nondiastereoisomeric systems in which the A-B discriminations arise from nearest-neighbor interactions such that a particular B can interact with a number of A and vice versa. The equilibrium conditions are determined by a balance between the racemization entropy favoring the racemate, and the discrimination energy term favoring the more stable enantiomer of A.

The source of the discriminations is postulated to be twofold: chiral perturbation of local solvent lattice structure between A and B; and purely electric dispersion terms varying with separation as R_{AB}^{-9} . It is hoped that future experimental studies will be directed to eliciting which of these two mechanisms leads to the predominant discrimination in aqueous systems.

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Base-Catalyzed Isotopic Exchange of Molecular Hydrogen. 4.¹ Hydrogen Isotope Effects in the Dimethyl Sulfoxide-Water System

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Abstract: lsotope effects for the hydrogen reacting as a hydride ion in the exchange reaction $HO^- + D_2 + H_2O \rightarrow (HOD + HOD)$ $D^- + H_2O$) \rightarrow HOD + DH + OH⁻ in H₂O-Me₂SO mixtures vary smoothly in the range 1.18-1.65 between 0 and 96.9 mol % Me₂SO, passing through a maximum at 65 mol % Me₂SO. Despite the smallness of the effects, model calculations suggest that they are consistent with rate-determining hydrogen transfer. The low zero point energy difference between isotopically substituted hydrogen molecules can give maximum isotope effects lower by a factor of 3 than in reactions of C-H, O-H, or N-H bonds. For reaction via a hydride intermediate the hydrogen separating as a hydride ion is not subject to tunnelling or a Westheimer effect, while $k_{\rm H}/k_{\rm D}$ for the transferred hydrogen, which is also small, should be sensitive to the low equilibrium isotope effect for its reaction ($K_H/K_D = 0.26$). In the more probable single step exchange mechanism, concerting hydrogen transfer reduces $k_{\rm H}/k_{\rm D}$, and a nonlinear configuration for the transition state may reduce it further. The possibilities of "hydride character" in the concerted transition state, [HO-H-H-H-OH][‡], and of formation of H-H-OH⁻ as an intermediate are considered.

Investigation of isotopic exchange between molecular hydrogen and H₂O in the condensed phase is of interest both from a theoretical viewpoint and also in the potential that the method could offer for separation of the deuterium isotope.⁵ The exchange is extremely slow in pure water, even at elevated temperatures, but it is catalyzed by the hydroxide ion.⁶⁻⁸ We have found that the catalyzed reaction is accelerated by using dimethyl sulfoxide (Me₂SO) as a cosolvent,^{9,10} although the increase in rate with increased Me₂SO content is not as large as in the case of many reactions involving rate-determining proton transfer.11,12

The mechanism of hydroxide catalysis, both of the isotope exchange and of the related para- to ortho-hydrogen conversion, has been extensively investigated,^{1,6-10,13-16} but the detailed course of the reaction remains unsettled. Wilmarth⁶ suggested that reaction occurs via a hydride intermediate (eq 1) or by a single concerted step through transition state A. He preferred the stepwise mechanism on the grounds that exchange is not subject to acid catalysis, and that the estimated

$$HO^{-} + D_2 + H_2O \longrightarrow HOD + D^{-} + H_2O \longrightarrow HOD + DH + OH^{-}$$

$$[HO---D---H---OH]^{*}$$
(1)

energy of formation of $H^{-}(aq)$ from H_2 was less than the activation energy of 24 kcal for the reaction.⁶ Olah et al. have more recently reported¹⁷ that exchange does occur slowly in 'magic acid" systems.

Subsequently, Ritchie reestimated the energy of formation of the hydride ion as 55 kcal, which would favor a concerted mechanism.¹⁴ However, Ritchie also noted^{14,18} that the observed activation energy corresponds to estimates of the energy for removing one water molecule from the solvation shell of the hydroxide ion.¹⁹ Calculations of the potential energy surface for reaction of H_2 with a hydroxide ion in the gas phase show an initial reaction without activation energy and exothermic by 12 kcal/mol to form a stable HHOH⁻ ion.¹⁴ Ritchie sug-

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Table I. Kinetic Data and Isotope Effect Values

