in which this semi-convergent series is satisfactory for the values of z as encountered here. In practice $z_1 = E^*/RT_4$, $z_2 = E^*/R(T_4 + 100)$.

2. Isothermal Build-up of Bromine Atoms.—Using the mechanism in Table I, assuming that $[H_2]$ and $[Br_2]$ are constant, $[HBr] << [Br_2]$, and $[H] = (k_2[H_2]/k_3[Br_2])\,[Br]$, the rate expression for Br formation becomes

$$\frac{d([H] + [Br])}{dt} = \left(\frac{k_2[H_2]}{k_3[Br_2]} + 1\right)\frac{d[Br]}{dt} = k_1^{f}[m][Br_2] - k_1^{r}[m][Br]^2 \cong \frac{d[Br]}{dt}$$

since if $[H_2] \cong [Br_2]$, $k_2[H_2] << k_3[Br_2]$. Then

$$[Br] = \left(\frac{k_1^{f}[Br_2]}{k_1^{r}}\right)^{1/2} \tanh At \qquad (8)$$

where $A = (k_1^{f}k_1^{r}[Br_2]^{1/2})\,[m]$ and the integration is from $t = 0$ to $t = t$. The rate expression for HBr formation then becomes

$$\frac{d[HBr]}{dt} = 2k_2\,[H_2][Br] = 2S \tanh At \qquad (9)$$

If the end of the induction period is set at $t = 2/A$, at which time [Br] has reached 96% of its steady-state value, $[HBr] = 2S/A \ln \cosh 2$. During the same period, the steady-state reaction produces $[HBr] = 4S/A$. Numerically, the results of this integration are in good agreement with the approximate method developed by Matsen.[20]

PRINCETON, N. J.

---

(20) F. A. Matsen and J. L. Franklin, THIS JOURNAL, **72**, 3337 (1950).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CORNELL UNIVERSITY]

Hydrolysis of Ethylene Oxide Derivatives in Deuterium Oxide–Water Mixtures[1]

BY J. G. PRITCHARD AND F. A. LONG

RECEIVED JULY 2, 1956

The hydrolysis of several simple epoxides by the acid-catalyzed, the base-catalyzed and the uncatalyzed hydrolysis paths has been studied in deuterium oxide-water mixtures as solvent. For the acid-catalyzed reaction k_{D_2O}/k_{H_2O} varies from 1.9 to 2.2 and data for intermediate mole fractions of deuterium fit the Nelson and Butler theory quite well. It is concluded that this reaction involves a preliminary equilibrium proton transfer. For the base-catalyzed reaction the effect of deuterium oxide as solvent is small, k_{D_2O}/k_{H_2O} varying from *ca.* 1.0 to 1.1. This is consistent with the accepted SN2 mechanism. For the uncatalyzed hydrolysis the values of k_{D_2O}/k_{H_2O} vary from 0.8 to 0.9. This result serves to eliminate a mechanism which involves reaction of the conjugate acid form of the epoxide with hydroxide ion. However, it does not appear to permit a distinction between possible *S*N1 and *S*N2 reactions of epoxide with solvent.

Introduction

Deuterium isotope effects on the kinetics of reactions frequently have been used to elucidate reaction mechanisms. In some cases deuterium is substituted for hydrogen in a reactant organic molecule; in others a protonated solvent is replaced by a deuterated solvent, for example water is replaced by deuterium oxide. Wiberg[2] has recently reviewed both types of application and in particular has tabulated data on the effect of deuterium oxide as solvent on rates of various hydrolytic reactions catalyzed by either acids or bases. Some of the latter data are reproduced in Table I for reactions which are relevant to the present study. The mechanism classifications in the third column of Table I are based on the work of several investigators and are reasonably well established.

One deficiency in the investigations to date is that the magnitudes of the deuterium oxide solvent effects have not been adequately studied either for variations of hydrolysis mechanism within a given class of compounds or for effects of variation of structure for a given mechanism. In these respects an interesting field of study is the hydrolysis of epoxides. These compounds undergo hydrolysis by three distinct paths[3] and the mechanisms are well understood for at least two of the three. We have determined the effects of deuterium oxide on the rates of these reactions by dilatometric meas-

TABLE I

EXAMPLES OF SOLVENT DEUTERIUM OXIDE ISOTOPE EFFECTS IN HYDROLYTIC REACTIONS

Reactant	Catalyst	Mechanism class	T, °C.	k_{D_2O}/k_{H_2O}[2]
Ethyl orthoformate	H^+	A-1[10]	25	2.35
Acetal	H^+	A-1[10]	15	2.68
Sucrose	H^+	A-1[4]	25	2.05
Ethyl formate	H^+	A-2[5]	15	1.37
Ethyl acetate	H^+	A-2[5]	. .	1.49[6]
Methyl acetate	H^+	A-2[5]	15	*ca.* 1.7
Acetamide	H^+ (0.1 *M*)	A-2[7,8]	25	1.45
Acetamide	OH^-	SN2[7,8]	25	0.91
Ethyl acetate	OH^-	$B_{Ac}2$[6]	. .	1.33
Methyl iodide	None	SN2[8]	52.5	1.0[9]
Methyl chloride	None	SN2[8]	52.5	1.0[9]
t-Butyl chloride	None	SN1[8]	25.2	0.7[9]

---

(1) Work supported by a grant from the Atomic Energy Commission.

