

ions inside the polyion or the effective charge is introduced. Therefore, the site-binding model, as proposed by Harris and Rice, may be the proper model for explaining the behavior of linear poly-electrolyte solutions.

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[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY, CORNELL UNIVERSITY, ITHACA, NEW YORK, AND HARPUR COLLEGE, ENDICOTT, NEW YORK]

Acid-Base Equilibria in Solvent Mixtures of Deuterium Oxide and Water^{1a}

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The dependence of the relative ionization constant of a weak acid on the atom fraction n of deuterium in a mixed deuterium oxide-water solvent is treated from a general point of view, with particular consideration of medium effects caused by the change in solvent. Various limiting formulations for comparison with experiment can be derived from the general equations, depending on the particular simplifying assumptions that are made. The Gross-Butler formulation, characterized by a cubic term in the denominator, results from assuming monohydrated protons and deuterons and additionally ignoring all medium effects, *i.e.*, neglecting free energies of transfer of the relevant species from one medium to another. A "linear" formulation (with a first order term in the denominator) results if one postulates non-specific solvation for the protons and deuterons and again neglects free energy of transfer. Finally a "medium effect" formulation can be derived by assuming that the entire effect is due to free energy of transfer, *i.e.*, that exchange fractionation is negligible. Comparison of these limiting formulations with experimental data for both ionization constants and rate coefficients of acid catalyzed reactions reveals that quite respectable fits may be obtained with each of them. However, for reactions that have K_H/K_D or k_D/k_H values close to unity the Gross-Butler formulation fits considerably less well than the other two. Since the most likely actual situation is some superposition of contributions from medium effects and exchange fractionation, it seems highly doubtful that acid-base studies in mixed solvents will permit unambiguous conclusions about the state of solvation of the protons. Furthermore, in view of the likelihood that medium effects are of consequence, it is doubtful whether rate studies in the mixed solvents will permit choices to be made among kinetic mechanisms, a conclusion which was recently also reached by Gold from a different line of reasoning.

The theory of the solvent isotope effect for water-deuterium oxide mixtures which was developed some time ago by Gross, Butler and their co-workers²⁻⁷ permits a prediction of the variation with solvent deuterium content both of ionization constants of weak acids and of rate coefficients of acid-catalyzed reactions which involve a pre-equilibrium proton transfer. Recently Purlee⁸ has re-examined and up-dated this theory, especially in its parametric aspects. He introduced the now firmly established value of $K = 4.0$ for the equilibrium



and also arrived at a new value of $L = 11$ for a second needed equilibrium constant, that for the exchange reaction



Purlee then utilized several sets of experimental data, both kinetic and equilibrium, to arrive at relevant values for a function $Q'(n)$ (see equation 3). To do this last he established best values for a pair of parameters, k_2^{+H} and k_3^{+H} , which enter in this function. However, Purlee also showed that the rule of the geometric mean⁹ would have sufficed to establish these latter and that in this sense $Q'(n)$ is really

only a function of the constant L and the atom fraction n of deuterium in the solvent. Purlee then gave a detailed comparison of the fit of the up-dated theory with the available data. Among other points he noted that the theory fails to agree with the experimental work for some well known acid catalyzed reactions, among them the mutarotation of glucose and the hydrolysis of methyl acetate.

Still more recently Gold¹⁰ has given further consideration to the Gross-Butler theory. He notes that the function $Q'(n)$ which appears to be rather complex in the Nelson and Butler formulation reduces, with the assumption of the rule of the geometric mean, to

$$Q'(n) = (1 - n + nl)^3 \quad (3)$$

where for this case $l = L^{-1/2}$. The resulting expressions for relative rates and ionization constants are

$$\frac{k_n}{k_H} = \frac{1 - n + nl^2(k_D/k_H)}{(1 - n + nl)^3} = \frac{1 - n + nL^{-1/2}(k_D/k_H)}{Q'(n)} \quad (4)$$

and

$$\frac{K_H}{K_n} = \frac{1 - n + nl(K_H/K_D)}{(1 - n + nl)^3} \quad (5)$$

where k refers to rate coefficients, K to ionization constants and the subscripts H, D and n to the solvents water, deuterium oxide and a mixed aqueous solvent with the atom fraction n of deuterium.

One point made by Gold was that the calculated values of k_n/k_H or K_H/K_n are rather insensitive to the value of L and he tabulates data to illustrate

(1) (a) Work supported in part by a grant from the Atomic Energy Commission. (b) On leave from Israel Institute of Technology, Haifa, Israel (1959-1960).

(2) P. Gross, H. Steiner and F. Krauss, *Trans. Faraday Soc.*, **32**, 877 (1936).

(3) P. Gross and H. Wischler, *ibid.*, **32**, 879 (1936).

(4) P. Gross, H. Steiner and H. Suess, *ibid.*, **32**, 883 (1936).

(5) J. C. Hornel and J. A. V. Butler, *J. Chem. Soc.*, 1361 (1936).

(6) W. J. C. Orr and J. A. V. Butler, *ibid.*, 330 (1937).

(7) W. E. Nelson and J. A. V. Butler, *ibid.*, 958 (1938).

(8) E. L. Purlee, *THIS JOURNAL*, **81**, 263 (1959).