Mol % Me2SO	Me₄NOH, <u>M</u>	$\frac{k_{D_2}}{\min^{-1} \times 10^3}$ at 338 K	<i>k</i> нD	2k _{HD} / a
0.0 <i>^b</i>	(0.1-0.8 KOH)			1.18 ^b
20.2	0.46	0.121	0.081	1.34
40.1	0.36	0.552	0.390	1.41
59.0	0.42	2.87	2.34	1.63
67.9	0.30	2.52	2.06	1.64
67.9	0.30	3.00	2.43	1.62
77.9	0.27	6.85	5.57	1.63
87.5	0.10	4.20	3.18	1.52
87.5	0.10	4,33	3.39	1.56
87.5	0.10	4.08	3.18	1.56
87.5	0.10	4.07	3.16	1.55
96.9	0.032	5.47	4.12	1.51
96.9	0.022	4.00	3.01	1.51

^a The statistical factor of 2 (ref 22) is used; estimated error in values is ± 0.03 . ^b Derived as explained in text from data of Wilmarth et al. (ref 6).

gested that the same ion is formed in solution and that its unactivated formation allows desolvation and association of hydroxide with H_2 to become rate determining. This is shown in the potential energy profile of Figure 1. The desolvation step can be imagined as occurring either by a direct displacement of H_2O by H_2 in the solvation shell of $OH^{-,1}$ or as accompanying a Grotthuss type proton transfer (first step of eq 2), in

$$HO^{-} \cdots H \longrightarrow O H \longrightarrow H \xrightarrow{\text{slow}} HOH \cdots O^{-} H \longrightarrow H$$

$$H \qquad H$$

$$H \qquad H$$

$$HO \longrightarrow H \longrightarrow H^{-} (2)$$

which relaxation of the solvent is rate determining. In principle, formation of $H-H-OH^-$ makes Ritchie's mechanism different from the concerted mechanism, but as the transition state for hydrogen transfer remains the same the chief point of distinction lies in whether or not hydrogen transfer is rate determining.

The relatively weak medium basicity dependence of the exchange rate in H₂O-Me₂SO mixtures,⁹ and also the measured enthalpies of transfer of the exchange transition state from water to aqueous Me₂SO,¹ suggest that formation of the transition state involves minimal desolvation of the hydroxide ion, which would be consistent with Ritchie's mechanism.¹ However, these results may also be reconciled with rate-determining hydrogen transfer if it is assumed that in the transition state negative charge is largely localized on the terminal hydroxyl groups.1 Apparently more compelling evidence, cited by Ritchie, is the magnitudes of hydrogen isotope effects observed in the reaction.¹⁸ For substitution of either atom of the hydrogen molecule $k_{\rm H}/k_{\rm D}$ is less than 1.5. This is much smaller than normally observed in hydrogen transfer reactions but is what might be expected of rate-determining desolvation, in which there is no formation or breaking of covalent bonds to the isotopically substituted molecule.

Because of the mechanistic significance of the isotope effects we have extended their measurement to H_2O-me_2SO mixtures of widely varying medium basicity, and have carried out model calculations to determine more precisely the magnitude to be expected for a primary isotope effect involving molecular hydrogen.

Experimental Section

The procedure employed in the isotope exchange runs involving molecular deuterium and alkaline aqueous Me₂SO solutions has been given previously.^{1,10} Some runs at selected solvent compositions were



Figure 1. Potential energy profile for base-catalyzed isotopic exchange occurring via the addition complex mechanism (eq 2).

Table II. Comparison of Experimental D₂, HD, and H₂ Data in a Typical Kinetic Run (67.9 mol % Me₂SO, 0.30 M Me₄NOH) with Theoretical Values Obtained by Computer Calculation Using $k_{D_2} = 2.52 \times 10^{-3} \text{ min}^{-1}$. Best Fit $k_{HD} = 2.06 \times 10^{-3} \text{ min}^{-1}$

Time,	%	%H ₂ %HD%D ₂		% HD		D ₂
min	Theor	Exptl	Theor	Exptl	Theor	Exptl
6	0.03	0.00	3.05	2.60	96.92	97.40
72	1.41	1.60	16.52	16.10	82.07	82.30
144	4.68	5.00	26.87	26.30	68.45	68.70
261	12.47	12.90	36.56	36.40	50.97	50.70
300	15,48	15.60	38.32	38.20	46.20	46.30
339	18.61	18.90	39.51	39.50	41.88	41.60
366	20.82	20.70	40.05	40.00	39.12	39.20
390	22.81	22.50	40.36	40.40	36.83	37.20
450	27.82	27.60	40.52	40.60	31.66	31.80
480	30.32	29.90	40.33	40.50	29.35	29.60

