Hydrogen-Bonded Intermediates and Stepwise Mechanisms for Proton-Exchange Reactions between Oxygen Atoms in Hydroxylic Solvents[1]

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Abstract: It is shown that such reactions as the hydrogen ion catalyzed exchange of the hydroxylic hydrogen atoms of phenol and benzoic acid in water and methanol solution, previously thought to be too fast for a stepwise mechanism to be plausible, actually proceed at rates that are reasonable when the reversible formation of hydrogen-bonded intermediates is included explicitly in the mechanism and when the basicities of the reactants are calculated by the method of Bunnett and Olsen. Relationships are derived expressing the equilibrium constants for hydrogen bonding between oxygen acids and bases in water and methanol in terms of the acidity and basicity of the reactants and solvent and the parameter τ (eq 7 and 8). A plausible value for τ permits calculation of the Brønsted α values for the exchange of meta- and para-substituted benzoic acids with methanol and for the donation of a proton from a benzoic acid molecule to a benzoate anion *via* a solvent methanol molecule.

Two of the generalizations most commonly applied by chemists to problems concerning structural effects on reaction rates may be referred to as the *product stability principle* and the *principle of least motion.*[2] Let us consider the application of these generalizations to the question of when a reaction will proceed by a stepwise mechanism and when it will proceed by a concerted mechanism.[3] In the case of most polar reactions a smaller "change in atomic position and electronic configuration[4]" might be expected to take place in a given step of a completely stepwise mechanism than in a fully concerted mechanism for the same reaction. Thus the principle of least motion will tend to favor stepwise reaction mechanisms. However, such mechanisms often necessitate the formation of highly unstable reaction intermediates, and according to the product stability principle the formation of such intermediates will tend to be slow. A combination of the two principles suggests the following possible generalization: *The making and breaking of bonds will tend to take place in separate steps except where the formation of a sufficiently unstable intermediate may be avoided by combining several such bond changes into one concerted step.* To test the validity of this generalization, which has been the implicit basis of many discussions of reaction mechanisms, and to learn something about how unstable a reaction intermediate has to be before it is by-passed by a concerted reaction mechanism, let us consider some relatively simple but well-understood reactions. The revealing studies of the kinetics of proton-transfer and proton-exchange reactions in solution that have been carried out during the last two decades should provide suitable examples. Dissociation of an acid to give a free proton followed by combination of the free proton with a base would constitute a fully stepwise mechanism for a proton-transfer reaction. However, the activation energies for typical proton transfers between oxygen atoms are more than 100 kcal/mol smaller than the energy that would be required to form a free proton. Hence the free proton is a sufficiently unstable intermediate to be avoided, and we shall assume that all proton transfers take place along a hydrogen bond with the proton forming a full bond to one base as it breaks its full bond to another. Such mechanisms will be referred to as stepwise in distinction to concerted mechanisms, which involve the transfer of two or more protons in the same step. Let us estimate the maximum rate constants that various proton-exchange reactions could have if they proceed by stepwise mechanisms and compare them with the experimental values. If some of the intermediates are so unstable that they are by-passed, the experimental rate constant should be larger than the estimated value.

Hydrogen-Bonded Intermediates in Proton Exchange between Oxygen Atoms. There are several acid-catalyzed proton-exchange reactions between oxygen atoms that have been reported to be too rapid to be stepwise protonation–deprotonation processes. Before considering one of these, the hydronium ion catalyzed exchange of phenol, we need to discuss the probable value of the acidity constant of the phenyloxonium ion in aqueous solution.

Spectrophotometric measurements were made on phenol in aqueous sulfuric acid at 0° and it was reported to be half protonated at an H_0 of -7.04 on the scale of Paul and Long.[5,6] However, a plot of log ([BH$^+$]/[B]) *vs.* the H_0 values used had a slope of 0.91, and when the improved H_0 values of Jorgenson and Hartter[7] were used the slope was 0.81. Thus phenol is apparently not a Hammett base. Accordingly, the pK was taken to be the intercept of a plot of $H_0 + \log([\mathrm{BH}^+]/[\mathrm{B}])$ *vs.* $H_0 + \log[\mathrm{H}^+]$, taking [H$^+$] as the molar concentration of sulfuric acid.[8] The value -6.1 ± 0.6

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[1] (a) This investigation was supported in part by Grant GP-14697 from the National Science Foundation. (b) Part XV in the series "Structural Effects on Rates and Equilibria." For part XIV see ref 2.

[2] *Cf.* J. Hine, *J. Amer. Chem. Soc.*, 93, 3701 (1971).

[3] The words "stepwise" and "concerted" are defined in terms of bond formation and cleavage. In a completely stepwise mechanism only one bond is formed or cleaved in any step. In a completely concerted mechanism all the bond formations and cleavages are combined into a single step.

[4] F. O. Rice and E. Teller, *J. Chem. Phys.*, 6, 489 (1938).

