Deuterium Solvent Isotope Effects on Reactions involving the Aqueous Hydroxide Ion

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The effect of solvent change from H_2O to D_2O on the ionic product of water and on rates of proton transfer from carbon acids to hydroxide ion can be quantitatively explained on the basis of the formula $OH^-_a(H_bOH_c)_3$ for the aqueous hydroxide ion, in which *a, b, c* denote non-equivalent positions and where it is assumed that different deuterium fractionation factors apply to the three hydrogen sites ($\phi_a \simeq 1{\cdot}2$—$1{\cdot}5$; $\phi_b \simeq 0{\cdot}65$—$0{\cdot}70$; $\phi_c \simeq 1$). It is thus possible to reconcile existing experimental results for deuterium fractionation in the aqueous hydroxide system and in the analogous methanolic methoxide system.

The formulation of the aqueous hydroxide ion as a trihydrate makes it improbable that proton transfer from a substrate to hydroxide ion is a simple process for which ' the degree of proton transfer in the transition state ' is a readily identifiable concept. Such considerations help to rationalise an apparent inconsistency in solvent and substrate isotope effects for the ionisation of 2-nitropropane. The primary substrate deuterium isotope effect [$k(Me_2CHNO_2)/k(Me_2CDNO_2)$] for methanolic methoxide is 7·6 ± 0·2 and 7·4 ± 0·1 for aqueous hydroxide, the agreement suggesting a close similarity in mechanism, whereas the solvent isotope effects in the two solvents do not correspond.

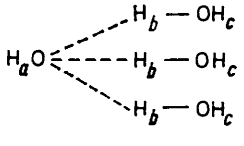
Experimental results are reported for the ionisation of 2-nitropropane and of 2-nitro[2-^{2}H]propane in aqueous sodium hydroxide (H_2O and D_2O as solvents, and mixtures for 2-nitropropane). There is a small interaction of solvent and substrate isotope effects.

SIGNIFICANT deuterium fractionation between hydroxylic positions of the 'methanolic methoxide ion' and methanol solvent is observable by n.m.r. measurements [1,2] and was first noticed and reported by More O'Ferrall.[1] Since CH_3O^- by itself contains no hydroxy-group, the phenomenon must be ascribed to fractionation between solvent molecules modified by the presence of methoxide ion and unperturbed solvent. Similar solvent–solute interactions must be presumed to exist in aqueous hydroxide solutions with corresponding implications for the measurement and interpretation of deuterium fractionation between the ' aqueous hydroxide ion ' and water. The present paper re-examines this fractionation effect and the deuterium solvent isotope effect on reactions in which the aqueous hydroxide ion is involved.

The absolute magnitude of the deuterium solvent isotope effect on several reactions in methanol solution in which a methoxide ion is neutralised supports [3] the formula $[MeO(HOMe)_m]^-$, with a value of $m \geqslant 3$. Since a stable primary co-ordination to oxygen of more than four groups appears improbable on steric grounds, the value $m = 3$ is indicated.

For the aqueous hydroxide ion there are similarly several observations which point to three-fold hydration of the hydroxide ion. Indeed, their existence has already been noted as corroborative evidence for the three-fold solvation of the methoxide ion.[2,3] For example, the solvation numbers 3 and 4 for aqueous OH^- and H^+ ions emerge from heat capacity measurements.[4] The parallel behaviour of methanolic methoxide and aqueous hydroxide is strikingly illustrated by their acidity functions. Following Bell and Bascombe's interpretation of the course of the H_0- function for aqueous acids in terms of four-fold hydration of the aqueous proton,[5] it has been shown that the basicity of these two lyate systems towards indicator acids can be explained [6,7] on the assumption that three solvent molecules are associated with OH^- and with OMe^-.

The ion shift of the hydroxide ion on the position of the proton magnetic resonance of water is *ca.* −15 p.p.m. (per unit atom fraction of protium in OH^-) when allowance is made for the contribution of the cation to the electrolyte shift of an alkali-metal hydroxide.† The hydroxide shift is in the same direction as, though numerically smaller than, the result for the aqueous hydrogen ion, *ca.* −36 p.p.m. (per stoicheiometric unit atom fraction of protium from HCl). In both cases the sign of the ion shift implies strong deshielding, and this is anomalous in the case of the hydroxide ion, since a proton in OH^- should be more shielded than a proton in H_2O. The anomaly can elegantly be removed [8,9] if it is assumed that the ' hydroxide ' shift is made up of opposing contributions from the single proton of the OH^- moiety (H_a) and from three protons in hydrogen bonds of attached water molecules (H_b). The outer hydrogen atoms of the solvating water molecules (H_c) are assumed to form part of the normal water structure and to make no significant contribution [see formula (I)]. (The details



(I)

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† Kresge was the first to point out the necessity for correcting for the cation effect.[8] However, he unfortunately applied the correction with the wrong algebraic sign, thereby calculating the hydroxide shift as −4·4 p.p.m., a value quoted in several recent publications. The mistake was independently noted by Dr. C. Tomlinson (personal communication) and the present authors.

