Calculated Isotope Effects for Reactions of Lyoxide Ion or Water in Mixtures of Light and Heavy Water[1-2]

By C. Gardner Swain and Edward R. Thornton

The nucleophilicity of DO$^-$ relative to HO$^-$ is calculated. Twelve equations relating isotope effect to atom fraction of deuterium in the solvent are derived for 21 extreme types of transition states for reactions of LO$^-$ or L$_2$O in L$_2$O at 25°, where L is H or D in any combination, with various substrates S, LS. SX and LSX without or with exchangeable L or displaceable halide ion X. Curves are shown for all of these equations for k_D/k_H values of 2, 1 and $^1/_2$.

Equations for the dependence of isotope effect on atom fraction of deuterium in the solvent for reactions of lyonium ion L$_3$O$^+$ in mixtures of light and heavy water at 25° were derived in the previous paper.[2] Using similar arguments, equations are derived below for reactions of lyoxide ion LO$^-$ or of water L$_2$O with substrates S, LS, SX and LSX at 25° where L is H or D in any combination in mobile equilibrium with the solvent water and X is a halogen atom.

Table I lists the transition states considered and the corresponding equations. A major factor

Table I
Equations Corresponding to Various Extreme Transition States[a]

Reactions of LO$^-$	Trans. state charge on LO or L$_2$O -1	0	$+1$
Substrate { S	1	4	....
SX	2	5	....
LS	3	4, 6	....
LSX	2, 3	5, 7	....
Reactions[b] of L$_2$O			
Substrate { S	8, 8′	1, 3	9
SX	8, 8′	2	10
LS	8, 8′	3	11, 11′
LSX	8, 8′	2, 3	12

[a] L is H or D in any combination; X is a halogen atom which is an incipient halide ion at the transition state. The L of LS or LSX is in mobile equilibrium with the solvent and is transferred to the nucleophile in the rate-determining step. [b] Water is considered as an electrophile (lyon donor) in the -1 column, but a nucleophile in the $+1$ column.

affecting the dependence of isotope effect on α, the atom fraction of deuterium in the solvent, is the change in charge on the oxygen of the nucleophile (LO$^-$ or L$_2$O) from initial state to transition state. At the transition state each LO bond at this oxygen is assumed to have the same zero-point energy difference as the LO bonds of either LO$^-$, L$_2$O or L$_3$O$^+$. These are the three extremes corresponding to the three captions in Table I (charges -1, 0 and $+1$). The distribution of H and D in these LO bonds and the resulting dependence of isotope effect on α is calculated for each kind of LO bond as a function of α for reactions in water at 25°. The approximations involved in this approach were discussed in the introduction of the previous paper.[2] By interpolating the observed dependence between the appropriate calculated

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(2) Previous paper (IV) in this series by C. G. Swain and E. R. Thornton, J. Am. Chem. Soc., 83, 3884 (1961).

extremes, one may be able to judge the actual strength of these LO bonds or the change in charge on oxygen or extent of bond formation with this oxygen at the transition state.

For halides SX reacting to give halide ions there is a further contribution to the dependence of isotope effect on α arising from differences in free energy of solvation of halide ions in H$_2$O and D$_2$O.[3] From the observed magnitude of this contribution one may be able to judge the extent of charge development on X or extent of bond breaking of the halogen bonds at the transition state.

Equations are also calculated for substrates which supply, to the nucleophile, lyons already in mobile equilibrium with the solvent. These substrates are denoted by LS and LSX.

Transition states of substrates SX and LSX in which the bonds to halogen are unchanged between initial state and transition state are listed in Table I and discussed below as reactions of S or LS. Transition states of LS or LSX in which the bonds to L are either unchanged or replace bonds to L of similar type in the initial state are treated as reactions of S or SX.

Equation 1.—Transition states LO$^-$---S (with the charge on oxygen still close to that in LO$^-$) for reaction of LO$^-$ with a substrate S are the simplest extreme case. For these to be transition states there must have been some movement of atomic nuclei and valence electrons within S. However, if S contains no halide or other leaving group having a significant effect on the structure of water, it is reasonable to expect that activity coefficients for S in ground state and transition state will cancel for all α. The adherence of data on hydrolysis of ethylene oxides and many other substrates to the Gross equation indicated that ratios of activity coefficients for numerous oxonium ion transition states to corresponding conjugate base ground states (γ^*/γ_S ratios) are independent of α.[8] Similarly for the present transition states, developing carbonium and alkoxide centers would not be expected to lead to a dependence on α because a carbonium center would have partial bonds with the approaching HO$^-$ and the developing alkoxide, leaving no face open for interaction with solvent molecules, while an incipient alkoxide center should interact with the solvent but to an extent independent of α, as do H$_2$O and HO$^-$.[8] The special case of a developing halide ion is treated as eq. 2 below. In the absence of such a compli-

(3) C. G. Swain, R. F. W. Bader and E. R. Thornton, Tetrahedron, 10, 200 (1960).

Table II
Parameters for Equations 2 and 4-12

| α	ξ_{F^-}	ξ_{Cl^-}	ξ_{Br^-}	ξ_{I^-}	β	ϕ	j_H	j_D	$(1-0.293\alpha)^2$	$(1-0.293\alpha)$
0.0	1.0000	1.0000	1.0000	1.0000	1.000	0.0000	1.0000	0.0000	1.0000	1.0000
.1	1.0165	0.9657	0.9543	0.9352	1.046	.0584	0.8603	.1711	0.9422	0.9146
.2	1.0327	.9337	.9121	.8766	1.097	.1224	.7294	.3264	.8862	.8343
.25	1.0407	.9185	.8922	.8495	1.124	.1568	.6672	.3981	.8589	.7960
.3	1.0487	.9038	.8730	.8236	1.153	.1930	.6073	.4659	.8391	.7588
.4	1.0644	.8760	.8372	.7757	1.215	.2711	.4941	.5896	.7793	.6880
.5	1.0798	.8500	.8039	.7322	1.284	.3582	.3897	.6975	.7285	.6217
.6	1.0948	.8258	.7732	.6926	1.361	.4556	.2941	.7896	.6793	.5599
.7	1.1096	.8031	.7449	.6572	1.448	.5656	.2073	.8659	.6319	.5023
.75	1.1168	.7924	.7315	.6406	1.496	.6260	.1672	.8981	.6088	.4750
.8	1.1239	.7821	.7187	.6247	1.547	.6906	.1294	.9264	.5861	.4488
.9	1.1379	.7625	.6946	.5953	1.660	.8340	.0603	.9711	.5421	.3992
1.0	1.1515	.7443	.6723	.5686	1.792	1.0000	.0000	1.0000	.5000	.3534

