[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE GEORGIA INSTITUTE OF TECHNOLOGY, ATLANTA 13, GA.]

Polar Effects on Rates and Equilibria. V. Relationships between Rates of Corresponding Acid-, Base- and Un-catalyzed Reactions[1]

BY JACK HINE AND RAYMOND P. BAYER

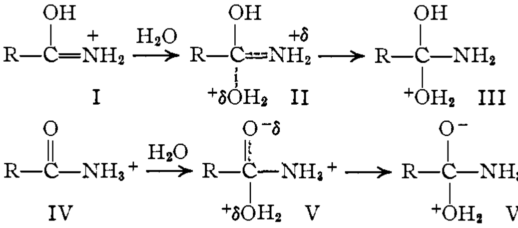
RECEIVED NOVEMBER 27, 1961

Existing qualitative generalizations about the effect of structure on reactivity are applied to certain acid- and/or base-catalyzed reactions. Upper and lower limits for the susceptibility of simple heterolysis reactions to acid catalysis are deduced. From the assumption that *if the equilibrium constant for the rate-determining step of a given acid-catalyzed reaction is equal to that of the corresponding base-catalzyed reaction the rate constants will also be equal,* quantitative relationships between the rates of acid and of basic hydrolysis of ethyl benzoates and between the rates of acid and basic hydrolysis of benzamides are derived. These relationships, whose application requires estimates of the acidity and basicity of such intermediate species as $ArC(OH)_2OEt$'s, are found to agree with the experimental values within a factor of 10^2, and therefore within the reliability of the various estimated K's and ρ's.

Bell has put certain qualitative ideas about the effect of structural changes in the reactants on the shape of the potential energy surface for the reaction into reasonable quantitative forms in discussing the basis of the Brönsted catalysis equation and other topics of importance in acid and base catalysis.[2] The methods of Bell and also the generalizations of Leffler and of Hammond concerning relationships between the nature of the transition state and that of the reactant and product[3,4] have suggested derivations of equations for limitations on the extent of acid and/or base catalysis to be expected in certain cases and also for quantitative relations between the catalytic constants for acid-, base- and un-catalyzed reactions in certain other cases. In addition, we shall make liberal use of the Hammett equation,[5] of Taft's equations,[6] and of the discussions these workers have presented concerning the basis and significance of their equations.

In this paper we shall use the term *corresponding reactions* in the following restricted sense. Corresponding acid- and base-catalyzed reactions are reactions in which the immediate reactants in and the immediate products of the rate-determining step differ only in the nature and extent of their protonation; the transition states differ in this manner and may also differ in the extent to which they resemble the immediate reactants and/or products. That is, the reactions must proceed by the same mechanism, but the transition states may lie at different points along the reaction coördinate. For example, the transformations of ethylene oxide to ethylene glycol by SN2 attack of hydroxide ion on ethylene oxide or its conjugate acid or by SN2 attack of water on ethylene oxide or its conjugate acid are all corresponding reactions.

Mechanism of the Acidic Hydrolysis of Amides.—The generalizations suggested in this paper may be applied qualitatively in a discussion of the mechanism of the acidic hydrolysis of amides. If it is accepted that this reaction involves the intermediate formation of $RC(OH)_2NH_2$[7] (or a protonated and/or deprotonated form of this species) and that in acidic solution amides are protonated largely at oxygen,[8,9] it may be shown that the reacting species is probably the oxygen-protonated rather than the nitrogen-protonated amide. This follows from the fact that the immediate reactant I is more stable than the immediate reactant IV and certainly the immediate product III is more stable than the immediate product VI. Therefore



I II III IV V VI

$$R{-}\overset{\overset{\displaystyle OH}{|}}{C}{=}\overset{+}{N}H_2 \xrightarrow{H_2O} R{-}\underset{\underset{\displaystyle {}^{+\delta}OH_2}{\vdots}}{\overset{\overset{\displaystyle OH}{|}}{C}}{\overset{+\delta}{\equiv\!\equiv}}NH_2 \longrightarrow R{-}\underset{\underset{\displaystyle {}^{+}OH_2}{|}}{\overset{\overset{\displaystyle OH}{|}}{C}}{-}NH_2$$

$$R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}NH_3{}^+ \xrightarrow{H_2O} R{-}\underset{\underset{\displaystyle {}^{+\delta}OH_2}{|}}{\overset{\overset{\displaystyle O^{-\delta}}{\|}}{C}}{-}NH_3{}^+ \longrightarrow R{-}\underset{\underset{\displaystyle {}^{+}OH_2}{|}}{\overset{\overset{\displaystyle O^-}{|}}{C}}{-}NH_3{}^+$$

if all properties (except the total energy contents) of the transition states may be expressed as linear combinations of the properties of the reactants and products,[3] the transition state II must be more stable than V and most of the reaction must proceed *via* the oxygen-protonated amide. Analogous arguments may be applied to the mechanism of acid-catalyzed ester hydrolysis and many other reactions.

