

peak at 18.0 min. was collected. It gave an immediate precipitate with AgNO_3 , showed a strong infrared band at 11.9μ (trisubstituted olefin) and had n_D^{20} 1.4477. *Anal.* C, 57.60; H, 8.72; Cl, 32.78. Calcd. for $\text{C}_5\text{H}_9\text{Cl}$: C, 57.47; H, 8.64; Cl, 33.90. It was accordingly identified as V, and the structure I assigned to the 6.6-min. product. Chlorination of 2-methyl-1-butene could give four allylic chlorides, II, III, IVA and IVB, none identical with I or V, and gas-liquid chromatographic analysis indeed gave four peaks at 10.0, 13.4, 16.0 and 18.0 min., the last appearing at the same time as V. Analysis at 109° also indicated addition product, considered to be 1-*t*-butoxy-2-chloro-2-methylbutane.

Chlorination of 2-methyl-2-butene, in turn, can give five allylic chlorides, I, II, IVA, IVB and V. Gas-liquid chromatographic analysis showed four peaks at 6.6 (I), 10.0, 16.0 and 18.0 min. (V plus another isomer). Since the 13.4-min. peak was absent, but present in the 2-methyl-1-butene product, it was thus identified as III. The 10.0-min. peak was collected and gave an infrared band at 11.05μ (disubstituted terminal olefin) but no bands at 12μ (trisubstituted olefin). It was accordingly assigned structure II. The 16.0- and 18.0-min. peaks were collected and showed an infrared doublet at 11.9 and 12.1μ (trisubstituted olefins) indicating that they contained the *cis-trans* isomers IVA and IVB together with V. Analysis at 111° also showed a higher-boiling product, believed to be 3-*t*-butoxy-3-chloro-2-methylbutane.

4,4-Dimethylpentenes.—Analysis of the reaction products from 4,4-dimethyl-1-pentene (C column, 58°) showed product peaks at 18.0 and 24.0 min. The major peak at 24.0 min. was collected and showed a strong infrared band at 10.3μ indicating *trans*-1-chloro-4,4-dimethyl-2-pentene, n_D^{20} 1.4404. The combined peaks were isolated by fractional distillation of a larger run; b.p. $29\text{--}32^\circ$ (9 mm.). *Anal.* Calcd. for $\text{C}_7\text{H}_{13}\text{Cl}$: C, 63.40; H, 9.88; Cl, 26.72. Found: C, 63.34; H, 9.71; Cl, 27.12. Analysis of the products from *cis*- and *trans*-4,4-dimethyl-2-pentene also showed product peaks at 18.0 and 24.0 min. The 24-min. peak from the *trans*-olefin had an index of refraction and infrared spectrum identical with that from the 1-olefin. However, that from the *cis*-olefin showed both *cis* and *trans* bands in the infrared. When the chlorination was carried out at -78° , only *cis*-olefin could be detected. This low-temperature product was collected and analyzed. It gave an immediate precipitate with AgNO_3 , n_D^{20} 1.4441. *Anal.* Found: C, 63.86; H, 9.79; Cl, 27.12. It was subsequently found that the *cis* and *trans* products could be partially resolved on a 10-ft. polysuccinate column at 110° . Reaction

products from each olefin were examined in this manner and the absence of *cis*-allylic chloride from 4,4-dimethyl-1-pentene and *trans*-4,4-dimethyl-2-pentene confirmed. The starting olefins were cleanly separated on a C column at 24° , and the lack of any isomerization demonstrated.

Reaction of Styrene with *t*-Butyl Hypochlorite.—Styrene (20.8 g., 0.2 mole) was placed in an erlenmeyer flask and a few drops of *t*-butyl hypochlorite added. As soon as the yellow color was discharged 10.8 g. (0.1 mole) of hypochlorite was added slowly keeping the mixture just below its boiling point. Distillation gave a 40% yield of product, b.p. 105° (44 mm), n_D^{20} 1.5017. The infrared spectra showed a strong ether doublet at $9.0\text{--}9.2 \mu$. Redistillation gave a center cut, n_D^{20} 1.5009, with the same infrared spectrum. *Anal.* Calcd. for $\text{C}_{12}\text{H}_{17}\text{Cl}$: C, 67.75; H, 8.06; Cl, 16.67. Found: C, 68.27; H, 8.27; Cl, 17.03. Since the product gave an immediate precipitate with AgNO_3 (indicating benzylic chlorine) it was considered to be 1-phenyl-1-chloro-2-*t*-butoxyethane. When a similar experiment was carried out adding the hypochlorite all at once and bubbling oxygen through the system, it showed a long induction period and then reacted very violently. The product had an infrared spectrum similar to the first product.

Two samples containing 0.1 mole of styrene, 0.05 mole of hypochlorite and 20 cc. of $\text{CF}_2\text{ClCH}_2\text{Cl}$ were degassed and stored at 0° , one illuminated by an incandescent lamp and the other in the dark. Reaction in the irradiated sample was complete in 30 min., and gave a product with the same infrared spectrum and other properties as the preparation above. The other still contained much hypochlorite after 24 hours.

Competitive Reactions by Product Analysis.—Approximately 2.45 cc. of each of two hydrocarbons were mixed in a 10-cc. reaction tube and a sample withdrawn for accurate gas-liquid chromatographic analysis. *t*-Butyl hypochlorite (0.25 cc.) was added and the tubes degassed, sealed, and irradiated at 40° . The products were then analyzed by gas-liquid chromatography essentially as described above and relative reactivities calculated as in our previous papers.²

Competitive Reactions by Reactant Analysis.—Small samples (0.25 cc.) of two hydrocarbons and the internal standard were mixed and a sample withdrawn for gas-liquid chromatographic analysis. Hypochlorite (0.1 cc.) was added, the tubes degassed, sealed and irradiated. Comparison of peak heights before and after reaction then was used to calculate relative reactivities as previously described.^{2,4}

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE, MASS.]