cation, the calculated isotope effect or ratio of ordinary experimental first-order rate constants in a mixture of light and heavy water with atom fraction of deuterium α compared to pure light water at the same concentration of lyoxide ion and same temperature (25°) is simply

$$k_\alpha/k_H = k_D/k_H = 1 \qquad (1)$$

There is no isotope effect.

Transition states (L$_2$O---S or S---LOL) with two L$_2$O-like LO bonds for reaction of L$_2$O (acting as either nucleophile or electrophile) with any substrate S should also fit eq. 1 because the LO bonds are similar in ground state and transition state.

Equation 2.—Transition states (LO$^-$---S$^{\delta+}$--X$^{\delta-}$) with an LO$^-$-like bond for reaction of LO$^-$ with an alkyl halide SX are of two types.

$$HO^- + SX \underset{}{\overset{K_H^*}{\rightleftarrows}} HO\text{-}SX$$

$$DO^- + SX \underset{}{\overset{K_D^*}{\rightleftarrows}} DO\text{-}SX$$
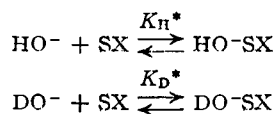
The isotope effect, now due solely to partial formation of X$^-$ (bond breaking), is

$$\frac{k_\alpha}{k_H} = \frac{[HO\text{-}SX]_\alpha^* + [DO\text{-}SX]_\alpha^*}{[HO\text{-}SX]_H^*}$$

where the starred concentrations are effective concentrations, which, like the K^* constants, include the velocity of crossing the potential maximum. Concentrations are expressed in moles per 55.5 moles of solvent. Hence

$$\frac{k_\alpha}{k_H} = \frac{[HO^-]_\alpha(\gamma_{HO^-})_\alpha(\gamma_{SX})_\alpha(\gamma_H^*)_H}{[HO^-]_H(\gamma_{HO^-})_H(\gamma_{SX})_H(\gamma_H^*)_\alpha} +$$
$$\frac{[DO^-]_\alpha(\gamma_{DO^-})_\alpha(\gamma_{SX})_\alpha)\gamma_H^*)_H}{[HO^-]_H(\gamma_{HO^-})_H(\gamma_{SX})_H(\gamma_D^*)_\alpha} = \frac{(\gamma_{SX})_\alpha(\gamma^*)_H}{(\gamma^*)_\alpha(\gamma_{SX})_H} =$$
$$[(\gamma_{X^-}^*)_H/(\gamma_{X^-}^*)_\alpha]^y = \xi^y \qquad (2)$$

$$k_D/k_H = [(\gamma_{X^-}^*)_H/(\gamma_{X^-}^*)_D]^y = \xi_D^y$$

where the exponent y is a measure of the extent of SX bond-breaking at the transition state. Since HO$^-$ and DO$^-$ do not change the structure of water, $(\gamma_{HO^-})_H = (\gamma_{HO^-})_\alpha = (\gamma_{DO^-})_\alpha$. Since isotopes have almost identical sizes and potential energies, $(\gamma_H^*)_\alpha = (\gamma_D^*) = (\gamma^*)_\alpha$. The final ratio in brackets is similar to the activity coefficient ratio for a free halide ion $(\gamma_{X^-})_H/(\gamma_{X^-})_\alpha$ calculated according to the method previously described[3] except that the number of water molecules coördinated is assumed to be one less than that for the free halide ion, i.e.,

3 for F$^-$, Cl$^-$ or Br$^-$ but 5 for I$^-$, because the S--X bond occupies one of the coördination positions.

$$(\Delta F_s^{F^-})^* = 14.67\,\alpha^2 - 98.28\,\alpha$$
$$(\Delta F_s^{Cl^-})^* = -35.28\,\alpha^2 + 210.24\,\alpha$$
$$(\Delta F_s^{Br^-})^* = -46.80\,\alpha^2 + 282.06\,\alpha$$
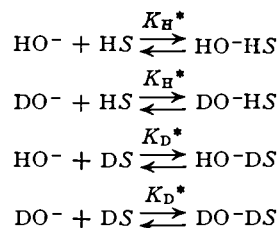$$(\Delta F_s^{I^-})^* = -69.60\,\alpha^2 + 404.10\,\alpha$$

in cal. mole-ion^{-1}. From the equation

$$(\Delta F_s^{X^-})_\alpha^* = -2.303\,RT\log((\gamma_{X^-}^*)_H/(\gamma_{X^-}^*)_\alpha) =$$
$$-2.303\,RT\log\xi$$

ξ can be calculated as a function of α for each halide ion. The exponent y should be independent of α, zero for negligible bond breaking and approximately one for complete bond breaking; it may be evaluated from eq. 2 for pure D$_2$O ($\alpha = 1.00$) and the ξ-values given in Table II. This is a solvent isotope effect arising from differences in strength of solvation of halide ions by light and heavy water.

Transition states (L$_2$O---S$^{\delta+}$--X$^{\delta-}$ or S$^{\delta+}$--X$^{\delta-}$---LOL) with two L$_2$O-like LO bonds for reaction of L$_2$O with a substrate SX should also fit eq. 2 because the LO bonds are not altered.