Acid Catalysis of Simple Heterolysis Reactions.—A somewhat more quantitative approach may be made to the possible extent of acid catalysis of simple heterolysis reactions. In the heterolysis of XY it seems clear that XYH^+ should react faster than XY and that X^+ should combine with Y^- faster than with HY. Whether the reaction is

$$XY \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} X^+ + Y^- \qquad (1)$$

$$XYH^+ \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} X^+ + HY \qquad (2)$$

$$k_2 > k_1;\ k_{-1} > k_{-2} \qquad (3)$$

subject to any significant acid catalysis also depends on the basicity of X–Y. If it is assumed that the

---

(1) For part IV see J. Hine and W. C. Bailey, Jr., *J. Org. Chem.*, **26**, 2098 (1961).

(2) R. P. Bell, "Acid–Base Catalysis," Oxford University Press, London, 1941, chap. VIII; "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, chap. X.

(3) J. E. Leffler, *Science*, **117**, 340 (1953).

(4) G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).

(5) L. P. Hammett, "Physical Organic Chemistry," McGraw–Hill Book Co., Inc., New York, N. Y., 1940, chap. VII.

(6) R. W. Taft, Jr., in M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, chap. 13.

(7) J. Hine, "Physical Organic Chemistry," McGraw–Hill Book Co., Inc., New York, N. Y., 1956, sec. 13-4c.

(8) A. R. Katritzky and R. A. Y. Jones, *Chem. & Ind.* (London), 722 (1961).

(9) I. R. Fox, P. L. Levins and R. W. Taft, Jr., *Tetrahedron Letters*, 249 (1961).

various proton-transfer reactions involved are much faster than the heterolysis reaction, then the rate constants in the experimentally observed rate equation

$$v_f = k_{H^+}[H^+][XY] + k_u[XY]$$

may be seen to have the significance

$$k_{H^+} = k_2/K_{XYH^+} \text{ and } k_u = k_1 \qquad (4)$$

where

$$K_{XYH^+} = [H^+][XY]/[XYH^+]$$

By combining the equilibrium expressions for reactions 1 and 2 it follows that

$$k_1k_{-2}/k_{-1}k_2 = K_{HY}/K_{XYH^+} \qquad (5)$$

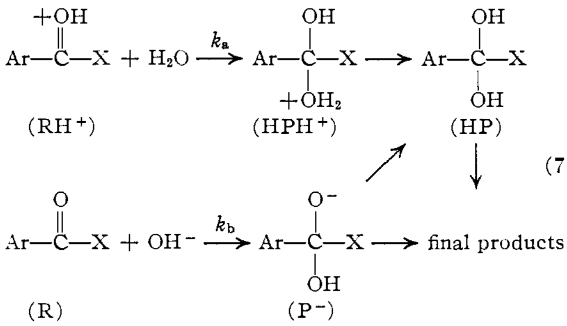
where $K_{HY} = [H^+][Y^-]/[HY]$. Combination of eqs. 3, 4 and 5 gives the following limitations for k_{H^+}/k_u, a fraction that measures the sensitivity of the reaction to acid catalysis. From eq. 6, in

$$1/K_{HY} > k_{H^+}/k_u > 1/K_{XYH^+} \qquad (6)$$

aqueous solution, heterolyses of RI's, RBr's and RCl's should be essentially insensitive to acid catalysis[10]; the heterolysis of RF's might be sensitive to acid catalysis[13]; the heterolysis of ROH's would probably be sensitive to acid catalysis, and that of RNH_2's should certainly be sensitive to acid catalysis.

A Quantitative Relation between the Rates of Corresponding Acid- and Base-catalyzed Reactions.—For the deduction of a quantitative relation between the rate of an acid-catalyzed reaction and that of the corresponding base-catalyzed (or uncatalyzed) reaction an additional hypothesis is required. Hammett and Taft have shown that there are large families of compounds and reactions for which correlations between rate and equilibrium constants may be made.[5,6] We shall assume that corresponding acid- and base-catalyzed reactions are in this category and therefore that *when the equilibrium constants for the rate-determining steps of such reactions are identical the rate constants will be also.*[14]

As specific examples of the application of this assumption we shall consider the effect of acid and base on the rates of hydrolysis of amides and esters of benzoic acid and its derivatives. We shall assume that these reactions involve the intermediate formation of the species HPH^+ and P^- in acidic and basic solutions, respectively, as



