The Hydrolysis of Ethyl Vinyl Ether. Part II.[1] Solvent Isotope Effects

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The deuterium isotope effect on hydrogen ion transfer from the hydronium ion to ethyl vinyl ether is 2·95, and that for transfer from formic acid is 6·8. Solvent isotope effects in H_2O–D_2O mixtures on the reaction with hydronium ion show that there is a secondary isotope effect of 0·65 and that the changes in the system which govern the magnitude of this effect are about half complete at the transition state. However, primary isotope effects calculated from this secondary effect and the observed rate ratio are only about half of their maximum values; this suggests that the two different parts of the reaction co-ordinate which govern the primary and the secondary isotope effects are not closely coupled. The hydronium ion reaction shows no tunnel effect near room temperature; the entropy of activation of this reaction is −11 cal. deg.$^{-1}$ mole^{-1}.

THE acid-catalysed hydrolysis of ethyl vinyl ether is a reaction whose initial and rate-determining step is proton transfer from the catalyst to the substrate.[1] In this reaction, therefore, unlike in many cases of acid catalysis where proton transfer occurs in a rapid pre-equilibrium, the proton transfer process is isolated kinetically, and kinetic measurements can lead directly to information about the proton transfer transition state. Since proton transfer is an important elementary chemical process, and since the number of acid-catalysed reactions in which it can be studied in isolation is still quite small, we have undertaken a detailed investigation of ethyl vinyl ether hydrolysis. We now report our results concerning solvent isotope effects.

RESULTS

Rates of hydrolysis were measured by following the decrease in absorbance of ethyl vinyl ether at 2280 Å; the kinetics were first-order to a high degree of precision.

Catalysis by Perchloric Acid.—Isotope effects on the hydrolysis of ethyl vinyl ether catalysed by the hydronium ion at 26·7° were determined by measuring rates of reaction in H_2O and in D_2O solutions of identical perchloric acid concentration (10^{-2}M) and in mixtures of these two solutions. The data are summarised in Table 1, and the variation of rate constant with solvent deuterium content is shown in Figure 1. These measurements provide a

TABLE 1

Rates of hydrolysis of ethyl vinyl ether catalysed by perchloric acid in H_2O, D_2O, and H_2O–D_2O mixtures at 26·7° *

Solvent composn. (parts)		$10^2 k_1$ (sec.$^{-1}$)	10^2 Std. devn. of mean value	No. of measurements
H_2O	D_2O †			
1·00	0·00	2·064	0·006	4
4·00	1·00	1·964	0·009	6
3·00	2·00	1·780	0·016	7
2·00	3·00	1·591	0·015	4
1·00	4·00	1·207	0·013	6
0·00	1·00	0·705	0·001	4

* Perchloric acid concentration, $9·57 \times 10^{-3}$M. † 99·5 atom % deuterium.

value of 2·93 ± 0·03 for the ratio of rate constants in H_2O to those in D_2O containing 99·5 atom % deuterium;

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[1] Part I, preceding Paper.

linear extrapolation to 100% D_2O gives 2·95 ± 0·03 as the deuterium isotope effect on catalysis by the hydronium ion.
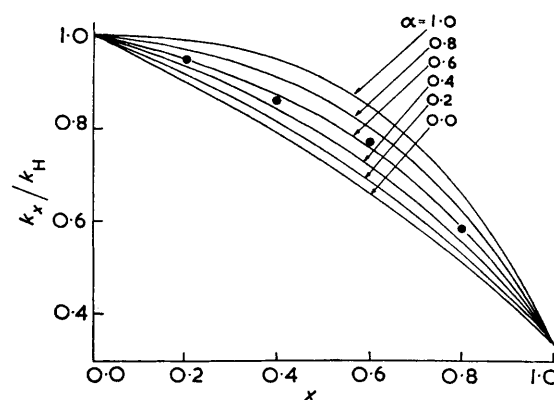

FIGURE 1 Relationship between solvent isotopic composition, x, and the solvent effect, k_x/k_H, on ethyl vinyl ether hydrolysis catalysed by perchloric acid in H_2O–D_2O mixtures; large dots represent observed values, and lines are calculated from equation (4) with $l = 0·7$
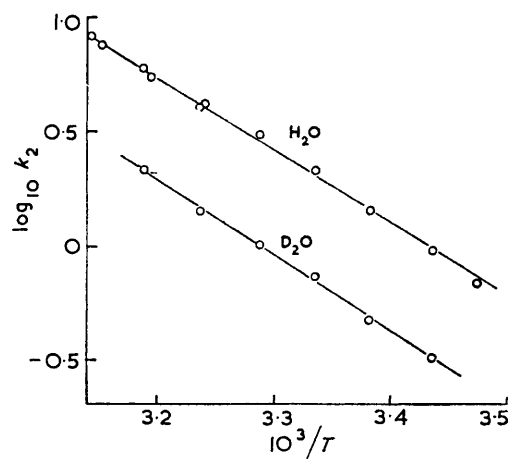