[5] E. M. Arnett and C. Y. Wu, *J. Amer. Chem. Soc.*, **82**, 5660 (1960).

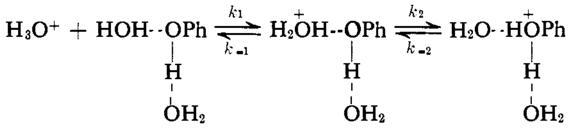
[6] C. Y. Wu, Ph.D. Thesis, University of Pittsburgh, Pittsburgh, Pa., 1961, pp 116, 184, 185.

[7] M. J. Jorgenson and D. R. Hartter, *J. Amer. Chem. Soc.*, **85**, 878 (1963).

[8] J. F. Bunnett and F. P. Olsen, *Can. J. Chem.*, **44**, 1899 (1966).

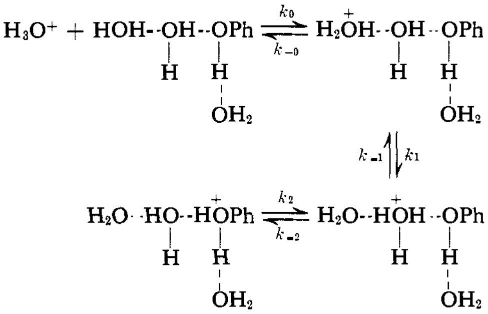
obtained[9] may suffer from the increasing uncertainty that attends the use of the method of Bunnett and Olsen when the molar concentration of sulfuric acid approaches and surpasses that of water in the solutions in which measurements are made. However, when the two points determined in the most concentrated acid solutions were neglected, the pK value obtained from the other five points was -4.9 ± 0.3.[9] Hence, it seems unlikely that the value -6.1 ± 0.6 overestimates the basicity of phenol.

As Grunwald and Puar have pointed out, if the hydronium ion catalyzed exchange of phenol proceeds by a stepwise mechanism the phenol–hydronium ion encounter complex should be a reaction intermediate.[11] In such a reaction, as seen in eq 1, the overall equilibrium constant $k_1k_2/(k_{-1}k_{-2})$ will be $10^{-6.1}$ M^{-1}. The assumptions[11] that the reaction governed by k_{-2} is ultrafast and that a conservative upper limit for k_{-1} is 10^{12} sec^{-1} seem plausible. It does not follow, however, that the step governed by k_{-1} may necessarily be treated as the rate-controlling step of the reverse reaction. In general, the rate constant for hydronium ion catalyzed exchange is that shown in eq 2. (A phenyloxonium ion formed from phenol and a hydronium ion will lose the old proton only half the time.) The only rigorous limit on the ultrafast reaction is a maximum rate constant of 10^{14} sec^{-1}, the vibrational frequency of an oxygen–hydrogen bond.[12] From this limit, the limit of 10^{12} sec^{-1} on k_{-1}, and eq 2, rate constants for exchange equal to or larger than the observed value of 1.46×10^7 M^{-1} sec^{-1} at 25°[11] may be calculated from any value of the equilibrium constant k_1/k_{-1} larger than about $10^{-4.3}$ M^{-1} (provided that it is not so large as to contradict the assumption that only relatively small concentrations of the intermediate are present). For example, the observed rate constant for exchange may be obtained from the values 4×10^{13} sec^{-1}, 10^{11} sec^{-1}, and 10^{-2} M^{-1} for k_{-2}, k_{-1}, and k_1/k_{-1}, respectively. Even smaller values of k_{-2} and k_{-1} could be used if phenol were taken to be more basic than indicated by the pK value -6.1 we have used. Since the stepwise mechanism can be accommodated by a value for k_{-2} in the vicinity of that (4.35×10^{13} sec^{-1}) reported for the donation of a proton from perchloric acid to water[13] and a value for k_{-1} smaller than that (6×10^{11} sec^{-1}) reported for the tranfer of a proton from a hydronium ion to an adjacent water molecule,[14] the stepwise mechanism is plausible if a value for k_1/k_{-1} greater than about $10^{-4.3}$ M^{-1} is plausible. In fact, even if k_1/k_{-1} is smaller than $10^{-4.3}$ M^{-1} the stepwise mechanism remains plausible provided that the value is significantly larger than the overall equilibrium constant for the reaction ($10^{-6.1}$ M^{-1}), as it would be expected to be.[15] In such a case it is merely necessary to make explicit an equilibrium that was implicit in mechanism 1. Since water is more basic than phenol, this new equilibrium, governed by the rate constants k_0 and k_{-0} as shown in mechanism 3, should have a significantly larger equilibrium constant than the equilibrium governed by k_1/k_{-1} in mechanism 1, which becomes the equilibrium governed by $k_0k_1/(k_{-0}k_{-1})$ in mechanism 3. If it does, then the rate constant for formation of phenyloxonium ions, which in the general case has the form $k_0k_1k_2/(k_{-0}k_{-1} + k_{-0}k_2 + k_1k_2)$, is well approximated as $k_0k_1k_2/(k_{-0}k_{-1})$. If this is true, then the rate constant for exchange is equal to $10^{-6.4}\cdot k_{-2}$. Hence, the observed rate of exchange may be fit with the plausible value $10^{12.6}$ sec^{-1} for k_{-2}.