(7)

The rates of formation of HPH^+ and of P^- may be expressed

$$v_{H^+} = k_{H^+}[H^+][R] \qquad (8)$$

and

$$v_{OH^-} = k_{OH^-}[OH^-][R] \qquad (9)$$

In terms of the reaction mechanism given it may be seen that k_{OH^-} is identical to k_b and that

$$k_{H^+} = k_a[H_2O]/K_{RH^+} \qquad (10)$$

where

$$K_{RH^+} = [R][H^+]/[RH^+]$$

The equilibrium constant for the formation of HPH^+ may be written

$$K_a = [HPH^+]/[RH^+][H_2O]$$

Similarly, for the equilibrium constant for the formation of P^-

$$K_b = [P^-]/[R][OH^-]$$

We do not know for what compound K_a will be equal to K_b (and therefore k_a equal to k_b), but if we denote the species derived from this compound by the subscript q it follows that

$$[HPH_q^+]/[RH_q^+][H_2O] = [P_q^-]/[R_q][OH^-] \qquad (11)$$

which may be rearranged to give

$$K_{RH_q^+}K_w = K_{HPH_q^+}K_{HP_q} \qquad (12)$$

where

$$K_w = [H^+][OH^-]/[H_2O]$$

$$K_{HPH_q^+} = [H^+][HP_q]/[HPH_q^+]$$

and

$$K_{HP_q} = [H^+][P_q^-]/[HP_q]$$

From the Hammett equation it follows that

$$\log K_{RH_q^+} = \log K_{RH_0^+} + \rho_{RH^+}\sigma_q$$

where RH_0^+ refers to the unsubstituted ion C_6H_5-$COHX^+$, ρ_{RH^+} is the reaction constant for the acidity of RH^+'s, and σ_q is the substituent constant for whatever substituent is required to make eq. 11 hold. Log $K_{HPH_q^+}$ and log K_{HP_q} may also be expressed in terms of the Hammett equation and substituted into eq. 12. Solution of the resulting equation for σ_q gives

$$\sigma_q = \frac{1}{(\rho_{RH^+} - \rho_{HPH^+} - \rho_{HP})} \log \frac{K_{HPH_0^+}K_{HP_0}}{K_{RH_0^+}K_w} \qquad (13)$$

Since $K_a{}^q$ is equal to $K_b{}^q$ and therefore $k_a{}^q$ is equal to $k_b{}^q$, it follows from eq. 10 and the preceding phrase that

$$k_{H^+}{}^q = k_{OH^-}{}^q[H_2O]/K_{RH_q^+} \qquad (14)$$

Substitution of the appropriate forms of the Hammett equation into 14 yields

$$\log \frac{k_{OH^-}{}^0}{k_{H^+}{}^0} = \log K_{RH_0^+} - \log [H_2O] + (\rho_{RH^+} + \rho_{H^+} - \rho_{OH^-})\sigma_q \qquad (15)$$

where the k^0's refer to the unsubstituted com-

---

[10] Although attempts to find acid catalysis in the solvolysis of certain chlorides in largely aqueous solution were unsuccessful,[11] such catalysis might be expected and has been observed in more weakly basic solvents such as nitrobenzene.[12]

[11] S. C. J. Olivier and G. Berger, *Rec. trav. chim.*, **41**, 637 (1922); S. C. J. Olivier and A. P. Weber, *ibid.*, **53**, 869 (1934).

[12] H. F. Herbrandson, R. T. Dickerson, Jr., and J. Weinstein, *J. Am. Chem. Soc.*, **76**, 4046 (1954).

[13] For observations of such catalysis see W. T. Miller, Jr., and J. Bernstein, *ibid.*, **70**, 3600 (1948); N. B. Chapman and J. L. Levy, *J. Chem. Soc.*, 1677 (1952).

[14] It may well be that this will prove to be a good approximation only in reactions in which the rate-determining step involves largely the formation or cleavage of only one bond. Such are the only cases considered quantitatively in the present article.

pounds and ρ_{H^+} and ρ_{OH^-} are the Hammett reaction constants for the rates of formation of HPH^+'s and P^-'s, respectively. Inserting the value of σ_{q} from eq. 13 gives

$$\log \frac{k_{\mathrm{OH}^-}{}^{0}}{k_{\mathrm{H}^+}{}^{0}} = \log K_{\mathrm{RH}_0{}^+} - \log\,[\mathrm{H_2O}] + \left(\frac{\rho_{\mathrm{RH}} + \rho_{\mathrm{H}^+} - \rho_{\mathrm{OH}^-}}{\rho_{\mathrm{RH}^+} - \rho_{\mathrm{HPH}^+} - \rho_{\mathrm{HP}}}\right) \log \frac{K_{\mathrm{HPH}_0{}^+}\,K_{\mathrm{HP}_0}}{K_{\mathrm{RH}_0{}^+}K_{\mathrm{w}}} \quad (16)$$