FIGURE 2 Arrhenius plots for the hydrolysis of ethyl vinyl ether catalysed by perchloric acid in H_2O and in D_2O solutions

Rates of hydrolysis of ethyl vinyl ether catalysed by perchloric acid in H_2O and in D_2O solution were also measured as a function of temperature. The results in both solvents (Table 2) conform to the Arrhenius equation within the limits of the accuracy of the measurements (Figure 2). Energies of activation and pre-exponential factors were evaluated by least-square analysis of plots of log k_2 against

TABLE 2

Temperature-dependence of rates of hydrolysis of ethyl vinyl ether catalysed by perchloric acid in H_2O and D_2O solutions

	T (°C)	k_2 (l. mole^{-1} sec.$^{-1}$)	Std. devn. of mean value	No. of measurements
H_2O: *	45·05	8·28	0·09	5
	44·30	7·69	0·07	4
	40·40	5·98	0·04	5
	39·80	5·29	0·03	4
	35·70	4·04	0·07	5
	35·45	4·08	0·05	5
	30·90	3·032	0·003	5
	26·60	2·138	0·011	5
	22·50	1·441	0·006	5
	17·85	0·954	0·001	5
	13·70	0·685	0·001	2
D_2O: †	40·40	2·140	0·008	5
	35·70	1·446	0·008	5
	30·90	1·019	0·008	5
	26·65	0·729	0·001	4
	22·50	0·746	0·002	4
	17·85	0·323	0·001	3

* Perchloric acid concentration, $5·16 \times 10^{-3}$M or $9·57 \times 10^{-3}$M. † 99·5 Atom % deuterium; perchloric acid concentration, $1·58 \times 10^{-2}$M.

$1/T$, and enthalpies and entropies of activation by analysis of plots of log (k_2/T) against $1/T$; the values of these parameters for both solvents are summarised in Table 3.

Catalysis by Formic Acid.—Rates of hydrolysis of ethyl vinyl ether were measured in formic acid–sodium formate buffer solutions in D_2O. Rate constants decreased with decreasing buffer acid concentration, and least-squares fitting of the data (Table 4) to a linear relationship gave the equation:

$$k_1 \text{ (sec.}^{-1}) = (4·65 \pm 0·07) \times 10^{-5} + (1·295 \pm 0·036) \times 10^{-3}[DA] \quad (1)$$

The catalytic coefficient for formic [²H]acid so obtained, when combined with that determined for ordinary formic acid under the same conditions of buffer ratio, buffer concentrations, and ionic strength,[1] gives $6·80 \pm 0·29$ as the ratio of rate constants for formic acid catalysis in H_2O to

TABLE 3

Activation parameters for the hydrolysis of ethyl vinyl ether catalysed by perchloric acid in H_2O and D_2O solutions *

	E_a (kcal./mole)	$10^{10}A$ (l. mole^{-1} sec.$^{-1}$)	$\Delta H^{\ddagger}$ (kcal./mole)	$\Delta S^{\ddagger}$ (cal./deg.)
H_2O:	$14·4 \pm 0·2$	$6·6 \pm 1·7$	$13·8 \pm 0·2$	$-11·1 \pm 0·5$
D_2O: †	$15·2 \pm 0·3$	$8·5 \pm 4·3$	$14·6 \pm 0·3$	$-10·5 \pm 1·0$

$E_a(H_2O) - E_a(D_2O) = 0·8 \pm 0·4$ kcal./mole
$A(H_2O)/A(D_2O) = 0·7 \pm 0·4$

* Uncertainties reported are standard deviations of mean values. † 99·5 Atom % deuterium.

those in D_2O containing 99·5 atom % deuterium; linear extrapolation to 100% D_2O gives $6·83 \pm 0·29$ as the deuterium isotope effect on catalysis by formic acid. The ratio

² P. Glascoe and F. A. Long, *J. Amer. Chem. Soc.*, 1960, **64**, 188; R. P. Bell and A. T. Kuhn, *Trans. Faraday Soc.*, 1963, **59**, 1789.