Calculated Isotope Effects for Reactions of Lyonium Ion in Mixtures of Light and Heavy Water¹⁻³

BY C. GARDNER SWAIN AND EDWARD R. THORNTON

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Relative nucleophilicities of D_2O , HDO and H_2O are calculated. Equations relating isotope effect to atom fraction of deuterium in the solvent are derived for reactions of L_2O^+ in water at 25° via (1) SL^+ , (2) $\text{S--LO}^+\text{L}_2$ or $\text{L}_2\text{O}^+\text{SL}$, and (3) $\text{L}_2\text{O}^+\text{L--SL}$ transition states, where L is H or D in any combination, S is any substrate, and L₂ is any substrate with exchangeable L. Curves are shown for the three types for k_D/k_H values of 3, 2, 1, 0.73 and $1/3$.

The Gross equation (1) for the dependence of isotope effect on atom fraction of deuterium in the solvent for reactions of L_2O^+ with substrates S in water solution at 25° proceeding via SL^+ transition states (L = H or D) was derived in a previous

paper.² It applies also to transition states involving water [S--L--OL_2]⁺ or [$\text{L}_2\text{O--SL}$]⁺ (L = H or D in any combination) for the extremes of these transition states which have the same charge on this oxygen as in a water molecule. A second equation (2), derived below, applies to the opposite extremes of these transition states, those with the same positive charge on this oxygen as in a lyonium ion. A third equation (3) will be derived for nearly complete attack of water in the special case where the water is removing a proton or deuterium which is in equilibrium with the solvent,

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(2) Paper II in this series by C. G. Swain, R. F. W. Bader and E. R. Thornton, *Tetrahedron*, **10**, 200 (1960).

(3) Previous paper III in this series by C. G. Swain, A. D. Ketley and R. F. W. Bader, *J. Am. Chem. Soc.*, **81**, 2353 (1959).

rather than attacking carbon or a non-exchangeable kind of hydrogen.

Each of the new transition states has a water portion, *i.e.*, an oxygen atom derived from solvent or lyonium ion with two non-migrating lyons (protons or deuterons) attached. When this oxygen is uncharged, these two LO bonds are considered to be just like those in water. When it is positively charged, these two LO⁺ bonds are considered to be just like those in a lyonium ion. Their composition may therefore be calculated from α , the atom fraction (previously² called mole fraction) of deuterium in the solvent. No assumption is made about the third L (the one associated with S). Its contribution to the isotope effect is determined instead from the experimental isotope effect between H₂O and D₂O, k_D/k_H .

The nature of the two LO bonds in the water portion of the transition state is thus considered to be affected only by the charge on this oxygen and by α . The approximation that deuteration of any HOR molecule brings about the same change in zero point energy of the molecule regardless of the nature of R or that deuteration of any HO⁺RR' bond brings about the same change in zero-point energy of the molecule regardless of the nature of R and R' was employed earlier.² For fractionation of deuterium between water and most compounds studied, experimental equilibrium exchange constants (K_D/K_H)_S/ K_D/K_H)_{L₂O} are near to the statistically expected value of unity. For example, the following exchange constants for LO bonds were found⁴ by making measurements in 32% and 16% D₂O and extrapolating linearly to 0% D₂O: succinic acid, 1.02; hydroquinone, 1.10; sodium hydroxide, 0.78. Sodium hydroxide should be exceptional since the oxygen atom has a negative charge. Brodskii obtained exchange constants of unity for sodium hydroxide and sulfuric acid solutions which were 50% by weight. Hence the fractionation constant must approach unity in concentrated solutions, but deviate from unity in dilute solutions. In general, exchange constants are unity for LOR or LNR₂ compounds regardless of the R groups. For 22 substances investigated by seven authors, the average exchange constant is 1.04, and most do not differ from unity by more than the experimental error (± 0.05).⁵ Therefore bonding of oxygen to carbon *per se* does not affect the nature of LO bonds significantly. Since our model considers all HO⁺ bonds to be equivalent (although different from DO⁺ or HO bonds), it does not distinguish between S---LO⁺L₂ and L₂O⁺SL transition states, but predicts the same curve for each. However, these will be considered separately to illustrate two theoretical approaches.

SLOL₂⁺ Transition States.—Since the lyon in transit may be either H⁺ or D⁺ and the L₂O portion remaining may be H₂O, HDO or D₂O, there are six species of this kind of transition state in a H₂O–D₂O mixture. If the transfer is nearly complete so that SL⁺ is remote from L₂O, the predicted dependence of isotope effect on atom fraction of deu-

terium α is the Gross equation (1), derived for SL⁺ transition states in an earlier paper.²

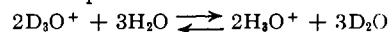
$$\frac{k_\alpha}{k_H} = \frac{[\text{SH}^+]_{\alpha^*} + [\text{SD}^+]_{\alpha^*}}{[\text{SH}^+]_{\text{H}^*} + [\text{SH}^+]_{\text{H}^*}} = g_H + (k_D/k_H)g_D \quad (1)$$

where

$$g_H = \frac{[\text{H}_2\text{O}^+]_{\alpha} [\text{H}_2\text{O}]_{\text{H}}}{[\text{H}_2\text{O}^+]_{\text{H}} [\text{H}_2\text{O}]_{\alpha}} = \frac{1 - \alpha}{(1 - \alpha + \alpha K_2^{-1/6})^3}$$

