DEUTERIUM SOLVENT ISOTOPE EFFECTS ON ACID–BASE EQUILIBRIA IN DIOXAN–WATER MIXTURES

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SCOPE OF INVESTIGATION

The problem considered in this article is the comparison of acid–base equilibrium constants in the solvent systems protium oxide–dioxan and deuterium oxide–dioxan. The two reactions considered specifically are the self-dissociation of water and the acid dissociation of acetic acid. Both processes have previously been studied in the binary solvent systems protium oxide–dioxan (up to 70 or 82 wt. per cent of dioxan respectively) and protium oxide–deuterium oxide (over the entire composition range). There has been no previous investigation of equilibria in the solvent system deuterium oxide–dioxan.

The available experimental data on the dissociation of water and acetic acid in protium oxide–dioxan mixtures are the result of very careful investigations by Harned and his school[1], but the theoretical interpretation of the effect of solvent variation has so far proved too difficult.

The present study was undertaken for two reasons. First, it was desired to establish to what extent the solvent isotope effects associated with the replacement of the protium oxide of water by deuterium oxide are modified if the solvent contains also a certain proportion of dioxan. This problem is of practical interest, since the use of pure water as a solvent is frequently impracticable. For instance, in the study of the velocity of an organic reaction the addition of an organic component to the solvent water may sufficiently raise the solubility of a reactant to make observations possible; or the velocity of the reaction may be modified in this way to fall into a convenient range. Dioxan is frequently used to achieve one or the other of these results, and the question then arises whether deuterium solvent isotope effects may still be relied on in such mixtures in order to obtain information about the rôle of proton-transfer steps in the reaction mechanism.

The second objective of the investigation was to find out whether experimental results of this kind could provide some pointers towards a better theoretical understanding of the mixed solvent dioxan–water and, more generally, of solvent mixtures consisting of water and a non-aqueous solvent.

THE DEUTERIUM SOLVENT ISOTOPE EFFECT IN AQUEOUS SOLUTION

It is well established that the dissociation constants of weak acids[2] and the ionic product of water[3] are reduced in magnitude on changing from

ordinary water to deuterium oxide as solvent. The size of the effect for acids shows a rough trend with acid strength, the larger values of K_H/K_D being associated with the weaker acids[4]. The correlation is by no means exact[2, 5, 6] and at present it is not altogether clear by what structural factors the size of the isotope effect is influenced[5, 6]. It appears to be common ground, however, that these factors influence intermolecular interactions in solution rather than the properties of the isolated species involved in the reaction. In aqueous solutions the most significant intermolecular interactions involve hydrogen bonds and are thus subject to a hydrogen isotope effect. This view has been well expressed by Bunton and Shiner[7] who also suggest empirical rules for the calculation of isotope effects on this basis. For the two equilibria considered in this article the isotope effects were determined with great care by La Mer and his collaborators. Their best value for acetic acid[8], log $(K_a^H/K_a^D) = 0{\cdot}52$, was considerably smaller than the corresponding value for the ionic product of water[9], log $(K_w^H/K_w^D) = 0{\cdot}81$. Our provisional values for these isotope effects in aqueous solution are 0·49 and 0·86, respectively.

ELECTROLYTE EQUILIBRIA IN PROTIUM OXIDE–DIOXAN MIXTURES

The effect of dioxan on the dissociation constants of water[1, 10] and of acetic acid[1, 11] (as well as on many other electrolyte phenomena) was studied by Harned and his collaborators. In both cases the equilibrium constant is reduced by a factor of about four powers of ten on going from water to a mixed solvent containing 70 per cent dioxan by weight. We have used these results as a criterion for the reliability of our procedure.