Relative Rates of Acidic and Basic Hydrolysis of Esters and Amides.—We shall first apply eq. 16 to the rates of hydrolysis of ethyl benzoates. If equilibrium between P^- and HP is established much more rapidly than the cleavage of P^-, $k_{\mathrm{OH}^-}{}^{0}$ is equal to the sum, $k_{\mathrm{h}}{}^{\mathrm{OH}^-} + 2k_{\mathrm{ex}}{}^{\mathrm{OH}^-}$, of the rate constant for the basic hydrolysis of the ester and twice the rate constant for the base-catalyzed oxygen exchange of the ester.[15] Recent work by Bender and Thomas, however, suggests that the rate of establishment of the HP–P^- equilibrium may be comparable to the rate of cleavage of P^-.[17] Therefore there may be some error in taking $k_{\mathrm{h}}{}^{\mathrm{OH}^-} + 2k_{\mathrm{ex}}{}^{\mathrm{OH}^-}$ as a measure of $k_{\mathrm{OH}^-}{}^{0}$. To whatever extent the rate of establishment of equilibrium between HPH^+ and HP is comparable to the rate of cleavage of HPH^+[18] in acid-catalyzed ester hydrolysis, any such error in $k_{\mathrm{OH}^-}{}^{0}$ will tend to be compensated in the ratio $k_{\mathrm{OH}^-}{}^{0}/k_{\mathrm{H}^+}{}^{0}$ if $k_{\mathrm{h}}{}^{\mathrm{H}^+} + 2k_{\mathrm{ex}}{}^{\mathrm{H}^+}$ is used as a measure of $k_{\mathrm{H}^+}{}^{0}$. The value of $k_{\mathrm{h}}{}^{\mathrm{H}^+}/k_{\mathrm{ex}}{}^{\mathrm{H}^+}$ for ethyl benzoate in water at 99° (5.2)[20] appears to be the only one that has been determined. It is about the same as the value of $k_{\mathrm{h}}{}^{\mathrm{OH}^-}/k_{\mathrm{ex}}{}^{\mathrm{OH}^-}$ at 25° (4.8)[20] and since $k_{\mathrm{h}}/k_{\mathrm{ex}}$ values do not appear to be *highly* temperature-dependent[16] we shall assume that $k_{\mathrm{h}}/k_{\mathrm{ex}}$ is the same for the acid as for the basic hydrolysis of ethyl benzoate. Therefore $k_{\mathrm{OH}^-}{}^{0}/k_{\mathrm{H}^+}{}^{0}$ will be taken as equal to the ratio of the second-order rate constants for the basic and acid hydrolysis of ethyl benzoate. We shall use the value 2.93×10^{-2} l. mole^{-1} sec.$^{-1}$ for the basic-hydrolysis rate constant at 25°.[21] The value 3.0×10^{-2} has been reported for 25.12°.[20] Combination with our value for the acid-hydrolysis rate constant at 25° (3.9×10^{-7} l. mole^{-1} sec.$^{-1}$ —extrapolated from data at higher temperatures) gives a value of 4.88 for log ($k_{\mathrm{OH}^-}{}^{0}/k_{\mathrm{H}^+}{}^{0}$). Since the ratio of $k_{\mathrm{OH}^-}{}^{0}$ to the over-all rate constant for basic ester hydrolysis and the ratio of $k_{\mathrm{H}^+}{}^{0}$ to the over-all rate constant for acid-catalyzed ester hydrolysis should be relatively independent of the nature of substituents on the aromatic ring, ρ_{OH^-} and ρ_{H^+} will be equated to the corresponding ρ's for ester hydrolysis. Least squares treatment of the data on ethyl benzoate and its *m*- and *p*-amino derivatives by Tommila and co-workers[21] and that on the *p*-nitro derivative by Connors and Bender[22] gives a ρ_{OH^-} of 1.566 in water at 25°, about the same value that would be obtained by extrapolation from data in various aqueous acetone and aqueous ethanol solvent mixtures.[21] Extrapolation from our own data at 50–90° gives a value of 0.062 for ρ_{H^+}.