$$\mathrm{H_3O^+ + HOH\cdots\underset{\substack{|\\ H\\ \vdots\\ OH_2}}{O}Ph \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} H_2\overset{+}{O}H\cdots\underset{\substack{|\\ H\\ \vdots\\ OH_2}}{O}Ph \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} H_2O\cdots H\underset{\substack{|\\ H\\ \vdots\\ OH_2}}{\overset{+}{O}}Ph} \qquad (1)$$

$$k_{\mathrm{exch}} = \frac{k_1k_2}{2(k_1 + k_2)} \qquad (2)$$



$$\begin{array}{ccc} \mathrm{H_3O^+ + HOH\cdots\underset{\substack{|\\ H}}{O}H\cdots\underset{\substack{|\\ H\\ \vdots\\ OH_2}}{O}Ph} & \underset{k_{-0}}{\overset{k_0}{\rightleftharpoons}} & \mathrm{H_2\overset{+}{O}H\cdots\underset{\substack{|\\ H}}{O}H\cdots\underset{\substack{|\\ H\\ \vdots\\ OH_2}}{O}Ph} \\ & & k_{-1}\Big\uparrow\Big\downarrow k_1 \\ \mathrm{H_2O\cdots H\underset{\substack{|\\ H}}{O}\cdots H\underset{\substack{|\\ H\\ \vdots\\ OH_2}}{\overset{+}{O}}Ph} & \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} & \mathrm{H_2O\cdots H\underset{\substack{|\\ H}}{\overset{+}{O}}H\cdots\underset{\substack{|\\ H\\ \vdots\\ OH_2}}{O}Ph} \end{array} \qquad (3)$$

The acid-catalyzed exchange of benzoic acid with methanol has also been reported to be too fast (by more than 10^4-fold) for a stepwise mechanism to be plausible.[16] However, when considered in terms of a mechanism like 1 or 3, in which explicit attention is given to the intermediate hydrogen-bonded species whose formation is believed to precede protonation of the weak base that is undergoing exchange, the exchange rate appears to be in the vicinity of that expected for a stepwise mechanism. Benzoic acid was reported to be half-protonated at an H_0 value of -7.62 in aqueous sulfuric acid and at an H_0 value of -8.85 in aqueous perchloric acid with slopes of the plots of H_0 *vs.* log ([BH$^+$]/[B]) of 0.84 and 0.83, respectively.[17] Using the sulfuric acid data to calculate what [BH$^+$]/[B] should have been in 76, 80, and 84% acid and applying the treatment of Bunnett and Olsen[8] gave a pK of -6.5 for benzoic acidium ions in aqueous solution. On the basis of Bell's observation that the pK values for 13 primary ammonium ions are 1.2 ± 0.3[9] units more positive in methanol than in water,[18,19] the pK of benzoic acidium ions is estimated to be -5.3 in methanol. A mechanism analogous to that in eq 3 will then give a rate constant for exchange of $10^{-5.6}k_{-2}$ if $k_0k_1/(k_{-0}k_{-1})$ is significantly larger than $10^{-5.3}$, k_0/k_{-0} is

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[9] The uncertainties listed are standard deviations.[10]

[10] W. J. Youden, "Statistical Methods for Chemists," Wiley, New York, N. Y., 1951, Chapter 5.

[11] E. Grunwald and M. S. Puar, *J. Phys. Chem.*, **71**, 1842 (1967).

[12] E. Grunwald, *Progr. Phys. Org. Chem.*, 3, 317 (1965).

[13] A. K. Covington, M. J. Tait, and Lord Wynne-Jones, *Discuss. Faraday Soc.*, 39, 172 (1965).

[14] S. Meiboom, *J. Chem. Phys.*, **34**, 375 (1961); A. Loewenstein and A. Szöke, *J. Amer. Chem. Soc.*, **84**, 1151 (1962); Z. Luz and S. Meiboom, *ibid.*, **86**, 4768 (1964).

[15] The value of k_1/k_{-1} obtained from an equation to be derived later in this paper is $10^{-3.6}$ M^{-1}.

[16] E. Grunwald and C. F. Jumper, *J. Amer. Chem. Soc.*, **85**, 2051 (1963).

[17] K. Yates and H. Wai, *Can. J. Chem.*, 43, 2131 (1965).

[18] R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p 44.