The fall in the value of the dissociation constant with increasing dioxan content (and therefore decreasing dielectric constant) suggests a dielectric effect on a charge-producing reaction. However, the pK value does not vary linearly with the inverse of the dielectric constant, as predicted by the Born equation for a purely electrostatic effect[12]. Instead, the pK value increases roughly linearly with the mole fraction of dioxan in the solvent[11] and this simpler behaviour argues against a straightforward electrostatic interpretation. A variety of acids conforms to this rule, which also applies to mixtures of other organic solvents with water[13].

In the case of benzoic acid the variation of the dissociation constant with the proportion of dioxan in the medium can be entirely accounted for by the change in the activity of the undissociated acid molecules, as measured by the solubility[14]. For 2,4-dinitrophenol similar measurements again point to a large effect of this kind, but the quantitative agreement with the variation of the dissociation constant is not good in this case[13], perhaps implying that a similar effect on the activity of the 2,4-dinitrophenoxide ion may also be significant.

EXPERIMENTAL PROCEDURE

The measurements on which the new results reported in this paper are based were carried out using the galvanic cell

glass electrode $|H^+, Cl^-$, *etc.* (aq.)$|$AgCl, Ag

in which the introduction of a liquid junction is avoided[3]. The procedure consisted essentially of the analysis by electronic computer (Ferranti Mercury, University of London Computer Unit) of complete potentiometric titration curves for the neutralization of either hydrochloric acid or acetic acid by potassium hydroxide. Barium hydroxide, used in analogous studies in entirely aqueous solution, is unsuitable because of its low solubility, and the use of sodium hydroxide, which would have made our measurements more directly comparable with Harned and Fallon's results[10, 11], was avoided because of possible complications in the response of the glass electrode. The computational programme was designed to correct for ionic strength effects, to minimize errors due to uncertainties in chemical composition and imperfections of cell behaviour by least-square routines, and to give the best agreement with Harned and Fallon's values[1, 10] for K_W in protium oxide–dioxan mixtures.

Details of the method will be published elsewhere, but we should like to state the assumptions on the correctness of which the reliability of our results depends. The most debatable assumption concerns the behaviour of activity coefficients. It was assumed that, for a given mole fraction of dioxan, ionic strength and cation, the activity coefficient ratio $\gamma_{Cl^-}/\gamma_{OH^-}$ in protium oxide–dioxan is identical with the ratio $\gamma_{Cl^-}/\gamma_{OD^-}$ in deuterium oxide–dioxan. More explicitly, we have taken the parameter B' in the expression

$$\log (\gamma_{Cl^-}/\gamma_{OH^-(OD^-)}) = B'I$$

to be invariant with the isotopic nature of the water constituent of the solvent, and have evaluated it by combination of our measurements with Harned and Fallon's results[10, 11]. (For solutions without dioxan, the value of B' is known from other data.) The ionic strength correction based on B' is significant in connection with the results on the self-dissociation of water but the rôle of the parameter corresponding to B' is negligible in our work on acetic acid. The behaviour of activity coefficients in water–dioxan mixtures is as yet not well understood, as Harned and his collaborators have stressed. However, Harned and Fallon[10] have also expressed the view that the resulting uncertainty is less in comparative measurements, such as are carried out to determine temperature coefficients of dissociation constants at a fixed composition. We believe that similar considerations apply to the isotope comparisons attempted in our work. We should perhaps point out that *qualitatively* the same conclusions emerge even if no correction for ionic strength is applied.

The results are expressed in molarity (moles litre^{-1}) units and for the interconversion of concentration scales it was assumed that the partial molar volume of deuterium oxide in a deuterium oxide–dioxan mixture is the same as that of protium oxide in a protium oxide–dioxan mixture containing the same mole fraction of dioxan. (The molar volumes of the two isotopic waters[15] are the same within 1/2 per cent.) Molality units which are more usually employed in the calculation of electrolyte equilibria are unsuitable for the isotope effect comparisons involving water in the solvent. (Isotopic solutions of equal mole-fraction composition have the same molarity for all solutes but different molalities). Our equilibrium constants

are not corrected for the changing concentration of water in the solvent mixtures[16], although it is formally involved in the reactions considered. Since the lowest mole fraction of water in this work was *ca.* 0·55, the correction would be small compared with the medium effect, and does not at all affect the size of the isotope effect.