of intercepts of plots of k_1 against buffer acid concentration for the experiments in the two solvents together with the known [2] ratio of dissociation constants for formic acid in H_2O and in D_2O gives $k_H/k_D = 2·85 \pm 0·06$ as the isotope

TABLE 4

Rates of hydrolysis of ethyl vinyl ether in deuterium oxide solutions of formic acid buffers at 26·7° *

Buffer ratio 0·75; μ 0·040

$10^2[HA]$ (M)	10^2k_1 (sec.$^{-1}$)	$10^2[HA]$ (M)	10^2k_1 (sec.$^{-1}$)
0·600	5·30	1·80	7·03
0·600	5·48	2·40	7·67
1·20	6·18	3·09	8·62
1·20	6·30	3·00	8·47

k_{obs} (sec.$^{-1}$) = $(4·65 \pm 0·07) \times 10^{-5} + (1·295 \pm 0·036) \times 10^{-3}[DA]$.

* 99·5 Atom % deuterium.

effect on catalysis by the hydronium ion. This is in good agreement with the value $2·93 \pm 0·03$ obtained directly from the experiments in perchloric acid solutions described above.

DISCUSSION

H_2O–D_2O *Mixtures.*—Although the solvent isotope effect in H_2O–D_2O mixtures is no longer considered to be a useful criterion of reaction mechanism,[3,4] it can, in favourable cases, provide valuable information concerning the nature of the transition state in reactions of known mechanism.[4] In particular, it can show the position which the transition state occupies on the reaction co-ordinate for reactions in which proton transfer from the hydronium ion to the substrate occurs in the rate-determining step and in which the limiting isotope effect, $k(H_2O)/k(D_2O)$, is appreciably greater than unity. The hydrolysis of ethyl vinyl ether is a process which meets these requirements.

The transition state in ethyl vinyl ether hydrolysis catalysed by the hydronium ion is a species (I) in which

$$[H_2O^{\delta+} \text{---} H \text{---} {}^{\delta+}S]^{\ddagger} \quad (I)$$
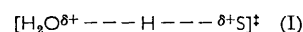
the proton being transferred is bonded partly to a water molecule and partly to the substrate, S. The structure of one part of this transition state (the part on the left) is intermediate between the structure of a hydronium ion and the structure of a molecule of liquid water; it is useful to describe the resemblance between this part of the transition state and a molecule of water in terms of a parameter α. This parameter will have the numerical limits zero and unity, and its value will measure the extent to which certain changes occurring in the system during this reaction step have progressed by the time the transition state is reached.

This transition state contains only two different kinds of hydrogen atom, and its isotopic composition, when it is formed in H_2O–D_2O mixtures, can therefore

³ V. Gold, *Trans. Faraday Soc.*, 1960, **56**, 255; P. Salomaa, L. L. Schaleger, and F. A. Long, *J. Amer. Chem. Soc.*, 1964, **86**, 1; H. H. Huang, R. R. Robinson, and F. A. Long, *ibid.*, 1966, **88**, 1866.
⁴ A. J. Kresge, *Pure Appl. Chem.*, 1964, **8**, 243.

be characterised by two fractionation factors.* Since the structure of the water-like portion of this transition state is intermediate between that of a hydronium ion and that of a water molecule, and since the position it occupies relative to these limits is measured by α, then the fractionation factor for the hydrogens in this part of the system can be expressed in terms of α and l, the fractionation factor for the hydronium ion, as $l^{1-\alpha}$. The fractionation factor for the other kind of hydrogen in this transition state, that being transferred, may be given the symbol ϕ. The theory of solvent isotope effects in H_2O–D_2O mixtures [4] then leads to the following expression relating x, the $D/(D + H)$ ratio of the solvent, to k_x/k_H, the isotope effect in a solvent composition x:

$$\frac{k_x}{k_H} = \frac{(1 - x + xl^{1-\alpha})^2(1 - x + x\phi)}{(1 - x + xl)^3} \quad (2)$$

Of the parameters in equation (2), l is known to be $0\cdot7$,[5] and ϕ can be expressed in terms of l, α, and k_D/k_H, the limiting solvent isotope effect, by taking the limit of equation (2) as x approaches unity:

$$k_D/k_H = l^{-(1 + 2\alpha)}\phi \quad (3)$$

Thus,

$$\frac{k_x}{k_H} = \frac{(1 - x + xl^{1-\alpha})^2(1 - x + xl^{1+2\alpha}k_D/k_H)}{(1 - x + xl)^3} \quad (4)$$

The parameter α can therefore be evaluated by comparing experimentally determined values of k_x/k_H with those calculated from equation (4). Figure 1 shows that the data of Table 1 for ethyl vinyl ether hydrolysis are consistent with a value for α of *ca.* $0\cdot6$.