Determination of the basicity of ethyl benzoate in $\mathrm{H_2O–H_2SO_4}$ gave a *pK* value of −7.36. We have assumed that ρ_{RH^+} for the basicity of ethyl benzoates will be equal to that (1.09) found by Stewart and Yates for benzoic acids.[23,24]

Stewart and Van der Linden have determined the acidities of a number of $\mathrm{ArC(OH)_2CF_3}$'s,[25] and their data provide a good basis for the estimate of K_{HP_0}, the acidity constant of $\mathrm{C_6H_5C(OH)_2OEt}$. The acidity of alcohols of the type $\mathrm{C_6H_5C(OH)_2X}$ is assumed to follow the Taft equation with the same value of ρ^*(1.42) as that observed for $\mathrm{XCH_2OH}$'s, the only series of alcohols that appears to have been studied.[26] Assuming that $\sigma_{\mathrm{OEt}}{}^*$ is equal to $\sigma_{\mathrm{OMe}}{}^*$, for which a value of 1.81 has been reported,[27] and that $\sigma_{\mathrm{CF_3}}{}^*$ is 2.49 (the value calculated from the Ballinger and Long correlation), the *pK* of $\mathrm{C_6H_5C(OH)_2OEt}$ must be 0.97 higher than that of $\mathrm{C_6H_5C(OH)_2CF_3}$, which is 10.00. Therefore log K_{HP_0} is −10.97. The value of ρ_{HP} is taken as 1.11, the ρ observed for $\mathrm{ArC(OH)_2CF_3}$'s.[25]

Probably the least reliable of our estimates of the terms in eq. 16 is for $K_{\mathrm{HPH}_0{}^+}$. Here we note that $\mathrm{HPH_0}^+$ is an acid of the form $\mathrm{XOH_2}^+$ where we already have a good estimate of the acidity of XOH ($\mathrm{HP_0}$). We shall therefore assume that, after correction for statistical factors, the ratio $K_{\mathrm{XOH_2}^+}/K_{\mathrm{XOH}}$ has the same value as for some other X (as closely related an X as possible). The choice of the other X is simplified by the fact that there appears to be only one organic X for which $K_{\mathrm{XOH_2}^+}$ and K_{XOH} have both been determined in aqueous solution. This X is phenyl and it at least has the virtue that the acidity of XOH (phenol) is comparable to that of $\mathrm{HP_0}$. Taking log $K_{\mathrm{PhOH_2}^+}$ as 7.04,[28] log K_{PhOH} as −9.95[29] and assuming that $4K_{\mathrm{HPH}_0{}^+}/K_{\mathrm{HP}_0}$ is equal to $K_{\mathrm{PhOH_2}^+}/K_{\mathrm{PhOH}}$, a log $K_{\mathrm{HPH}_0{}^+}$ value of 5.42 is calculated.[30] The value of ρ_{HPH^+} is probably near 1.0, like most ρ's for the acidity of hydrogens separated by two saturated atoms from the aromatic ring. We shall assume ρ_{HPH^+} is 1.11 just as we have for ρ_{HP}. Substitution of these ρ and K values into the right-hand side of eq. 16 gives a calculated value of 6.66 for log ($k_{\mathrm{OH}^-}{}^{0}/k_{\mathrm{H}^+}{}^{0}$) in comparison to the experimental value of 4.88. Considering the possibilities: that ethyl benzoate may not be

---

[15] This sum is the k_1 of Bender, Ginger and Unik's reaction scheme.[16]

[16] M. L. Bender, R. D. Ginger and J. P. Unik, *J. Am. Chem. Soc.*, **80**, 1044 (1958).

[17] M. L. Bender and R. J. Thomas, *ibid.*, **83**, 4189 (1961).

[18] It is unlikely that the rate of cleavage of HPH^+ to $\mathrm{H_2O}$ and RH^+ is rapid compared to the transformation of HPH^+ to HP. If this were the case the rate-determining step in acid-catalyzed ester hydrolysis would be a simple proton-transfer reaction and for this reason the reaction might be expected to proceed more slowly in heavy water than in light water. Actually, the opposite is observed for ethyl formate and methyl acetate, at least.[19]

[19] K. B. Wiberg, *Chem. Revs.*, **55**, 713 (1955).

[20] M. L. Bender, *J. Am. Chem. Soc.*, **73**, 1626 (1951).

[21] E. Tommila, A. Nurro, R. Murén, S. Merenheimo and E. Vuorinen, *Suomen Kemi.*, **B32**, 115 (1959).

[22] K. A. Connors and M. L. Bender, *J. Org. Chem.*, **26**, 2498 (1961).

[23] R. Stewart and K. Yates, *J. Am. Chem. Soc.*, **82**, 4059 (1960).

[24] The *pK* of benzoic acid (−7.26)[23] is very near that of ethyl benzoate.

[25] R. Stewart and R. Van der Linden, *Can. J. Chem.*, **38**, 399 (1960).