(9) J. Bigeleisen, *J. Chem. Phys.*, **23**, 2264 (1955).

(10) V. Gold, *Trans. Faraday Soc.*, **56**, 255 (1960).

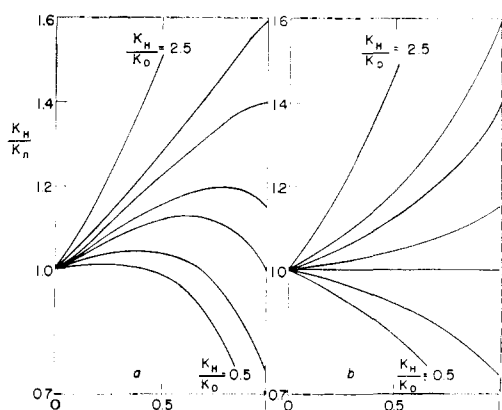
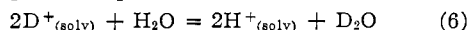


Fig. 1.—Comparison of predictions for Gross-Butler and "linear" formulations [equations 5 and 7] using best value parameters for each.

this. A second, rather different point made by him concerns the origin of and evidence for the cubic formulation for $Q'(n)$. Gold notes, following Gross,³ that the cubic dependence is a direct consequence of the use of the formula H_3O^+ for the proton in solution and in particular of the assumption that the three protons are equivalent. If, alternatively, one makes no specification of the solvation of the proton and writes for equation 2 the less specific equation



the resulting expression for $Q'(n)$ is

$$Q'(n) = 1 - n + nl^3 \quad (7)$$

Gold concludes that the comparisons of Purlee suffice to show that the linear formulation [equation 7] for $Q'n$ does not represent the data and that the cubic form is essential. This, in Gold's view, is evidence that the proton is indeed monohydrated in solution and that no further solvation is of any structural significance.

For three different reasons these last conclusions seem suspect to us. One is that the Gross-Butler development is given in thermodynamic terms and generally, in a thermodynamic discussion of dilute solutions, it is unnecessary to give consideration to the details of the ion solvation, *i.e.*, for such purposes the formula H^+ , for unspecified solvation, is fully as useful as H_3O^+ . A rather different reason is that the cubic formulation for $Q'(n)$ leads to predictions which seem intuitively to us to be rather unlikely. Hence, it seems of importance to be sure that the experimental data do, indeed, necessitate use of a cubic $Q'(n)$. This last is illustrated by a comparison of Figs. 1a and 1b, which summarize the predictions from a cubic and a linear $Q'(n)$. Qualitatively it is clear that the predictions are similar for large values of the K_H/K_D ratio but very different for values near unity, so different that one would expect rather ordinary experiments to distinguish between them. We shall show later that there is no evidence to support the belief that the cubic $Q'(n)$ is superior; and that in fact if one were forced to choose between equations with a cubic and a linear denominator, one would probably choose the latter. However, a third quite dif-

ferent point leads us to believe that the problem is actually more complex than implied by a simple choice between these two theories. The usual development of the Gross-Butler theory refers the activity coefficients of all the solutes to "infinitely dilute solution" as standard state without regard for the fact that, as the solvent composition changes from pure H_2O to pure D_2O , this standard state is continually shifting. We believe that this disregard is not legitimate and that the standard state problem must be given explicit attention.

Kingerley and LaMer¹¹ pointed up this last problem by noting that most deuterium exchange studies can actually be shown to involve two different types of process, an exchange reaction for a constant solvent and a transfer reaction which carries the exchanging species from one solvent to another. They therefore proposed a separation of the total free energy into a free energy of exchange and a free energy of transfer and went on to show that experimental values can be obtained for the separate terms and that the free energy of transfer is usually a substantial term. This term is, of course, the one which is being neglected if no consideration is given to the changes in standard state. Kingerley and LaMer went still farther and concluded both from their own studies and from those of Brodsky¹² that the free energy for exchange is generally close to zero (exchange factor of close to unity) so that the free energy of transfer term is often the dominant one.

Swain and co-workers¹³ have very recently also discussed the problem of the solvent isotope effect. Their approach involves detailed consideration of the structure of water and the relation of this to solvation, to activity coefficients of ions in solution, etc. Since we believe that the particular problem of acid-base equilibrium can be usefully discussed from a more general standpoint, we shall not at this time give consideration to this structure-oriented approach.

In the next section we shall give general equations for the deuterium solvent isotope effect for aqueous solutions and explore the various limiting expressions, emphasizing the assumptions which lead to them. Finally we shall compare the various expressions with experimental data.¹⁴

Formulation of Equations.—The acid dissociation constant for a weak acid, HA, in water can be expressed in either of the forms

$$K_H = \frac{a_{H^+}a_{A^-}}{a_{HA}} \quad (8)$$

or

$$K_H = \frac{a_{H_3O^+}a_{A^-}}{a_{HA}a_{H_2O}} \quad (9)$$

These expressions are equivalent by virtue of the conventional relationship defining a_{H^+} and $a_{H_3O^+}$

(11) R. W. Kingerley and V. K. LaMer, *THIS JOURNAL*, **63**, 3256 (1941).

(12) A. E. Brodsky, *Trans. Faraday Soc.*, **33**, 1180 (1937).