(2) K. B. Wiberg, *Chem. Revs.*, **55**, 713 (1955).

(3) (a) D. McIntyre and F. A. Long, THIS JOURNAL, **76**, 3240 (1954); (b) M. M. Kreevoy and R. W. Taft, Jr., *ibid.*, **77**, 3146 (1955); (c) F. Stasiuk, W. A. Sheppard and A. N. Bourns, *Can. J. Chem.*, **34**, 123 (1956).

(4) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1940, p. 275.

(5) R. P. Bell, A. L. Dowding and J. A. Noble, *J. Chem. Soc.*, 3106 (1955).

(6) W. F. K. Wynne-Jones, *Chem. Revs.*, **17**, 117 (1935).

(7) M. L. Bender, THIS JOURNAL, **77**, 348 (1955).

(8) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953.

(9) C. G. Swain, R. Cardinaud and A. D. Ketley, THIS JOURNAL, **77**, 934 (1955).

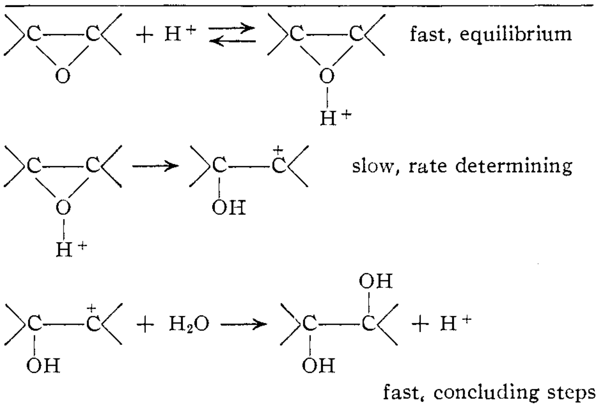
(10) (a) J. N. Brönsted, M. Kilpatrick and M. Kilpatrick, THIS JOURNAL, **51**, 428 (1929). (b) H. J. Lichtenstein and G. H. Twigg, *Trans. Faraday Soc.*, **44**, 905 (1948).

urements on the hydrolysis of several simple epoxides in different *p*H regions. The measurements lead to an experimental first-order rate coefficient, k_1. In the general case this can contain contributions from all of the hydrolysis paths

$$k_1 = k_{H^+}C_{H^+} + k_{OH^-}C_{OH^-} + k_{H_2O}C_{H_2O} \qquad (1)$$

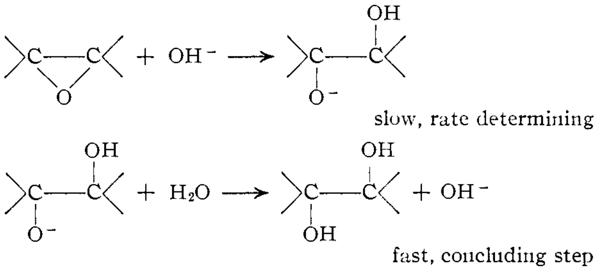
However, for all the epoxides studied there are *p*H regions where one of the above three terms accounts for at least 95% of the reaction. Hence, it has been possible to make separate studies of the influence of deuterium oxide on the three modes of hydrolysis. The sections which follow give information on the mechanisms for the three paths and on the expected influence of deuterium oxide.

I. Acid-catalyzed Hydrolysis.—Evidence is presented elsewhere[11] that the acid-catalyzed hydrolysis of epoxides follows an A-1, carbonium ion mechanism and may be represented as



