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A THEORETICAL INTERPRETATION OF ISOTOPE EFFECTS IN MIXTURES OF LIGHT AND HEAVY WATER[1-3]—II

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Abstract—Solvent isotope effects for H_2O—D_2O mixtures and for ionic hydration equilibria in such mixtures can be calculated from the structure difference between D_2O and H_2O and that between HDO and H_2O and the relative amounts of the three waters. The behavior of acids in H_2O—D_2O mixtures is considered in detail. Dissociation constants of acetic acid are calculated over the complete range of deuterium concentrations and found to agree with the experimentally determined ones. The Gross equation for the dependence of isotope effect on mole fraction of deuterium for acid-catalyzed reactions of substrates S proceeding via SL^+ transition states (L = H or D) is derived from first principles.

THE previous paper[2] was concerned with differences between pure light and pure heavy water or between ionic solutions in these solvents. The present paper will be concerned with differences between light water and mixtures of light and heavy water.

The first step in the discussion of isotope effects observed in mixtures of light and heavy water is the calculation of differences in thermodynamic properties between these mixtures and pure light water. For one mole of a mixture of H_2O, D_2O and HDO, the value of any extensive thermodynamic function G is given by

$$G = \Sigma N_j \bar{G}_j$$

where $\bar{G}_j$ are partial molal quantities and N_j are solvent mole fractions

$$\Sigma N_j = 1 \tag{1}$$

Since mixtures of the three isotopic forms of water, H_2O, D_2O and HDO, are ideal solutions,

$$\bar{G}_j = G_j + G_j{}^m$$

where G_j is the value of the property G for one mole of the pure component j and $G_j{}^m$ is the change in G_j from mixing in one mole of this component to form the ideal solution (e.g. $F_j{}^m = RT \ln N_j$). Now

$$G - G_1 = \Sigma_j N_j \bar{G}_j - G_1 = \Sigma_j N_j (G_j - G_1) + \Sigma_j N_j G_j{}^m$$

where the subscript 1 refers to H_2O, 2 to D_2O and 3 to HDO. The part of $G - G_1$ due to the properties of the component waters is defined as the isotopic excess function ΔG

$$\Delta G = \Sigma_j N_j (G_j - G_1) \tag{2}$$

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[1] Supported in part by the Atomic Energy Commission under Contract No AT(30-1)-905 and by the National Institutes of Health under Research Grant RG-3711 (C4 and C6).

[2] *Cf.* Part I: C. G. Swain and R. F. W. Bader, *Tetrahedron* **10**, 182 (1960).

[3] For further details, *cf.* R. F. W. Bader, Ph.D. Thesis in Organic Chemistry, M.I.T., December, 1957.

The thermodynamic differences characterizing any structure difference between a mixture and pure H_2O, or between solutions of ions in these solvents, are evaluated by considering only those contributions to the terms $(G_i - G_1)$ in equation 2 which arise from the librational degrees of freedom. The term $(H_2 - H_1)$ determined by only the librational motions was previously[2] designated as $\Delta H (= H^{D_2O} - H^{H_2O} = H_w' - H_w)$ and calculated to be -582 cal mole^{-1}, by treating the librational degrees of freedom as arising from isotropic three-dimensional harmonic oscillators of frequency ω_r and $\omega_r(I/I')^{1/2}$ where ω_r is the observed librational frequency of the light water molecule and I/I' is the mean of the ratios of the three principal moments of inertia for H_2O and D_2O molecules. The present ΔG_w quantities will also contain a librational contribution from the term $G_3 - G_1 (= G_w^{HDO} - G_w^{H_2O} = G_w'' - G_w)$ and this may be calculated from the value of ω_r in a similar fashion by assuming the librational frequency of an HDO molecule to be given by

$$\omega_r'' = \omega_r(I/I'')^{1/2}$$

where I/I'' is the mean of the ratios of moments of inertia for H_2O and HDO molecules. The factor $(I/I'')^{1/2}$ has a value of 1/1·1884. Therefore structure differences will be governed by the three librational frequencies ω_r (667 cm^{-1}), ω_r' (482 cm^{-1}) and ω_r'' (561 cm^{-1}). An almost identical result would have been obtained for ω_r'' (566 cm^{-1}) by employing the rule of the geometric mean.[4] The isotopic excess functions which characterize the structure differences between H_2O—D_2O mixtures and pure H_2O can now be calculated to be

$$\Delta H_w = -581{\cdot}9N_{D_2O} - 348{\cdot}0N_{HDO}$$
$$\Delta S_w = 1{\cdot}067N_{D_2O} + 0{\cdot}521N_{HDO}$$
$$\Delta F_w = -900{\cdot}1N_{D_2O} - 503{\cdot}4N_{HDO}$$

The equilibrium constant K_1 for the reaction

$$H_2O + D_2O \rightleftarrows 2HDO \tag{3}$$

has a value of 3·96 at 25°,[5] and the mole fraction of deuterium α is given by

$$\alpha = (2N_{D_2O} + N_{HDO})/2 \tag{4}$$

The values of the isotopic excess functions which characterize the structure differences between H_2O—D_2O mixtures and pure H_2O are shown in Fig. 1 as a function of the mole fraction of deuterium, α. The values of ΔH_w, $T\Delta S_w$ and ΔF_w are almost linear functions of α.