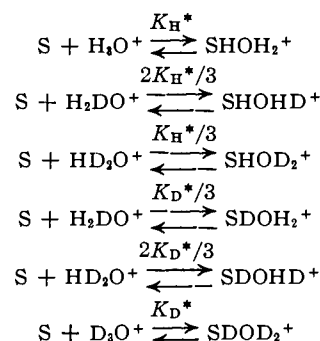
$$g_D = \frac{[\text{D}_2\text{O}^+]_{\alpha} [\text{D}_2\text{O}]_{\text{D}}}{[\text{D}_2\text{O}^+]_{\text{D}} [\text{D}_2\text{O}]_{\alpha}} = \frac{\alpha K_2^{-1/2}}{(1 - \alpha + \alpha K_2^{-1/6})^3}$$

and K_2 is the equilibrium constant for the reaction



evaluated there² as 8.2. The assumptions involved in setting the activity coefficient ratios equal to unity to obtain the final expression for eq. 1 were discussed in detail there,⁶ and therefore will not be repeated here. This isotope effect k_α/k_H combines an α -independent primary isotope effect for subsequent reactions of SD⁺ or SH⁺ (which should be close to unity if the transition state is close to a simple oxonium ion) and an α -dependent isotope effect due to conversion of two LO⁺ bonds in L₃O⁺ to LO bonds in L₂O.

At the other extreme is the case of six transition states close to the reactants in structure, *i.e.*, S---LO⁺L₂. The factors of 3 and 2 are statistical



factors; H₃O⁺ is three times as effective as HD₂O⁺ at the same concentration in supplying H⁺ because it has three equivalent HO⁺ bonds.

The predicted isotope effect or ratio of ordinary experimental first-order rate constants in a mixture of light and heavy water compared to pure light water at the same concentration of lyonium ion is then

$$\frac{k_\alpha}{k_H} = \frac{[\text{SHOH}_2^+]_{\alpha^*} + [\text{SHOHD}^+]_{\alpha^*} + [\text{SHOD}_2^+]_{\alpha^*}}{[\text{SHOH}_2^+]_{\text{H}^*}} + \frac{[\text{SDOH}_2^+]_{\alpha^*} + [\text{SDOHD}^+]_{\alpha^*} + [\text{SDOD}_2^+]_{\alpha^*}}{[\text{SHOH}_2^+]_{\text{H}^*}}$$

where the starred concentrations are effective concentrations, which, like the K^* constants,⁷ include the effective mass for crossing the barrier. Hence

$$\frac{k_\alpha}{k_H} = \frac{(\gamma_S)_\alpha (\gamma_H^*)_{\text{H}}}{(\gamma_S)_H (\gamma_H^*)_{\alpha}} \left(\frac{3[\text{H}_3\text{O}^+]_{\alpha} [\gamma_{\text{H}_3\text{O}^+}]_{\alpha} + 2[\text{H}_2\text{DO}^+]_{\alpha}}{3[\text{H}_2\text{DO}^+]_{\alpha} + [\text{HD}_2\text{O}^+]_{\alpha} (\gamma_{\text{HD}_2\text{O}^+})_{\alpha}} \right) + \frac{k_D (\gamma_S)_\alpha (\gamma_D^*)_{\text{D}}}{k_H (\gamma_S)_D (\gamma_D^*)_{\alpha}} \left(\frac{3[\text{D}_3\text{O}^+]_{\alpha} [\gamma_{\text{D}_3\text{O}^+}]_{\alpha} + 2[\text{HD}_2\text{O}^+]_{\alpha}}{3[\text{D}_3\text{O}^+]_{\text{D}} (\gamma_{\text{D}_3\text{O}^+})_{\text{D}}} \right) = (1 - \theta) + \frac{k_D}{k_H} \theta = 1 + \theta \left(\frac{k_D}{k_H} - 1 \right) \quad (2)$$

(6) Reference 2, p. 210.

(4) W. H. Hamill, *Proc. Indiana Acad. Sci.*, **48**, 110 (1939).

(5) A. R. Brodskii, *Trans. Faraday Soc.*, **33**, 1180 (1937); S. Korman and V. K. La Mer, *J. Am. Chem. Soc.*, **55**, 1396 (1936).

(7) Our K^* corresponds to K^\ddagger of A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, New York, N. Y. 1953, p. 88.

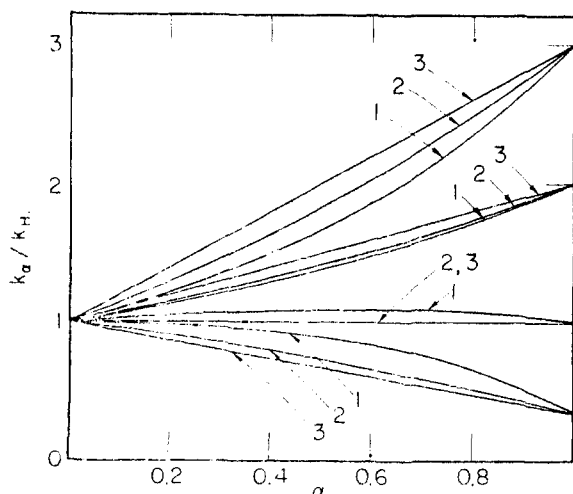


Fig. 1.—Calculated isotope effects at 25° vs. α , the atom fraction of deuterium in the water solvent, for k_D/k_H values of 3, 2, 1 and $1/3$. Curves 1, 2, and 3 correspond to eq. 1, 2 and 3.