[1] R. A. More O'Ferrall, *Chem. Comm.*, 1969, 114.

[2] V. Gold and S. Grist, *J. Chem. Soc.* (*B*), 1971, 1665.

[3] V. Gold and S. Grist, *J. Chem. Soc.* (*B*), 1971, 2282.

[4] T. Ackermann, *Discuss. Faraday Soc.*, 1957, **24**, 180.

[5] K. N. Bascombe and R. P. Bell, *Discuss. Faraday Soc.*, 1957, **24**, 158.

[6] G. Yagil and M. Anbar, *J. Amer. Chem. Soc.*, 1963, **85**, 2376.

[7] C. H. Rochester, *Quart. Rev.*, 1966, **20**, 511.

[8] A. J. Kresge, *J. Chem. Phys.*, 1963, **39**, 1360.

[9] R. Grahn, *Acta Chem. Scand.*, 1965, **19**, 153; see also G. M. Sheldrick, *Chem. Comm.*, 1966, 673.

of the analysis and the precise values of the parameters[9] δ_a and δ_b require revision in the light of more recent suggestions concerning the evaluation of single-ion shifts,[10] especially in view of the wrong sign of the cation correction used by previous authors.[8,9])

The corresponding ion shifts in methanol solution, with the best available correction for the effect of counterions, are $\delta = ca.\ -29$ p.p.m. (per stoicheiometric unit atom fraction of protium from HCl) for the methanolic hydrogen ion and $\delta = ca.\ -28$ p.p.m. (per unit mol fraction) for the methoxide ion.[2] Qualitatively these results support the foregoing interpretation of the hydroxide ion shift. The absence of the (shielded) H_b-atom in methoxide can be linked with the more marked downfield shift but the detailed analysis is not quite so simple.

The interpretation of the ion shift of the hydroxide ion as a composite of opposing contributions from several proton sites also accounts for the failure of the n.m.r. method to yield a value of the deuterium fractionation factor of the aqueous hydroxide ion[11] even remotely in line with results from other studies, although it is not yet clear whether the two-site (*a*, *b*) formulation of the hydroxide ion permits a rationalisation of the observations.

The only direct determination of this fractionation, due to Heinzinger and Weston,[12] is based on the isotopic composition of water vapour in equilibrium with concentrated (*ca.* 7—12M) aqueous solutions of potassium and sodium hydroxide. The fractionation factor (ϕ^*), calculated on the assumption that the fractionation is restricted to a single site in OH^-, was found to have the value $0{\cdot}47_5$ at 25 °C.

A different but, as will be shown below, complementary approach to the problem is the study of the solvent isotope effect on the ionic product of water. If the autoprotolysis of water can be written as equation (1), it follows[13] that the isotope effect on K_W is given by equation (2). On the basis of this assumption it is

$$2H_2O \rightleftharpoons H_3O^+ + OH^- \tag{1}$$

$$K_W^D/K_W^H = l^3\phi^* \tag{2}$$

possible to calculate ϕ^* from the experimentally determined ratio K_W^D/K_W^H and the independently derived fractionation factor (l) for the aqueous hydrogen ion.[11,14] The agreement of the directly determined value of ϕ^* with the result calculated from equation (2), on the basis of certain determinations[15] of K_W^D/K_W^H available in 1964, persuaded Heinzinger and Weston[12] of the essential correctness of equation (1) and the formula OH^- for the purposes of solvent isotope effect studies. However, the more accurate and consistent recent determinations[16,17] of K_W^D/K_W^H would require ϕ^* to have a somewhat smaller value (*ca.* 0·42), outside the range considered possible by Heinzinger and Weston for their directly determined fractionation factor. (This analysis assumes the adequacy of the rule of the geometric mean for the present purposes: the main conclusions are not significantly altered by a more elaborate treatment in which this assumption is avoided.)

The need for involving a larger number of hydrogen atoms than appear in equation (1) in the formulation of the hydroxide ion or in the interpretation of the solvent isotope effect on K_W was in different ways recognised by Swain and Bader[18] and by Bunton and Shiner.[19] The same conclusion emerges from the detailed examination of K_W values for H_2O–D_2O mixtures.[16] Agreement between measurements and theory[13,16] can be obtained by any one of several similar elaborations of equilibrium (1) in which either H_3O^+ or OH^- (or both) are formulated with several molecules of hydration (hydrogen-bonding). In these calculations the fractionation factor for the OH^--grouping [H_a position of formula (I)] was always taken to have a value in the region of 0·5, as required by the simpler model of equation (1), and ϕ-values for other protons in the range 0·9—1·0 were introduced in order to provide an improvement of the fit.