The solvent isotope effects, i.e. those due only to a change in the structure difference and not involving isotopic exchange with the substrate, should exhibit this same almost linear behavior. The addition of an anion to a solution of the light and heavy waters will change the librational frequencies of the water molecules in the 4-coordinated shell of the ion and thus the structure differences from those of the pure waters at that particular value of α. Calculations are done as before (Ref. 2, footnote 34) except that from the one new librational frequency for H_2O both ω_r' and ω_r'' and

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[4] G. N. Lewis and R. E. Cornish, *J. Amer. Chem. Soc.* **55**, 2616 (1933); B. Topley and H. Eyring, *J. Chem. Phys.* **2**, 217 (1934); J. Bigeleisen, *Ibid.* **23**, 2264 (1955).

[5] H. C. Urey, *J. Chem. Soc.* 569 (1947).

hence both $\Delta\theta$ values are calculated. The resulting thermodynamic differences $G_{D_2O} - G_{H_2O}$ and $G_{HDO} - G_{H_2O}$ calculated from the two $\Delta\theta$ values are multiplied by the mole fractions N_{D_2O} and N_{HDO} respectively and summed to give ΔG, the observed isotope effect.

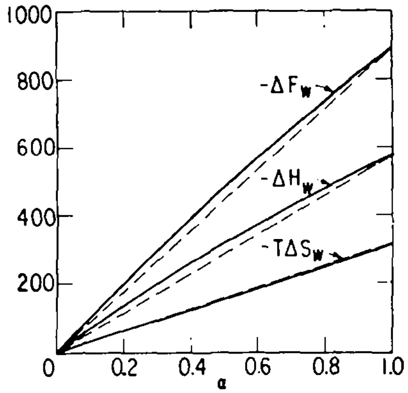

FIG. 1. The value of the isotopic excess functions characterizing the structure difference between H_2O—D_2O mixtures and light water at 25° in cal mole^{-1} as a function of the mole fraction of deuterium (D/D + H).

Calculation of isotope effect for heat of solution of a salt in H_2O—D_2O *mixtures*

The isotope effect on the heat of solution of sodium chloride in H_2O—D_2O mixtures as a function of x will be calculated and compared with experiment. The calculation will be carried out initially for the heat of solution at infinite dilution, ΔH_s. Values of the isotopic function ΔH_i will be determined using the libration frequencies of the water molecules coordinated to the sodium and chloride ions. These frequencies for the sodium ion are ω_r (635·0 cm^{-1}), ω_r' (459·8 cm^{-1}) and ω_r'' (534·5 cm^{-1}) and for the chloride ion ω_r (598·0 cm^{-1}), ω_r' (432·9 cm^{-1}) and ω_r'' (503·2 cm^{-1}) where the same reduced mass factors previously listed were employed in the calculation of ω_r' and ω_r''. One now calculates

$$\Delta H_i^{Na^+} = -537{\cdot}0 N_{D_2O} - 321{\cdot}5 N_{HDO}$$

and

$$\Delta H_i^{Cl^-} = -487{\cdot}0 N_{D_2O} - 292{\cdot}3 N_{HDO}$$

where the units of each are cal mole-ion^{-1}. These expressions for ΔH_i are more general than those given in part I[2] because they now refer to differences between any mixture of light and heavy water and pure light water. The values of ΔH_i and ΔH_s given earlier are for the special case where $N_{D_2O} = 1{\cdot}00$ and $N_{HDO} = N_{H_2O} = 0{\cdot}00$. The isotope effect per mole of salt at infinite dilution is

$$\begin{aligned}\Delta H_s &= \Delta H_s^{Na^+} + \Delta H_s^{Cl^-} \\ &= 4(\Delta H_i^{Na^+} - \Delta H_w) + 4(\Delta H_i^{Cl^-} - \Delta H_w)\end{aligned}$$

The factors of 4 are present to account for the four moles of water which are bound to each mole-ion. The calculated values of ΔH_s are shown in Fig. 2 as curve A, and the experimental points of Lange and Martin[6] are also given. These authors felt that their data were best represented by a simple linear relationship as indicated by curve C in Fig. 2. The calculated curve lies outside of all the experimental points. The maximum deviation from the straight line approximation is 25 cal mole^{-1} of salt, slightly larger than the reported experimental error of 20 cal mole^{-1} of salt. This simple approach to the problem has, however, resulted in a curve which is in good general agreement with the experimental one. It may well be that the correct form of the curve is slightly convex as indicated by the simple theoretical approach; certainly it is difficult to tell from the experimental data. Better agreement with the experimental results may be obtained by performing a more elaborate calculation, one which takes into account the displacement in the equilibrium brought about by the addition of the ions. This is the substance of the following section.