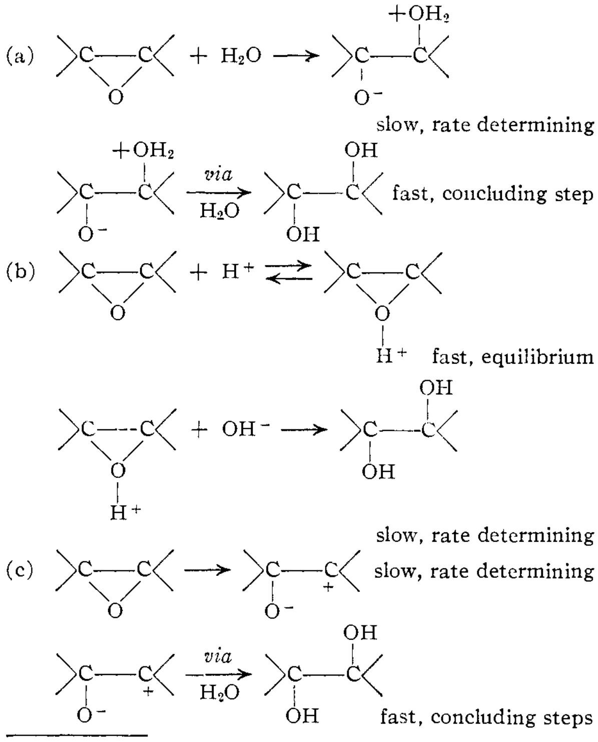
The mechanism proposes that there is an initial preliminary equilibrium with hydrogen ion followed by a rate determining reaction of the protonated (or deuterated) epoxide. From what is known about similar systems[12-16] the effect of substituting deuterium oxide for water as the solvent should be a substantial increase in rate. This is a direct result of the smaller dissociation of acids in deuterium oxide compared to normal water. The preliminary equilibrium will lie farther to the right in deuterium oxide than in water; and since the rate is directly proportional to the concentration of the conjugate acid form of the epoxide, a rate increase for deuterium oxide would be expected. Thus, for this general type of acid catalyzed hydrolysis k_{D_2O}/k_{H_2O} ratios of 2 or greater are commonly found, *cf.* Table I.

II. Base-catalyzed Hydrolysis.—This reaction is classed by Ingold[17] as SN2, and recent studies[18] on the direction of opening of the epoxide rings in propylene and isobutylene oxides during base-catalyzed hydrolysis in water containing H_2O^{18} have confirmed this classification. The O^{18} is found predominantly on the primary carbon atom in both cases. Hence, the mechanism appears to be



This mechanism does not involve any preliminary equilibrium and no bonds to H or D are broken in the rate-determining step. Hence any change in rate for OD^- compared to OH^- should result only from secondary causes. In view of the small influence of D_2O noted in Table I for similar reactions, only a small isotope effect would be predicted for mechanism II. A similar prediction follows from a qualitative consideration of theory.[19]

III. Neutral Hydrolysis.—For the *p*H range 7 to 12, it has been shown[10,18] that epoxides undergo a characteristic uncatalyzed reaction in aqueous solution. The mechanism of this reaction is not known with certainty even though it is frequently presumed that it involves a simple nucleophilic attack by a water molecule, mechanism (a), analogous to the SN2 base-catalyzed hydrolysis. There are, however, two other possibilities, as pointed out by Ingold.[17] One is nucleophilic attack of hydroxide ion on the conjugate acid form of the epoxide, (b), and the other is an SN1 reaction of the epoxide, (c). All three of these mechanisms predict a rate which is independent of *p*H.



---

[11] J. G. Pritchard and F. A. Long, THIS JOURNAL, **78**, 2667 (1956).

[12] K. F. Bonhoeffer and E. A. Moelwyn-Hughes, *Z. physik. Chem.*, **B26**, 272 (1934).

[13] W. K. F. Wynne-Jones, *Trans. Faraday Soc.*, **32**, 1397 (1936).

[14] Ph. Gross and A. Wischin, *ibid.*, **32**, 879 (1936).

[15] Ph. Gross, H. Steiner and H. Suess, *ibid.*, **32**, 883 (1936).

[16] W. J. C. Orr and J. A. V. Butler, *J. Chem. Soc.*, 330 (1937).

[17] Ref. 8, pp. 341-345

[18] F. A. Long and J. G. Pritchard, THIS JOURNAL, **78**, 2663 (1956).

[19] (a) J. Bigeleisen, *J. Phys. Chem.*, **56**, 823 (1952); (b) H. Eyring and F. W. Cagle, *ibid.*, **56**, 889 (1952).

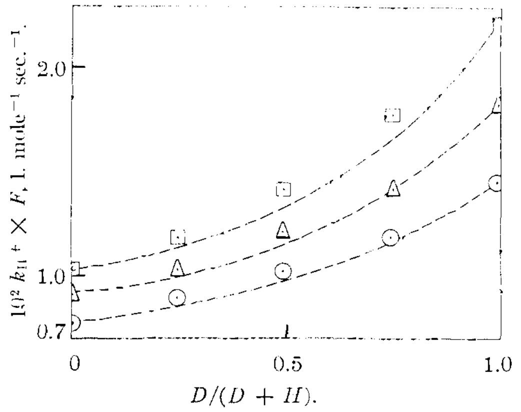


Fig. 1.—Effect of D_2O on the rates of hydrolysis of epoxides catalyzed by 0.097 *M* perchloric acid at 25°: ethylene oxide, ⊡ (*F* = 1.0); β-methylglycidol, ◬ (*F* = 0.8); epichlorohydrin, ⊙ (*F* = 10.0).