Heinzinger and Weston[12] likewise considered, but then rejected, the involvement of additional water molecules in terms of the general formula $OH^-\ (H_2O)_m$. However, they adopted the improbable assumption that all $(2m + 1)$ hydrogen atoms were equivalent. For example, their treatment of the case $m = 3$ [corresponding in composition to formula (I)] implicitly took $\phi_a = \phi_b = \phi_c$ for the seven protons.

Both these sets of calculations[12,16] thus ignored the possibility, suggested by the n.m.r. evidence,[1,2,9] that a range of values $\phi_a > 1$, $\phi_b < 1$, $\phi_c \sim 1$ is a more reasonable one to apply to formula (I). It is this model which is examined in the following.

It is assumed that the fractionation factor ϕ_c of the outer protons can be taken as unity, that the aqueous hydrogen ion is correctly described as H_3O^+, with $l = 0{\cdot}69$, and that medium effects other than those explicitly included in the formulation of hydrogen and hydroxide ions [formula (I)] can be neglected. The two sets of experimental data, *viz.* Heinzinger and Weston's experiments[12] and the K_W^D/K_W^H ratio, then provide

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[10] J. Davies, S. Ormondroyd, and M. C. R. Symons, *Chem. Comm.*, 1970, 1426.

[11] (*a*) V. Gold, *Proc. Chem. Soc.*, 1963, 141; (*b*) A. J. Kresge and A. L. Allred, *J. Amer. Chem. Soc.*, 1963, **85**, 1541; (*c*) C. Tomlinson, personal communication.

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[15] E. Abel, E. Bratu, and O. Redlich, *Z. Phys. Chem.* (*A*), 1935, **173**, 353; R. W. Kingerley and V. K. LaMer, *J. Amer. Chem. Soc.*, 1941, **63**, 3256; P. Salomaa, L. L. Schaleger, and F. A. Long, *ibid.*, 1964, **86**, 1.

[16] V. Gold and B. M. Lowe, (*a*) *Proc. Chem. Soc.*, 1963, 140; (*b*) *J. Chem. Soc.* (*A*), 1967, 936.

[17] (*a*) A. K. Covington, R. A. Robinson, and R. G. Bates, *J. Phys. Chem.*, 1966, **70**, 3820; (*b*) L. Pentz and E. R. Thornton, *J. Amer. Chem. Soc.*, 1967, **89**, 6931; (*c*) M. Goldblatt and W. M. Jones, *J. Chem. Phys.*, 1969, **51**, 1881.

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[19] C. A. Bunton and V. J. Shiner, *J. Amer. Chem. Soc.*, 1961, **83**, 42.

simultaneous equations which can be solved for ϕ_a and ϕ_b,[16] as is now shown.

Formula (I) is considered as a particular case of a solute with two sets of hydrogen nuclei (i, j), their respective numbers per formula being ν_i and ν_j. We define site fractionation factors (ϕ_i and ϕ_j) and a mean fractionation factor for the solute ($\bar{\phi}$) according to the conventional general expression (3), where n, μ_i, μ_j, and $\bar{\mu}$ are deuterium atom fractions, respectively in the solvent and in positions i and j, and overall in the solute. (More usually the symbol m is used for this quantity but it is not used here to avoid confusion.)

$$\phi = \mu(1 - n)/n(1 - \mu) \tag{3}$$

Rearrangement of (3) then leads to equations (4)—(6).

$$\mu_i = n\phi_i(1 - n + n\phi_i) \tag{4}$$

$$\mu_j = n\phi_j/(1 - n + n\phi_j) \tag{5}$$

$$\bar{\mu} = n\bar{\phi}/(1 - n + n\bar{\phi}) \tag{6}$$

For low deuterium abundance, $\mu \longrightarrow 0$, and multiple labelling in the same solute molecule can ·be neglected. The overall deuterium abundance in the solute will then be given by equation (7). The corresponding

$$\bar{\mu} = (\nu_i\mu_i + \nu_j\mu_i)/(\nu_i + \nu_j) \tag{7}$$

limiting forms of equations (4)—(6) are (8)—(10)

$$\mu_i = n\phi_i \tag{8}$$

$$\mu_j = n\phi_j \tag{9}$$

$$\bar{\mu} = n\bar{\phi} \tag{10}$$

which, when substituted in equation (7), lead to equation (11) according to which for low values of n, the overall fractionation factor of the solute is the arithmetic mean of the fractionation factors of the individual sites.

