

These reactions have transition states containing a water molecule and a +1 charge.⁷ It can be shown that the fit with eq. 4 is equivalent to having the activity coefficient of the transition state (f^*) equal to $f_{\text{H}_3\text{O}^+}$. As a provisional hypothesis, we propose that this category is characterized by cations in which the charge is centered on a H₂O⁺ moiety which is rather loosely held so that the interaction with solvent is much like that of H₃O⁺ itself and thus $f^* = f_{\text{H}_3\text{O}^+}$.

Fortunately, literature data indicate that the f behavior of most cations closely approach that of one of the three limiting categories.

Activity Coefficient Behavior of Neutral Molecules in Aqueous Sulfuric Acid.—Earlier it had been found⁴ that $d \log f$ behavior in water-sulfuric acid was similar for a wide variety of neutral molecules. To that list can now be added salicylic acid,

(7) M. A. Paul and F. A. Long, *Chem. Revs.*, **57**, 1, 935 (1957); R. W. Taft, Jr., N. C. Deno and P. A. Skell, *Ann. Rev. Phys. Chem.*, **9**, 306 (1958).

a difunctional compound with internal hydrogen bonding. The actual values of % sulfuric acid, solubility in (moles/l.) $\times 10^3$, and $d \log f$ were 0, 16.1, 0.014; 4.84, 11.6, 0.014; 9.82, 8.3, 0.018; 19.55, 6.3, 0.023, 29.59, 4.1, 0.23; 40.52, 2.0, 0.013; 50.83, 1.7, 0.0; 60.24, 4.0. The values of e increased with increasing concn. of sulfuric acid and the details of this change will appear in the Ph.D. thesis of Henry J. Peterson.

Experimental

The data used to calculate H_R appear in the Ph.D. Thesis of H. E. Berkleimer, Pennsylvania State Univ., 1959. The indicators that were used are listed in Table II. In all cases, values of $d \log (c_{\text{ROH}}/c_{\text{R}^+})/d c_{\text{O}^-}$ acid were independent of the indicator used.

The data on 4,4',4''-trimethoxytriphenylmethanol are presented in detail (Table V) to show that measurements were made in acids sufficiently dilute so that $H_R = pH$. Thus, H_R values in sulfuric, nitric and perchloric acids are all based on the same standard state assignment, namely, that $f = 1$ for all species in dilute aqueous solution.

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The Reaction of Chlorohydrins and Hydroxide Ion in the Solvents H₂O and D₂O^{1,2}

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The reaction between chlorohydrins and sodium hydroxide or tetramethylammonium hydroxide has been studied by combined kinetic and equilibrium measurements in the solvents H₂O and D₂O. The mechanism is known to involve specific hydroxide ion catalysis *via* a two-step mechanism and data are given for both the slow step and the prior equilibrium. Conductivity studies confirm the earlier conclusion of Twigg and co-workers that measurable amounts of the intermediate alkoxide ion are present. Some of the observed variation of second-order rate coefficients with concentration of reactants is due to this but there is also evidence that much of the variation is due to kinetic salt effects. The over-all rate coefficients in D₂O relative to H₂O are $k^D/k^H = 1.54$ for 2-chloroethanol and $k^D/k^H = 1.58$ for 2-chloropropanol. These values are in substantial agreement with the k^D/k^H ratio of 1.45 reported for the base-catalyzed decomposition of diacetone alcohol, a reaction which also involves specific hydroxide ion catalysis. Measurements of relative rates have been made for several mixtures of H₂O and D₂O and the dependence of rate on atom fraction of D agrees excellently with the revised Nelson-Butler equation, in contrast to the results for diacetone alcohol. The conductivity measurements lead to values of 4.9×10^{-16} and 1×10^{-15} for the acid ionization constant of 2-chloroethanol in the solvents H₂O and D₂O, respectively. From these values and the observed kinetic effect of D₂O, it is concluded that the unimolecular reaction of a 2-chloroalkoxide ion to give an epoxide goes about 15% faster in D₂O than in H₂O. Finally, the observed kinetic effects of D₂O are compared with the available data for other mechanisms of base catalysis. Relative rates in D₂O will probably distinguish between specific hydroxide ion catalysis and general base catalysis with a pre-equilibrium proton transfer but will probably not distinguish between specific catalysis and a one-step, slow proton transfer.

