. A. E., and Winter, E. R. S.: Trans. Faraday Soc. **44,** 171 (1948).

(172) Mackenzie, H. A. E., and Winter, E. R. S.: Trans. Faraday Soc. **44,** 243 (1948).

(173) Marshall, H. P., and Grunwald, E.: J. Am. Chem. Soc. **76,** 2000 (1954).

(174) MacCauley, C. E., and King, C. V.: J. Am. Chem. Soc. **74,** 6221 (1952).

(175) McIntyre, D., and Long, F. A.: J. Am. Chem. Soc. **76,** 3240 (1954).

(176) Nelson, W. E., and Butler, J. A. V.: J. Chem. Soc. **1938,** 957.

(177) Newman, M. S.: J. Am. Chem. Soc. **63,** 2431 (1941).

(178) Newman, M. S.: J. Am. Chem. Soc. **64,** 2324 (1942).

(179) Newman, M. S., Kuivila, H. G., and Garrett, A. B.: J. Am. Chem. Soc. **67,** 704 (1945).

(180) Noyce, D. S.: Personal communication.

(181) Noyce, D. S., and Pryor, W. A.: J. Am. Chem. Soc. **77,** 1397 (1955).

(182) Noyce, D. S., Pryor, W. A., and Bottini, A. H.: J. Am. Chem. Soc. **77,** 1402 (1955).

(183) Ogata, K., and Okano, M.: J. Am. Chem. Soc. **78,** 5423 (1956).

(184) Ogata, Y., Okano, M., and Ganke, T.: J. Am. Chem. Soc. **78,** 2962 (1956).

(185) O'Gorman, J. M., and Lucas, H. J.: J. Am. Chem. Soc. **72,** 5489 (1950).

(186) Olson, A. R., and Hyde, J. L.: J. Am. Chem. Soc. **63,** 2459 (1941).

(187) Olson, A. R., and Miller, R. J.: J. Am. Chem. Soc. **60,** 2687 (1938).

(188) O'Neill, R. J., Ludwig, F. J., Melillo, D., and Adams, K. H.: Unpublished data reported at the 124th Meeting of the American Chemical Society, Chicago, Illinois, September, 1953.

(189) Paul, M. A.: J. Am. Chem. Soc. **72,** 3813 (1950).