This value of α implies that the changes which occur in that part of the system which beomes a water molecule during the first step of ethyl vinyl ether hydrolysis catalysed by the hydronium ion are $0\cdot6$ complete by the time the transition state is reached, *i.e.*, that the transition state occupies a position which is $0\cdot6$ of the way along this part of the reaction co-ordinate for this elementary step. The exponent α in the Brönsted relationship is also believed to be a measure of the position occupied by the transition state in a proton transfer reaction,[6] and Brönsted's α for this reaction, based on the limited information so far available,[1] is *ca.* $0\cdot5$. The agreement between these two measures of transition state structure is therefore good.

Limiting Isotope Effects.—The data of Table 1 show that the limiting solvent isotope effect on hydrogen ion transfer from the hydronium ion to ethyl vinyl ether at $26\cdot7°$ is $2\cdot95(k_H/k_D)$. This isotope effect is the product of a normal primary isotope effect on the hydrogen in transit and an inverse secondary isotope effect which resides in the non-reacting (in the sense that they are not being broken) but isotopically substituted bonds of the hydronium ion.[7,8] Such a secondary isotope effect will, of course, be absent in the case of hydrogen ion transfer from an acid containing only one hydrogen atom which can exchange with the solvent, and it is not surprising, therefore, that the limiting solvent isotope effect on ethyl vinyl ether hydrolysis catalysed by formic acid, $k_H/k_D = 6\cdot8$, is appreciably larger than that on catalysis by the hydronium ion.

Solvent isotope effect theory predicts [8] that the secondary isotope effect on hydrogen ion transfer from the hydronium ion will be equal to $l^{2\alpha}$, where α is the parameter defined in the section above and l is the D–H fractionation factor for the hydronium ion. Since α has been determined for the present case from isotope effect measurements in H_2O–D_2O mixtures, the secondary isotope effect can be evaluated as $0\cdot65(k_H/k_D)$. The observed limiting isotope effect, $k_H/k_D = 2\cdot95$, is, of course, the product of this secondary effect and the primary isotope effect on the hydrogen in transit, and this primary effect is therefore $2\cdot95/0\cdot65 = 4\cdot5$.

Once α has been determined, still another primary isotope effect can be calculated. According to equation (3), ϕ, the fractionation factor for the hydrogen in transit, is equal to $l^{1+2\alpha}k_D/k_H$ or $0\cdot155$. The reciprocal of ϕ, $6\cdot5$, is the primary isotope effect (k_H/k_D) on the hypothetical reaction in which the initial state is ethyl vinyl ether plus a molecule of liquid water and the transition state is that depicted above for hydrolysis catalysed by the hydronium ion (I).

These two primary isotope effects on hydrogen ion transfer occurring through transition state (I), that on transfer from the hydronium ion and that on transfer from a molecule of water, are surprisingly small. The parameter α has a value close to $\frac{1}{2}$. This implies that those changes in the system which occur during the first step of the reaction and produce the secondary isotope effect are half complete at the transition state. It seems reasonable to expect that this part of the reaction co-ordinate should be coupled with the part governing the primary isotope effect, and that the changes occurring there would be half complete at the transition state as well. This implies that the hydrogen in transit is half transferred at the transition state, and this should give rise to primary isotope effects whose values are nearly maximum.[9] But the observed effects are considerably less than maximum values. Isotope effects

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* The fractionation factors employed in this discussion are defined in the usual way as the D/H ratio at some particular site divided by the D/H ratio of the solvent.

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[6] J. E. Leffler and E. Grunwald, " Rates and Equilibria of Organic Reactions," Wiley, New York, 1963, p. 158.

[7] C. A. Bunton and V. J. Shiner, jun., *J. Amer. Chem. Soc.*, 1961, **83**, 42, 3207, 3214; C. G. Swain and E. R. Thornton, *ibid.*, p. 3884; A. J. Kresge and Y. Chiang, *ibid.*, 1962, **84**, 3976.

[8] A. J. Kresge and D. P. Onwood, *J. Amer. Chem. Soc.*, 1964, **86**, 5014; M. M. Kreevoy, P. W. Steinwand, and W. V. Kayser, *ibid.*, p. 5013.