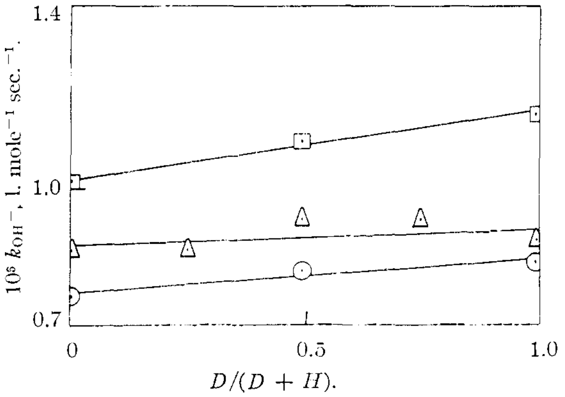


Fig. 2.—Effect of D_2O on the rates of hydrolysis of epoxides catalyzed by 1.02 *M* potassium hydroxide at 25°: ethylene oxide, ⊡; propylene oxide, ◬; isobutylene oxide, ⊙.

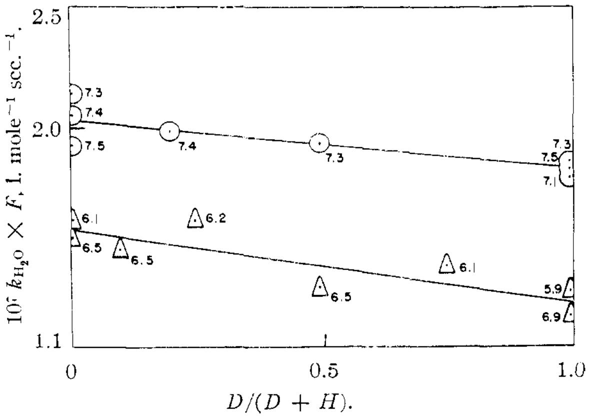


Fig. 3.—Effect of D_2O on the rates of hydrolysis of epoxides in neutral solution at 50°: isobutylene oxide ⊙ (*F* = 0.6); propylene oxide, ◬ (*F* = 1.0). Numbers adjacent to points give *p*H of the reaction mixtures.

The uncertainty of the mechanism for this reaction precludes any definite prediction of the effect of deuterium oxide. In fact, as discussed later, information on the isotope effect should help decide which of the mechanisms III(a), (b) and (c) are effective.

Experimental

Solutions of perchloric acid were made up in various mixtures of water and deuterium oxide by mixing weighed amounts of 60% perchloric acid with known weights of the solvents.[20] This procedure was checked by titrating aliquots of the acid solutions with standardized sodium hydroxide solution. The basic and "neutral" solutions were made up similarly by weighing out exact amounts of potassium hydroxide and buffer components, respectively. From the weight data, the mole fraction of deuterium in the water of the reaction solutions was calculated easily.

Dilatometers having a small (8 ml.) capacity were used for the rate studies. The initial concentrations of epoxides ranged from 0.25 to 0.4 *M*. These values gave volume diminutions for complete reaction in the dilatometer equivalent to the movement of the meniscus through about 15 cm. in a capillary tube of 0.05 cm. internal diameter. From the observed volume changes, first-order rate coefficients, k_1, were calculated using the Guggenheim procedure and were converted to second-order coefficients as in eq. 1. All reagents were of analytical grade; epoxide samples were distilled before use. Water-bath temperatures were maintained to within ±0.01°.

Many previous studies on hydrolysis under essentially neutral conditions have been made difficult by lack of suitable *p*H control. The basic forms of conventional buffer components have been shown to add rapidly to epoxides and this seriously complicates the "water" reaction.[13,21,22] This effect and the errors introduced by *p*H drift in unbuffered solutions become important when an attempt is made to detect small rate differences (10%) for the slow water reactions. This problem was overcome by using buffer solutions made from the organic bases 2,6-dimethylpyridine, pK_B = 6.7, and 2,4,6-trimethylpyridine, pK_B = 7.5. The perchlorates of these compounds were prepared and purified and buffer solutions were made by dissolving weighed quantities of the perchlorate (0.005 *M*) with the necessary quantities of potassium hydroxide to obtain the desired *p*H. In this way the *p*H was maintained constant to within ±0.1 unit for the "neutral" reaction mixtures.

The perchlorate ion is known to have negligible nucleophilic activity and similar behavior has been found for the *hindered* pyridine bases. For example, separate buffered solutions containing 0.0025 and 0.1 *M* free 2,6-dimethylpyridine (*p*H of 6.4) showed only a 20% difference in the rate of hydrolysis of propylene oxide. This is of the order of a general salt effect and shows that the buffer components react, if at all, at a very slow rate.