$$\bar{\phi} = (\nu_i\phi_i + \nu_j\phi_j)/(\nu_i + \nu_j) \tag{11}$$

Heinzinger and Weston[12] express their measurement of deuterium fractionation between the hydroxide ion and water at low values of n in terms of a parameter κ_H. We adapt their definition of this measured quantity to the ij-site case. The aqueous hydroxide ion $O_xH_h^-$ (where $h = \nu_i + \nu_j = 2x - 1$) is characterised by the overall fractionation factor $\bar{\phi}$ defined above [equations (12) and (13)]. We recognise that κ_H and $\bar{\phi}$ are functions of h by explicitly including h (or its particular numerical value) in the final position of the subscript. Combination of (12) and (13) establishes the interdependence of $\kappa_{\mathrm{H}h}$, $\bar{\phi}_h$, and h (equations 14—16, *cf.* Heinzinger and Weston's[12] equation 10). Heinzinger and Weston report the average value of κ_H1 as 4·21, with an average deviation of ±0·27, which implies $\bar{\phi}_1 = 0{\cdot}47_5$. The formula (I) represents the case $h = 4$, for which we then calculate $\bar{\phi}_4 = 0{\cdot}869$, and (17) as the special form of equation (11).

$$\kappa_{\mathrm{H}h} = \frac{[O_xH_h][HDO]}{[O_xDH_{h-1}][H_2O]} \tag{12}$$

$$\bar{\phi}_h = \frac{[O_xDH_{h-1}]}{h[O_xH_h]} \cdot \frac{2[H_2O]}{[HOD]} \tag{13}$$

$$\bar{\phi}_h = \frac{2}{h\kappa_{\mathrm{H}h}} \tag{14}$$

$$\kappa_{\mathrm{H}h}{}^{-1} = \frac{h - 1}{2} + \kappa_\mathrm{H1}{}^{-1} \tag{15}$$

$$\bar{\phi}_h = \frac{h - 1}{h} + \frac{2}{h\kappa_\mathrm{H1}} \tag{16}$$

$$\bar{\phi}_4 = (\phi_a + 3\phi_b)/4 \tag{17}$$

A trend of κ_H1 with hydroxide ion concentration over the range 7—12M is perceptible in the measurements and, although this is ' within or barely outside the limits of error ', one could argue that extrapolation to zero concentration is more compatible with $\kappa_\mathrm{H1} = 5{\cdot}6$, $\bar{\phi}_1 = 0{\cdot}356$, $\bar{\phi}_4 = 0{\cdot}839$. The discrepancy between the two sets of parameters reflects their limited accuracy even on the basis of careful and precise measurements.

Formula (I) requires the autoprotolysis to be written as equation (18), which implies that the solvent isotope effect $K_\mathrm{W}{}^\mathrm{D}/K_\mathrm{W}{}^\mathrm{H}$ is given by equation (19). Comparison

$$5H_2O \rightleftharpoons (OH(HOH)_3)^- + H_3O^+ \tag{18}$$

$$K_\mathrm{W}{}^\mathrm{D}/K_\mathrm{W}{}^\mathrm{H} = l^3\phi_a\phi_b{}^3 \tag{19}$$

of equations (2) and (19) shows the identity of the product $\phi_a\phi^3{}_b$ and ϕ^* for which the value 0·42 is calculated from our result[16,17] for $K_\mathrm{W}{}^\mathrm{D}/K_\mathrm{W}{}^\mathrm{H}$ (0·137).

Equations (17) and (19) can be combined to give (20) which allows evaluation of ϕ_b (and hence of ϕ_a) in terms of the experimentally determined qualities $\bar{\phi}_4$ and ϕ^*.

$$3\phi^4{}_b - 4\bar{\phi}_4\phi_b{}^3 + \phi^* = 0 \tag{20}$$

Table 1 gives solutions of equation (20) corresponding to a range of values of $\bar{\phi}_4$. There are two physically possible roots for ϕ_b for each pair of plausible values of ϕ^* and $\bar{\phi}_4$. One of these is always close to unity: this is in the range previously considered by Gold and Lowe[16] and for which the value of ϕ_a is close to that of ϕ^*. The other solution for ϕ_b, now considered to be the more acceptable one, lies in the range 0·64—0·68

TABLE 1

Values of ϕ_a and ϕ_b compatible with equations (17), (19), and (20), and $\phi^* = 0{\cdot}471$

		First root		Second root	
$\bar{\phi}_4$	κ_H1 †	ϕ_b	ϕ_a	ϕ_b	ϕ_a
0·829	6·33	0·936	0·508	0·700	1·22
0·839	5·62	0·963	0·467	0·684	1·30
0·849	5·05	0·988	0·433	0·670	1·39
0·859	4·59	1·011	0·404	0·658	1·46
0·869	4·20	1·032	0·380	0·648	1·53
0·879	3·88	1·053	0·357	0·639	1·60

† Heinzinger and Weston consider κ_H1 to have a value in the range 4·21 ± 0·27.

and requires a value of ϕ_a greater than unity (1·3—1·6). Because ϕ_b is cubed in (19), the complementary value of ϕ_a is sensitive to the precise value of ϕ_b. For this solution the values of ϕ_b and ϕ^* are quite different.