Introduction

Data on relative rates of reaction in D₂O and H₂O frequently have been used as a criterion of mechanism for acid catalysis and the behavior to be expected for various mechanisms is fairly well understood.^{3,4} Much less is known about base-catalyzed reactions. Some early work is available for the case of general base catalysis⁵⁻⁷ and Long and Watson recently have reported on a fairly complete study of the base-catalyzed keto-enol reaction.⁸

However, for the case of specific hydroxide ion catalysis there appears to have been only one investigation, that of Nelson and Butler on diacetone alcohol.⁹ Unfortunately these investigators found for mixtures of H₂O and D₂O that the relative rate was linear in the atom fraction of D and they interpreted this as evidence that the reaction did not involve a prior equilibrium, *i.e.*, did not go by specific hydroxide ion catalysis.¹⁰ In view of these facts it seemed useful to study the effect of D₂O as solvent for a reaction whose mechanism fairly surely involved specific base catalysis. The reaction chosen was the formation of an epoxide from a chlorohydrin. There were several reasons for this choice.

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

(2) Presented in part at 133rd Meeting of the American Chemical Society, San Francisco, California, April 1958.

(3) R. P. Bell, "Acid-Base Catalysis," Oxford Press, 1941, Chap. V11.

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

(5) O. Reitz and J. Kopp, *Z. physik. Chem.*, **A184**, 429 (1939).

(6) O. Reitz, *ibid.*, **A176**, 363 (1936).

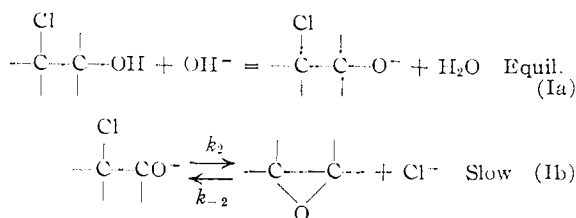
(7) S. K. Maron and V. K. LaMer, *THIS JOURNAL*, **60**, 2588 (1938).

(8) F. A. Long and D. Watson, *J. Chem. Soc.*, 2019 (1958).

(9) W. E. Nelson and J. A. V. Butler, *ibid.*, 957 (1938).

(10) On the basis of the presently available evidence it seems fairly certain that the diacetone alcohol reaction does in fact proceed by specific hydroxide ion catalysis. An excellent summary of the situation is to be found in A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, pp. 283-296.

One was that the work of a number of investigators on both the forward and reverse reactions had established that the mechanism was quite definitely¹¹⁻¹⁴



This clearly belongs to the category of specific hydroxide ion catalysis (even though hydroxide ion is actually used up in the process). A second reason is that the reaction goes essentially to completion in basic solution and is easy to follow.

A final reason for choosing this reaction is that Twigg and co-workers¹³ have proposed that, at least for 2-chloroethanol, a measurable amount of the intermediate alkoxide ion is formed and that a kinetic analysis of rates for reaction of fairly concentrated solutions can give information on the separate steps of the mechanism. Specifically these authors give an approximate steady-state development to show that a plot of $1/k_0$ vs. $[A_0 + B_0]$, where A_0 and B_0 are initial concentrations of reactants and k_0 is the observed second-order rate coefficient for the early part of the reaction, should be linear with a non-zero slope. From the observed slope and intercept it is possible to calculate both the equilibrium constant K for reaction (Ia) and the value of k_2 . This sort of analysis for reaction of ethylene chlorohydrin with sodium hydroxide led Twigg, *et al.*, to a value of the acid ionization constant of the alcohol of 3×10^{-15} . The possibility of a similar detailed analysis for reaction in D_2O implied that it would be feasible to determine the separate contributions of steps (Ia) and (Ib) to the over-all D_2O solvent effect. As will be seen this particular procedure involves some serious difficulties, but it fortunately has been possible to obtain the same kind of information in other ways.

Experimental

Materials.—Commercial 2-chloroethanol was fractionated (b.p. 51.0° (31 mm.)) over anhydrous calcium sulfate together with a little sodium carbonate to remove traces of acid. 2-Chloropropanol was prepared from α -chloropropionic acid *via* the acid chloride, followed by reduction with lithium aluminum hydride. The procedure of Fickett, Garner and Lucas¹⁵ was followed except that the lithium aluminum hydride complex was destroyed by the addition of water and the ether extract removed immediately without acidification. This minimized the formation of the isomeric 1-chloro-2-propanol by acid-catalyzed attack of chloride ion on any traces of propene oxide which might have been formed by hydrolysis of 2-chloropropanol. The product had b.p. 37.9° (12.5 mm.), n_D^{25} 1.4362, and was shown

(11) S. Winstein and H. J. Lucas, *THIS JOURNAL*, **61**, 1576 (1939).

(12) C. L. McCabe and J. L. Warner, *ibid.*, **70**, 4031 (1948), and earlier references therein.