(13) C. G. Swain, R. F. W. Bader and E. R. Thornton, *Tetrahedron*, **10**, 182 and 200 (1960). See also C. G. Swain, A. D. Ketley and R. F. W. Bader, *THIS JOURNAL*, **81**, 2353 (1959).

(14) To save space we shall restrict our development to ionization of weak acids. The extension to rate coefficients of acid and base catalyzed reactions is obvious from the developments of earlier workers.

in terms of each other, $a_{\text{H}_3\text{O}^+} = a_{\text{H}^+} a_{\text{H}_2\text{O}}$. The standard state for each solute is a hypothetical ideal dilute solution containing one mole of solute per liter of solvent. The standard state for the solvent is pure H_2O , and following normal practice we shall give solvent concentrations in mole fraction units. Therefore for sufficiently dilute solutions in H_2O

$$K_{\text{H}} = \frac{C_{\text{H}^+}C_{\text{A}^-}}{C_{\text{HA}}} \text{ or } K_{\text{H}} = \frac{C_{\text{H}_3\text{O}^+}C_{\text{A}^-}}{C_{\text{HA}}} \quad (10)$$

where the mole fraction term $x_{\text{H}_2\text{O}}$, in the second denominator is omitted because its value is unity. These two equations differ merely in the symbol used to denote the solvated proton.

Exactly similar considerations apply to the dissociation of DA in the solvent D_2O

$$K_{\text{D}} = \frac{a_{\text{D}^+}a_{\text{A}^-}}{a_{\text{DA}}} \quad (11)$$

or

$$K_{\text{D}} = \frac{a_{\text{D}_3\text{O}^+}a_{\text{A}^-}}{a_{\text{DA}}a_{\text{D}_2\text{O}}} \quad (12)$$

where by convention, $a_{\text{D}_3\text{O}^+} = a_{\text{D}^+}a_{\text{D}_2\text{O}}$. The standard state for each solute is now a hypothetical ideal dilute solution containing one mole of solute per liter of D_2O . For sufficiently dilute solutions in D_2O

$$K_{\text{D}} = \frac{C_{\text{D}^+}C_{\text{A}^-}}{C_{\text{DA}}} \text{ or } K_{\text{D}} = \frac{C_{\text{D}_3\text{O}^+}C_{\text{A}^-}}{C_{\text{DA}}} \quad (13)$$

where again the two equations differ merely in the symbol used to denote the solvated deuteron. Without further consideration of the difference in standard states, it cannot be assumed that K_{H} and K_{D} retain their pure solvent values for the case of ideal dilute solution in a *mixed* solvent of H_2O and D_2O .

For a mixed solvent (atom fraction n of deuterium) the operationally meaningful dissociation constant is that for the over-all dissociation of the combined isotopic acids, HA and DA. For sufficiently dilute solutions

$$K_{\text{n}} = \frac{(C_{\text{H}^+} + C_{\text{D}^+})C_{\text{A}^-}}{(C_{\text{HA}} + C_{\text{DA}})} \quad (14)$$

If solvation of protons and deuterons is taken into account explicitly by assuming that just one solvent molecule is involved this relationship takes the completely equivalent form

$$K_{\text{n}} = \frac{(C_{\text{H}_3\text{O}^+} + C_{\text{H}_2\text{DO}^+} + C_{\text{HD}_2\text{O}^+} + C_{\text{D}_3\text{O}^+})C_{\text{A}^-}}{(C_{\text{HA}} + C_{\text{DA}})(x_{\text{H}_2\text{O}} + x_{\text{HDO}} + x_{\text{D}_2\text{O}})} \quad (15)$$

We are here using the convention

$$a_{\text{H}^+} + a_{\text{D}^+} = \frac{\sum a''_{\text{H}_3\text{O}^+}}{\sum a''_{\text{H}_2\text{O}}} \quad (16)$$

where the sums are taken over all relevant isotopic species corresponding to the assumed degree of solvation.¹⁵ The standard state for each solute

(15) This convention is necessary in order that equations 14 and 15 be equivalent. It is *not* the same, however, as the convention employed by Gross or Butler or Purlee, all of whom adopted, even for the mixed solvents: $a_{\text{H}^+} = a_{\text{H}_3\text{O}^+}/a_{\text{H}_2\text{O}}$ and $a_{\text{D}^+} = a_{\text{D}_3\text{O}^+}/a_{\text{D}_2\text{O}}$ i.e., the same definitions as are employed for the pure media H_2O and D_2O , thus ignoring the difference in standard state. Moreover, when a_{H^+} and a_{D^+} are defined in this latter way, their sum does not in general reduce to the sum of the concentrations of the acid cations in dilute solution in the mixed solvent. Therefore, concentration equilibrium expressions derived in terms of them will contain activity coefficients of obscure significance (see e.g., footnote 13, page 210 of ref. 14a).

is a hypothetical ideal dilute solution containing one mole of solute per liter of mixed solvent. The standard state for each solvent species is the respective pure solvent (hypothetical in the case of HDO). Equations exactly equivalent to (15) could be written in terms of other assumed degrees of solvation (more than one solvent molecule per cation) provided that the appropriate convention corresponding with eq. 16 is introduced.