Further, though not quite independent, evidence concerning the values of ϕ_a and ϕ_b comes from the dependence of K_W on the isotopic composition n. According to equation (18) and formula (I) and on the assumption of validity of the rule of the geometric mean, the value of $(K_W)_n$ is given by equation (21) or, if this is combined with equation (19), by equation (22) [which is equation (32) of reference 16*b*]. Gold and

$$(K_W)_n = K_W{}^H[1 - n + nl]^3[1 - n + n\phi_a][1 - n + n\phi_b]^3 \quad (21)$$

$$(K_W)_n = K_W{}^H[1 - n + nl]^3[1 - n + n\phi_b]^3[1 - n + n(K_W{}^D/K_W{}^H)^{-3}\phi_b{}^{-3}] \quad (22)$$

Lowe[16] fitted their experimental data to equation (22) and deduced $\phi_b = 0{\cdot}92$. However, again this is not a unique solution. If one accepts that ϕ_b can be further removed from unity, as the present arguments require but was not considered in the earlier work,[16] a second solution, $\phi_b = 0{\cdot}70 \pm 0{\cdot}02$, gives an equally good least-squares fit to the data. [The existence of two possible values of the medium effect in Gold and Lowe's[16b] equation (30) was pointed out to the authors by Professor F. A. Long: this conclusion is mathematically, though not chemically, equivalent to the present treatment.] The evaluation of the best values of ϕ_a and ϕ_b from a least-squares procedure applied to equation (21), and the unsmoothed experimental values of $(K_W)_n$, in fact constitutes a better set of data than the extrapolated ratio $K_W{}^D/K_W{}^H$. Altogether, it does not seem that we can at this stage fix the values of the fractionation factors more closely than the approximate ranges 0·65—0·70 for ϕ_b and 1·2—1·5 for ϕ_a.

The deduction that ϕ_b is less than unity implies that the stabilisation caused by the hydrogen bonding of a water molecule to hydroxide ion is *diminished* in a deuteriated system. A similar conclusion follows even more directly from the n.m.r. determination of the fractionation factors for methanolic methoxide.[1,2] The value of ϕ tells us that (compared with MeOH) MeOD molecules prefer a site in the bulk of the solvent to one hydrogen-bonded to a methoxide ion.

From the deduction that D_2O is a more structured solvent than H_2O it is generally assumed that $-O-D \cdots O$ bonds are stronger than the corresponding $-O-H \cdots O$ bonds.[20] Superficially this appears to be the opposite conclusion from that now proposed, but in fact there need be no contradiction. It is the stability of a hydrogen-bonded system *relative to the isolated molecules* which seems to be enhanced by deuteriation of the hydrogen bonds. What we conclude from the value of the fractionation factor is that deuteriation enhances the stability of hydrogen bonds between hydroxide ion as solute and solvent by less (or decreases it more) than it affects the stability of hydrogen bonds between solvent molecules (which must be ruptured in order to provide solvent–solute bonding). In different terminology, these ideas are implicit in Bunton and Shiner's semi-quantitative rules for the estimation of solvent isotope effects.[19] This decreased differential stabilisation of the hydroxide ion by hydrogen-bonding from deuterium oxide also rationalises the generally accepted conclusion that OD^- is a better base than OH^-. It would also appear that formula (I), in which the O–H bonds of attached water molecules are unequal, should be used in the calculation of the solvent isotope effect from assumed vibrational and librational frequencies, in preference to the usual approach in which such a distinction is not made.[12,17c,18]

It is of interest to see to what extent these conclusions form a basis for discussing solvent isotope effects on rates of reaction in which the hydroxide ion is a reactant. One such case is the ionisation of 2-nitropropane in aqueous sodium hydroxide, a reaction by which hydroxide ions are being consumed. Equation (23) is a conventional representation for this type of process, equation (24) re-states this with explicit inclusion of the hydration of the hydroxide ions. The extreme

$$\mathrm{SH + OH^- \longrightarrow S^- + H_2O} \quad (23)$$

$$\mathrm{SH + OH^-(HOH)_3 \longrightarrow S^- + 4H_2O} \quad (24)$$

solvent isotope effect (k_D/k_H) on the ionisation of nitroethane and 2-nitropropane by reaction with hydroxide ion was first studied over 30 years ago by Maron and LaMer[21] whose values (for k_D/k_H at 5 °C, 1·39 and 1·36, respectively) are well confirmed by a more recent study of nitroethane[22] (1·40) and in the present work for 2-nitropropane (k_D/k_H at 25 °C = 1·35). A number of other hydroxide-destroying reactions also have solvent isotope effects (k_D/k_H) mainly in the range 1·3—1·4 [*e.g.* the hydrolyses of ethyl acetate,[23] (1·33), monochloroacetate ion[24] at 45 °C (1·2), phenyl acetate[25] (1·35), and of chloramine,[26] a case where a secondary isotope effect is included,(1·30); the racemisation of mandelate ion[27] (1·39) and hydrogen abstraction from acetone[28] (1·47); hydrogen isotope exchange in phenylacetylene,[29] (1·33), in t-butylmalononitrile[30] (1·72)