(13) G. H. Twigg, W. S. Wise, H. J. Lichtenstein and A. R. Philpotts, *Trans. Faraday Soc.*, **48**, 699 (1952).

(14) A. A. Frost and R. G. Pearson, ref. 10, give a detailed discussion of this reaction.

(15) W. Fickett, H. K. Garner and H. J. Lucas, *THIS JOURNAL*, **73**, 5066 (1951).

to be pure, and free from the isomeric compound by vapor phase chromatography. Other materials were purified as described previously¹⁶ and all solutions were prepared immediately before use.

Kinetics.¹⁷—Equimolar solutions of the chlorohydrin and of sodium or tetramethylammonium hydroxide were allowed to react at thermostat temperature and aliquots were removed and quenched in dilute nitric acid sufficient to leave only a slight excess after neutralizing the alkali. The progress of the reaction was followed by potentiometric titration of chloride ion and the addition of the necessary excess nitric acid was postponed until very near the end-point to prevent appreciable acid-catalyzed addition of chloride ion to the alkene oxide present. Apparent second-order rate coefficients (k_0) were calculated from the slope of a graph of $1/A$ versus t where A is the concentration of unreacted starting materials at time t .

Conductivity Measurements.—The electrical equipment has been described previously.¹⁶ The conductivity cell, shown in Fig. 1, was constructed from heavy-walled Pyrex tube. The cell constant, measured with carefully prepared potassium chloride solutions, was 0.412 cm.⁻¹ and the electrodes were of bright platinum to minimize retention of electrolyte when the cell was rinsed and dried between runs.

The principal use of the conductivity apparatus was for determination of the equilibrium constant of reaction (Ia). The theory of the method has been described previously.¹⁶ The specific procedure for the reactive 2-chloroethanol was to place 10 ml. each of solutions of the alcohol and of sodium hydroxide in the compartments of the inclined cell (previously flushed with carbon dioxide-free air). After a wait of ten minutes to establish constant temperature, the solutions were mixed quantitatively by vigorous agitation. The cell then was reoriented so that the electrodes were covered as deeply as possible and resistances were measured at frequent intervals. For non-reactive mixtures, *i.e.*, where the electrolyte was potassium chloride or where the alcohol was ethanol, the resistance attained a constant value within a few minutes after mixing. With the mixture of chlorohydrin and strong base the resistance increased with time owing to replacement of hydroxide ion by chloride ion. This increase was accurately linear with time for at least 15 minutes. Hence, it was possible to obtain the resistance at the instant of mixing by extrapolation to zero time. Blank experiments with electrolyte solutions but without the organic solute gave the resistance of the electrolyte itself.

TABLE I

THE VISCOSITIES OF ETHANOL-WATER AND 2-CHLOROETHANOL-WATER MIXTURES AT 25°

	Concn. (M)	Relative viscosity	Relative fluidity (ϕ)	$(\phi_0 - \phi) / \phi_0$, calcd. for a molar soln.
Ethanol	0.0	1.000	$1.000 = \phi_0$...
	1.00	1.198	0.834	0.197 ^a
2-Chloroethanol	0.09803	1.017	.983	.176
	.2936	1.050	.952	.172
	.3888	1.069	.936	.176
	.4818	1.085	.922	.176

^a This value calculated from data in "International Critical Tables."

If the data from a conductivity experiment are plotted as $R/(R_\infty - R)$ versus time, a determination of the slope and intercept permits calculation of the second-order rate coefficient.¹⁸ This procedure was tested for the chlorohydrin reaction and found to give highly reproducible data. However, the actual rate coefficients were invariably about 10% larger than those determined by titration of chloride ion. The difficulty probably stems from our inability to obtain a precise value for R_∞ . The normal assumption was that this is given by the resistance of a solution of sodium

(16) P. Ballinger and F. A. Long, *ibid.*, **81**, 1050 (1959).

(17) All rate coefficients are in l. mole⁻¹ sec.⁻¹ units at $25 \pm 0.005^\circ$.

(18) A. A. Frost and R. G. Pearson, ref. 10, p. 35-37.

TABLE II

CONCENTRATION EFFECTS FOR THE REACTION OF 2-CHLOROETHANOL WITH EQUIMOLAR HYDROXIDE ION, 25°									
Reactant concn. (M)	0.025	0.050	0.100	0.150	0.200	0.250	0.304	0.403	0.500
10 ³ k ₀ (NaOH)	10.3	9.89	9.33	9.05		8.80			7.77
	10.4	10.4	9.33	9.11		8.79			7.77
10 ³ k ₀ ((CH ₃) ₄ NOH)	10.7		10.5		10.4		10.2	10.3	
	10.6		10.7		10.4		10.2	9.5 ^a	9.6 ^a

^a With added 0.4 M sodium nitrate.

chloride of the same concentration as that of the initial sodium hydroxide. However, there was almost certainly some gradual contamination by carbonate so that this value is only a lower limit. Because of these difficulties we have only used rate coefficients from conductivities for relative considerations in spite of their excellent reproducibility.