RESULTS

Within the limits of experimental accuracy of this work and up to a dioxan mole fraction (N_2) of 0·25, the medium effect on the dissociation constant can in all cases be expressed in the form

$$pK = A + BN_2 \tag{1}$$

The "best" values of the constants A and B, obtained by a least-square fit of all data for a particular system to equation (1) are tabulated below. The K_w values were derived from measurements at ionic strengths (I) in the range 0·22–0·29; the K_a values rely on data $I = 0{\cdot}026 \pm 0{\cdot}001$. All values are corrected to zero ionic strength in the manner described. The values of A and B for acetic acid in protium oxide–dioxan differ somewhat from Harned and Fallon's[11] corresponding parameters $-C$ and C' which is in part due to the use of different concentration scales (molarity and molality). The slight discrepancy between the values of A and the previously cited pK values arises from the circumstance that the parameter A was obtained from the results for dioxan–water mixtures (excluding the point $N_2 = 0$), whereas the values for pK in water are the results of measurements in water alone.

It follows from equation (1) that the isotope effects should also be expressible in the form

$$\log (K^H/K^D) = a + bN_2 \tag{2}$$

where a and b are differences of the parameters A and B. For example, for the ionic product of water,

$$\begin{aligned} \log (K_w{}^H/K_w{}^D) &= pK_w{}^D - pK_w{}^H \\ &= (A_w{}^D - A_w{}^H) + (B_w{}^D - B_w{}^H)N_2 \\ &= a_w + b_wN_2 \end{aligned}$$

and, similarly, $\log (K_a{}^H/K_a{}^D) = a_a + b_aN_2$
(Subscripts and superscripts have the obvious connotations).

Although this treatment gives an adequate impression of the comparative insensitivity of the isotope effects to composition of the medium, it is better to calculate the isotope effects directly from the experimentally determined equilibrium constants. This avoids imparting an unconscious bias to the results by assuming equation (2) to hold. In fact, the directly calculated isotope effects do not confirm the validity of equation (2). This apparent contradiction arises because the b values in *Table 1* are small differences of larger values of B.

The variation of $\log (K^H/K^D)$ with composition is given in *Table 2*. Where

Table 1. Parameters of equations (1) and (2)

	A	*B*	*a*	*b*
Acetic acid				
H_2O–dioxan	4·73	10·61	0·54	−0·09
D_2O–dioxan	5·27	10·52		
Water				
H_2O–dioxan	14·02	11·67	0·84	−0·27
D_2O–dioxan	14·86	11·40		

Table 2. Solvent isotope effects on K_w and K_a

	Acetic acid		*Water*
N_2	log (K_aH/K_aD)	N_2	log (K_wH/K_wD)
0	$0{\cdot}49_3$	0	$0{\cdot}85_7$
0·0499	$0{\cdot}52_5$	0·0500	$0{\cdot}85_5$
0·1199	$0{\cdot}55_2$	0·1225	$0{\cdot}78_8$
0·1724	$0{\cdot}52_0$	0·1753	$0{\cdot}77_6$
0·2347	$0{\cdot}51_5$	0·2478	$0{\cdot}79_2$
0·4513	$0{\cdot}46_8$		

necessary, a short interpolation was carried out so that corresponding points for deuterium oxide–dioxan and protium oxide–dioxan referred to exactly the same mole fraction of dioxan.

DISCUSSION

The results summarized in the tables show that both isotope effects vary only slowly, decreasing as the mole fraction of dioxan in the solvent is raised, at least up to the compositions studied. The changes involved are so small that it is not easy to be confident about the exact manner of this variation, but it seems that the value of log (K_aH/K_aD) passes through a slight maximum about $N_2 = 0{\cdot}12$.