[19] The ΔpK of 0.8 used previously[16] was based on the average of the values for the anilinium ion (1.2) and the *N*-methylanilinium ion (0.4). Since I feel that the benzoic acidium ion should be very strongly hydrogen bonded to the solvent, the primary ammonium ions are taken as better models for estimating ΔpK.

still larger, k_{-1} is around 10^{13} sec^{-1}, and k_{-0} is near the upper limit ($10^{11.3}$ sec^{-1}) estimated[16] for such proton transfers in methanol. Hence a value of 10^{14} sec^{-1} for k_{-2} will give the observed rate constant for exchange (2.58×10^8 M^{-1} sec^{-1}).[16] This value is at the theoretical upper limit, but the overall uncertainty in the equilibrium and rate constants used in arriving at it may be as much as a factor of 10.

An analogous treatment of the acid-catalyzed exchange of phenol in methanol shows that a k_{-2} value of only $10^{13.1}$ sec^{-1} is needed to obtain the rate constant (8×10^7 M^{-1} sec^{-1}) at 25° that may be extrapolated, by use of the Arrhenius equation, from values determined at −80 and −42.5°.[20]

The rate constant for the hydrogen ion catalyzed exchange of water with water in aqueous *tert*-butyl alcohol solution has been found to be about 2.7 times as large as the rate constant for exchange of water with alcohol.[21] This was taken as evidence against a stepwise mechanism for exchange involving an intermediate *tert*-butyloxonium ion on the basis of the statement that the basicity of water is at least 10 times greater than that of *tert*-butyl alcohol. However, Raman spectral studies on methanol and isopropyl alcohol have been shown to yield pK values for the conjugate acids around −2.2 and −1.7, respectively,[2] and pmr chemical shift measurements have given a pK of −1.94 for the conjugate acid of ethanol.[22] It seems reasonable that the basicity of *tert*-butyl alcohol should be comparable to the basicities of these alcohols. It is therefore plausible that the basicity of *tert*-butyl alcohol is within a factor of three of that of water and that its acid-catalyzed exchange involves the intermediate formation of *tert*-butyloxonium ions.

The preceding calculations give such a plausible picture of a number of proton-exchange reactions at oxygen in terms of stepwise mechanisms involving hydrogen-bonded intermediates that it seems worthwhile to consider, in terms of such mechanisms, the way in which the rate constants for some such reactions change with the acidities and basicities of the reactants. First, however, we should consider how the equilibrium constants for hydrogen bonding between oxygen acids and bases might most reasonably be expected to change with the acidities and basicities of the reactants in hydroxylic solvents.

Hydrogen Bonding by Oxygen Acids and Bases in Hydroxylic Solvents. If we assume that oxygen acids and bases in a hydroxylic solvent are hydrogen bonded to the solvent, if not to anything else, equilibrium in hydrogen bonding will be a hydrogen-bond exchange reaction, as shown in eq 4, which, for convenience, re-

$$\text{AOH--OH}_2 + \text{HOH--OB} \overset{K'_{\text{AB}}}{\rightleftharpoons} \text{AOH--OB} + \text{HOH--OH}_2 \quad (4)$$

fers to hydrogen bonding between electrically neutral species in aqueous solution, with B being either a divalent group or two monovalent groups. This equation may be seen to be analogous to eq 5, which has

$$\text{X}_1\text{—N—Y}_1 + \text{X}_2\text{—N—Y}_2 \rightleftharpoons \text{X}_1\text{—N—Y}_2 + \text{X}_2\text{—N—Y}_1 \quad (5)$$

been used as a general representation of substituent effects, from which, by use of certain assumptions concerning the interaction of the groups X and Y across the common molecular framework N, such relations as the Hammett and Taft equations may be derived.[23] In eq 4 the groups X and Y have become A and B and the framework N has become the group OH--O, across which A and B must interact. According to the derivation given previously,[23] K'_{AB} should be expressed as shown in eq 6, where the τ and σ constants refer to the

$$\log K'_{\text{AB}} = -\tau(\sigma_{\text{A}} - \sigma_{\text{H}})(\sigma_{\text{B}} + \sigma_{\text{H}_2}) \quad (6)$$

OH--O framework. The σ constants are measures of the electron-donating or electron-withdrawing power of the substituents. In the present case it is convenient to equate the σ constants for A and H to the logarithms of the acidity constants of HOA and H_2O and those for B and H_2 to the logarithms of the acidity constants of the conjugate acids of BO and H_2O, respectively.[24] When this is done and the term [HOH--OH_2], which is taken as the concentration of water in an aqueous solution, is absorbed into K'_{AB} to give K_{AB}, the result is eq 7.[25] The equation for methanol (eq 8) is the same

$$K_{\text{AB}} = \frac{[\text{AOH--OB}]}{[\text{AOH--OH}_2][\text{HOH--OB}]} = \frac{[\text{AOH--OB}]}{[\text{AOH}][\text{OB}]}$$

$$\log K_{\text{AB}} = \tau(\text{p}K_{\text{HOA}} - \text{p}K_{\text{H}_2\text{O}})(\text{p}K_{\text{H}_3\text{O}} - \text{p}K_{\text{HOB}}) - \log 55 \quad (7)$$