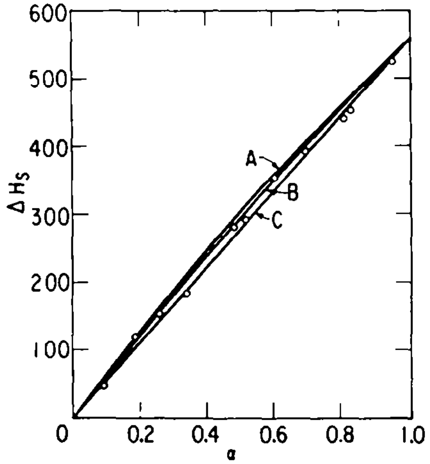

FIG. 2. The isotope effect for the heat of solution of sodium chloride in H_2O—D_2O mixtures at 25° in cal mole^{-1} of salt as a function of the mole fraction of deuterium in the solvent.

How does the addition of an ion to an H_2O—D_2O mixture affect the position of the equilibrium respresented by equation (3)? Previous considerations have illustrated that all monatomic singly-charged ions, with the exception of the fluoride ion, are preferentially solvated by light water rather than heavy water. The species HDO will lie somewhere between these waters in its solvating ability.

$$D_2O + X^{\ominus}(H_2O) \rightleftarrows H_2O + X^{\ominus}(D_2O) \qquad K < 1 \tag{5}$$

$$HDO + X^{\ominus}(H_2O) \rightleftarrows H_2O + X^{\ominus}(HDO) \qquad K < 1 \tag{6}$$

Qualitatively, one can see that this fractionation of the water molecules within the solution will decrease the value for the isotope effect for any property connected with ionic solvation. Since the mole fraction of deuterium in the immediate vicinity of the ion is less than that for the solution as a whole, i.e. less than the apparent mole fraction, the actual structure difference is less and isotope effects are correspondingly smaller.

To calculate the integral heat of solution taking into account the displacement in the equilibrium concentrations of the three waters, it is necessary to determine nine

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[6] E. Lange and W. Martin, *Z. Physik. Chem.* **A178**, 214 (1936).

water concentrations. These nine concentrations correspond to the mole fractions of the three waters bound to the anions, of the three waters bound to the cations and of the three in the bulk water of the solution. Nine independent relationships may be found between these quantities. The equilibrium constant K_1 of equation (3) is taken as governing the equilibrium between the unbound waters. The equilibrium constants, four in number, corresponding to processes 5 and 6 for both the anion and the cation may be calculated from the theory. The K values are related to one quarter of the ΔF_s values previously tabulated for the ions in Part I.[2] The remaining four relationships are obtained from material balance considerations.

The results of such a calculation are as anticipated. If the apparent mole fraction of deuterium in a H_2O—D_2O mixture α is defined as determined by the total amount of deuterium present in water of all kinds, then α is in every case greater than the value of α_i, the mole fraction of deuterium in the waters bound to the ions and slightly less than the mole fraction of deuterium in the unbound waters. The mole fraction of bound HDO is less than or greater than the mole fraction present in the entire solution depending on whether the mole fraction of deuterium is less than or greater than 0·5. The result of this fractionation is to lower the isotope effect for any value of α from the value calculated for infinite dilution. The values of ΔH_s calculated for a 0·2498m solution (as employed by Lange and Martin[6]) are plotted as curve B in Fig. 2. The calculated points now lie entirely within the experimental error of the data. While the calculated variation in ΔH_s is now closer to the straight line approximation, a definite curvature is still present. The percentage error between the two plots is, however, very small.

Reference should be made to some results obtained by La Mer and Noonan[7] for the integral heat of solution of potassium chloride in mixtures of light and heavy water. Their results show a very slight but definite concave curvature in the plot ΔH_s vs. the mole fraction of deuterium present in the solution. The calculated values for potassium chloride should lie even closer to a straight line than did those for sodium chloride because of the larger fractionation of the water molecules within the solution by potassium ion in comparison with the sodium ion, but still above a straight line. However, their cell involved transfer of the two waters between the two half cells, for which it is difficult to correct. Furthermore, the experimental concavity is very slight and the deviations are therefore still very small.

The behavior of acids in H_2O—D_2O *mixtures*

The addition of an acid to a mixture of light and heavy water results in the formation of four different forms of lyonium ion, H_3O^+, H_2DO^+, HD_2O^+ and D_3O^+, which differ in their protonating ability. Thus, any process, equilibrium or rate, which is a function of acidity will reflect in its own behavior the differences in the acidities of the four species. The problem is further complicated by the differing basicities of the three kinds of water present in a mixture of light and heavy water. Before treating any specific problem, one must be able to determine the equilibrium concentrations of the four lyonium ions for any mole fraction of deuterium present in the solvent.

For a given concentration of lyonium ion in solution (i.e. for a given molar concentration of a strong acid) there are seven equilibrium concentrations which must be determined, those of the three waters and the four forms of lyonium ion. To calculate

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[7] V. K. La Mer and E. Noonan, *J. Amer. Chem. Soc.* **61**, 1487 (1939).