where

$$\theta = \frac{3[D_2O^+]_{\alpha} + 2[HD_2O^+]_{\alpha} + [H_2DO^+]_{\alpha}}{3[D_2O^+]_{\beta}} \\ = \frac{\alpha K_2^{-1/3}}{1 - \alpha + \alpha K_2^{-1/3}} = \alpha \left(\frac{g_D}{\alpha} \right)^{1/3}$$

The units of concentration are moles in a fixed number of moles (e.g., 55.5) of solvent. The ratios of activity coefficients are set equal to unity in deriving the final expression for eq. 2 for the reasons discussed fully before.² The parameter θ is listed for convenience in Table I. The family

α	g_H	g_D	θ
0.0	1.0000	0.0000	0.0000
.1	0.9848	.0382	.0726
.2	.9606	.0839	.1497
.25	.9444	.1099	.1901
.3	.9251	.1384	.2318
.4	.8754	.2038	.3195
.5	.8082	.2822	.4132
.6	.7188	.3765	.5137
.7	.6017	.4903	.6216
.75	.5306	.5558	.6787
.8	.4496	.6280	.7380
.9	.2540	.7984	.8661
1.0	.0000	1.0000	1.0000

of curves for different values of k_D/k_H are labeled 2 in Fig. 1. They are quite different from the curves labeled 1 for the Gross equation (1) for most values of k_D/k_H . Ordinarily one would expect k_D/k_H to be less than unity for this mechanism but greater than unity for the Gross mechanism. This isotope effect k_{α}/k_H assumes a constant primary isotope effect for transfer of L, but takes into account the concentrations (which vary with α) and constant statistical factors of the various lyon donors.

L₂OSL⁺ Transition States.—Since the SL⁺ portion may be either SH⁺ or SD⁺ and the L₂O portion may be H₂O, HDO or D₂O, there are also

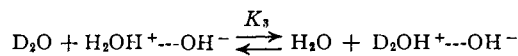
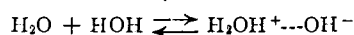
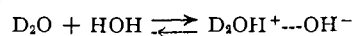
six species of this kind of transition state in a H₂O–D₂O mixture. If the L₂O is still very remote from SL⁺, the predicted dependence of isotope effect on the atom fraction of deuterium α is the Gross equation (1).

At the other extreme is the case of six transition states (L₂O⁺SL⁺)^{*} with practically complete bonding of water. This requires a calculation of the rela-

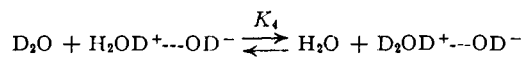
$$\frac{k_{\alpha}}{k_H} = \frac{[H_2OSH^+]_{\alpha}^* + [HDOSH^+]_{\alpha}^* + [D_2OSH^+]_{\alpha}^*}{[H_2OSH^+]_{H}^*} + \frac{[H_2OSD^+]_{\alpha}^* + [HDOSD^+]_{\alpha}^* + [D_2OSD^+]_{\alpha}^*}{[H_2OSH^+]_{H}^*}$$

tive equilibrium concentrations of transition states containing bound H₂O, HDO and D₂O but otherwise similar. Each relative concentration should include a factor for the relative nucleophilic reactivity of the water involved (relative to pure H₂O), in addition to the relative concentrations of the reactants from which they are derived and the appropriate activity coefficients for the equilibria forming these transition states.

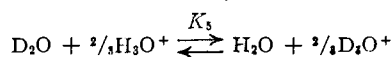
The relative nucleophilicities of H₂O, HDO and D₂O are independent of the reference substrate from the approximation that all HO⁺ bonds are the same. For example, the equilibrium constants are equivalent ($K_3 = K_4 = K_5 = K_6 = 0.50$) when comparing D₂O and H₂O in transition states for proton abstraction from H₂O



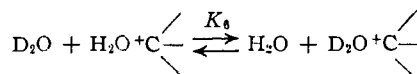
or deuteron abstraction from D₂O



or in electron donation to any substrate



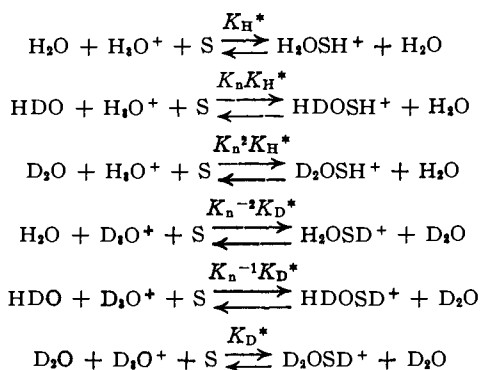
or in bonding to carbon.



K_3 is one third of $(Q_{H_2O}/Q_{D_2O})(Q_{D_2OH^+}/Q_{H_2OH^+}) = (1/3)(1/1436)(2178)$ because of a statistical factor of three arising from a symmetry difference between H₃O⁺ and D₂OH⁺: only one third of the orientations of H₃O⁺ are distinguishable because its three hydrogens are indistinguishable, whereas all are distinguishable for D₂OH⁺. There is no corresponding difference in the transition states to offset this. ($Q_{H_3O^+}$, the partition function for H₃O⁺, was defined² so that it is already divided by the symmetry number of 3.) Similarly K_4 is three times $(Q_{H_2O}/Q_{D_2O})(Q_{D_2OD^+}/Q_{H_2OD^+}) = 3 \cdot (1/1436)(242.0)$. The partition function ratios were derived in the earlier paper²; K_5 is the minus third root of the K_2 of that paper; K_6 is the same as K_4 from our approximation of neglecting other bonds. The nucleophilicity of HDO will be assumed to be the geometric mean of values for H₂O and D₂O. Half of the orientations of H₂O are indistinguishable because its two hydrogens are indistinguishable. However, this does not affect

the nucleophilic reactivity of H₂O compared to HDO because allowed transition states corresponding to reaction of the two unshared pairs are also indistinguishable for H₂O (but distinguishable for HDO).