Equivalent solutions of buffer components gave slightly higher *p*H values in deuterium oxide than in water as measured by a standardized Beckman *p*H meter with calomel and glass electrodes. The autoprotolysis constant for deuterium oxide at 25° is $C_{D^+}C_{DO^-} = 0.16 \times 10^{-14}$ so that the point of neutrality in deuterium oxide will be 7.4 on a scale defined by $pD = -\log_{10} C_{D^+}$.[23] However, a conventional *p*H meter still records the value of C_{D^+} on the *p*H scale quite accurately since the change of potential on substituting deuterium oxide for water as the solvent for simple cells is quite small.[24]

Results and Discussion

Figures 1, 2 and 3 give the experimental results for the influence of deuterium oxide as solvent on the reaction of some simple substituted ethylene oxides by the hydrolysis paths I, II and III, respectively. Each study was made so that a single mechanism was operative and the plots give values of the three second-order rate coefficients of eq. 1 as a function of mole fraction of deuterium.

---

[20] Deuterium oxide was supplied as "99.5% D_2O" from the Stuart Oxygen Company by permission of the Atomic Energy Commission. Densities were referred from T. L. Chang and J. Y. Chien, THIS JOURNAL, **63**, 1709 (1941).

[21] W. C. J. Ross, *J. Chem. Soc.*, 2257 (1950).

[22] C. G. Swain, THIS JOURNAL, **74**, 4108 (1952).

[23] V. K. LaMer and S. Karmau, *Science*, **83**, 624 (1936).

[24] E. Abel, E. Bratu and O. Redlich, *Z. physik. Chem.*, **A173**, 353 (1935).

Data for the acid-catalyzed hydrolysis of ethylene oxide, epichlorohydrin and β-methylglycidol at 25° are given in Fig. 1. For each case, a marked increase in rate with increasing deuterium oxide content is observed. Some duplicate runs for ethylene oxide showed the reproducibility of the results to be within ±1%. The dotted curves were calculated using the theory of Nelson and Butler.[25] This theory applies to acid and base-catalyzed hydrolyses which involve a preliminary equilibrium between the substrate and hydrogen or hydroxide ion. For mechanisms involving acid catalysis, the reaction rate in an acid solution containing water and deuterium oxide is assumed to be directly proportional to the total thermodynamic activity of the species H_3O^+, H_2DO^+, HD_2O^+ and D_3O^+. This activity may be calculated assuming that the activity coefficients of the various species do not vary with solvent composition. The final equation permits calculation of the dependence of rate on mole fraction of deuterium oxide for a given value of k_1/k_0, the experimental ratio of the rate in pure deuterium oxide to that in water. In our case the theory should apply to mechanisms I and III(b) if it enters, but not to the others.

Two aspects of the data of Fig. 1 indicate that the concept of a preliminary equilibrium proton transfer is correct. One is the fact that the observed value of k_1/k_0 is greater than unity and is in fact close to 2 for all three reactions. In addition to this, it is evident from Fig. 1 that there is close quantitative agreement between the results for k_n/k_0 at intermediate mole fractions of deuterium oxide and the theory of Nelson and Butler. We conclude that the first step of mechanism I is firmly established.[26]

The fact that the values of k_{D_2O}/k_{H_2O} are as large as two is in accord with the proposal that the mechanism is A-1 rather than A-2. As Table I shows, A-1 hydrolyses have values of two or more for this ratio whereas for the A-2 mechanism the ratio tends to be distinctly lower. This difference is quite reasonable. For the A-1 mechanism the unimolecular rate determining step should show only a small isotope effect. Consequently the k_{D_2O}/k_{H_2O} ratio will be given essentially by the ratio of the concentration of the conjugate acid in D_2O relative to that in H_2O, and a value of approximately two for this is in accord with equilibrium studies.[23] In contrast, the bimolecular rate step of mechanism A-2 would be expected to go more slowly with D_2O than with H_2O and this effect should lead to the observed lower over-all values of k_{D_2O}/k_{H_2O}.

Figure 2 shows the rates of base-catalyzed hydrolysis of ethylene, propylene and isobutylene oxides at 25°. Ethylene and isobutylene oxides show an almost linear increase of k_{OH^-} with increasing deuterium oxide content which appears to be beyond the experimental error and which amounts to a total of 10% at $D/(D + H) = 1$. Propylene oxide shows a maximum effect (7% increase) at $D/(D + H) = 0.5$ while the rates for $D/(D + H) = 0$ and 1 are almost identical. (A duplicate series of runs to check this unexpected behavior showed an average deviation from the mean of ±1.5%.) We conclude that deuterium oxide as solvent has a small but definite accelerating effect for at least two of the epoxide hydrolyses. To calculate the values of k_{D_2O}/k_{H_2O} (Table II), best straight lines were drawn through the experimental points, in spite of the apparently real deviations shown by propylene oxide.

Figure 3 shows the rates for the neutral reaction of propylene and isobutylene oxides at 50°. Overall, a small almost linear decrease in k_{H_2O} with increasing deuterium oxide concentration is observed. Although the accuracy is only about ±5% for the rates of these slower reactions, the decrease in rate is large enough to be quite definite for both of the oxides. No significant change of rate with *p*H was observed.