$$\log K_{\text{AB}} = \tau(\text{p}K_{\text{HOA}} - \text{p}K_{\text{MeOH}})(\text{p}K_{\text{MeOH}_2} - \text{p}K_{\text{HOB}}) - 1.4 \quad (8)$$

except that log 55 is replaced by log 25 (pure methanol is 25 M) and the τ and pK values refer to methanol solution. The proportionality constant for interactions across the OH--O grouping (τ) should be a positive number. To get some idea as to its probable magnitude, let us apply eq 7 to the formation of the complexes XH--Y^- and YH--X^- in the case where HX is a stronger acid than HY. This gives eq 9 and 10, which

$$\log \frac{[\text{XH--Y}^-]}{[\text{XH}][\text{Y}^-]} = \tau(\text{p}K_{\text{HX}} - \text{p}K_{\text{H}_2\text{O}})(\text{p}K_{\text{H}_3\text{O}} - \text{p}K_{\text{HY}}) - \log 55 \quad (9)$$

$$\log \frac{[\text{YH--X}^-]}{[\text{YH}][\text{X}^-]} = \tau(\text{p}K_{\text{HY}} - \text{p}K_{\text{H}_2\text{O}})(\text{p}K_{\text{H}_3\text{O}} - \text{p}K_{\text{HX}}) - \log 55 \quad (10)$$

may be combined and rearranged to give eq 11.[26] If

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(20) M. S. Puar and E. Grunwald, *Tetrahedron*, 24, 2603 (1968).

(21) E. K. Ralph and E. Grunwald, *J. Amer. Chem. Soc.*, 91, 2426 (1969).

(22) D. G. Lee and R. Cameron, *ibid.*, 93, 4724 (1971).

(23) J. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill, New York, N. Y., 1962, Chapter 4.

(24) Note that since the framework OH--O is written as being unsymmetrical, the substituent contants of A and B do not have to have identical definitions.

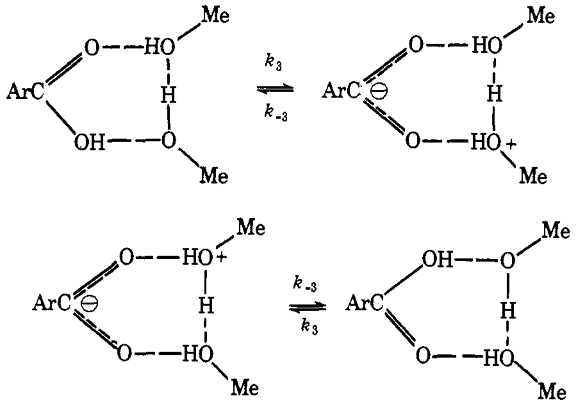
(25) The fact that the OH--O framework is neither as rigid nor as large as the molecular frameworks (*e.g.*, *m*- and *p*-phenylene) for which linear free energy relationships have been most successful suggests that eq 7 will be less precise than many other such relationships. This equation may also be "derived" from relationships obtained in the correlation of equilibrum constants for hydrogen bonding in carbon tetrachloride solution by W. H. Sachs and L. R. Green in this laboratory (unpublished observations, 1971), but in the end it will have to be considered a hypothesis whose validity must be judged on the basis of its ability to fit experimental observations.

(26) It seems likely that the errors in the application of an equation like 7–10, 14, 18, or 19 to several association reactions will be similar if each of the acids belongs to the same family and each of the bases belongs to the same family. If this is so, the errors in equations like 11, 20, and the partial derivative of 14 with respect to p$K_{\text{ArCO}_2\text{H}}$ will be relatively small if there have been no changes in the families (and therefore no changes in the electrical charge type) to which the acids or the bases involved belong.

$$\log\frac{[\mathrm{XH}\text{--}\mathrm{Y}^-]}{[\mathrm{YH}\text{--}\mathrm{X}^-]} = (\mathrm{p}K_{\mathrm{HY}} - \mathrm{p}K_{\mathrm{HX}})[\tau(\mathrm{p}K_{\mathrm{H_2O}} - \mathrm{p}K_{\mathrm{H_3O}}) - 1] \qquad (11)$$

there is only one potential energy minimum for movement of H between X and Y, then XH--Y$^-$ and YH--X$^-$ are identical and eq 11 is equal to zero. Since $\mathrm{p}K_{\mathrm{HY}} - \mathrm{p}K_{\mathrm{HX}}$ is a positive number by hypothesis, the bracketed term on the right side of eq 11 would be zero and τ would be the reciprocal of $15.74 - (-1.74)$ or 0.057. On the other hand if there are two potential minima and if the predominant species is the one with the hydrogen nearer the stronger base (*i.e.*, [YH--X$^-$] > [XH--Y$^-$]), then τ may be seen to be less than 0.057. Hence τ should be between zero and 0.057 in water at 25°; analogous calculations show that in methanol at 25° it should be between zero and 0.051.