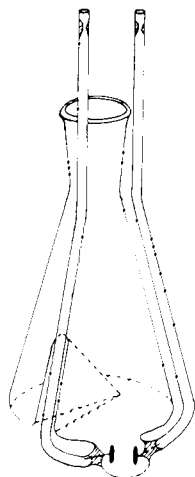


Fig. 1.—Conductivity cell for rapid mixing.

Calculation of the equilibrium constants from conductivity data involves corrections for changes in viscosity. The data of Table I were collected for this purpose. Measurements were made with an Ostwald viscosimeter and the listed values of viscosity are corrected for the small kinetic energy term. Even so, the values are only relative since the available data on density of the 2-chloroethanol solution are for 20°.¹⁹

Results and Discussion

Tables II and III give data on the rate of production of chloride ion from equimolar solutions of chlorohydrin and strong base for the solvents H₂O and D₂O. The recorded k's are the observed second-order coefficients for the initial stages of reaction (roughly the first 35%). The values of the coefficients for reaction with sodium hydroxide are in good agreement with those of earlier workers.^{20,21} Furthermore the variation of k₀ with concentration of reactants is quite similar to that reported at 20° by Twigg, *et al.*,¹³ and by Porret,²² as may be seen from Fig. 2.

In view of the results of Nelson and Butler with diacetone alcohol, it seemed of particular interest to

(19) J. Matejka and B. Jelinek, *J. chim. phys.*, **34**, 611 (1937).

(20) L. O. Winstrom and J. C. Warner, *THIS JOURNAL*, **61**, 1205 (1939).

(21) L. Smith, *Z. physik. Chem.*, **152**, 153 (1930).

(22) D. Porret, *Helv. Chim. Acta*, **24**, 80E (1941).

TABLE III
DEUTERIUM ISOTOPE EFFECTS²³

Substrate	Solvent	Reactant concn. (M)	10 ³ k ₀	k ₀ D ₂ O/k ₀ H ₂ O
2-Chloroethanol	H ₂ O	0.050	0.997	1.54
	99.5% D ₂ O	.0503	1.54	
2-Chloropropanol	H ₂ O	.0125	7.26	1.58
	99.5% D ₂ O	.0125	11.46	
	49.7% D ₂ O	.0125	8.60	
Diacetone alcohol ⁹	ca. 0.2 M alcohol			1.45
	.119 M NaOH			

make rate measurements for the chlorohydrin reaction at intermediate mole fractions of D₂O. Figure 3 gives the results for ethylene chlorohydrin.²⁴

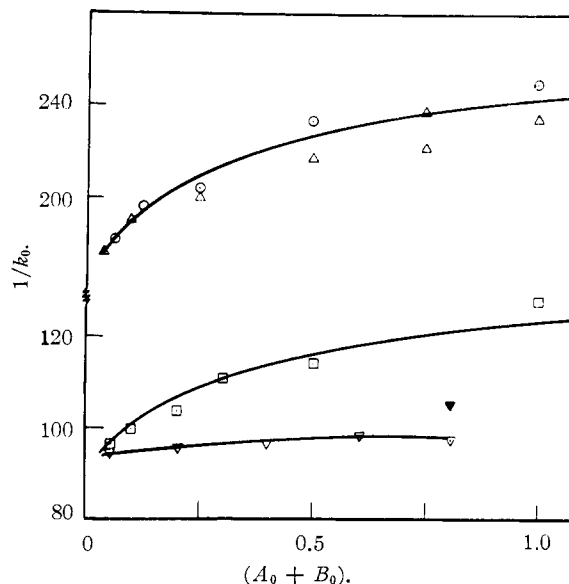


Fig. 2.—Second-order rate coefficients versus sum of initial reactant concentrations. Sodium hydroxide as base: Δ , Twigg and co-workers, 20°; \odot , Porret, 20°; \square , present work, 25°. Tetramethylammonium hydroxide as base: ∇ , 25°; \blacktriangle , with 0.4 M added sodium nitrate.

(23) We have learned recently (private communication) that C. G. Swain and co-workers have also measured k^D/k^H for reaction of 2-chloroethanol and sodium hydroxide and find a value of 1.54, in excellent agreement with that listed in Table III.