Table II summarizes values of the ratio of rates in pure deuterium oxide (obtained by extrapolation from $D/(D + H) = 0.99$) to rates in ordinary water for all the epoxide reactions studied. It is clear that there are three distinct classes of isotope effect corresponding to the three different mechanisms of hydrolysis. There are also variations of ratio with the structure of the epoxides but these are small and do not vitiate the classification by mechanism.

TABLE II

EFFECT OF DEUTERIUM OXIDE AS SOLVENT ON THE HYDROLYSIS OF EPOXIDES

Oxide	Catalyst concn.	T, °C.	k_{D_2O}/k_{H_2O}
Ethylene oxide	0.097 *M* $HClO_4$	25	2.20
Epichlorohydrin		25	1.89
β-Methylglycidol		25	2.05
Ethylene oxide	1.02 *M* KOH	25	1.14
Propylene oxide		25	1.04
Isobutylene oxide		25	1.10
Propylene oxide	*p*H *ca.* 6.4	50	0.8
Isobutylene oxide	*p*H *ca.* 7.4	50	.9

We noted earlier that the observed results for the acid catalyzed reaction are in accord with mechanism I. Similarly the data for the base-catalyzed reaction are in accord with mechanism II in that only a small effect is observed. The fact that the

---

[25] W. E. Nelson and J. A. V. Butler, *J. Chem. Soc.*, 957 (1938). The expression for acid-catalyzed hydrolysis is

$$k_n/k_0 = \{(1 - n)\phi(1 - n) + n\phi(n)Q'(1)k_1/k_0\}/Q'(n)$$

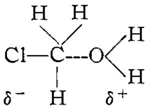
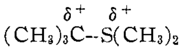
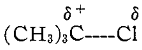
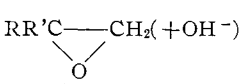
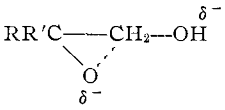
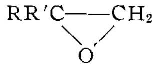
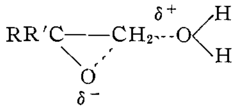
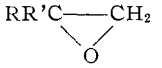
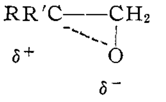
where n is mole fraction of deuterium in the solvent and k_1/k_0 is the rate ratio for reaction in pure deuterium oxide relative to that in pure normal water. The functions $Q'(n)$ and $\phi(n)$ have the following values, reproduced here for easy reference

n	0	0.25	0.50	0.75	1.00
$Q'(n)$	1.00	0.816	0.612	0.421	0.26
$\phi(n)$	1.103	1.055	1.025	1.01	1.00

[26] Swain[22] has given data to support the idea that acid-catalyzed nucleophilic displacements on epoxides, for example iodide ion with epichlorohydrin, show general acid catalysis. He concludes that for reaction in solutions of *p*H *ca.* 4.3 the transition state must involve epoxide, nucleophile and a general acid HA. He further concludes (in contrast to our conclusion above) that there is no pre-equilibrium between epoxide and its conjugate acid. It is of course conceivable that different mechanisms enter for different *p*H regions. However, another possible explanation of Swain's results is that at the high buffer concentration (4 *M* HOAc, 1 *M* NaOAc) the hydrogen ion concentration differs significantly from that in low concentration buffers of the same ratio. Swain attempted to minimize this effect by working at constant ionic strength. But at these high concentrations salt effects are quite specific and it is known that the effect of sodium perchlorate, the salt used by Swain, is normally quite different from that of sodium acetate. *cf.* F. A. Long and W. F. McDevit, *Chem. Revs.*, **51**, 143 (1952).

TABLE III

RELATION BETWEEN SOLVATION AND EFFECT OF DEUTERIUM OXIDE

Substance hydrolyzed	Transition state	Change in solvation, reactant to transition state	Obsd. $\frac{k_{D_2O}}{k_{H_2O}}$
CH_3Cl		Slight increase	0.9 to 1
$(CH_3)_3CS^+(CH_3)_2$	 $\overset{\delta^+}{(CH_3)_3C}\text{--}\overset{\delta^+}{S}(CH_3)_2$	Slight decrease	1
$(CH_3)_3CCl$	 $\overset{\delta^+}{(CH_3)_3C}\text{----}\overset{\delta^-}{Cl}$	Increase	0.7
 by Mech II		Decrease	1 to 1.1
 by Mech. III(a)		Slight increase	0.8 to 0.9
 by Mech. III(c)		Increase	

observed isotope effect for this mechanism is a small increase in rate in deuterium oxide is not surprising although it does not appear to be susceptible of quantitative explanation. It is probable that contributions enter from both general medium effects as discussed later and secondary structural effects caused by a change from O–H to O–D in the transition state. The unexpected behavior of propylene oxide at intermediate mole fractions of deuterium oxide may conceivably be due to interplay of these two effects.