Equation 3.—Transition states (LO$^-$---L$^{\delta+}$--S$^{\delta-}$) with an LO$^-$-like bond for reaction of LO$^-$ with a substrate LS are

$$HO^- + HS \underset{}{\overset{K_H^*}{\rightleftarrows}} HO\text{-}HS$$

$$DO^- + HS \underset{}{\overset{K_H^*}{\rightleftarrows}} DO\text{-}HS$$

$$HO^- + DS \underset{}{\overset{K_D^*}{\rightleftarrows}} HO\text{-}DS$$

$$DO^- + DS \underset{}{\overset{K_D^*}{\rightleftarrows}} DO\text{-}DS$$

The isotope effect is

$$\frac{k_\alpha}{k_H} =$$
$$\frac{[HO\text{-}HS]_\alpha^* + [DO\text{-}HS]_\alpha^* + [HO\text{-}DS]_\alpha^* + [DO\text{-}DS]_\alpha^*}{[HO\text{-}HS]_H^*}$$

$$= \frac{[HS]_\alpha}{[HS]_H}\left(\frac{[HO^-]_\alpha + [DO^-]_\alpha}{[HO^-]_H}\right) +$$
$$\frac{k_D[DS]_\alpha}{k_H[DS]_D}\left(\frac{[HO^-]_\alpha + [DO^-]_\alpha}{[DO^-]_D}\right)$$

if we cancel all activity coefficients as before.[2] If there is no fractionation between LS and solvent (L$_2$O), this leads to the linear relationship

$$\frac{k_\alpha}{k_H} = 1 - \alpha + \frac{k_D}{k_H}\alpha$$

$$= 1 + \left(\frac{k_D}{k_H} - 1\right)\alpha \qquad (3)$$
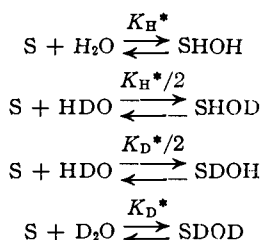
This isotope effect arises from weakening of the LS bond (without concomitant formation of a new OL bond to the LO⁻).

Transition states (L$^\delta$+--S$^\delta$----LOL) with two L₂O-like LO bonds for reaction of L₂O (acting as an electrophile or lyon donor) with LS are

$$HS + H_2O \underset{}{\overset{K_H^*}{\rightleftharpoons}} HSHOH$$

$$HS + HDO \underset{}{\overset{K_H^*/2}{\rightleftharpoons}} HSHOD$$

$$HS + HDO \underset{}{\overset{K_H^*/2}{\rightleftharpoons}} HSDOH$$

$$HS + D_2O \underset{}{\overset{K_H^*}{\rightleftharpoons}} HSDOD$$

$$DS + H_2O \underset{}{\overset{K_D^*}{\rightleftharpoons}} DSHOH$$

$$DS + HDO \underset{}{\overset{K_D^*/2}{\rightleftharpoons}} DSHOD$$

$$DS + HDO \underset{}{\overset{K_D^*/2}{\rightleftharpoons}} DSDOH$$

$$DS + D_2O \underset{}{\overset{K_D^*}{\rightleftharpoons}} DSDOD$$
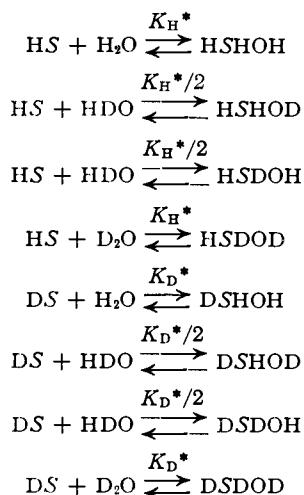
Each $1/2$ is a statistical factor. Using the same method and assumptions, this isotope effect also fits eq. 3.

Transition states (S$^\delta$---L$^\delta$+--OL) with one L₂O-like bond for reaction of L₂O (acting as an electrophile or lyon donor) with a substrate S are

$$S + H_2O \underset{}{\overset{K_H^*}{\rightleftharpoons}} SHOH$$

$$S + HDO \underset{}{\overset{K_H^*/2}{\rightleftharpoons}} SHOD$$

$$S + HDO \underset{}{\overset{K_D^*/2}{\rightleftharpoons}} SDOH$$

$$S + D_2O \underset{}{\overset{K_D^*}{\rightleftharpoons}} SDOD$$

One lyon is still like that in L₂O since this limiting case is one in which any increase in negative charge occurs on S or (less probably) on the other lyon being transferred, but not on the oxygen. Each $1/2$ is a statistical factor. The isotope effect is

$$\frac{k_\alpha}{k_H} = \frac{[H_2O]_\alpha + 1/2[HDO]_\alpha}{[H_2O]_H} + \frac{k_D}{k_H}\frac{1/2[HDO]_\alpha + [D_2O]_\alpha}{[D_2O]_D}$$

$$= 1 + \left(\frac{k_D}{k_H} - 1\right)\alpha$$

which is again eq. 3. Transition states (L₂O---L--S) also fit eq. 3.

Transition states (LO⁻---L$^\delta$+--S$^\delta$---X$^\delta$⁻) with an LO⁻-like bond for reaction of LO⁻ with LSX lead to an isotope effect combining two effects (halide ion solvation and LS bond weakening) which would be difficult to separate experimentally. Therefore the equation is not included for this case.

Equation 4.—Transition states (LOS⁻) with an L₂O-like bond for reaction of LO⁻ with S are

$$HO^- + S \underset{}{\overset{K_H^*}{\rightleftharpoons}} HOS^-$$

$$DO^- + S \underset{}{\overset{K_n'K_H^*}{\rightleftharpoons}} DOS^-$$
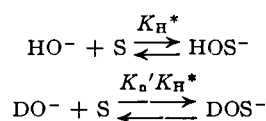
and are the alkaline analogs of reactions of L₃O⁺ for which the Gross equation was derived earlier.[3]
The isotope effect is

$$\frac{k_\alpha}{k_H} = \frac{[HOS^-]_\alpha{}^* + [DOS]^-{}_\alpha{}^*}{[HOS^-]_H{}^*} = \frac{[HO^-]_\alpha}{[HO^-]_H} +$$

$$\frac{K_n'[DO^-]_\alpha}{[HO^-]_H} = \frac{K_n'}{\alpha + (1 - \alpha)K_n'} = \beta \qquad (4)$$