Let us now introduce auxiliary, hypothetical dissociation "constants" for the two isotopic acids defined for the mixed solvent medium. These may be defined for ideal dilute solutions in two non-equivalent ways, where the symbol $K_{\text{H}(n)}$ etc., is used to indicate that the constant is for the solvent containing atom fraction n of deuterium

$$K_{\text{H}(n)} = \frac{C_{\text{H}^+}C_{\text{A}^-}}{C_{\text{HA}}} \text{ and } K_{\text{D}(n)} = \frac{C_{\text{D}^+}C_{\text{A}^-}}{C_{\text{DA}}} \quad (17)$$

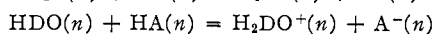
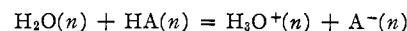
or

$$K'_{\text{H}(n)} = \frac{C_{\text{H}_3\text{O}^+}C_{\text{A}^-}}{C_{\text{HA}}x_{\text{H}_2\text{O}}} \text{ and } K'_{\text{D}(n)} = \frac{C_{\text{D}_3\text{O}^+}C_{\text{A}^-}}{C_{\text{DA}}x_{\text{D}_2\text{O}}} \quad (18)$$

If we now introduce the value of $K = 4$ for eq. 1 (which is equivalent to assuming the rule of the geometric mean for the solvent water), we can conveniently rewrite eq. 18 as

$$K'_{\text{H}(n)} = \frac{C_{\text{H}_3\text{O}^+}C_{\text{A}^-}}{C_{\text{HA}}(1-n)^2} \text{ and } K'_{\text{D}(n)} = \frac{C_{\text{D}_3\text{O}^+}C_{\text{A}^-}}{C_{\text{DA}}n^2} \quad (19)$$

Equation 17 represents equilibrium among the same species as in eq. 8 and 11, whereas eq. 18 and 19 represent equilibrium among the same species as in eq. 9 and 12. Thus $-RT \ln (K_{\text{H}(n)}/K_{\text{H}})$ or $-RT \ln (K'_{\text{H}(n)}/K_{\text{H}})$ measures the respective free energies of transfer from pure H_2O to the mixed solvent and $-RT \ln (K_{\text{D}(n)}/K_{\text{D}})$ or $-RT \ln (K'_{\text{D}(n)}/K_{\text{D}})$ measures the respective free energies of transfer (for the deuterated species) from pure D_2O to the mixed solvent. The difference between eq. 17 and 19 is that the latter equations imply specific solvation with single monomeric water molecules. They differentiate in principle among such processes as



and the like, treating the ions, H_3O^+ , H_2DO^+ , HD_2O^+ , D_3O^+ as thermodynamically well defined species. Equation 17 on the other hand, implies ignorance with regard to the structure of liquid water and the solvated cations. This view neglects local isotopic fluctuations in the composition of the solvation shell, assuming that on the average they will be smoothed out. In effect, it ascribes a mean base strength to the mixed solvent (for given n) and mean acid strengths to protons and deuterons, respectively, solvated by it. The values of the K' constants will not in general be the same as those for the analogous K constants, since the former involve a specific hydration of the cation and degree of polymerization of the water (which is assumed to be monomeric in equations 18 and 19).¹⁶

(16) If one were to assume a more general model, in which the degree of polymerization of the water is q and the proton is p -fold hydrated (say $p = 4$, as suggested, see e.g., E. Wicke, M. Eigen and Th. Ackermann, *Z. Phys. Chem.*, 1, 340 (1954), equation 15 would be re-

For further discussion it is convenient to define some additional symbols. Let α be the isotopic abundance of deuterium in the HA species and let β be the isotopic abundance of deuterium in the cationic species, *i.e.* in H^+ or H_3O^+ etc. In contrast to α and to the earlier defined n , the value of β will depend on the model chosen for the acid cation, *i.e.*, on the number of equivalent exchangeable hydrogens. Let φ be the isotopic fractionation factor between weak acid and water, defined $\varphi = \alpha(1-n)n(1-\alpha)$. For a monobasic acid HA this is $C_{DA}(1-n)/nC_{HA}$. Let ϵ be the fractionation factor between water and the acid cation. Assuming non-specific hydration, this gives $\epsilon = \beta(1-n)/n(1-\beta) = C_{D^+}(1-n)/C_{H^+}n$. For the specific case of three equivalent protons and assuming the rule of the geometric mean for these acid species

$$\epsilon' = \frac{\beta(1-n)}{n(1-\beta)} = \left(\frac{C_{D_3O^+}}{C_{H_3O^+}}\right)^{1/3} \frac{1-n}{n}$$

Using these definitions, we can develop expressions relating ionization constants in the pure solvents and in the mixtures. For the case of unspecified solvation

$$\frac{K_{H(n)}}{K_n} = \frac{1-\beta}{1-\alpha} = \frac{1-n+n\varphi}{1-n+n\epsilon} \quad (20)$$

But since

$$\frac{K_{H(n)}}{K_{D(n)}} = \frac{(1-\beta)\alpha}{\beta(1-\alpha)} = \epsilon^{-1}\varphi \quad (21)$$

we obtain

$$\frac{K_{H(n)}}{K_n} = \frac{1-n+n\epsilon(K_{H(n)}/K_{D(n)})}{1-n+n\epsilon} \quad (22)$$