The data of Table II for the "water" reaction permit the definite conclusion that this reaction cannot go extensively by mechanism III(b). The rate expression for this mechanism may be written

$$\text{Rate} = kC_{H^+}C_{OH^-}C_{\text{oxide}} = k'C_{SH^+}C_{OH^-}$$

where $C_{SH}{}^+$ is concentration of conjugate acid of the oxide. For a given concentration of H^+ or D^+ (and hence a given *p*H) a shift from H_2O as solvent to D_2O will have two effects. It will increase the concentration of $C_{SH}{}^+$, and from a consideration both of deuterium oxide effects on rates for other acid-catalyzed reactions and of studies of equilibrium ionization of weak acids[23] a reasonable prediction is that C_{SD^+} for D_2O will be larger than C_{SH^+} by a factor of roughly two. This effect alone would lead to the prediction of a faster rate in D_2O. However, the ion product, $C_{D^+}\cdot C_{OD^-}$, for D_2O is smaller than that for water by a factor of six and this, for a given concentration of H^+ or D^+, will lead to a sixfold *decrease* in rate in D_2O. The over-all prediction, then, is that reaction by mechanism III(b) should be *slower* in D_2O by a factor of about three. Since the observed effect from D_2O is only about a 15% decrease in rate, this mechanism cannot be contributing to any significant extent.

A choice between mechanisms III(a) and III(c) on the basis of isotope effects is not obvious. Just as expected for attack by hydroxide ion, any isotope effect from nucleophilic reaction of D_2O *vs.* H_2O should be due only to secondary effects and hence should be small. It is known that the subsitution of deuterium for hydrogen in positions adjacent to the reaction center produces a retardation in the rates of hydrolysis of alkyl derivatives by carbonium ion mechanisms.[27–29] This is believed to be due to hyperconjugation of the bound hydrogen or deuterium atoms near the reaction site. From similar considerations, it is plausible that the direction of the effect for mechanism III(a) should be such as to give a smaller rate with D_2O. A reasonable transition state for this mechanism is shown in line 5 of Table III. It is likely that as the result of the developing positive charge in this transition state, the vibrational force constants and hence the zero point energies of the attacking H_2O or D_2O molecules would be decreased. Since D–O bonds have a lower initial zero point energy this should lead to a slightly higher total energy of activation for the deuterium oxide case and hence a slower rate of reaction than for water. A similar but somewhat more general argument can be made by a consideration of solvation. Data on the influence of deuterium oxide on the solubility of salts[30] and on their heats of solution[31] indicate that water is a better solvating agent than deuterium oxide for both positive and negative charge centers. Hence, if only secondary effects are operating, a reaction which involves an increase in solvation in going from reactants to transition state should go more slowly in deuterium oxide than in water. This same conclusion is implicit in the discussion of Swain, Cardinaud and Ketley,[9] some of whose data are reproduced in Tables I and III. The latter table compares the magnitude of solvent isotope

---

(27) V. J. Shiner, Jr., THIS JOURNAL, **75**, 2925 (1953).

(28) C. E. Boozer and E. S. Lewis, *ibid.*, **76**, 794 (1954).

(29) E. S. Lewis and G. M. Coppinger, *ibid.*, **76**, 4495 (1954).

(30) R. D. Eddy and A. W. C. Menzies, *J. Phys. Chem.*, **44**, 207 (1940).

(31) E. Lange and W. Martin, *Z. physik. Chem.*, **A180**, 233 (1937).

effects for several reactions with the probable change in extent of solvation of the reactants on going to the transition state.

The data in Table III on alkyl halides and sulfides appear to support the suggestion that increased solvation for the transition state leads to a smaller value of the rate ratio k_{D_2O}/k_{H_2O}. The data for the base-catalyzed hydrolysis of epoxides are also consistent with this. For the water reaction of epoxides, mechanisms III(a) and (c) both involve increased solvation upon reaction but the increase should be much more for the latter. The observed low value of k_{D_2O}/k_{H_2O} is hence consistent with the proposal that III(c) may contribute at least to some extent. However, a decision on the relative contributions of mechanisms III(a) and (c) must await the results of other types of experiments since the differences of Table III are not large enough to be more than suggestive.

ITHACA, N. Y.

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

Kinetics of the Solvolysis of Alkyl Borates[1a]

BY GILBERT T. PERKINS[1b] AND THOMAS I. CROWELL

RECEIVED JULY 5, 1956

The rate of ethanolysis of *sec*-butyl borate has been measured dilatometrically at 0 and 25°. The first-order rate constants are linear in the concentrations of hydrogen ion and acetic acid, and are increased in a more complex manner by ethoxide ion and acetate ion, indicating general acid-base catalysis. The reaction is markedly accelerated by small amounts of water, except that water inhibits oxonium-ion catalysis. Uncatalyzed methanolysis is faster than ethanolysis and has a lower apparent activation energy. The order of reactivity of several alkyl borates with ethanol at 25° is *n*- and iso-Bu >> iso-Pr > *sec*-Bu >> *t*-Bu.