followed for up to 3 half-lives, with as many as ten hydrogen samples being taken per run. Analysis by mass spectrometry gave the mole percent D_2 , HD, and H_2 in these vapor phase samples: the rate constants obtained directly from log (mole percent D_2) vs. time plots were converted to in-solution values by multiplying by the factor (total moles D_2 in the system)/(moles of D_2 dissolved in the liquid phase) in the normal manner.^{1,10} The base concentration was constant for a given solvent system but was varied from one solvent to another so as to bring the reaction rate within a conveniently measurable range (Table I). In the Me₂SO rich media, base-catalyzed equilibration of the hydrogen isotopes of CH₃SOCH₃ and H₂O molecules occurs readily so that the overall effective H:D ratio remains large under all conditions of exchange.²⁰

The observed trend in the relative analyses for D₂, HD, and H₂ was consistent with a simple consecutive pseudo-first-order kinetic system. Thus, during a run the D₂ level decreased in an exponential manner. the HD increased to a maximum (generally about 40 mol %) before declining, while the H₂ concentration increased steadily. It was thus possible to determine k_{HD} by the following procedure. First, k_{D2} was obtained from a least-squares treatment of the D₂ vs. time data as before. A computer program based on the equations for a consecutive first-order system²¹ was then utilized to calculate the expected percent HD vs. time data from this k_{D2} value and an initial estimate of k_{HD} . By means of an iterative process, the experimental and calculated HD data were compared, and the value of k_{HD} was adjusted incrementally to minimize the average deviation between the two sets. The data obtained for a sample run are given in Table 11.

Results and Previous Isotope Measurements

The kinetic data obtained are given in Table I. The rate constants measured were for the stepwise exchange of D_2 with H_2O at 65 °C (eq 3).



Figure 2. Medium dependence of kinetic isotope effect in Me_2SO -water system.

$$HO^{-} + D_{2} + H_{2}O \xrightarrow{k_{D_{2}}} HOD + DH + OH^{-}$$
$$HO^{-} + DH + H_{2}O \xrightarrow{k_{HD}} HOD + H_{2} + OH^{-}$$
(3)

Combination and correction for the symmetry number²² of 2 for D₂ give a kinetic isotope effect $k_{\rm H}/k_{\rm D} = 2k_{\rm HD}/k_{\rm D_2}$ which can be seen from the stoichiometry of the exchange reactions to refer to the hydrogen reacting as a hydride ion. The variation of the isotope effect with solvent composition is shown in Figure 2. Errors in the isotope effects were estimated to be ±0.03. The value for pure water was derived from the rate constant data of Wilmarth et al.⁶ at 100 °C using the equation $k_{\rm HD}/k_{\rm D_2} =$ exp($\Delta E_a/RT$) to convert it to 65 °C.

Combining the present results with the more fragmentary earlier measurements, isotope effects for substitution at different isotopic positions can conveniently be summarized under the transition state formulation B (although B is not intended





to imply a mechanism for the reaction). For the hydrogen transferred from H₂ as a proton $k_{\rm H}/k_{\rm D} = 1.3$ was obtained from measurements of the rate constants $k_{\rm HD}$ for exchange of HD and $k_{\rm H_2}$ for conversion of para to ortho hydrogen.⁶ The solvent isotope effect $k_{\rm H_2O}/k_{\rm D_2O}$ comes from rates of para to ortho conversion in H₂O and D₂O and includes contributions from substitution of all hydrogens other than those of the H₂ molecule. The values of 1.4 and 2.2 for the solvent isotope effect had to be crudely estimated from measurements in different laboratories,^{6,15,16} but the other isotope effects must be considered reliable. It is unlikely that the high temperature is significant in contributing to the small effects because similar values are seen at -50 °C in the analogous exchange reaction between hydrogen molecules and liquid ammonia.²⁵

Discussion

Two points are apparent from the dependence of $k_{\rm H}/k_{\rm D}$ upon the Me₂SO content of the medium in water-Me₂SO mixtures shown in Figure 2 and the summary of isotope measurements in B. Firstly, the generality of small isotope effects in the hydroxide-catalyzed exchange of molecular hydrogen is clearly established. For isotopic substitution in the hydrogen molecule, measurements under a wide range of conditions yield isotope effects within the limits 1.2-1.65. Secondly, for the

Table III. Isotopic Partition Function Ratios,^a Excluding Symmetry Numbers, at 25 °C