and

$$\frac{k_D}{k_H} = K_n'$$

K_n' is the isotope effect (k_D/k_H) for changing one LO⁻ bond to one LO bond, or the factor by which DO⁻ is a stronger base than HO⁻. It is 1.79, the square root of the constant 3.21 derived earlier[4] for the equilibrium

$$2DO^- + H_2O \underset{}{\overset{K_n'^2}{\rightleftharpoons}} 2HO^- + D_2O$$
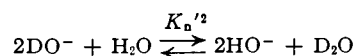
Since it is greater than one, it disfavors DO⁻ bonds relative to HO⁻ bonds. Other equilibria involving K_n' are

$$DO^- + HDO \underset{}{\overset{K_n'/2}{\rightleftharpoons}} HO^- + D_2O$$

$$DO^- + H_2O \underset{}{\overset{2K_n'}{\rightleftharpoons}} HO^- + HDO$$
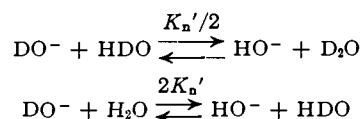
The factors of two are statistical factors.
In deriving eq. 4 we have made use of the relations

$$N_{H_2O} + N_{HDO} + N_{D_2O} = 1$$

$$\alpha = (2N_{D_2O} + N_{HDO})/2$$

$$N_{HDO}{}^2/N_{H_2O}N_{D_2O} \cong 4$$

which lead to

$$N_{H_2O} = (1 - \alpha)^2; \quad N_{HDO} = 2\alpha(1 - \alpha); \quad N_{D_2O} = \alpha^2$$

Table II contains values of β for various values of α.

This isotope effect arises solely from the greater basicity of DO⁻ than of HO⁻, i.e., the isotope effect for changing an LO⁻ to an LO bond.

Transition states (LOL---S⁻) with the LO bond like that in water and the OL bond like the LS bond in the reactant also fit eq. 4.[5]

Equation 5.—Transition states (LOS$^\delta$---X$^\delta$⁻) with L₂O-like bonds for reaction of LO⁻ with SX combine the features of eq. 2 and 4. The symbol δ is used to indicate any partial charge; the two δ⁻ charges may be of any relative magnitudes. The result is
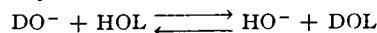
$$k_\alpha/k_H = \xi^y\beta$$

and

$$k_D/k_H = K_n'\xi_D{}^y$$

(4) C. G. Swain and R. F. W. Bader, *Tetrahedron*, **10**, 182 (1960).
(5) W. E. Nelson and J. A. V. Butler, *J. Chem. Soc.*, 957 (1938), derived the equation

$$\frac{k_\alpha}{k_H} = \frac{1 + \alpha((k_D/k_H K_n') - 1)}{1 + \alpha((1/K_n') - 1)}$$

for transition states of this type. However, k_D/k_H must equal K_n' because it is the equilibrium constant for
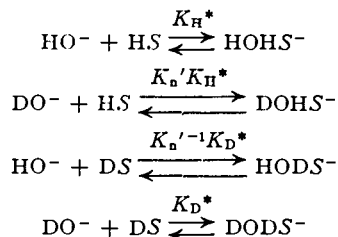
$$DO^- + HOL \rightleftharpoons HO^- + DOL$$

This reduces their equation to eq. 4.

This isotope effect combines factors for halide ion solvation and lyoxide ion basicity.

Transition states (LOL---$S^{\delta-}$---$X^{\delta-}$) with the LO bond like that in water and the OL bond like the LS bond in the reactant also fit eq. 5.

Equation 6.—Transition states (LO--L--S^-) with one (or two) L$_2$O-like bonds for reaction of LO$^-$ with LS are

$$HO^- + H\mathit{S} \underset{}{\overset{K_H^*}{\rightleftharpoons}} HOH\mathit{S}^-$$

$$DO^- + H\mathit{S} \xrightarrow{K_n'K_H^*} DOH\mathit{S}^-$$

$$HO^- + D\mathit{S} \xrightarrow{K_n'^{-1}K_D^*} HOD\mathit{S}^-$$

$$DO^- + D\mathit{S} \underset{}{\overset{K_D^*}{\rightleftharpoons}} DOD\mathit{S}^-$$

If there is no fractionation of deuterium between the substrate LS and the solvent the isotope effect should be

$$\frac{k_\alpha}{k_H} =$$

$$\frac{[HOH\mathit{S}^-]_\alpha^* + [DOH\mathit{S}^-]_\alpha^* + [HOD\mathit{S}^-]_\alpha^* + [DOD\mathit{S}^-]_\alpha^*}{[HOH\mathit{S}^-]_H^*}$$

$$= (1 - \alpha)\left[\frac{[HO^-]_\alpha + K_n'[DO^-]_\alpha}{[HO^-]_H}\right] +$$

$$\frac{k_D\alpha}{k_H}\left[\frac{K_n'^1[HO^-]_\alpha + [DO^-]_\alpha}{[DO^-]_H}\right]$$

$$= 1 + \left(\frac{k_D}{k_H} - 1\right)\phi \tag{6}$$

where

$$\phi = \frac{\alpha}{\alpha + (1 - \alpha)K_n'} = \frac{\alpha\beta}{K_n'}$$

using the β of eq. 3. Table II contains values of ϕ for various values of α. This isotope effect combines a primary isotope effect for the difference in the lyon being transferred from DS or HS to LO$^-$ and a secondary isotope effect for the differing nucleophilicities of DO$^-$ and HO$^-$.

Equation 7.—Transition states (LO--L--S---X$^-$) with one (or two) H$_2$O-like bonds and with the halide ion essentially fully formed from reaction of LO$^-$ with LSX combine the features of eq. 2 and 6. The equation contains y and k_D/k_H and cannot be solved for y in terms of k_D/k_H. However, if one assumes a value of unity for y corresponding to no effect of X on the structure of the water in the ground state and complete formation of X$^-$ solvated by 3 or 5 water molecules at the transition state, then

$$\frac{k_\alpha}{k_H} = \xi\left(1 + \left(\frac{k_D}{k_H\xi_D} - 1\right)\phi\right) \tag{7}$$

where ξ is the same as in eq. 2 and ξ_D means ξ for $\alpha = 1.00$.