these quantities six more relationships are necessary besides the given total concentration of acid. For dilute solutions of the acid, it is possible to employ the same three relationships which were used to determine the concentration of the three waters in pure H_2O–D_2O mixtures (equations 1, 3 and 4). The three remaining expressions are given by the conditions governing the equilibrium between the various forms of lyonium ion and the three waters. The reaction

$$2D_3O^{\oplus} + 3H_2O \rightleftarrows 2H_3O^{\oplus} + 3D_2O \qquad (7)$$

is equivalent to equation 7 of part I[2], and its equilibrium constant (K_2) was evaluated there as 8·200. The equation, as written above, omits the waters necessary for the solvation of the ions. However, it was previously pointed out that hydronium ion leaves the frequencies of the surrounding four water molecules unaffected and therefore the same equilibrium constant is obtained with or without their contribution. In other words there is no free energy of transfer or solvent isotope effect of the "usual kind" for H_3O^+ and D_3O^+. The same will, of course, hold true for the other two lyonium ions in mixtures of light and heavy water. This is equivalent to assuming that the ratio of the activity coefficient of H_3O^+ to that of any of its isotopic isomers is unity and is independent of the mole fraction of deuterium in the solution. This is equivalent to the assumptions made by Nelson and Butler[8] and Schwarzenbach[9] in their treatment of similar problems. However, their reasons for making these assumptions were simply out of necessity, since they possessed no experimental evidence to favor such a procedure. Furthermore, for K_2, Nelson and Butler used the value of 15·3 which is the equilibrium constant for the reaction

$$2D_3O^{\oplus}(D_2O) + 2Cl^{\ominus}(D_2O) + 3H_2O \rightleftarrows 2H_3O^{\oplus}(H_2O) + 2Cl^{\ominus}(H_2O) + 3D_2O$$

i.e. they were not able to allow for the free energy of transfer of the chloride ion and hence could not determine the value of K_2 (8·2) employed in the present calculations. Purlee[10] used a value of K_2 of 11·0 to obtain an improved fit to the pertinent experimental data. To arrive at this value he calculated that the free energy of transfer of chloride ion from H_2O to D_2O is $-\frac{1}{2}RT \ln (11{\cdot}0/17{\cdot}4) = 140$ cal mole^{-1} from e.m.f. measurements of Schwarzenbach on liquid junction cells by assuming equal liquid junction potentials between HCl solutions in either H_2O or D_2O vs. a saturated KCl solution in H_2O. This correction is in the right direction, but is less than our calculated value of $\Delta F_s = 233$ cal mole^{-1}, which is free from this dubious use of liquid junction cells and these assumptions about liquid junction potentials.

In order to calculate the equilibrium concentrations of the species H_2DO^+ and HD_2O^+ it is necessary to determine their partition function ratios. These cannot be calculated directly since their spectra cannot be observed. However, a very reasonable assumption may be made, equivalent to one used earlier by Schwarzenbach[9]. The assumption is

$$Q_{H_2DO^+}/3Q_{H_3O^+} = 3Q_{D_3O^+}/Q_{HD_2O^+} = Q_{HD_2O^+}/Q_{H_2DO^+}$$

where each Q_i is a partition function. This application of the rule of the geometric

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[8] J. C. Hornel and J. A. V. Butler, *J. Chem. Soc.* 1361 (1936); W. J. C. Orr and J. A. V. Butler, *Ibid.* 330 (1937); W. E. Nelson and J. A. V. Butler, *Ibid.* 957 (1938).

[9] G. Schwarzenbach, *Z. Electrochem.* **44**, 46 (1938).

[10] E. L. Purlee, *J. Amer. Chem. Soc.* **81**, 263 (1959).

mean[4] is equivalent to assuming that progressive substitution of deuterium for hydrogen in hydronium ion brings about equal stepwise increments in thermodynamic differences. In effect, each HO bond is considered as an independent entity in the sense that the HO bond of HD_2O^+ is considered to have the same fundamental frequencies as an HO bond in H_3O^+. The factors of three take into account the different statistical probabilities of the species, i.e. the species H_3O^+ and D_3O^+ possess symmetry numbers of three while the symmetry numbers of H_2DO^+ and HD_2O^+ are unity. The symmetry number is the number of indistinguishable orientations obtainable by rotation of the molecule and is a divisor reducing the partition functions. The partition function ratio $Q_{D_3O^+}/Q_{H_3O^+}$ may be calculated from the value of K_2 and the calculated value of the partition function ratio of light and heavy water.[2]

$$Q_{D_2O}/Q_{H_2O} = 1437$$

$$Q_{D_3O^+}/Q_{H_3O^+} = 19023$$

From this value and the above relationships the other ratios are

$$Q_{HD_2O^+}/Q_{H_2DO^+} = 26{\cdot}70$$

$$Q_{H_2DO^+}/Q_{H_3O^+} = 80{\cdot}08$$

$$Q_{D_3O^+}/Q_{HD_2O^+} = 8{\cdot}898$$

Two more equilibria may now be written which involve the species H_2DO^+ and HD_2O^+ and their equilibrium constants calculated.

$$H_2O + H_2DO^{\oplus} \rightleftarrows HDO + H_3O^{\oplus} \qquad K_3 = 0{\cdot}9420 \tag{8}$$

$$H_2O + D_3O^{\oplus} \rightleftarrows HDO + HD_2O^{\oplus} \qquad K_4 = 8{\cdot}478 \tag{9}$$

According to the assumptions made above concerning the two intermediate forms of lyonium ion, the constants K_3 and K_4 should, aside from statistical factors, be of equal magnitude. Therefore $K_4/6$ should equal $3K_3/2$, as indeed it does.