Similar manipulation of the equations for the case of specifically monohydrated protons and deuterons yields

$$\frac{K'_{H(n)}}{K_n} = \frac{1-n+n\epsilon'^3(K'_{H(n)}/K'_{D(n)})}{(1-n+n\epsilon')^3} \quad (23)$$

The relation of K_H , the observed ionization constant in H_2O , to K_n assumes the forms, for unspecified solvation and monohydration, respectively

$$\frac{K_H}{K_n} = \frac{K_H}{K_{H(n)}} \frac{1-n+n\epsilon(K_{H(n)}/K_{D(n)})}{1-n+n\epsilon} \quad (24)$$

$$\frac{K_H}{K_n} = \frac{K_H}{K'_{H(n)}} \frac{1-n+n\epsilon'^3(K'_{H(n)}/K'_{D(n)})}{(1-n+n\epsilon')^3} \quad (25)$$

These equations are formally similar to those of earlier workers [see for example Gold's¹⁰ equations 7 and 8], but it should be emphasized that at this stage, the quantities $K_{H(n)}$, $K_{D(n)}$, ϵ , etc. are not necessarily independent of n . More significantly, these quantities are not presently accessible to measurement so that to obtain equations which involve measurable quantities we are forced to make assumptions. We wish now to show that different sets of plausible simplifying assumptions

placed by

$$K_n = \frac{\left(\sum_i C_{H(H_2O)_i} p^+\right) C_A^-}{(C_{HA} + C_{DA}) \left(\sum_j x_{(H_2O)_j} q\right)^{p/q}} \quad (15')$$

where the summations in each case are over all of the isotopic species. This remains equivalent to (14) if we adopt the convention

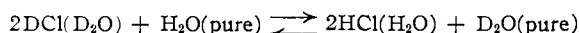
$$a_{H^+} + a_{D^+} = \frac{\sum_i a_{H(H_2O)_i} p^+}{\left(\sum_j a_{(H_2O)_j} q\right)^{p/q}} \quad (16')$$

yield quite different limiting forms for the dissociation constant ratio.

1. The Gross-Butler Formulation.—Equation 25 leads directly to this formulation if one assumes that the ionization constants expressed in the form of $K'_{H(n)}$ and $K'_{D(n)}$ are independent of medium and so can be replaced by the experimental values K_H and K_D , respectively. This assumption gives

$$\frac{K_H}{K_n} = \frac{1-n+n\epsilon'^3(K_H/K_D)}{(1-n+n\epsilon')^3} \quad (26)$$

The problem of ϵ' remains. A reasonable extension of the above ideality assumption suggests that the proper value for ϵ'^{-3} would be 18.02, the Kingerley and LaMer¹¹ value for the equilibrium constant L' of the exchange reaction



This of course implies that free energies of transfer can be neglected entirely. Actually, Purlee concluded that the value 11 fits the data better than does 18, a result which suggests that a complete neglect of free energies for transfer is probably not justified. It is also probable that the free energy of transfer will depend on the anion involved. This if true would cause ϵ' to vary slightly from one acid molecule to another.

2. The Linear Formulation for Unspecified Solvation.—This follows from eq. 24 if we assume that the constants $K_{H(n)}$ and $K_{D(n)}$ of eq. 17 can be replaced by the experimental values for the pure solvents, K_H and K_D . Then

$$\frac{K_H}{K_n} = \frac{1-n+n\epsilon(K_H/K_D)}{1-n+n\epsilon} \quad (27)$$

Even though the denominator here is similar to the $Q'(n)$ function of equation 7, it does not follow that ϵ must be equal to $L'^{-1/2}$ where L' is again the Kingerley and LaMer equilibrium constant. Here too, as above, worries about neglect of free energy of transfer remain. A more serious difficulty is that this equivalence only follows if one treats the acidic cation as if it were *non-solvated*. Since the unspecified solvation equations must hold for any degree of solvation,¹⁶ there can be no unique link between ϵ and L' . For both reasons, it is necessary to treat ϵ as a parameter. It will be shown later that for this formulation a value of $\epsilon = 0.45$ gives a good fit to the data.

3. Medium Effect Formulation.—A particularly extreme position to adopt is to assume that the variations in K are due solely to medium effects, *i.e.*, to changes in the standard state for the ionization process. This is equivalent to postulating that $K_{H(n)} = K_{D(n)}$ for all values of n . We also need some assumption for the variation of $K_{H(n)}$ with the medium. An obvious assumption is that

$$\Delta F^0(n) = (1-n)\Delta F^0(H_2O) + n\Delta F^0(D_2O) \quad (28)$$

which leads to the relation

$$\frac{K_H}{K_{H(n)}} = \left(\frac{K_H}{K_D}\right)^n \quad (29)$$

Substituting into equation 24 gives¹⁷

(17) The same result can be obtained from equation 25, but it is here necessary to make the additional assumption that $\epsilon' = 1$. This is altogether reasonable for this model implying as it does that the free energy of exchange between the acid cation species and the solvent is zero.

$$\frac{K_H}{K_n} = \left(\frac{K_H}{K_D}\right)^n \quad (30)$$

The complete neglect of exchange fractionation that leads to equation 30 is almost certainly too extreme, but the same can be said about the neglect of free energy of transfer implicit in the earlier two formulations.