This isotope effect is a composite of three effects: a secondary effect for halide ion solvation, a primary effect for LS transfer, and a secondary effect for LO$^-$ basicity.

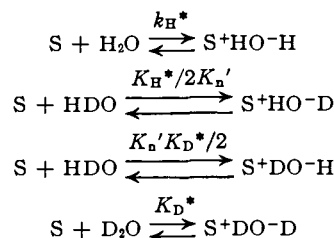An equation for mechanisms intermediate between the extremes of eq. 7 and 6 is

$$\frac{k_\alpha}{k_H} = \xi^z\left(1 + \left(\frac{k_D}{k_H\xi_D^z} - 1\right)\phi\right)$$

where z, $0 \leq z \leq 1$, is a measure of the amount of bond-breaking of the halogen atom in the transition

state. When $z = 0$, it is eq. 6; when $z = 1$, it is eq. 7. Intermediate mechanisms[2] may have curves which do not fall between the two extremes of mechanism represented by eq. 6 and 7 in the regions

$$2.11 < k_D/k_H < 2.50 \text{ for F}$$
$$1.59 < k_D/k_H < 2.24 \text{ for Cl}$$
$$1.44 < k_D/k_H < 2.24 \text{ for Br}$$
$$1.22 < k_D/k_H < 2.26 \text{ for I}$$

Equation 8.—Transition states (S$^{\delta+}$--L$^{\delta+}$---O$^-$L, with $\delta+$ charges of any relative magnitude) with a LO$^-$-like bond for reaction of L$_2$O (acting as an electrophile or lyon donor) with a substrate S are

$$S + H_2O \underset{}{\overset{k_H^*}{\rightleftharpoons}} S^+HO^-H$$

$$S + HDO \xrightarrow{K_H^*/2K_n'} S^+HO^-D$$

$$S + HDO \xrightarrow{K_n'K_D^*/2} S^+DO^-H$$

$$S + D_2O \underset{}{\overset{K_D^*}{\rightleftharpoons}} S^+DO^-D$$

K_n' is the isotope effect for changing LO$^-$ to LO (see eq. 4) and each $1/2$ is a statistical factor. The isotope effect is

$$\frac{k_\alpha}{k_H} = \frac{[S^+HO^-H]_\alpha^* + [S^+HO^-D]_\alpha^* + [S^+DO^-H]_\alpha^* + [S^+DO^-D]_\alpha^*}{[S^+HO^-H]_H^*}$$

$$= \frac{[H_2O]_\alpha}{[H_2O]_H} + \frac{[K_n']^{-1}}{2}\frac{[HDO]_\alpha}{[H_2O]_H} +$$

$$\frac{k_D}{k_H}\left(\frac{K_n'[HDO]_\alpha}{2[D_2O]_D} + \frac{[D_2O]_\alpha}{[D_2O]_D}\right)$$

$$= (1 - \alpha)^2 + (K_n')^{-1}\alpha(1 - \alpha) +$$

$$\frac{k_D}{k_H}(K_n'\alpha(1 - \alpha) + \alpha^2)$$

$$= (1 - 1.442\,\alpha + 0.442\,\alpha^2) + \frac{k_D}{k_H}(1.79\,\alpha - 0.79\,\alpha^2)$$

$$= j_H + (k_D/k_H)j_D \tag{8}$$

Values of j_H and j_D for various values of α are listed in Table II.

Equation 8 is similar to the Gross equation except that it applies to systems in which L$_2$O rather than L$_3$O$^+$ is the lyon donor. The isotope effect combines a primary isotope effect for transfer of L and a secondary isotope effect for basicity of the remaining LO$^-$.

If the L is completely transferred to form an O$^+$L bond like that in L$_3$O$^+$ at the transition state, then

$$k_D/k_H = K_n/K_n' = 0.707/1.79 = 0.394$$

$$\frac{k_\alpha}{k_H} = j_H + \frac{K_n}{K_n'}j_D \tag{8'}$$

Mechanisms intermediate between the extremes of eq. 8 and 3 should follow

$$\frac{k_\alpha}{k_H} = (1 - \alpha)^2 + K_n'^z\alpha(1 - \alpha) +$$

$$\frac{k_D}{k_H}(K_n'^{-z}\alpha(1 - \alpha) + \alpha^2)$$

where z approximates the fractional charge on oxygen at the transition state. This is eq. 8 when $z = -1$ and is eq. 3 when $z = 0$. For $0.311 < k_D/k_H < 1$, there are intermediate mechanisms which have curves not falling between eq. 3 and 8.