[9] F. W. Westheimer, *Chem. Rev.*, 1961, **61**, 265; J. Bigeleisen, *Pure Appl. Chem.*, 1964, **8**, 217; A. V. Willi and M. Wolfsberg, *Chem. and Ind.*, 1964, 2097; R. P. Bell, *Discuss. Faraday Soc.*, 1965, **39**, 16.

calculated on the basis of complete loss of the zero-point energy of one stretching vibration are 7·8 for hydrogen ion transfer from the hydronium ion ($\omega = 2900$ cm.$^{-1}$) [10] and 11 for hydrogen ion transfer from a water molecule ($\omega = 3400$ cm.$^{-1}$); these are nearly twice the experimental values of 4·5 and 6·5, respectively. The discrepancy is even greater if bending vibrations are included in the estimation of maximum effects.*

This discrepancy is, of course, dependent on arguments based on the current theory of solvent isotope effects, and this theory may be inadequate. Assuming, however, that the theory does describe the situation correctly, it would seem that different parts of the reaction co-ordinate for the first step of ethyl vinyl ether hydrolysis are not closely coupled in the sense that the changes which govern the secondary isotope effect are being completed at the same rate as the changes which control the primary isotope effect.

Temperature Coefficients of Reaction Rates.—The tunnel effect is known to occur in some hydrogen transfer reactions.[12] This phenomenon can lead to anomalous isotope effects, and these might invalidate an analysis such as that presented above. Two criteria are commonly applied to detect tunneling in hydrogen transfer reactions: the tunnel effect can produce a curved Arrhenius plot, and it is usually accompanied by a ratio of pre-exponential factors in the Arrhenius equations for protium and deuterium transfer (A_H/A_D) which is less than 0·5.[13] For ethyl vinyl ether hydrolysis catalysed by the hydronium ion, both of these criteria indicate that the tunnel effect is absent; Arrhenius plots show no systematic deviation from linearity (Figure 2) and $A_H/A_D = 0·7$ (Table 3).

It is perhaps not unexpected that the hydrolysis of ethyl vinyl ether catalysed by the hydronium ion should show no tunnel effect, for the energy of activation of this reaction is only 14 kcal./mole (Table 3). Theoretical calculations [13,14] predict that sizeable tunnel effects will occur only in reactions with fairly large energy barriers; this is borne out by experience.[12]

The entropy of activation for ethyl vinyl ether hydrolysis catalysed by the hydronium ion is −11 cal. deg.$^{-1}$ mole^{-1} (Table 3). Not many reactions are known in which rate-determining proton transfer from the hydronium ion is uncomplicated by other effects, and entropies of activation have been measured for very

few of these. One example, however, does exist to which the present value may be compared: $\Delta S^{\ddagger} = -12$ cal. deg.$^{-1}$ mole^{-1} in the cleavage of allylmercuric iodide catalysed by the hydronium ion.[15] The secondary isotope effect has also been measured for this reaction, and the value of α based on this is *ca.* 0·6.[15]

It may be significant that the entropies of activation of these two reactions, both with α approximately $\frac{1}{2}$, are roughly midway between the values near zero usually observed in A-1 processes and the values near −20 cal. deg.$^{-1}$ mole^{-1} usually observed in A-2 processes.[16] The origin of the entropy changes in A-1 and A-2 reactions is still incompletely understood, but an attractive hypothesis attributes the difference to the constraint imposed on the system by the water molecule which has taken on positive charge in the slow step of the A-2 process.[17] The situation in rate-determining proton transfer from the hydronium ion is somewhat similar, for here a water molecule is in the process of losing positive charge. At one extreme of transition state structure ($\alpha = 0·0$), this water molecule still has a full positive charge and the entropy of activation should therefore be near that for an A-2 reaction; at the other extreme ($\alpha = 1·0$), the positive charge is completely lost and the entropy of activation should be near that for an A-1 reaction. This rationalisation is consistent with the fact that $\Delta S^{\ddagger} = -3$ cal. deg.$^{-1}$ mole^{-1} for the hydration of isobutene catalysed by the hydronium ion;[18] it has recently been inferred [19] that this reaction is a rate-determining proton transfer from the catalyst to the substrate, for which the value of α is *ca.* 0·9.

EXPERIMENTAL

* The somewhat unorthodox view has, however, been expressed [11] that bending vibrations may be stronger in a symmetrical transition state than in the initial state; this would reduce the theoretically estimated maximum isotope effects.

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[18] R. W. Taft, jun., E. L. Purlee, P. Riesz, and C. A. DeFazio, *J. Amer. Chem. Soc.*, 1955, **77**, 1584.
[19] V. Gold and M. A. Kessick, *J. Chem. Soc.*, 1965, 6718.