These relationships enable one to calculate the ratios

$$[H_3O^+]/[D_3O^+] = K_2^{1/2}([H_2O]/[D_2O])^{3/2} = 1/\lambda_1$$

$$[H_3O^+]/[H_2DO^+] = K_3[H_2O]/[HDO] = 1/\lambda_2$$

$$[HD_2O^+]/[D_3O^+] = K_4[H_2O]/[HDO] = \lambda_3/\lambda_1$$

If the total lyonium ion concentration is denoted by $[L_3O^+]$, then

$$[L_3O^+] = (1 + \lambda_1 + \lambda_2 + \lambda_3)[H_3O^+] = \lambda[H_3O^+];$$

$$\lambda = 1 + \frac{[D_2G]^{3/2}}{K_2^{1/2}[H_2O]^{3/2}} + \frac{[HDO]}{K_3[H_2O]} + \frac{K_4[D_2O]^{3/2}}{K_2^{1/2}[HDO][H_2O]^{1/2}} \tag{10}$$

The units of concentration are moles in a fixed number of moles (e.g. 55·5) of solvent. The four lyonium ion concentrations may be calculated for any value of the deuterium content of the solution and any total lyonium ion concentration. The ratios of the lyonium ion concentrations are fixed by the above four equilibrium constants and independent of any other processes occurring in the solution.

A strong acid in a mixture of H_2O and D_2O is completely dissociated into its conjugate base and the four different types of lyonium ions. If, for convenience, the total acid concentration $[L_3O^+]$ $(= [H_3O^+] + [H_2DO^+] + [HD_2O^+] + D_3O^+])$ is taken as unity, all four lyonium ion concentrations may be calculated for varying mole fractions of deuterium. The results of such a calculation are illustrated in Fig. 3. The most important feature of this plot is the lack of symmetry, which is a direct consequence of the differing acidities of the four lyonium ions. The progressive substitution of deuterium for hydrogen increases the acidity of the ion with the result that the ratio of D/H is greater in the solvent than in the ions. When the mole fraction of deuterium in the solvent is 0·50, the mole fraction of deuterium in the ions is only 0·41; similarly for a solvent deuterium mole fraction of 0·90, the deuterium mole fraction in the ions is 0·87. The OH bond strength is greater for water than for the ion. The zero-point energy is thus greater for water than for the ion and thus the deuterium should concentrate in the water as found.

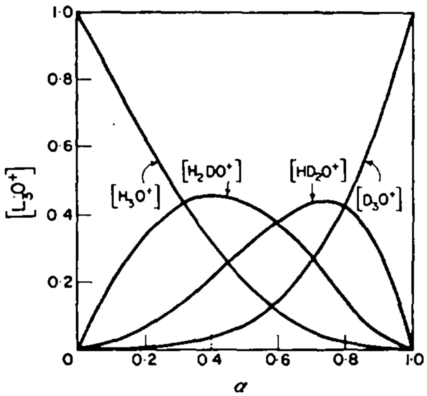

FIG. 3. The lyonium ion concentrations for a strong acid in H_2O—D_2O mixtures at 25° where total acid concentration $[L_3O^+] = 1·00$.

Calculation of ionization constants of weak acids in H_2O—D_2O *mixtures*

To test the assumptions made in the above analysis, the dissociation constant of a weak acid in mixtures of light and heavy water will be calculated and the values obtained compared with experimentally determined ones.

Other acids than lyonium ion are generally dissociated to a greater extent in light water than is the deuterated form of the acid in heavy water.

$$HA + H_2O \rightleftarrows H_3O^{\oplus} + A^{\ominus} \qquad K_{HA}$$

$$DA + D_2O \rightleftarrows D_3O^{\oplus} + A^{\ominus} \qquad K_{DA}$$

One reason why the ratio K_{HA}/K_{DA} possesses a value greater than unity is the fact that deuteronium ion is a stronger acid than hydronium ion. The other determining factor is the strength of the acid HA. The weaker this acid is, the stronger is the HA bond and thus the greater the zero-point energy difference between the acid and its deuterated form. Therefore, the lower the acidity possessed by HA, the greater will be the tendency for the deuterium to concentrate in the undissociated form of the acid.

This effect enhances the former one with the result that K_{HA}/K_{DA} should increase as the acidity of HA is decreased.

Dissolving a weak acid in a mixture of light and heavy water establishes equilibria between HA, DA and all four different lyonium ions. The dissociation constant in a mixture of deuterium mole fraction α is

$$K_\alpha = \frac{[L_3O^+][A^-]\gamma_{L_3O^+}\gamma_{A^-}}{[LA][L_2O]\gamma_{LA}\gamma_{L_2O}}$$

where $[LA] = [HA] + [DA]$, $[L_2O] = [H_2O] + [HDO] + [D_2O]$, and each γ is an activity coefficient. Combining equations for K_α, K_{HA} and K_{DA} gives

$$\frac{K_{HA}}{K_\alpha} = \frac{[H_3O^+][L_2O]\gamma_{H_3O^+}\gamma_{L_2O}}{[L_3O^+][H_2O]\gamma_{L_3O^+}\gamma_{H_2O}} + \frac{K_{HA}[D_3O^+][L_2O]\gamma_{D_3O^+}\gamma_{L_2O}}{K_{DA}[L_3O^+][D_2O]\gamma_{L_3O^+}\gamma_{D_2O}} \tag{11}$$