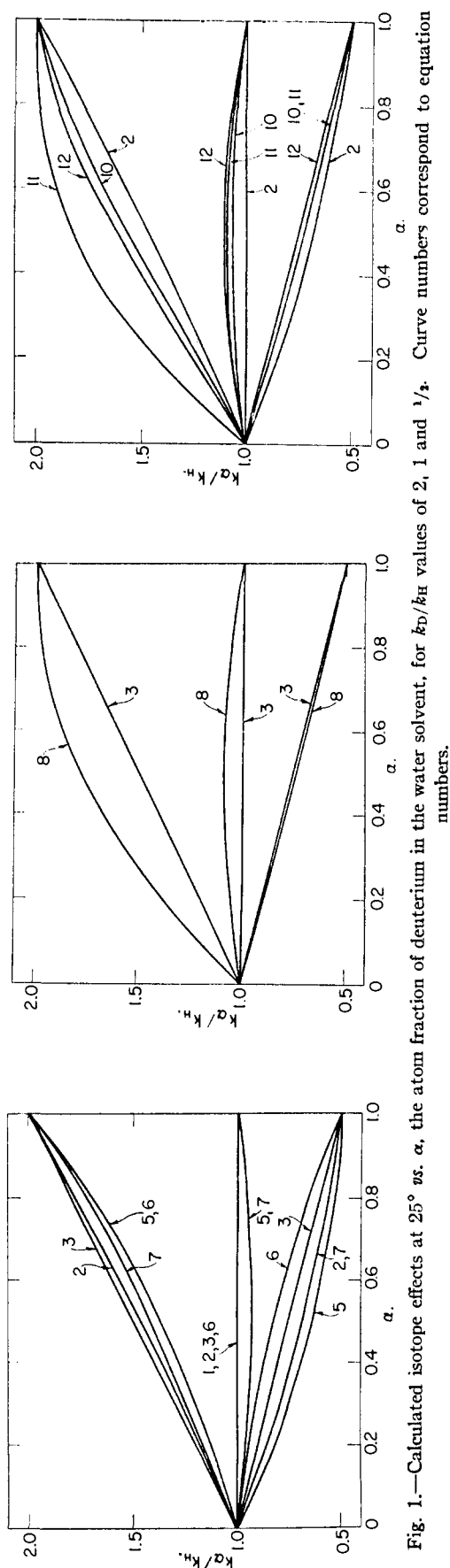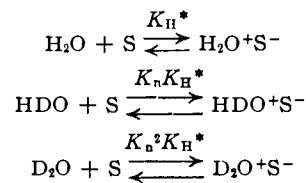Fig. 1.—Calculated isotope effects at 25° *vs.* α, the atom fraction of deuterium in the water solvent, for k_D/k_H values of 2, 1 and $\frac{1}{2}$. Curve numbers correspond to equation numbers.

Equation 9.—Transition states $(L_2O^+S^-)$ with L_3O^+-like bonds for reaction of L_2O with S are

$$H_2O + S \underset{}{\overset{K_H^*}{\rightleftharpoons}} H_2O^+S^-$$

$$HDO + S \underset{}{\overset{K_nK_H^*}{\rightleftharpoons}} HDO^+S^-$$

$$D_2O + S \underset{}{\overset{K_n^2K_H^*}{\rightleftharpoons}} D_2O^+S^-$$

K_n, the isotope effect for conversion of one LO bond to an LO^+ bond, was evaluated previously[3] as $\sqrt{2}/2$. The isotope effect is

$$\frac{k_\alpha}{k_H} = \frac{[H_2O^+S^-]_\alpha^* + [HDO^+S^-]_\alpha^* + [D_2O^+S^-]_\alpha^*}{[H_2O^+S]_H^*}$$

$$= \frac{[H_2O]_\alpha + K_n[HDO]_\alpha + K_n^2[D_2O]_\alpha}{[H_2O]_H}$$

$$= (1 - 0.293 \alpha)^2 \tag{9}$$
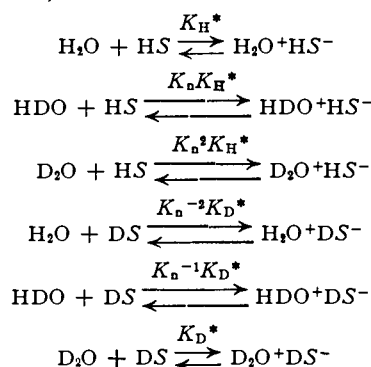
$$k_D/k_H = K_n^2 = 0.50$$

Values of $(1 - 0.293\alpha)^2$ are listed in Table II for various values of α. This isotope effect arises solely from the lower basicity of D_2O than of H_2O (or higher acidity of H_3O^+ than of D_3O^+), *i.e.*, the isotope effect for changing an LO to an LO^+ bond.

Equation 10.—Transition states with L_3O^+-like bonds for reactions of L_2O with a substrate SX $(L_2O^+S^\delta---X^{\delta-})$ give

$$k_\alpha/k_H = \xi^\nu(1 - 0.293 \alpha)^2 \tag{10}$$

$$k_D/k_H = K_n^2\xi_D^\nu = 0.50\xi_D^\nu$$

combining isotope effects of eq. 2 for halide ion solvation and eq. 9 for L_2O basicity.

Equation 11.—Transition states with L_3O^+-like bonds for reactions of L_2O with a substrate LS $(L_2O^+L---S^-)$ are

$$H_2O + HS \underset{}{\overset{K_H^*}{\rightleftharpoons}} H_2O^+HS^-$$

$$HDO + HS \underset{}{\overset{K_nK_H^*}{\rightleftharpoons}} HDO^+HS^-$$

$$D_2O + HS \underset{}{\overset{K_n^2K_H^*}{\rightleftharpoons}} D_2O^+HS^-$$

$$H_2O + DS \underset{}{\overset{K_n^{-2}K_D^*}{\rightleftharpoons}} H_2O^+DS^-$$

$$HDO + DS \underset{}{\overset{K_n^{-1}K_D^*}{\rightleftharpoons}} HDO^+DS^-$$

$$D_2O + DS \underset{}{\overset{K_D^*}{\rightleftharpoons}} D_2O^+DS^-$$

The isotope effect is

$$\frac{k_\alpha}{k_H} = (1 + (K_n - 1)\alpha)^2 \left(1 - \alpha + \frac{k_D\alpha}{k_HK_n^2}\right)$$

$$= (1 - 0.293 \alpha)^2 \left(1 + \left(\frac{k_D}{K_n^2k_H} - 1\right)\alpha\right) \tag{11}$$

as calculated by the methods used before if there is no fractionation of deuterium between LS and the solvent.

If the LS bond in the initial state is like an LO bond of L_2O

$$k_D/k_H = K_n^3$$

$$k_\alpha/k_H = (1 - 0.293 \alpha)^3 \tag{11'}$$

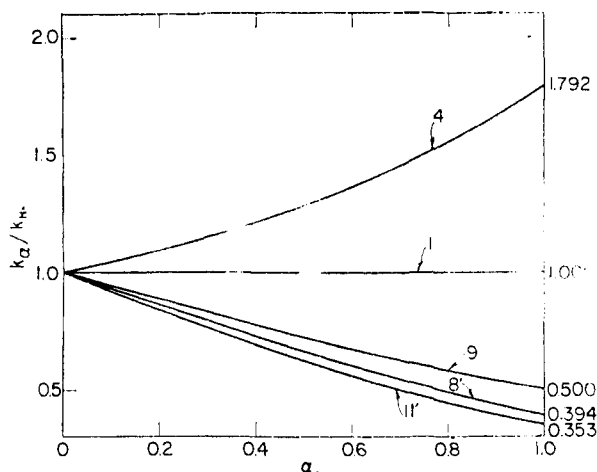This isotope effect arises because three LO bonds are changed to LO^+ bonds.