[26] P. Ballinger and F. A. Long, *J. Am. Chem. Soc.*, **82**, 795 (1960).

[27] H. K. Hall, Jr., *ibid.*, **79**, 5441 (1957).

[28] E. M. Arnett and C. Y. Wu, *ibid.*, **82**, 5660 (1960).

[29] C. M. Judson and M. Kilpatrick, *ibid.*, **71**, 3110 (1949).

[30] The "4" is a statistical factor.[31]

[31] S. W. Benson, *J. Am. Chem. Soc.*, **80**, 5151 (1958).

a Hammett base, with the result that our $K_{RH_0^+}$ is in error; that $K_{HPH_0^+}$ is quite difficult to estimate; that the ρ's and the other K's are subject to some uncertainty; and that the ratio of the rate constant for basic ester hydrolysis to that for acidic ester hydrolysis may not be exactly equal to $k_{OH^-}^0/k_{H^+}^0$, the ratio of k's for the formation of P^- and HPH^+; the agreement is believed to be good enough to lend some support to the hypothesis on the basis of which eq. 16 was derived.

Equation 16 may also be applied to the hydrolysis of benzamides, but in this case we have less confidence that $k_{OH^-}^0/k_{H^+}^0$ can really be approximated well from available experimental data. As in the case of ester hydrolysis we shall use the rate constants for hydrolysis plus twice the rate constants for exchange as a measure of $k_{OH^-}^0$ and of $k_{H^+}^0$. Because of the great ability of the amino group to donate electrons to sp^2-carbon, however, the cleavage of P^- and of HPH^+ would be expected to be much faster than in the case of esters,[17] and therefore perhaps faster than equilibration with HP. If this error is present, both in our estimate of $k_{OH^-}^0$ and $k_{H^+}^0$ the error in the ratio $k_{OH^-}^0/k_{H^+}^0$ will be less, though perhaps still considerable.[32]

Extrapolation of Bender, Ginger and Unik's values of $k_h + 2k_{ex}$ for the basic hydrolysis and ^{18}O-exchange of benzamide, determined at 40.7°, 80° and 109°, to 25° gives the value 4.42×10^{-5} l. mole^{-1} sec.$^{-1}$.[16] In the acid hydrolysis of benzamide there is no detectable ^{18}O-exchange at 109°,[33] and we shall assume that there is none at 25°. Therefore $k_{H^+}^0$ is equal to the second-order rate constant for the acid hydrolysis of benzamide in water at 25°, for which a value of 1.94×10^{-7} l. mole^{-1} sec.$^{-1}$ may be calculated from the data of Edward and Meacock[34] if it is assumed that the hydrolysis rate is a linear function of the acid concentration at concentrations up to 1 M hydrochloric acid. The "experimental" value of $\log (k_{OH^-}^0/k_{H^+}^0)$ is thus 2.36.

The pK of benzamide (-2.16) and ρ_{RH^+} for the basicities of benzamides (1.30) have been determined by Edward, Chang, Yates and Stewart.[35] From our previous assumption that ρ^* for the acidity of $C_6H_5C(OH)_2X$'s is 1.42 and the value 0.62 for $\sigma_{NH_2}^*$,[28] the pK of $C_6H_5C(OH)_2NH_2$ is estimated to be 12.66. Assuming that a ρ^* of 1.42 is also applicable to the acidities of $C_6H_5COHXOH_2^+$'s (HPH^+'s) and using the pK we estimated for the case X = OEt, a pK of -3.73 is estimated for the case X = NH_2. We assume the same values of ρ_{HPH^+} and ρ_{HP} (1.11) as those used in the application of eq. 16 to ester hydrolysis. In order to estimate the value of ρ_{OH^-} appropriate for the correlation of k_{OH^-}'s for various benzamides we should like to learn how k_h/k_{ex} changes with changes in substituents on the aromatic ring. Since such data do not appear to be available, however, we shall simply estimate ρ_{OH^-} for the basic hydrolysis of benzamides in water at 25°, assuming that the value of k_h/k_{ex} is independent of the nature of the substituents. We shall also make this assumption for acid hydrolysis, for which it is probably an excellent approximation, and estimate ρ_{H^+} for the acid hydrolysis of benzamides under the desired conditions. Since ρ for the basic hydrolysis of benzamides at 100° is essentially the same in pure water (1.068) as it is in 60% ethanol (1.100)[36] we shall assume it is also the same at 25°.[37] The best straight line through a plot of the ρ's at 52.8°, 64.5°, 80.3° and 100.1° in 60% ethanol *vs.* $1/T$ leads to a ρ value of 1.54 at 25°. For the acid hydrolysis of benzamides in water ρ is 0.119 at 100°.[36] In 60% ethanol ρ for acid hydrolysis decreases from -0.222 at 99.6° to -0.483 at 52.4°.[36] There appear to be no data available for hydrolysis in dilute aqueous acid at temperatures below 100°, but from a report on hydrolysis in concentrated acid[34] it seems that in water ρ may actually be somewhat larger at 25° than at 100°. The data are limited, however, and it would be be difficult to calculate a very reliable ρ. In our application of eq. 16 we have used the ρ value (0.119) obtained at 100°. The calculated value of $\log (k_{OH^-}^0/k_{H^+}^0)$ is 1.03.[39] The agreement with the experimental value (2.36) is slightly better than that obtained in the case of esters, and in spite of the greater uncertainty involved in the application of eq. 16 to amide hydrolysis we believe that this agreement constitutes some added evidence for the hypothesis on the basis of which eq. 16 was derived.