The *n*-alkyl borates (tris-*n*-alkoxyboranes) are liquids which hydrolyze rapidly in water. Branched chain borates such as neopentyl, isopropyl[2] and *t*-butyl,[3] react much more slowly, a generalization which has been verified in a recent, more comprehensive study of hydrolysis rates.[4] No careful consideration has been given to the possibility of acid or base catalysis.

We have investigated the kinetics of alcoholysis of several alkyl borates, especially the reaction of *sec*-butyl borate with ethanol

$$(s\text{-}C_4H_9O)_3B + 3C_2H_5OH \longrightarrow (C_2H_5O)_3B + 3s\text{-}C_4H_9OH \quad (1)$$

The stoichiometry of this type of ester interchange has been established in the preparation of many alkyl borates.[5] The rate was most conveniently measured dilatometrically; a few cases in which titrations were used are described in the Experimental section.

Experimental

Reagents.—*sec*-Butyl borate was prepared by the methods of Bannister[6] and Lippenscott.[7] Analysis by titration with standard aqueous sodium hydroxide, in the presence of mannitol and phenolphthalein, gave 100.4% of the theoretical titer. *t*-Butyl, isobutyl and isopropyl borates were prepared according to Lippenscott, *n*-butyl borate according to Bannister, and methyl borate obtained from Anderson Laboratories. All were purified by distillation and protected from the atmosphere.

Commercial absolute ethanol was dried by distillation from magnesium ethoxide. Karl Fischer titration indicated a maximum water content of 0.02%. Methanol was dried by the same procedure. Sodium ethoxide solutions were prepared from clean sodium and ethanol, then standardized against aqueous hydrochloric acid. Ethanolic hydrogen chloride solutions were prepared by passing the gas through concentrated sulfuric acid and into ethanol; the solutions were standardized against aqueous sodium hydroxide.

Reagent grade sodium acetate and lithium chloride were oven-dried. Lithium acetate was prepared by adding excess acetic acid to a solution of lithium carbonate, evaporating to dryness, and fusing the residue. Acetic acid was dried by distillation with benzene in a fractionating column. Standard ethanol solutions of acetic acid appeared to esterify to the extent of nearly 1% per day, and consequently were always freshly prepared.

Rate by Titration.—Meerwein[8] reported that methyl borate in methanol could be titrated to a sharp end-point with sodium methoxide, using thymolphthalein indicator, but that larger alkyl groups reversed the reaction. Accordingly, we attempted to determine ethyl borate in the presence

$$B(OCH_3)_3 + OCH_3^- \rightleftarrows B(OCH_3)_4^- \quad (2)$$

of *sec*-butyl borate by titration and thus follow the kinetics of ethanolysis. Although Meerwein's results were qualitatively confirmed, the end-points faded badly due to ester interchange, catalyzed by the titrant. The rough values of *k* so obtained for ethanolysis of *sec*-butyl borate at 0° are 0.003, 0.005 and 0.007 min.$^{-1}$.

The uncatalyzed solvolysis of *t*-butyl borate was followed by pipetting samples of the reaction mixtures into cold water. While *t*-butyl borate (m.p. 18°) separated as a solid, primary borates were quickly hydrolyzed and titrated as boric acid with sodium hydroxide in the presence of mannitol. The titer at complete reaction was obtained by hydrolyzing a sample overnight in aqueous hydrochloric acid.

Rate by Dilatometer.—The dilatometer consisted of a Pyrex bulb (capacity 20 ml.) bearing a 12-cm. length of 0.5 mm. precision-bore capillary tubing with etched millimeter scale. A stopcock and funnel were also attached to the bulb.

In the kinetic runs, the reaction mixtures were quickly made up at the temperature of the thermostat and poured into the dilatometer, which was immersed in the thermostat. Zero time was taken as the time of mixing. The decrease in volume with time was observed until the reading became constant. The exact borate concentration was determined after the run by hydrolyzing a sample and titrating for boric

---

[1] (a) From the Dissertation of Gilbert T. Perkins, University of Virginia, 1956. Presented in part at the Southeastern Regional Meeting of the American Chemical Society, Columbia, South Carolina, November 1955. (b) Du Pont Fellow, 1955–1956.

[2] A. Scattergood, W. H. Miller and J. J. Gammon, THIS JOURNAL, **67**, 2150 (1945).

[3] P. D. George and J. R. Ladd, *ibid.*, **77**, 1900 (1955).

[4] H. Steinberg and D. L. Hunter, Abstracts of Papers, American Chemical Society, Minneapolis, Minn., September, 1955, p. 36-O.

[5] H. Wuyts and A. Duquesne. *Bull. soc. chim. Belg.*, **48**, 77 (1939).

[6] See J. R. Johnson and S. W. Thompkins, *Org. Syntheses*, **13**, 16 (1933).

[7] S. B. Lippenscott, U. S. Patent 2,642,453 (1954).

[8] H. Meerwein and T. Bersin, *Ann.*, **476**, 122 (1929).