Brønsted Correlations of Proton-Exchange Rates between Oxygen Atoms in Methanol. In an nmr study of proton exchange in solutions of benzoic acid in methanol, a term first order in benzoic acid was found in the rate equation for exchange of the methanol and also in the rate equation for exchange of the acid.[27] Since the coefficient of the term in the methanol rate equation was almost twice that of the term in the acid rate equation, these terms are due to a mechanism or mechanisms in which two methanol molecules undergo proton exchange every time one benzoic acid molecule does. Grunwald has explained these observations in terms of a stepwise mechanism involving an intimate ion pair as an intermediate,[12,27] as shown in eq 12. Albery has argued that the stepwise mechanism is implausible, but his argument is based in part on an assumption that the equilibrium constant for complexing between a carboxylate anion and a solvated hydrogen ion must be quite small.[28] Calculations based on eq 7 suggest a larger value for this equilibrium constant and support the Grunwald mechanism. Since a benzoate ion is much more basic than a methanol molecule, k_{-3} in mechanism 12 should be much larger than k_4, and therefore the rate equation expected for the reaction is eq 13. The equilibrium constant k_3/k_{-3} may be calculated, as shown in eq 14, by combining the ionization constant of the carboxylic acid with the equilibrium constant for the hydrogen bonding of methyloxonium ions to the carboxylate anions.



(12)

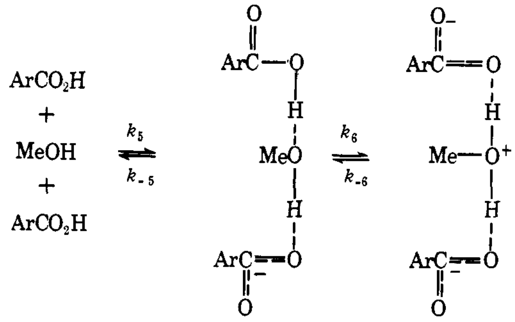
$$k_{\mathrm{exch}} = (k_3/k_{-3})k_4 \qquad (13)$$

$$\log(k_3/k_{-3}) = -(1 - 19.5\tau)(\mathrm{p}K_{\mathrm{ArCO_2H}} + 1.4) \qquad (14)$$

Inasmuch as k_4 is the rate contant for a reaction whose equilibrium constant is unity, not only for benzoic acid but for any derivative of it, it seems likely, from the product stability principle, that its value will not be changed much by the presence of meta and para substituents on the benzene ring. Hence changes in the rate of exchange should be very largely reflections of changes in k_3/k_{-3}. From eq 14 it follows that the Brønsted α for exchange should be about $1 - 19.5\tau$.[26] To get agreement with the value 0.53 observed using the substitutents *m*-nitro, *p*-nitro, and 3,5-dinitro,[29] it is necessary to use a τ of 0.024. This value is in the permissible range for methanol solution, 0–0.051, but it should be more informative to see how well a value of τ chosen to fit one set of data agrees with further data.

A value of $2 \times 10^{-6}\ M^{-1}$ for k_3/k_{-3} for benzoic acid itself may be calculated from eq 14 using a τ of 0.024. To give the observed rate of exchange, this must be combined with a k_4 value of 7×10^{10} sec^{-1}. This value for a proton transfer within a hydrogen bond with no net energy change is small enough to leave room for the fact that eq 13 overestimates the rate by not allowing for other types of hydrogen bonding between the methanol and the acid or ion pair.[27]

The rate equation for proton exchange of benzoic acid in methanol also contains a term first order in benzoic acid and first order in benzoate ions.[27] The analogous term for proton exchange of methanol has a coefficient that is almost as large, showing that the mechanism of exchange involves at least largely one benzoic acid, one methanol, and one benzoate ion. A stepwise mechanism could involve formation of a methyloxonium ion hydrogen-bonded to two benzoate anions, as shown in eq 15. Such a methyloxonium ion would lose its old proton to give exchange half the times it was formed. The overall rate constant for exchange is then given in eq 16. It might be thought at first glance that the proton donation from carboxylic acid to methanol that occurs in eq 15 should not differ much from proton donation to some other methanol molecule in the solution. However, this particular methanol molecule is hydrogen bonded to a carboxylate ion. This will make it more basic than a methanol molecule surrounded only by other methanol molecules. If we consider the analogous reaction of



(15)

$$k_{\mathrm{exch}} = \frac{k_5k_6}{2(k_{-5} + k_6)} \qquad (16)$$

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[27] E. Grunwald, C. F. Jumper, and S. Meiboom, *J. Amer. Chem. Soc.*, **85**, 522 (1963).

[28] W. J. Albery, *Progr. React. Kinet.*, **4**, 353 (1967).