Other Applications of Eq. 16.—It seems unlikely that the proposed quantitative relationship will ever permit the correlation of rate and/or equilibrium constants with the reliability of such simpler linear free-energy relationships as the Hammett equation or the Taft equation. Considering that *no* relation between the rate constants of corresponding acid- and base-catalyzed reactions seems to have been proposed previously, however, the present crude correlation is a vast improvement. The predictive power of the relationship may appear to be somewhat marred by the necessity of having to know the k's whose ratio is predicted in order to learn the ρ's whose values are needed in the prediction. This need not always be the case, though, since ρ's for rate processes can be determined without a knowledge of any rate constants—by competition experiments, for example, and, less precisely, by use of an equation of the form $\rho = \tau(\sigma_{\pm} - \sigma_{\text{reactant}})$.[40] Furthermore, since the proposed relation was designed only for cases in which the acid- and base-catalyzed reactions proceed by the same mechanism, it may be useful in the diagnosis of changes in reaction mechanism.

---

(32) For recent observations and discussion of the mechanism of the base-catalyzed hydrolysis and oxygen exchange of amides, see M. L. Bender and R. J. Thomas, *J. Am. Chem. Soc.*, **83**, 4183 (1961).

(33) M. L. Bender and R. D. Ginger, *ibid.*, **77**, 348 (1955).

(34) J. T. Edward and S. C. R. Meacock, *J. Chem. Soc.*, 2000 (1957).

(35) J. T. Edward, H. S. Chang, K. Yates and R. Stewart, *Can. J. Chem.*, **38**, 1518 (1960).

(36) H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

(37) From Reid's data on the basic hydrolysis of *m*- and *p*-nitrobenzamides in water at 60–100°[38] and the data on benzamide,[16] it is clear that ρ increases significantly with decreasing temperature in pure water.

(38) E. E. Reid, *Am. Chem. J.*, **24**, 397 (1900); **45**, 327 (1911).

(39) A measure of the sensitivity of this value to the choice of ρ and K values may be found in the fact that the use of Edward and Meacock's preliminary ρ_{RH^+} value (0.933)[34] gives an experimental log ($k_{OH^-}^0/k_{H^+}^0$) of 1.98.

(40) J. Hine, *J. Am. Chem. Soc.*, **81**, 1126 (1959).

Experimental

Reagents.—The ethyl benzoates used were Eastman Kodak Co. white label products, except for the *p*-chlorobenzoate, a gift from Mr. D. F. Brown of Washington State College. The melting points of the solids were within 2° and the refractive indices of the liquids within 0.0011 of values reported in the literature.

The perchloric acid, sodium hydroxide and potassium hydrogen phosphate used were J. T. Baker analyzed reagents. The boric acid was Merck & Co., Inc., reagent.

Kinetics of Acidic Hydrolysis of Ethyl Benzoates.—Our method of determining the rate constants for the acid hydrolysis of ethyl benzoates is based on that used by Chmiel and Long for methyl benzoate and methyl mesitoate.[41] A solution (*ca.* $10^{-4}M$) of ester in about 1.05 *M* aqueous perchloric acid was kept in a constant temperature bath. At intervals, 20-ml. samples were pipetted into measured amounts of cold sodium hydroxide and buffer, the unreacted ester was extracted with methylene chloride and the amount of acid produced was determined by spectrophotometric measurements on the acidified solution. With the benzoate and *p*-methoxybenzoate a borate buffer was used, giving a *p*H of 8.5–9.0. With the other esters, however, basic hydrolysis was found to be a significant source of error at this *p*H and therefore a phosphate buffer, giving a *p*H of 6.0–6.3, was used. Check experiments showed that known solutions could be analyzed with no more than about 5% error by these techniques. The coefficient of expansion of 1 *M* perchloric acid was determined over the range 25–90° and found to be essentially equal to that of water. From this result, the concentration of ester used and the extinction coefficient of the acid produced, D_∞ (the optical density at infinite time) was calculated. Using points taken between 5 and 75% reaction and between 0.5 hour and 12 hours, first-order rate constants were determined by visual fit of the best straight lines through plots of $2.303 \log [D_\infty/(D_\infty - D)]$ *vs.* time. The first-order rate constants were transformed to second-order rate constants by division by the hydrogen-ion concentration.[41] Two runs, with an average of five points per run, were made on each compound at each temperature. Like Chmiel and Long, we estimate the accuracy of the rate constants determined to be ±10%.