(24) These measurements were made with the conductivity procedure partly because of its high precision, partly because we wished to work at low concentrations of reactants where perturbations from changing concentrations of intermediate would be minimized. As noted earlier, rate coefficients from this procedure are somewhat higher than those obtained by titration of chloride ion. However, the rate ratio for pure D₂O relative to water agrees very well for the two methods and we have confidence in the ratios for intermediate mole fractions.

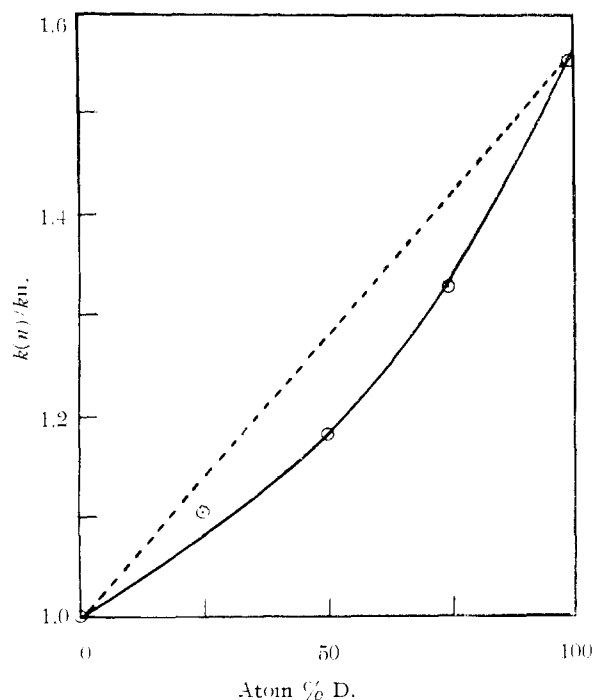
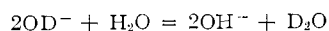


Fig. 3.—Relative rates in $\text{H}_2\text{O}-\text{D}_2\text{O}$ mixtures for reaction of 2-chloroethanol and sodium hydroxide.

Each point of Fig. 3 gives a value for the mean of two experimental determinations. The dashed line is a linear interpolation between the 0 and 100% D_2O values. The solid line is calculated from the Nelson-Butler equation

$$\frac{k(n)}{k^H} = \frac{1 + k^D/k^H [(D_2O)/N(H_2O)]^{1/2}}{1 + [(D_2O)/N(H_2O)]^{1/2}}$$

where $k(n)$ is the rate coefficient at atom fraction (n) of deuterium, (D_2O) and (H_2O) are concentrations in mole fraction units and N is the equilibrium constant for the reaction



The value of N has been calculated as 3.88 using modern values for the various equilibrium constants which enter.²⁵ The agreement between experiment and calculation is excellent and lends support to the prediction made by Nelson and Butler for this mode of reaction. Equally good agreement is shown by the less extensive data for reaction of 2-chloropropanol (Table III).²⁶

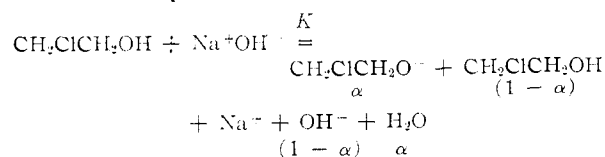
A major reason for studying the reaction of sodium hydroxide over a wide range of concentration was to obtain values of K and k_2 for the mechanism (I), using the procedure of Twigg, *et al.*¹³ However, the pronounced curvature of the sodium hydro-

(25) E. L. Purlee, *THIS JOURNAL*, to be published, recently has revised the Nelson and Butler equilibrium constants. The new values are, in the terminology of Nelson and Butler: $K = 4.0$, $L = 11$ and $K_{H_2O}/K_{D_2O} = 6.5$.

(26) NOTE ADDED IN PROOF: We have just been informed (Y. Pöcker, private communication) that a reinvestigation of the reaction between diacetone alcohol and hydroxide ion has led to relative rates which agree well with the revised Nelson-Butler predictions for specific hydroxide ion catalysis. The discrepancy reported earlier thus appears to be removed.

droxide data of Fig. 2 casts considerable doubt on the utility of this procedure since there clearly is no easily established linear dependence of $1/k_0$ on concentration of reactants. Furthermore the slope for reaction with tetramethylammonium hydroxide differs markedly from that for reaction with sodium hydroxide. Both of these results are consistent with the proposal that much of the observed behavior is due to kinetic salt effects since it is known that sodium hydroxide is a strong salting out agent and that the salt effects of sodium and tetramethylammonium ions differ markedly.²⁷ The still different dependence of rate on concentration reported by Winstrom and Warner²⁰ using another base, barium hydroxide, is further evidence for specific salt effects. We conclude, as did Twigg, *et al.*, that the data of Fig. 2 are indeed evidence for the existence of measurable amounts of the alkoxide intermediate of mechanism (I), but we also conclude that the data by themselves do not permit quantitative measurement of its concentration.