	ZPE _R ⁻¹	MMl_R^{-1}	Qd/Qн
>C-H->C-D	32.1	1.10	36.0
H_2 -HD	4.03	2.45	9.86
$H\bar{D}-D_2$	5.23	2.31	12.07
X-H-X-D ^b	9.00	2.00	18.00
H-D	1.00	2.83	2.83
H ₂ O-HDO	32.10	1.02	37.74
HDO-D ₂ O	33.20	1.02	38.87

^a See "Details of Calculations" for explanation. ^b With harmonic force constant for H_2 but X has infinite mass. Lack of anharmonic corrections to HX should affect difference from H_2 -HD and HD-D₂ by only 2-3%.

measurements in aqueous Me₂SO a distinct maximum in $k_{\rm H}/k_{\rm D}$ is observed at a composition of approximately 65% Me₂SO.

Such behavior is quite unusual for primary isotope effects. Small effects are possible and have been associated with reactant-like or product-like transition states,²³ but in going from water to Me₂SO one would expect the huge change in basicity of the hydroxide ion, revealed by H_{-} measurements,¹² to modify the transition state and lead to a much larger increase in isotope effect than observed.²⁴ Moreover, while an isotope maximum is normally characteristic of primary isotope effects, in this case the magnitude at the maximum is so small as to be quite uncharacteristic.

On the face of it the results favor Ritchie's mechanism, with formation of what Kreevoy²⁶ calls the "reaction complex" rather than hydrogen transfer being rate determining. Before drawing a firm conclusion, however, it is necessary to make a proper estimate of the isotope effects to be expected of ratedetermining proton transfer in this system.

Isotope Contributions from Reactants. An obvious difference of primary isotope effects for exchange of molecular hydrogen from those normally measured in organic reactions is that the reacting hydrogen originates not from a C-H, O-H, or N-H bond but from a hydrogen molecule. Isotope effects may be expressed in terms of partition functions for isotopic reactants and transition states, Q and Q^{\pm} , and a tunnelling correction:

$$\frac{k_{\rm H}}{k_{\rm D}} = \frac{Q_{\rm H}^{\pm}Q_{\rm D}}{Q_{\rm D}^{\pm}Q_{\rm H}} {\rm TUN}$$
(4)

From Table III, which lists values of partition function ratios, Q_D/Q_H , for deuterium and hydrogen modifications of various stable molecules, it can be seen that for H₂ and HD Q_D/Q_H is little more than one-quarter that of a typical C-H bond.

The origin of this difference is shown by separating the contribution of zero point energy to Q_H/Q_D from that of rotational and translational partition functions. The zero point energy (ZPE_R²⁷) depends upon the H and D vibration frequencies,

$$ZPE_{R} = \exp\left\{\frac{\sum h(\nu_{H} - \nu_{D})}{2kT}\right\}$$
(5)

which are determined by force constants and atomic masses, as shown for a diatomic molecule:

$$\nu_{\rm H} = \frac{1}{2\pi} \sqrt{f\left(\frac{1}{m_{\rm H}} + \frac{1}{m_{\rm X}}\right)} \tag{6}$$

For hydrogen isotope effects the zero point energy is often the only important contribution to $Q_{\rm H}/Q_{\rm D}$, but with simple hydrides, including hydrogen molecules, translational and rotational contributions must also be considered.²³ These can be expressed either as ratios of molecular masses and moments of inertia ($\rm MMI_R^{27}$) or, by use of the product rule,²⁸ as ratios of vibration frequencies:

$$MMI_{R} = \left(\frac{m_{H}}{m_{D}}\right)^{3/2} \prod_{3n=6} \frac{\nu_{H}}{\nu_{D}}$$
(7)

Thermal excitation of hydrogen vibrations (EXC_R) is important only for vibrations of unusually low frequency.

From Table III we can see that the contribution of zero point energy (ZPE_R^{-1}) to k_H/k_D for H₂ and HD is only one-eighth that of a typical C-H bond. In part this is because H2 possesses no bending vibrations and in part because isotopic substitution occurs next to another hydrogen rather than next to a heavy atom. The latter factor leads to an isotopic shift in frequency of $\sqrt{3}/2$ (0.866) instead of $1/\sqrt{2}$ (0.707), as is apparent from eq 6 and is illustrated in Table III by comparison of ZPE_{R}^{-1} for H_2 and HD with that for the hypothetical molecules HX and DX in which the force constant is the same but the mass of X is infinite. The slightly larger difference in zero point energy between HD and D_2 than between H_2 and HD is also due to the greater mass of D than H. The small zero point energy contribution to $Q_{\rm D}/Q_{\rm H}$ for hydrogen molecules is in some degree compensated by isotopically sensitive rotational and translational partition functions (eq 8) but far from completely so.