[29] E. Grunwald and S. Meiboom, *J. Amer. Chem. Soc.*, **85**, 2047 (1963).

a more strongly acidic carboxylic acid, the acid will be a better proton donor. However, the methanol molecule to which it must donate a proton in eq 15 will now be hydrogen bonded to a more weakly basic carboxylate ion, and so it, too, will be more weakly basic. Hence, when we increase the acidity of the carboxylic acid one factor will tend to increase the rate of proton donation and the other will tend to decrease it. These qualitative arguments may be put in rough quantitative form by use of the hydrogen-bonding equations.

Since both the carboxylic acid and carboxylate ion reactants are hydrogen bonded to methanol in their initial states, the equilibrium governed by k_5/k_{-5} may be regarded either as complexing of the acid with a molecule of methanol that is hydrogen bonded to a carboxylate ion or as complexing of the carboxylate ion with a molecule of methanol that is hydrogen bonded to a carboxylic acid molecule. Regarding it in the former way, in order to use eq 8 to calculate the equilibrium constant we must know the acidity constant of HX where X is a molecule of methanol that is hydrogen bonded to a carboxylate ion. From its definition in eq 17, K_{HX} may be seen to be simply the

$$K_{HX} = \frac{[MeOH_2^+][MeOH\text{--}^-O_2CAr]}{[MeOH_2^+\text{--}^-O_2CAr]} \quad (17)$$

reciprocal of the equilibrium constant for hydrogen bonding of methyloxonium ions to carboxylate ions. Hence K_{HX} may be calculated by use of eq 8 and the resultant value substituted into the appropriate form of eq 8 to obtain the value for log (k_5/k_{-5}) shown in eq 18. The equilibrium governed by k_6/k_{-6} is the

$$\log (k_5/k_{-5}) = 19.5\tau^2(18.1 - pK_{ArCO_2H})(1.4 + pK_{ArCO_2H}) - 1.4 \quad (18)$$

transfer of a proton within a hydrogen bond, in this case to give a carboxylate ion and the HX whose acidity constant is defined by eq 17. The treatment is similar to that by which eq 14 was obtained and yields eq 19.

$$\log (k_6/k_{-6}) = -(1 - 19.5\tau)^2(pK_{ArCO_2H} + 1.4) \quad (19)$$

For benzoic acid itself the values −0.35 and −3.03 may be calculated for log (k_5/k_{-5}) and log (k_6/k_{-6}), respectively. The observed value of log k_{exch} at 24.8° (8.08) may be obtained from these results with various sets of plausible values for the rate constants involved. It is the relatively small value of the Brønsted α (0.26), however, that has been taken as the strongest argument against the stepwise mechanism.[28,29] The logarithm of the overall equilibrium constant for reaction 15 is expressed by the sum of eq 18 and 19. The negative of the partial derivative of this sum with respect to pK_{ArCO_2H}, which is shown in eq 20, is the Brønsted α

$$-\frac{d(\log k_5k_6/k_{-5}k_{-6})}{d(pK_{ArCO_2H})} = -19.5\tau^2(16.7 - 2pK_{ArCO_2H}) + (1 - 19.5\tau)^2 \quad (20)$$

for the equilibrium.[26] Because of the first term, which arises from the k_5/k_{-5} equilibrium, it is a function of pK_{ArCO_2H}. However, over the range of pK_{ArCO_2H} values covered this term remains in the region 0.00 ± 0.02. The second term, arising from the k_6/k_{-6} equilibrium, is dominant and has the value 0.28. If the reverse of this uphill proton-transfer reaction is random, and if the rate-controlling step for exchange is the one governed by k_6, then the predicted α for the exchange reaction should be about 0.28. If k_{-6} decreases somewhat as the equilibrium constants increase, then α should be somewhat less than 0.28, as observed.

The preceding paragraph demonstrates that the Brønsted α for proton donation from a carboxylic acid to a solvent molecule that is hydrogen bonded to the corresponding carboxylate ion is smaller than the α for proton donation to a solvent molecule that is surrounded only by other solvent molecules. The same kind of arguments leads to the conclusion that the value of α will be intermediate in the protonation of a solvent molecule that is hydrogen bonded to a second solvent molecule that is hydrogen bonded to a carboxylate ion. The first step in mechanism 12 is a special case of this type, in which the carboxylate ion is the one produced by the proton donation process, but this fact was neglected in the treatment of the reaction. A complete quantitative application of eq 8 would be quite complicated (since, for example, the carboxylate ion that is hydrogen bonded to the second solvent molecule is not an ordinary solvent-coordinated carboxylate ion, but one that is hydrogen bonded to a methyloxonium ion), but it seems qualitatively clear that it would lead to a somewhat smaller calculated value of α. For this reason the value of τ we have calculated from data on this reaction should be somewhat too large.