Fortunately it appears that a fairly precise measurement of the equilibrium constant for reaction Ia can be made by a conductivity procedure.¹⁶ Data on the necessary measurements are listed in Table IV. For the process involved



the degree of dissociation α , and hence ultimately the equilibrium constant K , may be calculated from the expression

$$\frac{R_{(\text{cor})}}{R_0} = \frac{\Delta_{\text{NaOH}}}{\lambda_c \text{Na}^+ + (1-\alpha)\lambda_c \text{OH}^- + \alpha\lambda_c \text{CH}_2\text{ClCH}_2\text{O}^-}$$

where R_0 and Δ_{NaOH} are the resistance and equivalent conductivity, respectively, of the sodium hydroxide solution by itself and $\lambda_c \text{Na}^+$, etc., refer to the equivalent conductivity of the various ions. $R_{(\text{cor})}$ is the resistance which the alkaline solutions of the chlorohydrin would exhibit if no "viscosity effect" were present. Since the viscosity correction is difficult to measure directly, it has been made by assuming that the effect of change in viscosity is the same for solutions of sodium hydroxide as it is for solutions of potassium chloride. Studies with ethanol (Table IV) indicate that this assumption is a conservative one.

The viscosity correction has been applied in Table V and the last column of this table gives values of the equilibrium constant as calculated from the relation $K = \alpha/(1-\alpha)C_{\text{SH}}$ where C_{SH} is molar concentration of unreacted substrate. As noted previously¹⁶ the resulting K is to a good approximation the thermodynamic equilibrium constant for the reaction.

It is noteworthy that the very slow decrease (*ca.* 0.1% per hour) in the resistance of solutions of potassium chloride containing 2-chloroethanol, together with the high resistance of solutions of the latter alone (Table IV), show that the degree of possible gradual contamination of solutions of 2-

(27) F. A. Long and W. P. McDevit, *Chem. Revs.*, **51**, 119 (1952); F. A. Long and R. L. Bergen, *J. Phys. Chem.*, **60**, 1131 (1956).

TABLE IV

THE CONDUCTIVITY OF ELECTROLYTES IN WATER AND IN DEUTERIUM OXIDE CONTAINING ETHANOL AND 2-CHLOROETHANOL

Solvent	Organic substrate	Concn. (M)	Electrolyte	Concn. (M)	Resistance (ohm)	Equivalent conductivity (Δ)	$\frac{(\Delta_1 - \Delta_2)}{\Delta_2}$ (= "L")	"L" Calcd. for 1 M substrate		
H ₂ O	Ethanol	0.0	KCl	0.001	2744	147.0	0.0323	0.129		
		.25	KCl	.001	2833	142.4				
		.0	NaOH	.002	870.0	236.8				
		.25	NaOH	.002	894.6	230.4				
H ₂ O	2-Chloroethanol	.10	ca. 10 ^b0686	.143		
		.0	KCl	.0024	1172	146.5				
		.4808	KCl	.0024	1252	137.1				
		.4808	KCl	.0024	1226 ^a	...				
		.0	NaOH	.00375	459.8	239.0				
		.1098	NaOH	.00375	484.0 ^b	227.1			.0524	.477
		.2069	NaOH	.00375	506.0 ^b	217.2			.1004	.485
		.3000	NaOH	.00375	528.0 ^b	208.1			.1485	.495
		D ₂ O	2-Chloroethanol	.0	KCl	.002815			1210	121.0
.08525	KCl			.002815	1222	119.8				
.0	NaOD			.004057	680.2	149.4				
.1001	NaOD			.004057	711.8 ^b	142.7	.0470	.470		
.2041	NaOD			.004057	748.0 ^b	135.8	.1001	.491		
.3037	NaOD			.004057	811.0 ^b	125.0	.1952	.643		
.0	NaOD			.002847	984.5	147.1	.0396	.465		
.08525	NaOD			.002847	1023 ^b	141.5				

^a After 16 hr. ^b Mean of 2 measurements.