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[27] Y. Pocker, *Chem. and Ind.*, 1958, 1117.

[28] Y. Pocker, *Chem. and Ind.*, 1959, 1383.

[29] E. A. Halevi and F. A. Long, *J. Amer. Chem. Soc.*, 1961, **83**, 2809.

[30] F. Hibbert and F. A. Long, *J. Amer. Chem. Soc.*, 1971, **93**, 2836.

and in the 9-position of 9-fluorenylmethanol[31] (1·49); elimination reactions of four β-arylethyl-sulphonium and -ammonium bromides[32] (1·57—1·79) and hydroxide addition to substituted *N*-methylfluoroacetanilides[33] (nine values between 1·23 and 1·41, one value 1·71). The general result is well recognised and has been discussed in recent reviews from different points of view.[34]

These solvent isotope effects are consistently lower than corresponding effects for similar reactions with methoxide ions in methanol solution. This is most unambiguously shown for the ionisation of 2-nitropropane (k_D/k_H in methanol[3] = 2·28, in water = 1·35) under precisely comparable conditions.

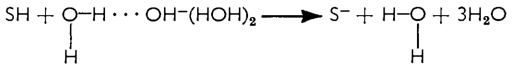
At a somewhat superficial level the difference could simply be ascribed to the role of H_a in formula (I), since this evidently has no counterpart in the methoxide ion. The maximum observable solvent isotope effect for reaction (24) should presumably correspond to a completely product-like transition state, *i.e.* $(k_D/k_H)_{max.} = (\phi_a\phi_b^3)^{-1} = (\phi^*)^{-1} = 2{\cdot}4$ and this is, in fact, though only slightly, less than the corresponding maximum isotope effect for methanol solution, *i.e.* $(k_D/k_H)_{max.} = \phi_b^{-3} = 2{\cdot}5$ (N.B.: ϕ_b for methoxide differs from ϕ_b for hydroxide). One might then expect the transition state for the actual reaction to correspond to partial progress (β, where $1 > \beta > 0$) of the hydroxide group towards being water-like and accordingly expect the actual isotope effect to be given by[33] equation (25).

$$k_D/k_H = (k_D/k_H)^{\beta}_{max.} \qquad (25)$$

The observed values of k_D/k_H would then suggest very different values of β for the ionisation of 2-nitropropane in water (0·35) and in methanol (0·9), since $1{\cdot}35 = 2{\cdot}4^{0{\cdot}35}$ and $2{\cdot}28 = 2{\cdot}5^{0{\cdot}9}$. However the observed primary substrate deuterium isotope effects [*i.e.* $k(Me_2CHNO_2)/k(Me_2CDNO_2)$] are almost identical in the two media (7·6 ± 0·2 with hydroxide in H_2O, 7·4 ± 0·1 with methoxide[3] in MeOH) suggesting a close similarity between the transition states (and in the value of β). Furthermore, the large size of the primary isotope effect points to a value of β in the region of one-half.[35] Similar conclusions can be reached from solvent isotope effects in water and methanol for triton abstraction from 9-fluorenylmethanol.[31,36]

We recognise that it would be an oversimplification to assume that only the two fractionation factors of the two sites, ϕ_a and ϕ_b, and their change on formation of the transition state, characterised by β, need enter into the calculation of the solvent isotope effect. Other sites, particularly those concerned in hydrogen-bonding to the incipient anionic oxygen atoms of the forming nitroalkanate ion, may also be expected to be involved to a significant extent. Goodall and Long[37] have discussed a related problem in connection with the conjugate base of nitroethane and have inferred that $CH_2NO_2^-$ is considerably more destabilised (or less stabilised) on transfer from H_2O to D_2O than the acetate ion. The kinetic solvent isotope effects of the hydroxide ion-destroying reactions can be thought similarly to require a positive free energy of transfer of the transition state from H_2O to D_2O, thereby causing the ratio k_D/k_H to be smaller than expected. The occurrence of a normal solvent isotope effect in methanol would, on this view, imply smaller transfer effects and weaker hydrogen bonding in the methanol system. This is a reasonable supposition, though the size of the difference in isotope effect between the aqueous and the methanol system would still be puzzling.