Fig. 2.—Calculated isotope effects at 25° vs. α, the atom fraction of deuterium in the water solvent for curves which do not involve k_D/k_H. Curve numbers correspond to equation numbers.

An equation intermediate between eq. 11 and 3 is

$$\frac{k_\alpha}{k_H} = \left(1 + \left(K_{n}{}^{z} - 1\right)\alpha\right)^{2}\left(1 + \left(\frac{k_D}{k_H K_{n}{}^{2z}} - 1\right)\alpha\right)$$

where z approximates the fractional charge on oxygen at the transition state. This is eq. 3 when $z = 0$ and is eq. 11 when $z = +1$. For $0.352 < k_D/k_H < 1$, there are intermediate mechanisms which have curves not falling between curves 3 and 11.

Equation 12.—Transition states $(L_2O^+L\text{---}S^{\delta-}\text{--}X^{\delta-})$ with L_3O^+-like bonds for a reaction of L_2O with a substrate LSX having a L_2O-like LO bond in its initial state lead to

$$k_\alpha/k_H = \xi^{y}(1 - 0.293\,\alpha)^{2} \qquad (12)$$

combining the isotope effects of eq. 2 and 11′.

Calculated Curves.—Figure 1 presents calculated curves at 25° for eq. 1–3 and 5–7 (for reactions of LO^-), eq. 3 and 8 (for reactions of L_2O acting as an electrophile) and eq. 2, 10, 11 and 12 (for reactions of L_2O as a nucleophile). Figure 2 presents calculated curves at 25° for eq. 1, 4, 8′, 9 and 11′, these equations being independent of k_D/k_H.

For certain values of k_D/k_H the values of y in the appropriate equations will be not between 0 and 1, but negative or greater than 1. The curves then correspond to unrealistic types of transition states: e.g., a negative y would correspond to a transition state in which the halogen atoms were more tightly bound than in the ground state, and a y greater than 1 to a transition state in which the halogen atom broke up the structure of water more than a free halide ion. However, except as noted above, the experimental points should fall between the curves for two extreme types of mechanism even if one extreme is unrealistic.

The same type of unrealism occurs in equations which do not involve y, whenever the k_D/k_H value is unreasonable for the transition state assumed.

It is likely that two similar substrates reacting by different mechanisms will show the predicted difference in dependence of isotope effect on α (with the mechanisms then characterized by the magnitudes of deviations from the theoretical curves)
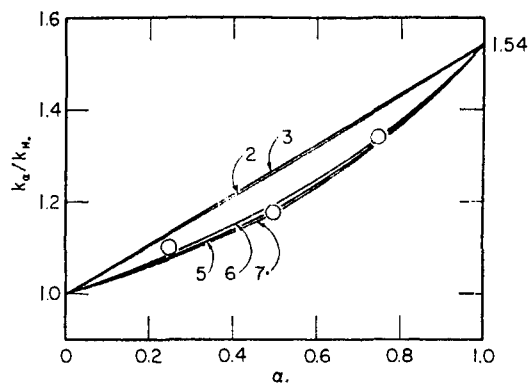

Fig. 3.—Reaction of lyoxide ion with 2-chloroethanol at 25°. Curve numbers correspond to equation numbers.

even if perfect fits to the individual curves are not obtained because of slight inaccuracies in the present parameters or differences in activity coefficients which were assumed equal for initial state and transition state. The main conclusion is that additional mechanistic information is almost certain to be obtained from the variation of isotope effect with α which is not obtainable from k_D/k_H alone. Since few reliable experimental data of this sort have yet been collected, it should be useful to collect such data for a variety of reactions of lyoxide ion or of water in water solution.

Reaction of Lyoxide Ion with 2-Chloroethanol.—This reaction, forming water and ethylene oxide, probably proceeds by abstraction of L from the LO group of 2-chloroethanol followed by rate-determining cyclization of 2-chloroethoxide ion.[6] The isotope effect, $k_{D_2O}/k_{H_2O} = 1.54$,[6] favors this mechanism by itself. Ballinger and Long[6] determined k_α/k_H for mixtures. The calculated curves for eq. 2 and 3 fall close together, while those for eq. 5, 6 and 7 fall close together but far from those for eq. 2 and 3. If the oxygen atom of the attacking LO^- had a full negative charge at the transition state, the experimental points should fall near the curves for eq. 2 and 3 (they do not). If it had a partial negative charge, they should fall between the curves for eq. 2 and 3 and those for eq. 5, 6 and 7 (they do not). Instead the points fall on the curves for eq. 5, 6 and 7, indicating that the oxygen atom has zero charge at the transition state, in accord with the proposed mechanism.

Reaction of Nucleophiles with Ethylene Oxide.—In the previous section it was shown that the cyclization of 2-chloroethanol probably involves formation of 2-chloroethoxide ion, i.e., the transition state has lost a water molecule. Therefore, by the principle of microscopic reversibility, the transition state for the reverse reaction, the nucleophilic attack of chloride ion on ethylene oxide, also involves no water molecule. The transition states for nucleophilic reactions of water and hydroxide ion with ethylene oxide should be similar to that of chloride. The solvent isotope effect for

$$X^{\delta\ominus}\text{--}CH_2\text{--}O^{\delta\ominus}$$
$$\diagdown\!\diagup$$
$$CH_2$$
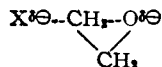
(6) C. G. Swain, A. D. Ketley and R. F. W. Bader, J. Am. Chem. Soc., 81, 2353 (1959); P. Ballinger and F. A. Long, ibid., 81, 2347 (1959).