where all concentrations and activity coefficients refer to a mixture of deuterium mole fraction α. Since H_2O, HDO and D_2O form ideal solutions, $\gamma_{H_2O} = \gamma_{D_2O} = \gamma_{L_2O}$ in any mixture. Since lyonium ions leave the structure of water undisturbed, $\gamma_{H_3O^+} = \gamma_{D_3O^+} = \gamma_{L_3O^+}$ in any mixture. Therefore the activity coefficient ratios in equation 11 are unity. The concentration ratios $[H_2O]/[L_2O]$ and $[D_2O]/[L_2O]$ can be calculated from K_1 (equations 1, 3 and 4); likewise $[H_3O^+]/[L_3O^+]$ and $[D_3O^+]/[L_3O^+]$ can be calculated from K_2, K_3 and K_4 (equations 7–10). Therefore K_{HA}/K_α and hence K_α can be calculated for any deuterium mole fraction α. Fig. 4 shows the calculated results for 0·02 M stoichiometric acid concentration ($[LA] + [L_3O^+]$).

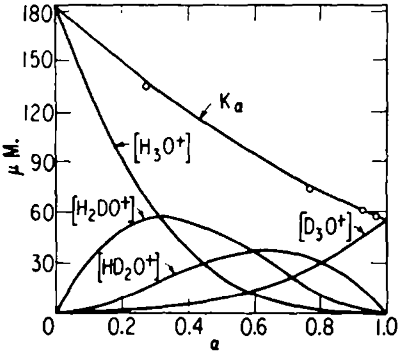

FIG. 4. The dissociation constant of acetic acid and the hydronium ion concentrations in H_2O—D_2O mixtures at 25° in micromolar units where $K\alpha = [L_3O^+]$.

La Mer and Chittum[11] have determined K_{HA}, K_{DA} and a number of K_α values for acetic acid in 0·02 M stoichiometric concentration by a conductivity method. Their values of K_{HA} and K_{DA} are $1{\cdot}84 \times 10^{-5}$ and $0{\cdot}555 \times 10^{-5}$ respectively. By convention $[H_2O]\gamma_{H_2O}$, $[D_2O]\gamma_{D_2O}$ and $[L_2O]\gamma_{L_2O}$ are set equal to unity. Also γ_{A^-}/γ_{HA} was assumed to be independent of α. This is reasonable because A^- and HA are of similar size and the charge on A^- is on oxygen, just as in hydroxide ion, which is known to leave the structure of water undisturbed.[2] The agreement between the calculated results (line) and experimental results (circles) in Fig. 4 is excellent. The pronounced dip in the value of K_α as noted by La Mer and Chittum is predicted by the calculations.

[11] V. K. La Mer and J. P. Chittum, *J. Amer. Chem. Soc.* **58**, 1642 (1936).

Their results show a maximum deviation from linearity of -12 per cent and the calculated ones give a value of -11 per cent. The good agreement between the experimental and calculated results provides an *a posteriori* proof of the assumptions made in calculating the partition function ratios for the species H_2DO^+ and HD_2O^+. Fig. 4 also illustrates the variations in the concentrations of the four lyonium ions for acetic acid where $K_\alpha = [L_3O^+]$, i.e. when $[A^-] = [LA]$.

Acid-catalyzed reactions in mixtures of light and heavy water. As first noted by Gross[12] and later elaborated by Butler[8] and Purlee[10], a study of the variation in the rate of an acid-catalyzed reaction as a function of the deuterium content of the solvent may allow one to differentiate between possible reaction mechanisms.

First consider a mechanism in which the substrate S reacts with acids via a transition state of composition $(SH^+)^*$, i.e. one not containing the elements of any additional solvent molecule or base. The rate of such a reaction is proportional to the concentration of the protonated transition state $[SH^+]^*$.

Among other possible mechanisms for an acid-catalyzed reaction are ones in which the transition state has the composition $(SHX)^*$ (as it might if the proton transfer from the acid HX were rate determining) or $(XSH)^*$ (as it might for a slow reaction of a base X^- with SH^+). The rate is then dependent on the nature of X.

For the first transition state $(SH^+)^*$, the isotope effect can be calculated as a function of α (the mole fraction of deuterium) as shown below. If instead the transition state is $(SHX)^*$ or $(XSH)^*$, the isotope effect need not follow this calculated dependence on α. The present calculations are based entirely upon the results that have been obtained by the use of the present theory. In a mixture of light and heavy water there will be a second term in the rate expression proportional to the concentration of the deuterated transition state $[SD^+]^*$. The two transition states are in equilibrium with all four kinds of lyonium ions. However, these equilibria are not all independent, and it is sufficient for the present purpose to consider only two.