TABLE V

EQUILIBRIUM CONSTANTS FOR THE REACTION OF 2-CHLOROETHANOL WITH HYDROXIDE ION IN WATER AND IN DEUTERIUM OXIDE

Solvent	Substrate concn. (M)	Alkali concn. (M)	R(cor.)	$\lambda_0\text{Na}^+$ (calcd.)	$\lambda_0\text{CH}_2\text{Cl}-\text{CH}_2\text{O}^-$	α	K (l. mole ⁻¹)	Mean K (l. mole ⁻¹)
H ₂ O	0.0	0.00375	459.8 = R ₀	48.1 ^a				
	.1098	.00375	476.5	48.1	32 ^c	0.0496	0.48	
	.2069	.00375	491.5	48.1	32	.0913	.49	0.49
	.3000	.00375	506.3	48.1	32	.130	.50	
D ₂ O	.0	.004057	680.2 = R ₀	39.8 ^b				
	.1001	.004057	703.6	39.8	26.4 ^d	.0597	.64	
	.2041	.004057	730.6	39.8	26.4	.124	.71	
	.3037	.004057	783.2	39.8	26.4	.236	1.02	.66 ^e
	.0	.00285	984.5 = R ₀	40.1 ^b	26.4			
	.08525	.00285	1013	40.1	26.4	.0514	0.64	

^a Calculated from best available literature value for $\lambda_0\text{Na}^+$ and the variation of λNaCl with concentration. ^b Calculated from mean value of $\lambda_0\text{Na}^+$ in D₂O = 41.6.²⁸ ^c The anion has approximately the same size as the trifluoroethoxide anion, ref. 16. ^d Using the relation $\lambda\text{H}_2\text{O}/\lambda\text{D}_2\text{O} = 1.21$. ^e Neglecting the value 1.02.

chloroethanol by "strong" acid is extremely slight and cannot account for more than ca. 0.2% of the resistance increment of the alkaline solutions.²⁹

An important consequence of the data of Table V is that they permit calculation of the thermodynamic ionization constant for the chlorohydrin as an acid. Using the relation $K = K_{\text{SH}}/K_{\text{H}_2\text{O}}$ along with values of 1×10^{-14} and 0.154×10^{-14} for $K_{\text{H}_2\text{O}}$ and $K_{\text{D}_2\text{O}}$, respectively, one calculates $K_{\text{SH}} = 4.9 \times 10^{-15}$ and $K_{\text{SD}} = 1.0_2 \times 10^{-15}$ where K_{SD} is for ionization of the deuterioalcohol in D₂O as solvent. The value of K_{SH} for water as solvent agrees approximately with the figure given by

(28) L. G. Longworth and D. A. McInnes, *THIS JOURNAL*, **59**, 1666 (1937), and O. F. Frivold, O. Hassel and E. Hetland, *C. A.*, **35**, 2055 (1941).

(29) Assuming no difficulties from adventitious impurities, there remain several sources of error in the K values, the largest of which probably is the viscosity correction. Our estimate is that the K values are accurate to about $\pm 25\%$. Several of these errors will partially cancel when one takes a ratio of K 's; hence we believe that the ratio $K_{\text{H}}/K_{\text{D}}$ is accurate to about $\pm 10\%$.

Twigg, *et al.*^{13,30} The ratio of ionization constants of $K_{\text{H}}^{\text{H}}/K_{\text{D}}^{\text{D}} = 4.8$ is in reasonable accord with an extrapolation of the Rule and LaMer plot.³¹

The observed values for the equilibrium constant for reaction Ia are in accord with the conclusions of Twigg, *et al.*,¹³ that measurable amounts of the intermediate alkoxide ion are present in the ordinary reaction mixtures. For example, with 0.01 M reactants about 0.5% of the initial chlorohydrin is actually present as the alkoxide ion and for 0.1 M reactants this percentage increases to about five

(30) Our value of the ionization constant of 2-chloroethanol is considerably higher than that listed by Winstein and Grunwald (*THIS JOURNAL*, **70**, 828 (1948)) who estimate a value for pK_{A} of 16.9. However, this estimate is based on an assumed value of $pK_{\text{A}} = 18$ for ethanol. Actually there is good reason to believe that ethanol has about the same acid strength as water (see, for example, Hine and Hine, *ibid.*, **74**, 5266 (1952)). If one assumes this and therefore uses a pK_{A} value for ethanol of 15.7, the procedure of Winstein and Grunwald leads to an estimate of $pK_{\text{A}} = 14.6$ for 2-chloroethanol, in reasonable agreement with the measured value.

(31) Figure 2 of C. K. Rule and V. K. LaMer, *ibid.*, **60**, 1981 (1938).

(assuming that K remains at its dilute solution value). However, the percentages for these concentrations are not large enough to cause any significant drift in the second-order rate coefficients, at least for the first 50% of the reaction, and the ratio of the observed rate coefficients for reaction in H_2O and D_2O is therefore a true measure of the over-all effect of this solvent change.