The kinetic data obtained are listed in Table I. In only one case does a direct comparison with the literature seem possible. Extrapolation of our results gives a *k* of 2.8×10^{-4} l. mole^{-1} sec.$^{-1}$ for ethyl benzoate at 99° in comparison with the value 3.9×10^{-4} l. mole^{-1} sec.$^{-1}$ at 99 ± 1° reported by Bender.[20]

TABLE I

ACID HYDROLYSIS OF ETHYL BENZOATES

Substituent	$10^6 k$, l. mole^{-1} sec.$^{-1}$ 50°	70°	90°	E_a, kcal./mole
p-Methoxy	3.7	23	107	19.5
None	5.1	28	143	19.4
p-Chloro	6.0	28	105	16.7
m-Nitro	4.2	28	144	20.7
p-Nitro	6.3	36	182	19.5

Since the activation energies reported may well be in error by 1 kcal./mole the only significant statement we can make about the relative values is that the activation energy for the *p*-chlorobenzoate appears to be lower than the others.

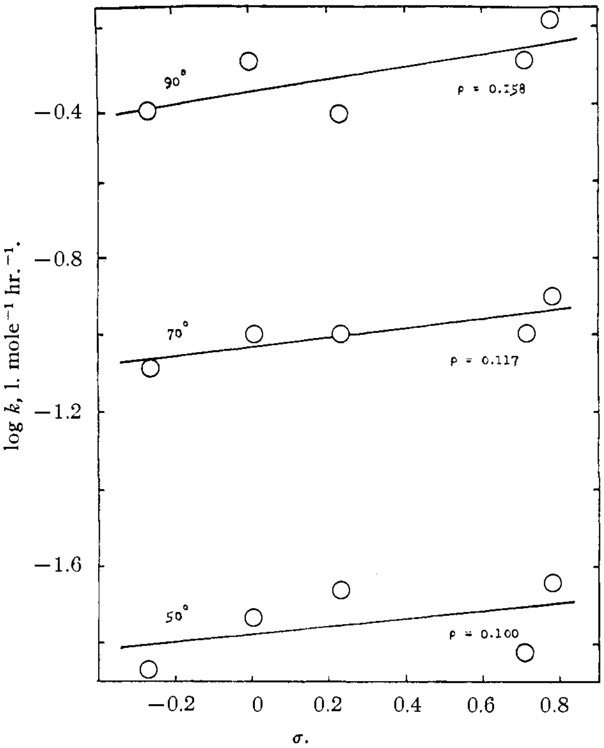


Fig. 1.—Hammett plots for acid hydrolysis of ethyl benzoates.

In Fig. 1 are Hammett-equation plots for the three temperatures at which the rates were determined. The Hammett ρ obtained by extrapolation to 25° is 0.062.

Determination of the pK of Ethyl Benzoate.—Sulfuric acid–water solutions, prepared from reagent grade concentrated sulfuric acid and distilled water or reagent grade 30% fuming sulfuric acid, were standardized by titration; H_0-values were obtained from the values listed by Paul and Long.[42] Standard solutions of ethyl benzoates in these sulfuric acid–water solutions were prepared as described by Stewart and Yates for acetophenones.[43] From measurements at the absorption maxima of ethyl benzoate (234 mμ) and its conjugate acid (262 mμ) *pK* values (−7.33 and −7.40 in two determinations) were calculated by the method of Davis and Geissman.[44]

Acknowledgment.—Support of this investigation by a grant from the National Science Foundation is gratefully acknowledged.

---

[41] C. T. Chmiel and F. A. Long, *J. Am. Chem. Soc.*, **78**, 3326 (1956).

[42] M. A. Paul and F. A. Long, *Chem. Revs.*, **57**, 1 (1957).

[43] R. Stewart and K. Yates, *J. Am. Chem. Soc.*, **80**, 6355 (1958).

[44] C. T. Davis and T. A. Geissman, *ibid.*, **76**, 3507 (1954).