As an alternative to mechanism 15 for proton transfer from an acid to its conjugate base *via* one solvent molecule a mechanism may be written, as shown in eq 21, in which the symmetrical intermediate contains a

$$HA + SH + A^- \rightleftharpoons AH\text{--}SH\text{--}A^- \rightleftharpoons AH\text{--}S^-\text{--}HA \quad (21)$$

deprotonated solvent molecule. By use of equations like 7 and 8 the equilibrium constant for the formation of this intermediate and for a species containing a protonated solvent molecule, such as the one formed in eq 15, may be expressed in terms of pK_{HA}, τ, pK_{SH}, and pK_{SH_2}. According to these equations the equilibrium constants for the formation of the two different intermediates should be identical for an acid whose pK is one-half the autoprotolysis pK of the solvent. For stronger acids, the intermediate with protonated solvent will be more stable and for weaker ones the intermediate with deprotonated solvent will be more stable. From the product stability principle, mechanisms like 15 would be expected to be the dominant mechanisms for the stronger acids, and mechanisms like 21 should be dominant for the weaker acids. In actuality, however, the linear Brønsted plot with a positive slope in the case of benzoic acid and its nitro derivatives in methanol shows that all these compounds probably react by mechanism 15, in spite of the fact that the pK of the unsubstituted acid is more than half as large as the autoprotolysis pK of methanol. A greater deviation from expectations probably occurs with *p*-bromophenol and *p*-nitrophenol in methanol at −80°.[30] From the α of about 0.19 that may be calculated for the kinetic term of the form k[ArOH][MeOH][ArO$^-$] in the exchange of these phenols from pK values at 25°, it appears that the *p*-nitro compound (pK 11.2), at least,

[30] E. Grunwald, C. F. Jumper, and M. S. Puar, *J. Phys. Chem.*, 71, 492 (1967).

is exchanging largely by a mechanism like 15. Perhaps part of the exchange is taking place by a mechanism like 21, especially for *p*-bromophenol; this could contribute to making α smaller than the calculated value (somewhat less than 0.37). These data suggest that for phenols and carboxylic acids there are systematic deviations from our hydrogen-bonding equations that make intermediates of the type formed in mechanism 15 more stable and/or those formed in mechanism 21 less stable than calculated.[26]

Hydrogen Bonding and Exchange in Aqueous Solution. In order to assess the applicability of eq 7 to data in aqueous solution more critically, we need a value for τ in water. However, in the absence of a plausible method for determining this value, we shall simply use the same value we have used in methanol.

The value 0.024 for τ in water yields a value of $10^{-3.6}$ for the equilibrium constant $k_0k_1/(k_{-0}k_{-1})$ in mechanism 3, which is in the range required to explain the acid-catalyzed exchange of phenol in terms of a stepwise mechanism.

The value of log (k_3/k_{-3}) calculated from the water analog of eq 14 for acetic acid in water is larger by 1.93 than that for benzoic acid in methanol. The value of log k for exchange of water with acetic acid at 25°,[31] presumably by a mechanism analogous to 12, is larger by 2.86 than that for exchange of methanol with benzoic acid at 24.8°.[27] Thus the hydrogen-bonding equations give at least a crude explanation for what is probably largely a solvent effect on the exchange rate.

How are the known facts on hydrogen bonding in aqueous solution fit by eq 6 and a τ of 0.024? The extent of hydrogen-bond complexing should increase with the acidity of the acid, the basicity of the base, and the concentrations of both. The strongest base that can exist in large concentrations in the presence of the acid HX is its conjugate base X^-. According to eq 7, the largest equilibrium constant for hydrogen bonding by such a pair should be found when pK_{HX} is 7.0 (at 25°). For such a pK, log K_{AB} would be 0.1; for a pK of 3 or 11 it would be -0.3. Association *via* equilibrium constants this small or smaller may be difficult to distinguish from other reasons for deviation from ideality. For example, one method of calculation gave log K values around -0.3 for the association of formate, acetate, propionate, and butyrate ions with their conjugate acids (which may be compared with values around 0.0 that may be calculated from eq 6), but an "improved" method gave values around -1,[32,33] and the values may even be much smaller.[34] The values of log K for the association of $H_2PO_4^-$ with itself and H_3PO_4[35,36] are larger than would be calculated, but there is an excellent chance for the formation of two or three hydrogen bonds in these cases. The log K value of 0.6 reported for the complexing of iodic acid with iodate ions[37] is larger than the calculated value (-0.8), but X-ray structural studies on $KIO_3 \cdot HIO_3$ suggest that there is a rather strong interaction between the iodine atom of the acid and one or more oxygen atoms of the anion.[38]

All in all it seems that the existing data on hydrogen bonding in aqueous solution are too sparse and unreliable and their interpretation too uncertain to provide much useful information concerning the validity of eq 7. The field invites systematic study. Equilibrium constants for hydrogen bonding in alcoholic solvents seem to have received even less study. Such complications as greater ease of ion pairing, less detailed knowledge of solvent properties, etc., would make the determination of such constants difficult.

The apparent success of the preceding treatment of relatively simple proton-exchange reactions suggests its future application to other general acid- and base-catalyzed reactions, such as the hydration of carbonyl compounds[39] and enzyme-catalyzed reactions.

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