4. Superposition of Exchange and Transfer.—

There are evidently a large number of ways to combine contributions from terms of these two sorts. As one typical combination let us assume, not that $K_{H(n)} = K_{D(n)}$, but rather that $K_{H(n)}$ varies only from its value K_H in water to some other value $K_{H(D)}$, in D_2O , the free energy change as a function of medium composition following an equation analogous to (28). A similar equation would hold for $K_{D(n)}$. This gives as the analog to (29)

$$\frac{K_H}{K_{H(n)}} = \left(\frac{K_H}{K_{H(D)}}\right)^n \quad (29')$$

Applying this to the case of unspecified solvation, and hence using equation 21 for $K_{H(n)}/K_{D(n)}$, (assumed to hold at $n = 1$), we arrive at

$$\frac{K_H}{K_{H(n)}} = \left(\frac{K_H}{K_D}\right)^n (\epsilon \varphi^{-1})^n$$

which, combined with equation 20 yields

$$\left. \begin{aligned} \frac{K_H}{K_n} &= \left(\frac{K_H}{K_D}\right)^n \frac{1 - n + n\varphi \left(\frac{\epsilon}{\varphi}\right)^n}{1 - n + n\epsilon \left(\frac{\epsilon}{\varphi}\right)^n} \\ &= \left(\frac{K_H}{K_D}\right)^n \frac{(1 - n)\varphi^{-n} + n\varphi^{(1-n)}}{(1 - n)\epsilon^{-n} + n\epsilon^{(1-n)}} \end{aligned} \right\} \quad (31)$$

If there is no isotopic fractionation, $\epsilon = \varphi = 1$, so that (31) reduces to (30). At the other limit, where there is no free energy of transfer, it reduces to (27). Actually, the general equation 31 (and also the similar generalization which can be derived for specific mono-solvation) is difficult to work with because of our lack of knowledge about the fractionation factors. If it can be assumed that the contribution from exchange is small, one might reasonably replace (31) by the approximation

$$\frac{K_H}{K_n} = \left(\frac{K_H}{K_D}\right)^{n\gamma} \quad (32)$$

where the empirical parameter γ is presumably not very different from unity.

It is quite probable that the actual behavior does result from some superposition of this general sort. However, since it is somewhat doubtful *a priori* whether the experimental data will permit the detailed analysis implied by this treatment, the useful question to ask is how well each of the limiting forms fits the experimental data and whether they differ sufficiently among themselves to make any postulated superposition amenable to experimental verification.

Comparison with Experiment.—The available experimental data have been reviewed by Purlee.⁸ The reactions may conveniently be ordered in several groups, according to the magnitude of K_H/K_D (or k_D/k_H for kinetic data). The cases in which equilibrium constants have been measured are limited, but considerably more data are available from kinetic studies of acid catalyzed reactions. On the assumption that these reactions involve a preliminary acid-base equilibrium, k_D/k_H is equivalent to K_H/K_D .

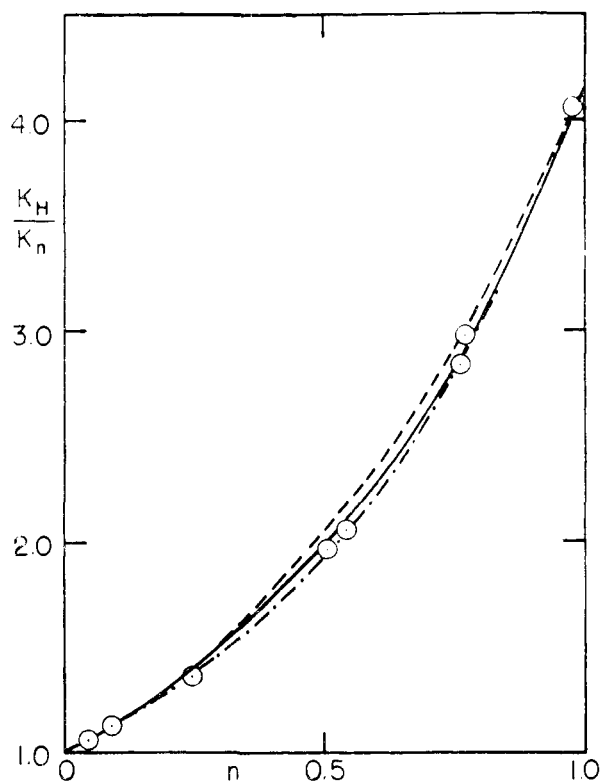


Fig. 2.—Comparison of limiting formulations with data for ionization of hydroquinone: “linear,” —: Gross-Butler, — · —; “medium effect” ($\gamma = 1$), - - - - -.

As noted briefly above, Purlee used a value of 11.0 for ϵ'^{-6} in his equivalent of equation 26, and we have retained this value in the Gross-Butler computations. In the linear formulation, equation 27, we use as a “best” value $\epsilon = 0.45$. The simple medium effect formulation, equation 30, has no adjustable parameter.

Figure 2 shows K_H/K_n vs. n for the ionization constant of hydroquinone, as measured by Rule and LaMer.¹⁸ This plot is typical of other acid ionization constants for which K_H/K_D is in the range 3–4 such as the ionization of acetic,¹⁹ benzoic¹⁸ and formic acids. In all these cases there is little to choose between the Gross-Butler and the linear formulations. The simple medium effect plot fits almost as well.