However, it seems doubtful to us that the kinetic solvent isotope effect for rates of hydroxide (and methoxide) ion-destroying reactions can be formulated on the basis of a transition state which is simply characterised by partial progress (β) from reactants to products in a single process (23) or (24). If the aqueous hydroxide ion is correctly formulated as (I) then it is not possible for direct proton transfer from SH to OH^- to take place without simultaneous expansion of the co-ordination of the hydroxide oxygen from four to five. Conversely, it would follow that the reverse reaction, proton transfer from water to the conjugate base of 2-nitropropane, would involve a water molecule with *three* other water molecules hydrogen-bonded to its oxygen. These implications seem unattractive and, accordingly, we believe that proton abstraction from SH by hydroxide ions would involve steps which avoid the five-co-ordinate oxygen atom. Equations (26) and (27) represent two such schemes (without explicit inclusion of any water molecules hydrogen-bonded to S^- or the incipient S^- of the transition state).



$$SH + \underset{\displaystyle H}{\underset{|}{O}}{-}H\cdots OH^-(HOH)_2 \longrightarrow S^- + H{-}\underset{\displaystyle H}{\underset{|}{O}} + 3H_2O \qquad (26)$$

$$SH + OH^-(HOH)_3 \rightleftharpoons SH + OH^-(HOH)_2 + H_2O \longrightarrow S^- + 4H_2O \qquad (27)$$

In equation (26) proton transfers occur from SH to one of the hydrogen-bonded water molecules of the hydroxide ion and from that water molecule to the hydroxide moiety. According to (27) the reactive species is an incompletely hydrated hydroxide ion. Such ions are bound to be present to some extent in a solution which is not perfectly ordered. On the available evidence it does not seem possible to assess the

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[31] R. A. More O'Ferrall and S. Slae, *J. Chem. Soc.* (*B*), 1970, 260.

[32] L. J. Steffa and E. R. Thornton, *J. Amer. Chem. Soc.*, 1967, **89**, 6149.

[33] L. D. Kershner and R. L. Schowen, *J. Amer. Chem. Soc.*, 1971, **93**, 2014.

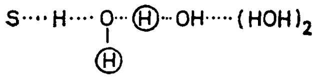
[34] P. M. Laughton and R. E. Robertson, in 'Solute-Solvent Interactions,' J. F. Coetzee and C. D. Ritchie, eds., Dekker, New York, 1969; R. L. Schowen, *Progr. Phys. Org. Chem.*, to be published; E. K. Thornton and E. R. Thornton, in 'Isotope Effects in Chemical Reactions', eds. C. J. Collins and N. B. Bowman, Van Nostrand–Reinhold, New York, 1971.

[35] F. H. Westheimer, *Chem. Rev.*, 1961, **61**, 265; J. Bigeleisen, *Pure Appl. Chem.*, 1964, **8**, 217; R. P. Bell and D. M. Goodall, *Proc. Roy. Soc.* (*A*), 1966, **294**, 273; J. E. Dixon and T. C. Bruice, *J. Amer. Chem. Soc.*, 1970, **92**, 905, and references cited therein.

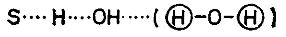
[36] R. A. More O'Ferrall, *J. Chem. Soc.* (*B*), 1970, 268.

[37] D. M. Goodall and F. A. Long, *J. Amer. Chem. Soc.*, 1968, **90**, 238.

absolute or relative merits of these schemes. However, they have one feature in common which is germane to the discussion of the solvent isotope effect. The respective transition states [(II) and (III)] do not only



(II)



(III)

contain exchangeable hydrogen atoms (ringed) which are intermediate in character between reactants and products. (Of course, the proton in transit from SH likewise occupies in the transition state a position which, in strength of bonding for example, is not intermediate between its initial and final states but, since it is not in isotopic exchange equilibrium with the solvent, we must not include it here.) Consequently, we cannot simply describe the fractionation factors of these atoms in terms of their fractionation factors in the reactant and product states, raised to an exponent to express the partial progress from reactants to products. It follows that the exponent β in (25) is not a straightforward index of transition-state structure.

If proton transfer to lyate ions (and, conversely, proton transfer from solvent to a solute) is a co-operative process, as in equation (26), then that marked difference between the aqueous and methanolic lyate ions in their kinetic behaviour is at least not without parallel. The ionic mobility of aqueous hydroxide ions is abnormally high and indicative of a chain conduction mechanism, whereas the mobility of methoxide ions in methanol is normal.[38] This contrasts with the behaviour of the corresponding hydrogen ions: their conductance is abnormally high in both solvent systems. In fact, none of these difficulties [and hence a need to invoke complex mechanisms, such as (26) or (27)] arises with catalysis by hydrogen ions, for which the solvent isotope effect in methanol solution appears to be closely analogous to that in aqueous solution. (Similarly, one would expect the reverse process, proton abstraction by the solvent acting as a base, to be uncomplicated.)