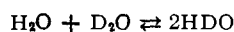
K_n will be used to represent the isotope effect (k_D/k_H) for converting *one* LO bond to *one* LO⁺ bond. It is $K_n^{1/2} = (1/2)^{1/2} = \sqrt{2}/2$. Since it is less than unity it disfavors DO⁺ relative to HO⁺. In terms of K_n , the equilibria between the reactants and the six transition states have the constants shown below.



With these approximations

$$\frac{k_\alpha}{k_H} = \left(\frac{[\text{H}_2\text{O}]_\alpha + K_n [\text{HDO}]_\alpha + K_n^2 [\text{D}_2\text{O}]_\alpha}{[\text{H}_2\text{O}]_H} \right) \cdot \left(\frac{[\text{H}_2\text{O}^+]_\alpha [\text{H}_2\text{O}]_H (\gamma_{\text{H}_2\text{O}^+})_\alpha (\gamma_{\text{H}_2\text{O}})_H (\gamma_B)_\alpha (\gamma_H^*)_H}{[\text{H}_3\text{O}^+]_H [\text{H}_2\text{O}]_\alpha (\gamma_{\text{H}_3\text{O}^+})_H (\gamma_{\text{H}_2\text{O}})_\alpha (\gamma_B)_H (\gamma_H^*)_\alpha} + \frac{k_D [\text{D}_2\text{O}^+]_\alpha [\text{D}_2\text{O}]_D (\gamma_{\text{D}_2\text{O}^+})_\alpha (\gamma_{\text{D}_2\text{O}})_D (\gamma_B)_\alpha (\gamma_D^*)_D}{K_n^2 k_H [\text{D}_3\text{O}^+]_D [\text{D}_2\text{O}]_\alpha (\gamma_{\text{D}_3\text{O}^+})_D (\gamma_{\text{D}_2\text{O}})_\alpha (\gamma_B)_D (\gamma_D^*)_\alpha} \right) = (1 - 0.293 \alpha)^2 \left(g_H + \frac{k_D g_D}{k_H K_n^2} \right)$$

where g_H and g_D are the parameters defined under eq. 1. In evaluating the $(1 - 0.293\alpha)^2$ factor, K_1 for



is approximated as 4 (rather than the 3.96 used previously²). The four is a statistical factor arising because formation of each HDO molecule by random selection of hydrogens from an infinite supply of equimolar H and D sources is twice as likely as formation of either H₂O or D₂O. This is true because the chance that two random hydrogens will be different is 1/2, while the chance that they will both be H, *e.g.*, is 1/4. Since $N_{\text{H}_2\text{O}} + N_{\text{HDO}} + N_{\text{D}_2\text{O}} = 1$ and $\alpha = (2N_{\text{D}_2\text{O}} + N_{\text{HDO}})/2$, $N_{\text{H}_2\text{O}} = (1 - \alpha)^2$, $N_{\text{HDO}} = 2\alpha(1 - \alpha)$, $N_{\text{D}_2\text{O}} = \alpha^2$ and the first factor reduces to $(1 + (K_n - 1)\alpha)^2$. In evaluating the second factor the ratios of activity coefficients are again set equal to unity. The ratios g_H and g_D are the parameters of the Gross equation and are tabulated *vs.* atom fraction of deuterium α in Table I. The units of concentration are moles in a fixed number of moles (*e.g.*, 55.5) of solvent. By use of equilibrium K_5 ($K_5 = K_n^2$), the assumption of the geometric mean, *i.e.*

$$\frac{Q_{\text{HD}_2\text{O}^+}}{Q_{\text{H}_3\text{O}^+}} = 3 \left(\frac{Q_{\text{D}_2\text{O}^+}}{Q_{\text{H}_2\text{O}^+}} \right)^{1/2}; \quad \frac{Q_{\text{H}_2\text{DO}^+}}{Q_{\text{H}_3\text{O}^+}} = 3 \left(\frac{Q_{\text{D}_2\text{O}^+}}{Q_{\text{H}_2\text{O}^+}} \right)^{1/2}$$

the expressions for $N_{\text{H}_2\text{O}}$, N_{HDO} and $N_{\text{D}_2\text{O}}$, and considerable algebra, this equation may be further reduced to eq. 2, for which the parameter θ is

already listed in Table I. Representative curves for different values of k_D/k_H are labeled 2 in Fig. 1. For the extreme case represented by this mechanism, k_D/k_H should be very nearly 1, becoming greater than one as the mechanism approaches the Gross mechanism. This isotope effect k_α/k_H combines the isotope effect associated with the Gross equation (1) and a secondary isotope effect which takes into account the differing nucleophilicities and concentrations of D₂O, HDO and H₂O.

Intermediate Transition States.—Gold⁸ derived an equation for rate-determining proton transfer which encompasses transition states intermediate between eq. 1 and 2 of the present paper. In the present notation

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

where z , $0 \leq z \leq 1$, is a measure of the amount of positive charge on the oxygen atom of transition states L₂O^{δ+}--SL^{δ+} or S^{δ+}--L--O^{δ+}+L₂. When $z = 0$ (the fractional positive charge on oxygen is 0), it is eq. 1. When $z = 1$ (the fractional positive charge on oxygen is 1), it is eq. 2.