By using the data of Table V on the effect of D_2O on the equilibrium (Ia), it is possible to calculate the effect of this solvent on the slow step (Ib). In terms of the mechanism one can write

$$\frac{k^{\text{D}}}{k^{\text{H}}} = \frac{k_2^{\text{D}} K^{\text{D}}}{k_2^{\text{H}} K^{\text{H}}}$$

where $k^{\text{D}}/k^{\text{H}}$ is the observed over-all rate ratio, $K^{\text{D}}/K^{\text{H}}$ is the ratio of equilibrium constants for step (Ia) and $k_2^{\text{D}}/k_2^{\text{H}}$ is the ratio of rates for the slow step of the reaction, step (Ib). From the listed values of the first two ratios we calculate that $k_2^{\text{D}}/k_2^{\text{H}}$ is 1.15. Since the alkoxide ion reactant for this step is clearly identical in D_2O and H_2O it follows that this is a case of a reaction which is significantly faster in D_2O because of general solvent effects. Solvent effects of this magnitude are frequently encountered but generally the direction is for slower rates in D_2O .³² However, a few cases of faster rate in D_2O (due to general solvent effects) have been observed and have been correlated with a decrease in solvation in going from reactants to transition state.³³ A similar large decrease in solvation is quite reasonable for the present reaction. Hence the observed D_2O effect for step (Ib) is not at all surprising.

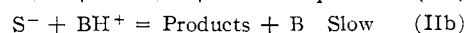
Returning to the over-all effect of the change from H_2O to D_2O as solvent, it is noteworthy that the measured $k^{\text{D}}/k^{\text{H}}$ ratios for the chlorohydrin reaction and also for the reaction of hydroxide ion and diacetone alcohol are substantially greater than unity. Since both of these are examples of specific hydroxide ion catalysis, it seems reasonable to conclude that reaction by this particular mechanism will generally be slightly faster in D_2O than in water. A plausible estimate of the limit of variation for $k^{\text{D}}/k^{\text{H}}$ for specific hydroxide ion catalysis might be a range of from 1 to 1.8.

An important question which now can be considered is: are the results for other mechanisms of

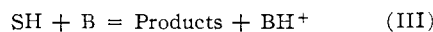
(32) P. M. Laughton and R. E. Robertson, *Can. J. Chem.*, **34**, 1714 (1956).

(33) J. G. Pritchard and F. A. Long, *THIS JOURNAL*, **78**, 6008 (1956).

base catalysis sufficiently different from this as to permit data from a study of relative rates in D_2O to be used as a general criterion of mechanism? One other mechanism for consideration is that of general base catalysis with a preequilibrium proton removal



An example of this is the reaction of an enol to give a ketone. For this reaction, and presumably also for other examples of this mechanism, there is good reason to believe that the reaction will be considerably *slower* in D_2O than in H_2O , for reaction of hydroxide ion as well as of other bases.^{8,34} Another mechanism to consider is a single-step, slow proton removal



Examples of this reaction are the base-catalyzed transformation of a ketone to an enol and the reaction between a base and a nitroparaffin. For the particular case of reaction of a nitroparaffin with hydroxide ion,⁷ $k^{\text{D}}/k^{\text{H}}$ has been reported as 1.4 and data for other bases are not very different.^{4,35} A summary of these various estimates is

Mechanism	Catalyst	Approx. $k^{\text{D}}/k^{\text{H}}$
I, specific OH^-	OH^-	1 to 1.8
II, pre-equil., gen. base	OH^- or other	0.2 to 0.4
III, one step, gen. base ³⁵	OH^- or other	0.8 to 1.5

On the basis of these estimates it would appear that studies of relative rates in D_2O should distinguish mechanism II from I and III. In contrast the latter two probably are not distinguishable in this way. This last conclusion is perhaps less serious since III, the one step slow proton removal, presumably will occur only for rather distinctive reactants, most characteristically for removal of a proton from carbon.

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(34) No direct study of the D_2O effect for reaction of hydroxide ion by this mechanism appears to have been made. Ref. 8 however shows that this reaction is about 1/4th as fast in D_2O for the bases acetate ion and water and the general prediction would be quite similar for reaction of hydroxide ion. The conclusion in ref. 8 that D_2O is a considerably weaker acid than H_2O would lead to the same prediction since the slow step for the hydroxide ion reaction is the transfer of a proton from either H_2O or D_2O to the α -carbon of the enolate ion.

(35) The usual situation, to which these data relate, is that the reactant is present as SH in the solvent D_2O as well as in H_2O , *i.e.*, that exchange of the proton being attacked is slow. If this is not true, this mechanism will also exhibit much slower rates in D_2O . See ref. 8 for amplification of this point.