Finally, attention is drawn to the observation, made for both methanolic and aqueous solutions, that the primary deuterium isotope effect in the ionisation of 2-nitropropane by reaction with lyate anions is slightly greater in the light solvent as compared to the deuteriated solvent. A solvent isotope effect on a primary isotope effect in the same direction has previously been noted for the zero-order iodination of pentan-3-one catalysed by pyridine and by 2,6-lutidine.[39] Taken together, these various examples suggest that the observations are genuine and that this phenomenon merits more systematic attention. It could be that involvement of solvent as in equation (27) would result in some interaction between solvent and solute effects and a closer study might shed some light on this.

TABLE 2

Reaction of 2-nitropropane with hydroxide ions in H_2O–D_2O mixtures

(Ionic strength = 0·1M)

n	$10^4[OL^-]/M$	$10^5k/s^{-1}$	$10^5k_2 l/ mol^{-1} s^{-1}$
0·0	90·1	287	318
0·0	189	659	349
0·0	266	953	359
0·0	362	1277	352
0·0	453	1600	353
0·0	550	1950	354
0·0	638	2280	358
0·0	728	2530	348
0·0	832	2930	352
0·0	890	3230	363
0·0	1000	3530	353
0·0	1000	3570	357
0·0	1000	3650	365
0·0924	330	1190	361
0·0947	500	1781	356
0·2066	330	1202	364
0·2067	500	1824	365
0·2969	331	1221	370
0·3907	331	1242	374
0·4017	496	1891	381
0·4884	499	1989	399
0·4991	332	1301	392
0·5853	502	2100	418
0·6503	333	1359	409
0·6907	501	2080	415
0·6922	500	2030	406
0·6945	333	1381	414
0·7503	333	1460	438
0·7995	501	2230	445
0·9114	501	2240	447
0·9946	175	782	447
0·9946	180	834	463
0·9946	271	1360	501
0·9946	341	1640	480
0·9946	366	1730	472
0·9946	467	2250	482
0·9946	513	2440	476
0·9946	544	2600	478
0·9946	641	3070	479
0·9946	851	4070	478
0·9946	1000	4640	464
0·9946	1000	4680	468

TABLE 3

Primary substrate isotope effect on the reaction of 2-nitropropane with hydroxide ion in H_2O and in D_2O

(Ionic strength = 0·1M)

A. In H_2O					
Approx. $10^3[OH^-]/M$	16	24	34	42	50
$10^5k(Me_2CHNO_2)/s^{-1}$	577 560	857 852	1177 1260	1466 1468	1752 1775
$10^6k(Me_2CDNO_2)\ s^{-1}$	796 757	1148 1146	1555 1587	1928 1890	2250 2270
Mean ratio	7·32	7·45	7·58	7·76	7·80
B. In D_2O					
Approx. $10^3[OD^-]/M$	13	21	26	40	54
$10^5k(Me_2CHNO_2)/s^{-1}$	624 616	998 994	1235 1221	1931 1894	2550 2659
$10^6k(Me_2CDNO_2)/s^{-1}$	849 852	1352 1388	1663 1722	2601 2629	3662 3415
Mean ratio	7·29	7·27	7·30	7·31	7·37

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[38] See S. Glasstone, K. J. Laidler, and H. Eyring, 'The Theory of Rate Processes,' McGraw-Hill, New York, 1941, ch. X.

[39] J. P. Calmon, M. Calmon, and V. Gold, *J. Chem. Soc.* (*B*), 1969, 659.

EXPERIMENTAL

The sample of 2-nitropropane was identical with that used for kinetic work in methanol solution.[3] Solutions of sodium hydroxide in water and in deuterium oxide were made up and handled only in a CO_2-free glove box. The concentration of protium introduced by the use of NaOH to make up the dilute hydroxide solutions in D_2O is trivially small. The kinetic procedures were the same as for the experiments in methanol, except that potassium chloride was used in the present work to maintain the ionic strength constant.

The results for the rate measurements of the ionisation of 2-nitropropane are given in Table 2. Second-order rate constants for different concentrations of deuterium in the solvent (atom fraction n) ($k_2 = k_{obs}/[OL^-]$) were fitted to a polynomial (28), the extrapolation of which gives the extreme solvent isotope effect, $k_D/k_H = 1{\cdot}35$. Primary (substrate) isotope effects were determined as in previous work [3] and on the same materials (Table 3).

$$k_n = 0{\cdot}352 + 0{\cdot}0434n + 0{\cdot}0658n^2 + 0{\cdot}0144n^3 \quad (28)$$

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