Mechanisms intermediate between eq. 1 and 2 may have experimental curves which do not fall between the curves for eq. 1 and 2 only if $k_D/k_H < 2.83$ (calculated using the present parameters, which differ slightly from Gold's). It is therefore necessary to use the equation involving z for predicting theoretical curves for intermediate mechanisms.

If k_D/k_H is as great as 2, the mechanism almost certainly involves a prior equilibrium (eq. 1) since a k_D/k_H of 2 is predicted for the isotope effect on conversion of 2 HO⁺ bonds to HO bonds. When $k_D/k_H \sim 2$, the predicted curves for various values of z fall near eq. 1 except when z is very close to 1. For $k_D/k_H = 1.10$, a possible value for either extreme mechanism, the largest deviation for any z from falling between eq. 1 and 2 is <0.1% below the curve for eq. 2, while the curve for eq. 1 is as much as 8% above the curve for eq. 2. Thus when k_D/k_H is reasonable for both types of mechanism, it should be straightforward to interpolate between the curves for the two mechanistic extremes to determine what kind of intermediate mechanism actually fits the data. When $k_D/k_H < 1$, the mechanism very likely involves a slow proton transfer but interpolation should be straightforward here also.

L₂OLSL⁺ Transition States.—A more complicated situation arises when the attacking water molecule bonds not a fixed proton or deuteron or carbon atom of the substrate but instead to a lyon of the substrate which is in mobile equilibrium with the solvent. Then we may describe the transition state as L₂OLSL⁺ (from the substrate LS) rather than as L₂OSL⁺ (from the substrate S). If the L₂O is very remote from LSL⁺ and the first LS bond is like the original bond in the initial state, the predicted dependence of isotope effect on α is the Gross equation (1).

At the other extreme is the case of twelve transition states L₂OL--SL in equilibrium with the re-

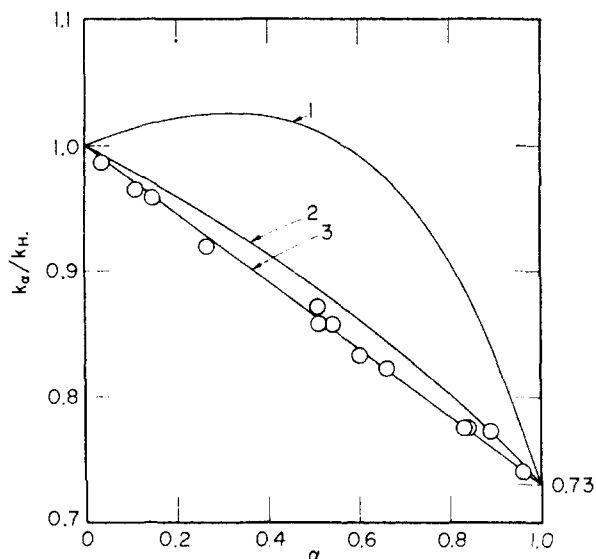
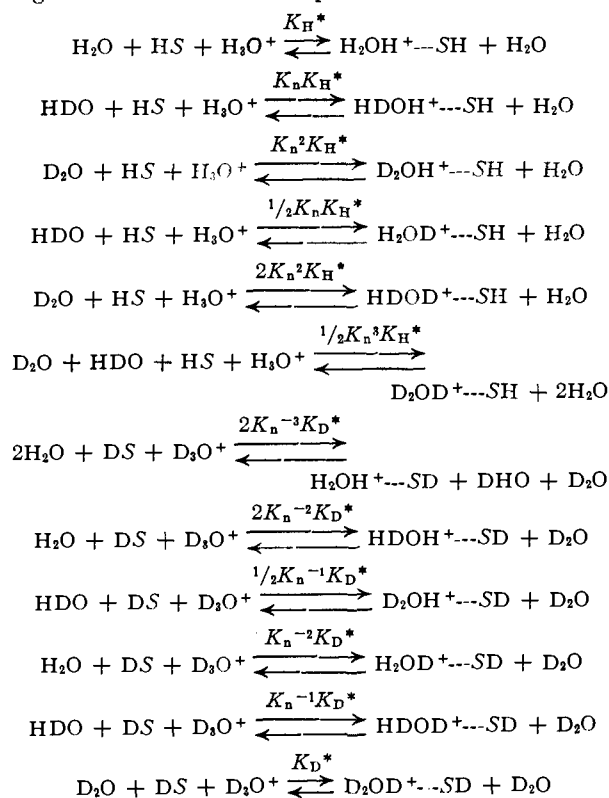


Fig. 2.—Lyonium ion-catalyzed mutarotation of glucose at 25°. Curves 1, 2, and 3 are for the corresponding equations.

actants. In the most common examples of this situation, the lyon of LS is attached to an uncharged oxygen atom in the reactant LS. Therefore the mole fraction of deuterium in LS is approximately the same as that in the solvent (α). In the transition state this LS bond has broken but a new SL bond has formed. This new bond will ordinarily also be an HO bond, but the following derivation does not require it to be.



The second equilibrium differs from the first by converting one DO to DO^+ and one HO^+ to HO.