$$H_3O^+ + S \rightleftarrows SH^{+*} + H_2O \qquad K_H^*$$

$$D_3O^+ + S \rightleftarrows SD^{+*} + D_2O \qquad K_D^*$$

The ratio of the ordinary experimental first-order rate constant in a mixture of H_4O and D_4O to that in H_4O is

$$\frac{k_\alpha}{k_H} = \frac{[SH^+]_\alpha^*}{[SH^+]_H^*} + \frac{[SD^+]_\alpha^*}{[SH^+]_H^*}$$

where the starred concentrations are effective concentrations, which, like the K^* constants, include the effective mass for crossing the barrier. Hence

$$\frac{k_\alpha}{k_H} = \frac{[H_3O^+]_\alpha[H_2O]_H(\gamma_{H_3O^+})_\alpha(\gamma_{H_2O})_H(\gamma_S)_\alpha(\gamma^*_{SH^+})_H}{[H_3O^+]_H[H_2O]_\alpha(\gamma_{H_3O^+})_H(\gamma_{H_2O})_\alpha(\gamma_S)_H(\gamma^*_{SH^+})_\alpha} + \frac{k_D[D_3O^+]_\alpha[D_2O]_D(\gamma_{D_3O^+})_\alpha(\gamma_{D_2O})_D(\gamma_S)_\alpha(\gamma^*_{SD^+})_D}{k_H[D_3O^+]_D[D_2O]_\alpha(\gamma_{D_3O^+})_D(\gamma_{D_2O})_\alpha(\gamma_S)_D(\gamma^*_{SD^+})_\alpha} \qquad (12)$$

The ratios of activity coefficients may be set equal to unity for the following reasons.

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[12] P. Gross, H. Steiner and F. Krauss, *Trans. Faraday Soc.* **32**, 877 (1936); P. Gross and A. Wischin, *Ibid.* **32**, 879 (1936); P. Gross, H. Steiner and H. Suess, *Ibid.* **32**, 883 (1936).

Since H_2O, D_2O and HDO form ideal solutions, $(\gamma_{H_2O})_\alpha = (\gamma_{H_2O})_H$ and $(\gamma_{D_2O})_\alpha = (\gamma_{D_2O})_D$. Since H_3O^+ and D_3O^+ do not change the structure of water[2], $(\gamma_{H_3O^+})_\alpha = (\gamma_{H_3O^+})_H$ and $(\gamma_{D_3O^+})_\alpha = (\gamma_{D_3O^+})_D$. The remaining assumptions that $(\gamma^*_{SH^+})_\alpha/(\gamma^*_{SH^+})_H = (\gamma_S)_\alpha/(\gamma_S)_H$ and $(\gamma^*_{SD^+})_\alpha/(\gamma^*_{SD^+})_D = (\gamma_S)_\alpha/(\gamma_S)_D$ are equivalent to assuming that solvation of the transition state changes in the same way with α as solvation of the ground state of S. If the transition state and S are large they both will cause considerable breakdown of the structure of water, and more as α increases because D_2O has the most structure to start with. However, such changes with α should be practically the same because of the closely similar sizes of SH^{+*} and S. There might be a difference associated with the electrical effect of protonating one atom in S. However, a transition state like protonated ethylene oxide, for example, probably would have hydrogen bonds between the proton and H_2O and between the remaining unshared pair and H_2O quite similar to hydrogen bonds formed by H_3O^+ or H_2O, already shown to be unaffected by α. Therefore at least in this case there is reason to expect the electrical contribution likewise to be unaffected by α. With these assumptions[13]

$$\frac{k_\alpha}{k_H} = g_H + \frac{k_D}{k_H} g_D \tag{13}$$

where

$$g_H = \frac{[H_3O^+]_\alpha [H_2O]_H}{[H_3O^+]_H [H_2O]_\alpha}, \quad g_D = \frac{[D_3O^+]_\alpha [D_2O]_D}{[D_3O^+]_D [D_2O]_\alpha}$$

A knowledge of the isotope effect k_D/k_H for the reaction in question together with the

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[13] This last assumption seems to be the weakest one and may not be valid for all substrates. The success of equation (13) is probably the best test of its validity.

Previous authors[8,10,12] have assumed instead that $\gamma_{H_3O^+}/\gamma^*_{SH^+}$ is independent of α. This is *not* valid. Although $\gamma_{H_3O^+}$ is independent of α because H_3O^+ does not change the structure of water, it is certainly untrue that γ_{SH^+} is independent of α except fortuitously, since large ions in general break down the structure of water.[2]

Alternatively one can write all lyon equilibria in terms of H^+ and D^+ instead of H_3O^+ ,H_2DO^+, HD_2O^+ and D_3O^+.[14] Substituting into equation (12) from the equilibria

$$H^+ \text{ (solvated)} + H_2O \text{ (solvated)} \overset{K_5}{\rightleftarrows} H_3O^+ \text{ (solvated)}$$

$$D^+ \text{ (solvated)} + D_2O \text{ (solvated)} \overset{K_6}{\rightleftarrows} D_3O^+ \text{ (solvated)}$$

yields the seemingly somewhat simpler equation

$$\frac{k_\alpha}{k_H} = \frac{[H^+]_\alpha (\gamma_{H^+})_\alpha (\gamma_S)_\alpha (\gamma^*_{SH^+})_H}{[H^+]_H (\gamma_{H^+})_H (\gamma_S)_H (\gamma^*_{SH^+})_\alpha} + \frac{k_D [D^+]_\alpha (\gamma_{D^+})_\alpha (\gamma_S)_\alpha (\gamma^*_{SD^+})_D}{k_H [D^+]_D (\gamma_{D^+})_D (\gamma_S)_D (\gamma^*_{SD^+})_\alpha}$$