$$MMI_{R} = (M_{H_{2}}/M_{D_{2}})^{3/2}(I_{H_{2}}/I_{D_{2}})$$
(8)

If there were no compensation in the transition state, the low values of Q_{DH}/Q_{H_2} and Q_{D_2}/Q_{DH} would alone account for unusually small isotope effects. Thus the possibility that the observed effects are consistent with primary isotope effects has to be taken seriously and in what follows we attempt the more difficult part of an evaluation of kinetic isotope effects, estimating partition function ratios and tunnelling corrections for transition states.

Isotope Contributions from Transition States. Calculation of isotopic partition function ratios for transition states requires assignments of force constants and geometries to suitable transition state models. Such assignments must in some degree be arbitrary but are here based on a procedure^{29,30} that gives reasonable isotope effects for "nonconcerted" hydrogen transfer between heavy atoms, and in a general way takes into account the results of calculations from ab initio and semiempirical potential surfaces for simple hydrogen transfer reactions.^{31,32}

For hydrogen transfer from carbon, oxygen, or nitrogen the calculated isotope effects are dominated by the Westheimer effect.³² That is, they show a maximum value roughly corresponding to the zero point energy difference between H and D stretching vibrations in the reactants for a transition state in which the partial bonds to the reacting hydrogen are of equal strength.^{32,33} For this transition state, which is referred to as symmetrical, the only stretching vibration in which the hydrogen is in motion is that for the reaction coordinate (ν_1^{\pm}) . Hence isotopic substitution leads to no change of zero point energy in the stretching vibrations, and it follows that contributions to the isotope effect from zero point energy changes in bending vibrations, in the transition state and in the reactants, and from tunnelling substantially cancel. In practice force constants are assigned to yield quite small tunnelling corrections and this leads to transition state bending frequencies not much greater than in the reactants and comparable with those of hydrogen bonds.

$$\begin{array}{ccc} \overleftarrow{\mathbf{C}} & - \overrightarrow{\mathbf{H}} & - \overrightarrow{\mathbf{C}} & \overleftarrow{\mathbf{C}} & - \overrightarrow{\mathbf{H}} & - \overrightarrow{\mathbf{C}} \\ f_1 & f_2 & & f_1 & f_2 \\ v_{\mathbf{L}}^{\dagger} & & v_{\mathbf{R}}^{\dagger} \end{array}$$

With smaller or larger degrees of hydrogen transfer the force constants relax from their values in the symmetrical transition state and approach values in the reactants or products. This leads to a smooth variation of the isotope effect with the degree of hydrogen transfer from $1.0 - (k_H/k_D)_{sym} - K_H/K_D$, where $(k_H/k_D)_{sym}$ and K_H/K_D are respectively the isotope effect for a symmetrical transition state and the isotope effect upon the equilibrium constant for the reaction. The main factor responsible for the variation is a shift in isotopic sensitivity from the reaction coordinate mode to a real stretching mode (v_R^{\pm}) . The product rule constrains the combined isotopic sensitivity of the two frequencies to $\sim 1/\sqrt{2}$. In previous papers^{29,30,34} k_H/k_D has been calculated for various degrees of hydrogen transfer, but given the limitations of the model, $(k_H/k_D)_{sym}$ and K_H/K_D should normally suffice, and this simplification is followed here.³⁵

The Westheimer effect applies only to linear transition states, and for nonlinear structures with comparable force constants much smaller isotope effects are calculated.³⁴ Small isotope effects and nonlinear transition states may be a feature of hydride transfer reactions³⁶ and this could be a factor in the H₂-hydroxide isotope exchange. The most controversial aspect of the transition state model is probably the magnitude of the tunnelling correction. Detailed discussions of this point are available.^{23,37,38}