The practical implication of the results is that dioxan–water mixtures are admissible as media for the study of deuterium solvent isotope effects. It is obviously impossible to say whether this conclusion would apply to mixtures considerably richer in dioxan.

The results also dispose of the facile prediction that the isotope effect might be more marked in the mixtures with dioxan, on the fallacious reasoning that smaller acid dissociation constants are generally associated with more pronounced isotope effects. The argument is altogether too superficial to be of help.

More properly, the results can be interpreted as throwing some light on the nature of the solutions. Since the substitution of dioxan for part of the solvent water is found to have only little influence on the size of the isotope effect (especially in the case of acetic acid), the dioxan molecules can exert only a small effect on the hydrogen-bonding interactions in solution to which a considerable proportion of the isotope effect must be due[7]. The same conclusion follows even more clearly from the lack of correlation

between the value of B^H (measuring the sensitivity of the equilibrium constant to solvent change by the addition of dioxan) and the solvent-sensitivity of the isotope effect. The values of $B_a{}^H$ and $B_w{}^H$ are nearly the same, whereas the isotope effect on K_w changes much more quickly with dioxan content than that on K_a. (For example, $b_w \sim 3b_a$.) On the other hand, b seems to bear some relation to A^H and a. The self-dissociation of water is the reaction with the smaller equilibrium constant and the larger isotope effect. Since the larger isotope effect is also associated with a larger change in hydrogen-bonding interactions it follows that the solvent sensitivity of the isotope effect is a measure of the (small) extent to which the presence of dioxan interferes with this hydrogen bonding. It is also reasonable that this interference should be greater for the compound with the larger isotope effect and, as has already been noted, this is also likely to be the weaker acid. The size of B seems to be, in the main, concerned with interactions other than hydrogen-bonding.

These conclusions are more or less expected, as far as the ionic species involved in the equilibria are concerned. It is generally thought that the solvation shells of ions in dioxan–water mixtures are composed only of water molecules[12, 13]. However, the very slow variation of $K_a{}^H/K_a{}^D$ with solvent composition also leads us to think that the hydrogen bonds between acetic acid molecules and water must likewise remain substantially unaltered even when a large volume fraction of the solvent is dioxan. This can hardly mean that dioxan is altogether excluded from the vicinity of the acetic acid molecules for the inverse correlation between solubility and dissociation constant of certain acids in mixed solvents[13, 14] implies a marked interaction between the acid molecules and the non-aqueous component of the solvent. A simple way of picturing this situation would be to regard the two ends of an acetic acid molecule as exerting their different preferences for the components of the solvent mixture in a substantially independent fashion. On this view dioxan addition does not affect the reaction sites of these reactions, being excluded from the vicinity of reactive and charged regions of molecules. It therefore affects the dissociation constant but hardly the isotope effect, and the isotope effect should be largely independent of B. The solvent effect on the dissociation constant is thus mainly concerned with order and disorder in the solution and it seems very significant that the large effect of added dioxan concerns almost entirely the entropy of ionization of acetic acid[1]. The model is undoubtedly naïve but it may contain the germ of a satisfactory theory in metaphoric form.

The isotope effect on the self-dissociation of water is substantially more sensitive to dioxan content of the medium, but even here this solvent dependence is surprisingly small. Again the addition of dioxan influences mainly the entropy of ionization, with very little effect on the enthalpy. These facts suggest that the energetically important interactions concerned in the reaction are not much changed by the presence of dioxan. The picture is bound to differ from the preceding one, since the uncharged reagent is now the water molecule which, in a mixed solvent, must form some contacts with dioxan near reactive sites of the small water molecule.

In summary, the data suggest that the study of solvent isotope effects could be a useful tool in the study of mixtures. The conclusions reached here

are likely to have some validity for other solvent systems in which an organic component forms a small number of comparatively weak hydrogen bonds with water, but they must not be applied to grossly different situations.

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