the reaction of lyoxide ion with ethylene oxide is due principally to the change of an LO^- bond in lyoxide to an $LO^{\delta-}$ bond in the transition state. Therefore $k_D/k_H = (K_n')^{1-z}$ where z approximates the fractional negative charge on the oxygen atom of the $LO^{\delta-}$ at the transition state. Pritchard and Long found $k_D/k_H = 1.14$ at $25°$,[7] which gives $z = 0.775$, *i.e.*, only a small amount of bond making at the transition state. For the reaction of water with ethylene oxide $k_D/k_H = K_n^{2z}$ where z is the fractional positive charge on the oxygen atom of the $L_2O^{\delta+}$ of the transition state. The isotope effect for isobutylene oxide at $50°$ is 0.9, while that for propylene oxide at $50°$ is 0.8. The result for ethylene oxide at $25°$ is not available, but is probably not much less than 0.8, which gives $z = 0.32$, still a small amount of bond formation at the transition state.

Acid-catalyzed Hydrolysis of Ethylene Oxide.— With H_2O^{18} and propylene oxide in $0.1–0.25$ M perchloric acid at $25°$, O^{18} appears in the glycol predominantly on the secondary carbon atom.[8] The order of rates is propylene oxide > ethylene oxide > epichlorohydrin (1-chloro-2,3-epoxypropane), but data on ten different oxides show some positive curvature on a Taft–Hammett $\rho\sigma^*$ plot.[9] Rates of ethylene oxide and five substituted ethylene oxides are more nearly proportional to the Hammett acidity function h_0 than to $[H_3O^+]$ above 1 M perchloric acid.[8] Entropies of activation are -4 and -6 cal. $mole^{-1}$ $deg.^{-1}$ for propylene and ethylene oxide, compared to $+6$ to $+9$ for hydrolysis of acetals or esters of tertiary alcohols and -21 to -25 for hydrolysis of esters of primary alcohols.[10] The solvent isotope effect k_α/k_{H_2O} for acid-catalyzed hydrolysis of ethylene oxide at $25°$ follows the Gross equation,[2,3] with $k_{D_2O}/k_{H_2O} = 2.20$.[7] These data were interpreted as indicating an A-1 mechanism, with ring opening of the conjugate acid of the oxide (epoxonium ion) to give a primary carbonium ion in the rate-determining step and no bonding of water at the transition state.[7–10]

The evidence of h_0 dependence shows only that the transition state has an activity coefficient which changes with acidity like that of a Hammett indicator acid. It does not exclude water as a reactant because the activity of water is almost constant out to 3 M acid.[11] If there were a carbonium ion intermediate, an h_R dependence might have been expected.[11] The adherence to the Gross equation also does not exclude involvement of water because in this case an intermediate mechanism with moderate bonding of water happens to give the same calculated curve as one with no bonding of water.

(7) J. G. Pritchard and F. A. Long, *J. Am. Chem. Soc.*, **78**, 6008 (1956).

(8) F. A. Long and J. G. Pritchard, *ibid.*, **78**, 2663 (1956).

(9) J. G. Pritchard and F. A. Long, *ibid.*, **78**, 2667 (1956).

(10) F. A. Long, J. G. Pritchard and F. E. Stafford, *ibid.*, **79**, 2362 (1957).

(11) C. G. Swain and A. S. Rosenberg, *ibid.*, **83**, 2154 (1961).

A quantitative treatment of the solvent isotope effect can nevertheless put some limits on the magnitude of positive charge on various atoms in the transition state. For the transition state

$$\overset{z\oplus}{L_2O}\text{-}\text{-}\overset{z''\oplus}{CH_2}\text{-}\text{-}\overset{z'\oplus}{O}\text{-}\text{-}L$$
$$\diagdown\diagup$$
$$CH_2$$
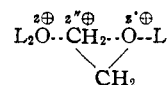
where z, z' and $z'' = 1 - z - z'$ are fractional charges on the water oxygen, oxide oxygen and carbon, respectively, the calculated solvent isotope effect is

$$k_H/k_D \cong K_n^{2(1-z)}K_n^{(1-z')} = K_n^{3-2z-z'}$$

because the contribution from the two water lyons varies from K_n^2 to 1 depending on z and the contribution from the other lyon varies from K_n to 1 depending on z'. The observed $k_H/k_D (0.454)$ requires

$$2z + z' = 0.73$$

Hence the extremes are $z = 0$, $z' = 0.73$, $z'' = 0.27$ and $z = 0.36$, $z' = 0$, $z'' = 0.64$.

This charge distribution is quite consistent with the proposed[7–10] carbonium ion mechanism. The maximum charge on the water oxygen (0.36) is indeed fairly low. The first extreme is close to what would be expected for the epoxonium ion intermediate, while the second extreme is reasonable for a primary carbonium ion solvated by a water molecule. The transition state may be anywhere between these limits in structure. However, in energy it is certainly much higher than epoxonium ion, because the epoxonium ion should be no more acidic than the cation from acetone $(pK_A \cong -6)$, generally considered to be in mobile equilibrium with acetone and hydronium ion.

An alternative and simpler interpretation is a rate-determining reaction of water with epoxonium ion to give directly the dipolar ion tautomer of the glycol, not *via* a primary carbonium ion intermediate. The transition state in such a process could come close to water and epoxonium ion in structure because these are so much less stable than the products, which are free of ring strain. This is consistent with the expectation that the bonding of water in such a process should be less than in the uncatalyzed hydrolysis, shown in the previous section to have only a small amount of bonding of water at the transition state. Since the conjugate acid has a better leaving group, it should require less help from nucleophilic attack of water, and water should be involved to a smaller extent at the transition state. Although bonding of water has not progressed very far relative to ring opening at the transition state, it may be occurring in the critical imaginary vibration at the transition state and it may become complete relatively rapidly in the subsequent continuous descent to a product in which the OC bond is fully formed. Since this is a simpler picture, we prefer it until carbonium ions are demonstrated as necessary intermediates by competition experiments, *e.g.*, by a change in product on introduction of a suitable nucleophile, without change in rate.