Its equilibrium constant should therefore differ from the first by K_{n} because K_{n}^2 is the equilibrium constant which converts two DO to DO^+ and two HO^+ to HO. The same difference occurs between the third and second equilibrium. The fourth involves the same kinds of bond changes as the second. Statistical factors have been included. In this way all of the equilibrium constants are related to K_{H}^* and K_{D}^* . Expressing the isotope effect again as a sum of transition state concentrations in the mixed solvent divided by the transition state concentration in pure H_2O and replacing these ratios by ratios involving the equilibrium constants and water concentrations gives

$$\begin{aligned} \frac{k_{\alpha}}{k_{\text{H}}} = (1 - \alpha)g_{\text{H}} &\left(\frac{[\text{H}_2\text{O}]_{\alpha}}{[\text{H}_2\text{O}]_{\text{H}}} + \frac{3K_{\text{n}}}{2} \frac{[\text{HDO}]_{\alpha}}{[\text{H}_2\text{O}]_{\text{H}}} + \right. \\ &\left. 3K_{\text{n}}^2 \frac{[\text{D}_2\text{O}]_{\alpha}}{[\text{H}_2\text{O}]_{\text{H}}} + \frac{K_{\text{n}}^3}{2} \frac{[\text{D}_2\text{O}]_{\alpha}[\text{HDO}]_{\alpha}}{[\text{H}_2\text{O}]_{\text{H}}} \right) + \\ \frac{k_{\text{D}}\alpha g_{\text{D}}}{k_{\text{H}}K_{\text{n}}^3} &\left(\frac{2[\text{H}_2\text{O}]_{\alpha}^2}{[\text{HDO}]_{\alpha}[\text{D}_2\text{O}]_{\text{D}}} + \frac{3K_{\text{n}}[\text{H}_2\text{O}]_{\alpha}}{[\text{D}_2\text{O}]_{\text{D}}} + \frac{3K_{\text{n}}^2[\text{HDO}]_{\alpha}}{2[\text{D}_2\text{O}]_{\text{D}}} + \right. \\ &\left. \frac{K_{\text{n}}^3[\text{D}_2\text{O}]_{\alpha}}{[\text{D}_2\text{O}]_{\text{D}}} \right) = \left(g_{\text{H}} + \frac{k_{\text{D}}g_{\text{D}}}{k_{\text{H}}K_{\text{n}}^3} \right) (1 - 0.293\alpha)^3 \end{aligned}$$

By use of equilibrium K_5 and the rule of the geometric mean this may be simplified further to

$$\frac{k_{\alpha}}{k_{\text{H}}} = 1 + \left(\frac{k_{\text{D}}}{k_{\text{H}}} - 1 \right) \alpha \quad (3)$$

The reason for this simple result is that L_3O^+ is a reactant, and our model assumes that the L_3O^+ group in the transition state $\text{L}_2\text{O}^+\cdots\text{SL}$ is just like the hydronium ion. This linear equation is also plotted for various $k_{\text{D}}/k_{\text{H}}$ values in Fig. 1. This isotope effect k_{α}/k_{H} is due to conversion of the LS bond in the reactant to the SL bond in the product (because these lyons may be on different atoms within S).

If the new SL bond in the transition state is equivalent to the LO^+ bond of a lyonium ion, the isotope effect is calculable even without an experimental value of $k_{\text{D}}/k_{\text{H}}$ because the difference between the last and first equilibria is then the conversion of one DO to DO^+ and one HO^+ to HO. Therefore $K_{\text{D}}^*/K_{\text{H}}^* = K_{\text{n}} = 0.71$. The experimental value for mutarotation of glucose is very close to this, *viz.*, 0.73.

The hemiacetal lyon of glucose (LOG) was assumed to be a normal hydroxylic lyon in respect to exchange with the solvent. Measurements of fractionation of deuterium between tetramethylglucose and water gave⁹

$$K = \frac{[\text{DOG}][\text{H}_2\text{O}]}{[\text{HOG}][\text{HDO}]} = 0.78$$

The method of measurement is open to some question since the H_2O - D_2O mixture used for equilibration was evaporated completely and then analyzed for deuterium content. The equilibrium may have shifted during evaporation. A more recent investigation of glucose (not tetramethylglucose) gave $K = 0.55^{10}$ in contrast with 0.63.⁹ The value of $K = 0.55$, close to the statistically expected value of 0.50, was obtained with water containing considerably less D_2O than the water

(9) W. H. Hamill and W. Preudenberg, *J. Am. Chem. Soc.*, **57**, 1427 (1935). The data have been corrected by E. L. Purlee, *ibid.*, **81**, 270 (1959).

(10) K. M. Koizumi and T. Titani, *Bull. Chem. Soc. Japan*, **13**, 427 (1938), considered 0.55 to be an upper limit.

used by Hamill and Freudenberg,⁹ so that isotopic fractionation on evaporation may have been less important. Since there is little fractionation of deuterium between many compounds and water,⁵ it is reasonable to assume that the true K for the hemiacetal lyon of glucose is very close to 0.50.

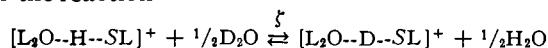
Curves 1, 2 and 3 and the experimental data¹¹ are shown in Fig. 2.

If mutarotation of glucose had a transition state close to $\text{LOG}^{\cdots}\text{LO}^+\text{L}_2$, the isotope effect should be close to 1.0 (it is not) and the points close to curve 2. If it were $\text{LOG}^+\text{L}^{\cdots}\text{OL}_2$, or $\text{LO}^+\text{GL}^{\cdots}\text{OL}_2$, the isotope effect should be larger than 1.0 and the points on curve 1. For a transition state between these extremes, the isotope effect should be smaller than 1.0, but the points should lie between curves 1 and 2 (they do not). For a concerted transfer of both lyons, an isotope effect of less than 0.5 would be expected. Instead the results fit a $\text{L}_2\text{O}^+\text{L}^{\cdots}\text{OGL}$ transition state quite closely (curve 3). A $[\text{L}_2\text{O}^{\cdots}\text{L}^{\cdots}\text{OGL}]^+$ transition state, *i.e.*, a rate-determining second step, was previously suggested from other kinds of evidence.¹² However, this new comparison gives the further detail that there is a large fractional positive charge on the left oxygen. Since this is a symmetrical system (*i.e.*, OLO), this implies that transfer of the second lyon is nearly complete.