(190) PAUL, M. A.: J. Am. Chem. Soc., **74,** 141 (1952).
(191) PAUL, M. A.: J. Am. Chem. Soc. **76,** 3236 (1954).
(192) PAUL, M. A., AND HAMMETT, L. P.: J. Am. Chem. Soc. **58,** 2182 (1936).
(193) PAUL, M. A., AND LONG, F. A.: Chem. Revs. **57,** 1 (1957).
(194) PEARCE, J. N., AND THOMAS, M. E.: J. Phys. Chem. **42,** 455 (1938).
(195) PEARSON, D. E., AND BALL, F.: J. Org. Chem. **14,** 118 (1949).
(196) PINNOW, J.: Z. Elektrochem. **21,** 380 (1915).
(197) PINNOW, J.: Z. Elektrochem. **23,** 243 (1917).
(198) POLANYI, M., AND SZABO, A. L.: Trans. Faraday Soc. **30,** 508 (1934).
(199) PRITCHARD, J. G., AND LONG, F. A.: J. Am. Chem. Soc. **78,** 2667 (1956).
(200) PRITCHARD, J. G., AND LONG, F. A.: J. Am. Chem. Soc. **78,** 6008 (1956).
(201) PURLEE, E. L., AND TAFT, R. W., JR.: J. Am. Chem. Soc. **78,** 5807 (1956).
(202) RABINOVITCH, B. S., AND WINKLER, C. A.: Can. J. Research **B20,** 73 (1942).
(203) RANDLES, J. E. B., AND TEDDER, J. M.: J. Chem. Soc. **1955,** 1218.
(204) REID, E. E.: Am. Chem. J. **21,** 284 (1899); **24,** 397 (1900).
(205) REITZ, O.: Z. Elektrochem. **44,** 693 (1938).
(206) REITZ, O.: Z. physik. Chem. **A183,** 371 (1939).
(207) RITCHIE, P. F., AND MCBURNEY, L. F.: J. Am. Chem. Soc. **71,** 3736 (1949).
(208) RITCHIE, P. F., AND MCBURNEY, L. F.: J. Am. Chem. Soc. **72,** 1197 (1950).
(209) ROBERTS, J. D., REGAN, C. M., AND ALLEN, I.: J. Am. Chem. Soc. **74,** 3679 (1952).
(210) ROČEK, J.: Chem. Listy **50,** 726 (1956); Collection Czechoslov. Chem. Communs. **22,** 1 (1957).
(211) ROČEK, J.: Chem. Listy **50,** 1602 (1956).
(211a) ROSENTHAL, D., AND TAYLOR, T. I.: J. Am. Chem. Soc. **79,** 2684 (1957).
(211b) SALOMAA, P.: Acta Chem. Scand. **11,** 125, 132, 141, 235, 239 (1957).
(211c) SALOMAA, P.: Acta Chem. Scand. **11,** 247 (1957).
(211d) SALOMAA, P.: Acta Chem. Scand. **11,** 461 (1957).
(212) SATCHELL, D. P. N.: J. Chem. Soc. **1956,** 3911.
(212a) SATCHELL, D. P. N.: J. Chem. Soc. **1957,** 2878.
(213) SCHUBERT, W. M.: J. Am. Chem. Soc. **71,** 2639 (1949).
(214) SCHUBERT, W. M., AND BURKETT, H.: J. Am. Chem. Soc. **78,** 64 (1956).
(215) SCHUBERT, W. M., DONOHUE, J., AND GARDNER, J. D.: J. Am. Chem. Soc. **76,** 9 (1954).
(216) SCHUBERT, W. M., AND LATOURETTE, H. K., J. Am. Chem. Soc. **74,** 1829 (1952).
(217) SCHUBERT, W. M., AND MYHRE, P. G.: Unpublished data presented at the 130th Meeting of the American Chemical Society, Atlantic City, New Jersey, September, 1956.
(218) SCHUBERT, W. M., AND ZAHLER, R. E.: J. Am. Chem. Soc. **76,** 1 (1954).
(219) SCHUBERT, W. M., ZAHLER, R. E., AND ROBINS, J.: J. Am. Chem. Soc. **77,** 2293 (1955).
(220) SKRABAL, A., AND EGER, H. H.: Z. physik. Chem. **122,** 349 (1926).
(221) SKRABAL, A., AND SKRABAL, R.: Z. physik. Chem. **A181,** 449 (1938).
(222) SLUITER, C. H.: Rec. trav. chim. **24,** 372 (1905).
(223) SOMMER, L. H., BARIE, W. P., AND GOULD, J. R.: J. Am. Chem. Soc. **75,** 3765 (1953).
(224) STASIUK, F., SHEPPARD, W. A., AND BOURNS, A. N.: Can. J. Chem **34,** 123 (1956).
(225) STIMSON, V. R.: J. Chem. Soc. **1955,** 2010.
(226) STIMSON, V. R.: J. Chem. Soc. **1955,** 2673.
(227) STIMSON, V. R.: J. Chem. Soc. **1955,** 4020.
(228) STIMSON, V. R., AND WATSON, E. J.: J. Chem. Soc. **1954,** 2848.
(229) SULLIVAN, M. J., AND KILPATRICK, M. L.: J. Am. Chem. Soc. **67,** 1815 (1945).
(230) SWAIN, C. G.: J. Am. Chem. Soc. **74,** 4108 (1952).
(231) *Tables of Chemical Kinetics*, National Bureau of Standards Circular 510, Washington, D. C. (1951).
(232) TAFT, R. W., JR.: J. Am. Chem. Soc. **74,** 3120 (1952).
(233) TAFT, R. W., JR.: J. Am. Chem. Soc. **74,** 5372 (1952).
(234) TAFT, R. W., JR.: J. Am. Chem. Soc. **75,** 4231 (1953).
(235) TAFT, R. W., JR.: Personal communication

(236) Taft, R. W., Jr., Purlee, E. L., Riesz, P., and De Fazio, C. A.: J. Am. Chem. Soc. **77,** 1584 (1955).
(237) Taylor, T. I., and Rosenthal, D.: See reference 211a.
(238) Taylor, T. W. J.: J. Chem. Soc. **1930,** 2741.
(239) Treffers, H. P., and Hammett, L. P.: J. Am. Chem. Soc. **59,** 1708 (1937).
(240) Walker, J. F., and Chadwick, A. F.: Ind. Eng. Chem. **39,** 974 (1947).
(241) Westheimer, F. H., and Kharasch, M. S.: J. Am. Chem. Soc. **68,** 1871 (1946).
(242) Whitford, E. L.: J. Am. Chem. Soc. **47,** 953 (1925).
(243) Whitmore, F. C.: J. Am. Chem. Soc. **54,** 3274 (1932).
(244) Wiberg, K. B.: Chem. Revs. **55,** 713 (1955).
(245) Wiig, E. O.: J. Am. Chem. Soc. **52,** 4729 (1930).
(246) Wiig, E. O.: J. Am. Chem. Soc. **52,** 4737 (1930).
(247) Williams, G., and Clark, D. J.: J. Chem. Soc. **1956,** 1304.
(248) Winstein, S., and Henderson, R. B.: *Heterocyclic Compounds*, edited by R. C. Elderfield, Vol. 1, Chap. 1. John Wiley and Sons, Inc., New York (1950).
(249) Winstein, S., and Lucas, H. J.: J. Am. Chem. Soc. **59,** 1461 (1937).
(250) Zucker, L., and Hammett, L. P.: J. Am. Chem. Soc. **61,** 2779 (1939).
(251) Zucker, L., and Hammett, L. P.: J. Am. Chem. Soc. **61,** 2785 (1939).
(252) Zucker, L., and Hammett, L. P.: J. Am. Chem. Soc. **61,** 2791 (1939).