Figure 3 shows a similar plot derived from kinetic data for the acid catalyzed bromination of acetone.²⁰ Here the linear plot fits well and the Gross-Butler slightly less well. The simple medium effect plot is less satisfactory, but an excellent fit can be obtained (not shown in figure) if one uses $\gamma = 1.4$ in equation 32. Similar behavior is shown by other kinetic data with k_D/k_H in the range 2–3, e.g., hydrolysis of ethyl orthoformate,²¹ hydrolysis of several epoxides²² and hydrolysis of acetal.⁶

Figure 4 shows a comparison of the Gross-Butler and linear formulations for the acid-catalyzed hydrolysis of methyl acetate.⁷ Here, with

(18) C. K. Rule and V. K. LaMer, *THIS JOURNAL*, **60**, 1975 (1938).

(19) V. K. LaMer and J. P. Chittum, *ibid.*, **58**, 1642 (1936).

(20) O. Reitz, *Z. physik. Chem.*, **179A**, 119 (1937).

(21) E. Brescia and V. K. LaMer, *THIS JOURNAL*, **60**, 1963 (1938).

(22) J. G. Pritchard and F. A. Long, *ibid.*, **78**, 6008 (1956).

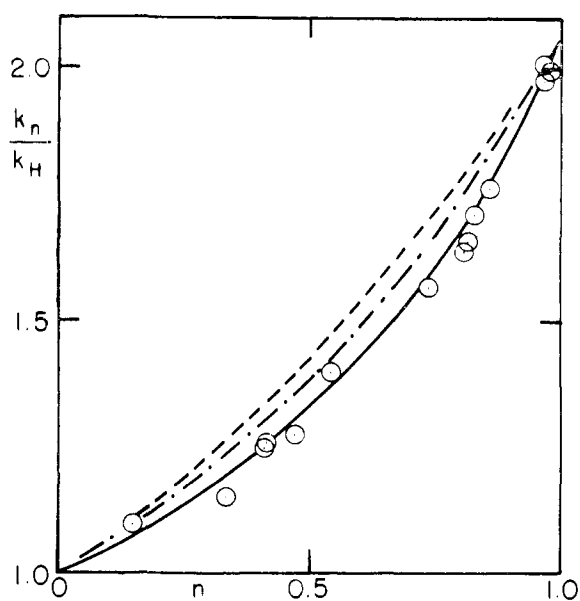


Fig. 3.—Comparisons with data for bromination of acetone; curves identified as in Fig. 2.

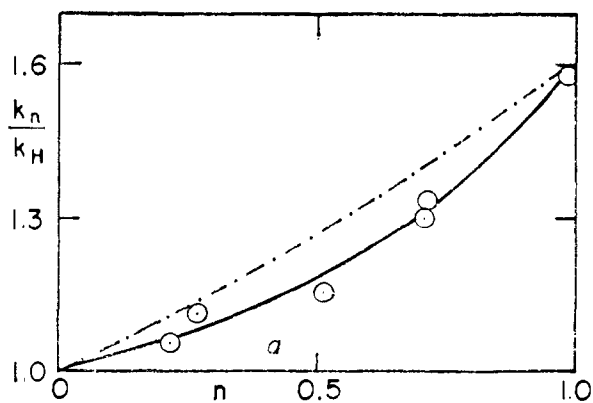


Fig. 4.—Hydrolysis of methyl acetate: Gross-Butler, — · — · —; linear —.

a k_D/k_H value as small as 1.6, the two formulations diverge sufficiently to allow a choice to be made between them. Clearly the linear formulation allows the better fit. This is also true for the hydrolysis of ethyl formate.⁷ The medium effect formulation of equation 30 gives a relatively poor fit to these data, the actual curve for methyl acetate being virtually identical to that for the Gross-Butler formulation. An excellent fit is, however, obtained by using equation 32 with $\gamma = 1.4$.

In Fig. 5 data are plotted for the acid catalyzed hydrolysis of methyl-1-cyclopentene and 2-methyl-2-butene,²³ for both of which k_D/k_H is not far from unity (0.8–1.2). In these cases the curvatures of the plots for the Gross-Butler and linear formulations are quite different and yield different extrapolated values. Although the two curves for each of the two alkenes are qualitatively dissimilar, the entire spread of the data is in both cases such as to preclude a clear decision as to which gives the better fit. The simple medium effect formulation is equally good, its plot (not shown in

(23) E. L. Purlee and R. W. Taft, Jr., *THIS JOURNAL*, **78**, 5807 (1956).

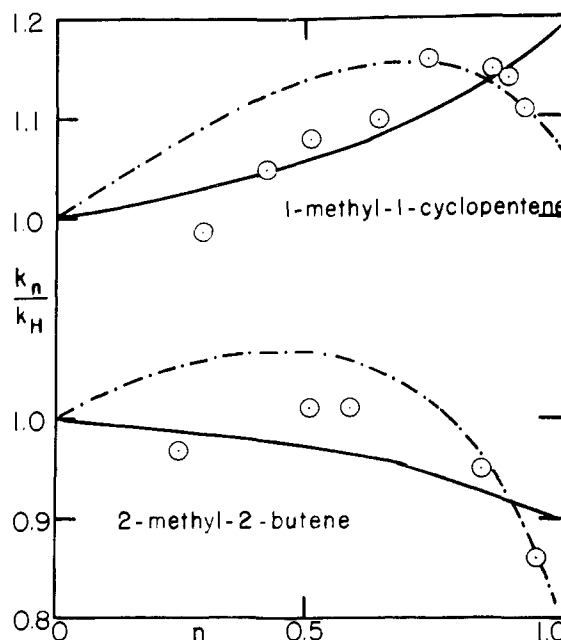


Fig. 5.—Hydration of olefins; curves identified as in Fig. 4.