For mechanisms intermediate between eq. 1 and 3

$$\frac{k_\alpha}{k_H} = \frac{[1 + \alpha(K_n^* - 1)]^2 [1 + \alpha(\zeta - 1)] \left[1 + \alpha \left(\frac{k_D K_n^3}{k_H \zeta K_n^{2z}} - 1 \right) \right]}{[1 + \alpha(K_n - 1)]^2}$$

If $z = 0$ and $\zeta = 1$ this equation is eq. 1, while if $z = 1$ and $\zeta = K_n$ it is eq. 3. Physically z approximates the fractional positive charge on the oxygen atom in the transition state $[\text{L}_2\text{O}^{\cdots}\text{L}^{\cdots}\text{SL}]^+$ ($0 \leq z \leq 1$), and ζ is the equilibrium constant for the reaction



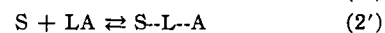
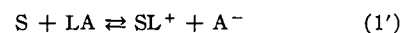
Although this equation is complex in having three parameters, k_D/k_H , z and ζ , in the case of glucose mutarotation it happens that the experimental points can be fitted only if $z > 0.9$, giving $\zeta \sim 0.7$. These values of z and ζ correspond to almost complete transfer of the lyon in the transition state.

Lyon Location in Transition States.—The degree of transfer of a lyon from one atom to another at the transition state is very difficult to determine in other ways, since a small isotope effect can generally result from either relatively incomplete

transfer (*e.g.*, 10%) or relatively complete transfer (*e.g.*, 90%). This new comparison may be a useful tool for distinguishing between the two and determining the actual location of the lyon in transition states of the types that have been discussed.¹³

Aside from the cancellation of activity coefficient ratios, the largest errors to be found in this theory probably go back to the evaluation of K_n and especially g_H and g_D . Hopefully, better experimental values for K_2 will be determined, so that the comparison of highly accurate experimental data with corrected theoretical curves can be made with confidence.

(13) Reactions similar to these lyonium ion reactions can also occur with weak acids.



The derivation of equations for k_α/k_H for these mechanisms is not of the same interest as for lyonium ion reactions because mechanisms 1' and 2' can be distinguished readily by the common ion effect of A^- . Also, since A contains no L, there is no secondary isotope effect of the type possible for, *e.g.*, $\text{S-L}^{\cdots}\text{OL}^+$ transition states, so that no information is given about the extent of transfer of L in mechanism 2', which applies to any degree of transfer of L as long as A^- has not become a separate species as in mechanism 1'. Of course, 2' also applies to transition states A-S-L where A^- is acting as a nucleophile. The equations can be derived in the same way as the Gross equation 1, using the dependence on α of the ionization constants of weak acids.² For mechanism 1'

$$\frac{k_\alpha}{k_H} = \frac{[\text{HA}]_\alpha [\text{A}^-]_H}{[\text{HA}]_H [\text{A}^-]_\alpha} + \frac{k_D}{k_H} \frac{[\text{DA}]_\alpha [\text{A}^-]_D}{[\text{DA}]_D [\text{A}^-]_\alpha}$$

if activity coefficients are cancelled.² Using the equations²

$$\frac{K_{HA}}{K_\alpha} = g_H + \frac{K_{HA}}{K_{DA}} g_D$$

$$K_{HA} = \frac{[\text{H}_3\text{O}^+]_\alpha [\text{A}^-]_\alpha}{[\text{H}_2\text{O}]_\alpha [\text{HA}]_\alpha}$$

and

$$K_\alpha = \frac{[\text{L}_2\text{O}^+]_\alpha [\text{A}^-]_\alpha}{[\text{L}_2\text{O}]_\alpha [\text{LA}]_\alpha}$$

$$\frac{k_\alpha}{k_H} = \frac{g_H}{[g_H + (K_{HA}/K_{DA})g_D]^{1/2}} + \frac{k_D}{k_H} \frac{g_D}{[g_D + (K_{DA}/K_{HA})g_H]^{1/2}} \quad (1')$$

if the acid is only slightly dissociated, *i.e.*, $[\text{LA}]_\alpha = [\text{DA}]_D = [\text{HA}]_H$. For solutions of weak acids

$$g_H = [\text{H}_3\text{O}^+]_\alpha [\text{L}_2\text{O}]_\alpha / [\text{L}_2\text{O}^+]_\alpha [\text{H}_2\text{O}]_\alpha$$

rather than

$$[\text{H}_3\text{O}]_\alpha [\text{H}_2\text{O}]_H / [\text{H}_3\text{O}^+]_H [\text{H}_2\text{O}]_\alpha$$

because the extent of dissociation of the acid is a function of α . Similarly, for mechanism 2'

$$\frac{k_\alpha}{k_H} = \frac{K_{DA}g_H + (k_D/k_H)K_{HA}g_D}{K_{DA}g_H + K_{HA}g_D} \quad (2')$$

if the acid is only slightly dissociated, *i.e.*, $[\text{LA}]_\alpha = [\text{DA}]_D = [\text{HA}]_H$. For example, for $k_D/k_H = 2$, k_α/k_H at $\alpha = 0.50$ is 1.39 for 1' and 1.54 for 2'; for $k_D/k_H = 0.5$, k_α/k_H at $\alpha = 0.50$ is 0.806 for 1' and 0.732 for 2' for acetic acid.

(11) W. H. Hamill and V. K. LaMer, *J. Chem. Phys.*, **4**, 395 (1936).
 (12) For references, *cf.* ref. 3, p. 2354.