However, in comparing this equation with experiment it is *not* valid to assume that $(\gamma_{H^+})_\alpha = (\gamma_{H^+})_H$ or that $(\gamma_{D^+})_\alpha = (\gamma_{D^+})_D$, because H^+ is smaller than Li^+ and so should increase the structure of water, since large ions like Na^+ and Cl^- decrease the structure of water, H_3O^+ and Li^+ leave it unchanged and the small fluoride ion increases it[2] (i.e. $(\gamma_{Na^+})_\alpha > (\gamma_{Na^+})_H$, $(\gamma_{Cl^-})_\alpha > (\gamma_{Cl^-})_H$, $(\gamma_{H_3O^+})_\alpha = (\gamma_{H_3O^+})_H$, $(\gamma_{Li^+})_\alpha = (\gamma_{Li^+})_H$ and $(\gamma_{F^-})_\alpha < (\gamma_{F^-})_H$ for $\alpha \neq 0{\cdot}00$). Instead $(\gamma_{H^+})_\alpha/(\gamma_{H^+})_H$ and $(\gamma_{D^+})_\alpha/(\gamma_{D^+})_D$ must be calculated as functions of α. For example

$$\frac{[H_3O^+]_\alpha (\gamma_{H_3O^+})_\alpha}{[H_2O]_\alpha (\gamma_{H_2O})_\alpha [H^+]_\alpha (\gamma_{H^+})_\alpha} = K_5$$

and

$$\frac{[H_3O^+]_\alpha [H_2O]_H [H^+]_H (\gamma_{H_3O^+})_\alpha (\gamma_{H_2O})_H (\gamma_{H^+})_H}{[H_2O]_\alpha [H_3O^+]_H [H^+]_\alpha (\gamma_{H_3O^+})_H (\gamma_{H_2O})_\alpha (\gamma_{H^+})_\alpha} = 1$$

Therefore

$$\frac{(\gamma_{H^+})_\alpha}{(\gamma_{H^+})_H} = \frac{[H_3O^+]_\alpha [H_2O]_H [H^+]_H (\gamma_{H_3O^+})_\alpha (\gamma_{H_2O})_H}{[H_2O]_\alpha [H_3O^+]_H [H^+]_\alpha (\gamma_{H_3O^+})_H (\gamma_{H_2O})_\alpha}$$

This shows that the ratio $(\gamma_{H^+})_\alpha/(\gamma_{H^+})_H$ is not unity and is a function of α. Indeed substitution of this ratio and the similar expression for $(\gamma_{D^+})_\alpha/(\gamma_{D^+})_D$ into the above equation for k_α/k_H again gives equation (12).

[14] F. A. Long, private communication.

variations in g_H and g_D allows one to predict k_α/k_H for various α. Agreement of the calculated values of k_α/k_H with experiment is evidence that the transition state is $(SH^+)^*$ rather than $(SHX)^*$ where X is water or any other base.

TABLE 1. VARIATIONS IN THE GROSS EQUATION PARAMETERS IN H_2O—D_2O MIXTURES AT 25°

α	N_{D_2O}	N_{HDO}	g_H	g_D
0·000	0·0000	0·0000	1·0000	0·0000
0·100	0·0101	0·1798	0·9839	0·0383
0·250	0·0628	0·3743	0·9425	0·1100
0·400	0·1606	0·4788	0·8732	0·2035
0·500	0·2506	0·4987	0·8062	0·2815
0·600	0·3606	0·4788	0·7174	0·3754
0·750	0·5628	0·3743	0·5303	0·5541
0·900	0·8101	0·1798	0·2544	0·7961
1·000	1·0000	0·0000	0·0000	1·0000

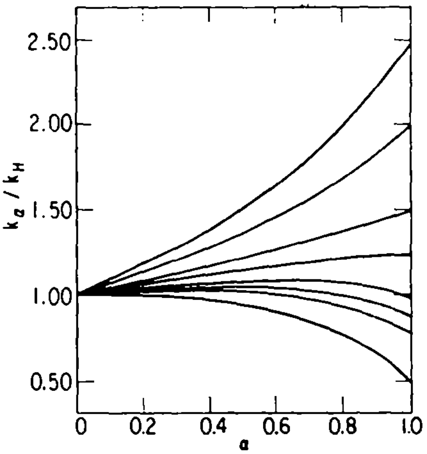

FIG. 5. The predicted variations in the rate ratio k_α/k_H for a number of values of the isotope effect k_D/k_H for acid catalyzed reactions involving specific hydrogen-ion catalysis at 25°.

Values of g_H and g_D for selected values of α are listed in Table 1. They are simply ratios of concentrations of H_2O, D_2O, H_3O^+ and D_3O^+ as defined under equation (13). These concentrations were calculated previously in the section entitled *The behavior of acids in* H_2O—D_2O *mixtures.* Fig. 5 illustrates the variation in k_α/k_H for a number k_D/k_H values.

The agreement of calculation with experiment was shown for a number of reactions by Purlee[10] using a K_2 of 11·0. The agreement is similar with our K_2 of 8·2. Both fit better than the value of 15·3 used by Nelson and Butler[8].