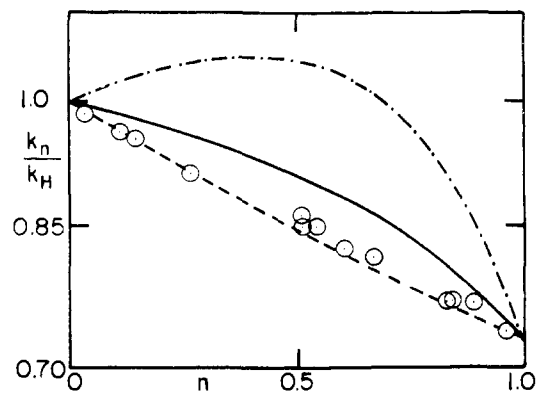


Fig. 6.—Mutarotation of glucose; curves as in Fig. 2.

this fig.) almost coinciding with the "linear" plot.

The apparent maxima in the plots for these two examples of olefin hydration, if real, might be taken as evidence for the validity of the Gross-Butler formulation since both the unspecified solvation and medium effect formulations give straight lines of zero slope when $K_H/K_D = 1$. That such a conclusion would not be justified follows directly from equation 31, which represents a superposition of these two formulations. This equation leads to the conclusion that even with $K_H/K_D = 1$, the curve for K_H/K_n may pass through either a maximum or a minimum, depending only on which of the two fractionation factors, ϵ or φ , deviates more from unity.

The mutarotation of glucose,²⁴ the data for which are plotted in Fig. 6, is exceptional among acid catalyzed reactions in that its k_D/k_H value is considerably less than unity. The Gross-Butler plot fits very poorly. That of the linear formulation does much better, and the simple medium

(24) W. H. Hamill and V. K. LaMer, *J. Chem. Phys.*, **4**, 395 (1936).

effect formulation fits best of all.²⁵ Purlee has taken the large deviation from the Gross-Butler plot as evidence that there is no acid-base pre-equilibrium in this reaction. Since a pre-equilibrium is in fact indicated by several lines of evidence,^{26,27} we believe that this lack of agreement is another illustration of the inadequacy of the Gross-Butler formulation.

It is perhaps worth noting that when K_H/K_D (or k_D/k_H) is much smaller than unity there may be a possibility of distinguishing experimentally between the formulations for unspecified solvation and for the medium effect. In this region the former exhibits the typical downward concavity of Fig. 1b. Plots for the latter would be slightly concave upwards. It is doubtful, however, whether suitable test reactions could be easily found.

The two formulations based on neglect of free energy of transfer yield equations of identical form for base catalysis. This arises in the Gross-Butler treatment since OH^- unlike H_3O^+ has only a single exchangeable proton. The "unspecified solvation" treatment is less restrictive in that it allows the same equation to be derived without assumptions about the degree of solvation and solvent polymerization. The medium effect formulation is independent of whether the catalysis is acid or base and in general seems to give for base catalysis the same sort of agreement as noted in the preceding discussions of acid catalysis.

(25) Purlee⁸ has noted that k_H for this reaction seems to be a weighted mean of k_H and k_D (arithmetic, rather than geometric as required by our equation 28) but his interpretation is quite different from ours.

(26) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1940, p. 337.

(27) B. C. Challis, F. A. Long and Y. Pocker, *J. Chem. Soc.*, 4679 (1957).

Conclusions.—The comparison of experiment with the various limiting formulations makes it evident that there is no case to be made for the superiority of the Gross-Butler equation. In fact if one chooses to neglect medium effects, the unspecified solvation treatment actually leads to distinctly better agreement with the data. It of course follows that these mixed solvent studies do not in themselves give any information about the state of solvation of the proton in solution, a conclusion which is only reinforced by the fact that complete neglect of medium effects is probably not justified.

Since the medium effect formulation can by itself give almost as good agreement with the data as does either of the other two limiting equations, one can be sure that a properly chosen superposition of a medium effect on the linear formulation (and presumably also on the Gross-Butler formulation) will give entirely satisfactory fits in all cases. However, because of the small differences among the various limiting forms themselves, this is not a very enlightening conclusion.

In view of the uncertainty about the relative importance of medium and exchange effects for these systems, it is very doubtful whether studies of acid or base catalysis in mixed $\text{H}_2\text{O}-\text{D}_2\text{O}$ media can yield useful information on the mechanisms of reactions. Actually, Gold¹⁰ reached the same conclusion on very different grounds, by showing that, even neglecting medium effects and assuming specific monohydration of the proton, a plausible case could be made for expecting pre-equilibrium and slow proton transfer mechanisms to show very similar behavior in the mixed solvents.