Details of Calculations. Partition function ratios for the stable molecules in Table III were calculated from vibration frequencies, making use of the product rule. For H₂ and H₂O (gas) full anharmonic corrections to the zero point energy were included, in the manner described by Wolfsberg.^{39,40} For H₂O, HDO, and D₂O harmonic frequencies were based on Kuchitsu and Bartell's valence force field,⁴¹ and the anharmonic corrections were those listed by Wolfsberg, Massa, and Pyper.⁴⁰ The value of 3.54 at 25 °C (MMI_R = 0.736, EXC_R = 1.00) calculated for the exchange equilibrium

$$H_2O(g) + HD \rightleftharpoons HDO(g) + H_2$$

compares very well with the value of 3.53 based on a leastsquares analysis of experimental measurements at various temperatures, although the precise agreement probably reflects cancellation of neglected corrections to the classical treatment of rotations for H₂ and use of the Born-Oppenheimer approximation.⁴² Partition function ratios for liquid water were obtained using $p_{H_2O}/p_{D_2O} = 1.156$ and $p_{H_2O}/p_{HDO} = 1.079$ at 25 °C.43 Separation into ZPE, MMI, and EXC was made on the assumption that the contributions were in the proportions calculated for a tetrahedrally hydrogen bonded water model.⁴⁴ Q_D/Q_H for the C-H reactant was based on a fractionation factor of 0.94 with respect to liquid water (cf. Table V, p 216 of ref 23); the corresponding values of MM_{1R} , ZPE_{R} , and EXC_R are reasonable but arbitrary. Symmetry numbers are excluded from the partition function ratios, as they are from calculated isotope effects.

For transition states Q_{D}^{+}/Q_{H}^{+} was based on harmonic frequencies calculated from assigned geometries and force constants. Usually the transition state involved symmetrical binding of the reacting hydrogen and for nonreacting bonds bond lengths and force constants were the mean of their values in reactants and products. For reacting bonds bond lengths were obtained from Pauling's relationship;²⁹ stretching force constants $(f_1 = f_2)$ were 1.0 or 2.0 mdyn/Å; force constants for bending about a reacting hydrogen were the same as in the bifluoride ion²⁹ (0.212 mdyn/Å); and force constants for bending about atoms flanking the reacting hydrogen were one-quarter their values in reactants or products.45 The interaction force constant between reacting bonds, f_{12} , was most commonly chosen to give a tunnelling correction of $\sim 40\%$ (and $k_{\rm H}/k_{\rm D} = 7-8$) for hydrogen transfer between heavy atoms. The tunnel correction used was a truncated version of Bell's expression³⁷ for a parabolic barrier:

$$\Gamma = 1 + \frac{u^2}{24} + \frac{7u^4}{5760}$$
 where $u = hv_{\rm L}^{\pm}/kT$

 Table IV. Calculated Isotope Effects for Hydrogen Transfer to a Hydroxide Ion at 25 °C

Symmetrical transition State Equilibrium						
MMI	TUN	$\left(\frac{k_{\rm H}}{k_{\rm D}}\right)_{\rm sym}^{b}$	MMI	$K_{\rm H}/K_{\rm D}$		
1.05	1.39	7.43	1.08	0.95		
1.39	1.02	1.53¢	0.87	3.49		
1.94	1.41	2.44	2.40	0.261		
2.75	1.42	4.39	1.96	1.12		
1.97	1.39	4.19	1.96	0.477		
	Symme MMI 1.05 1.39 1.94 2.75 1.97	Symmetrical tra MMI TUN 1.05 1.39 1.39 1.02 1.94 1.41 2.75 1.42 1.97 1.39	Symmetrical transition StaMMITUN $\left(\frac{k_H}{k_D}\right)^b_{sym}$ 1.051.397.431.391.021.53c1.941.412.442.751.424.391.971.394.19	Symmetrical transition State EquilMMITUN $\left(\frac{k_{\rm H}}{k_{\rm D}}\right)_{\rm sym}^{b}$ MMI1.051.397.431.081.391.021.53 c0.871.941.412.442.402.751.424.391.961.971.394.191.96		

^a For transfer of a proton to hydroxide. The transferred atom is that adjacent to OH, e.g., C-C-D + OH⁻ \rightarrow C-C⁻ + DOH. The isotopically substituted atom is indicated by D. Isotopic transition states are shown in Table V. ^b k_D refers to the reactants as written, k_H to the reaction with D replaced by H. ^c Increasing $f_{DH} = f_{HO}$ from 1.0 to 2.0 mdyn/Å in the transition state reduced k_{H}/k_{D} to 1.06. ^d k_{D2}/k_{H2} . ^e The mass of X is 1000 for the kinetic isotope effect and infinite for the equilibrium.

The correction depends on the reaction coordinate frequency $\nu_{\rm L}^{\pm}$ which in the symmetrical case is determined by $f_1 - f_{12}$ (since $\nu_{\rm L}^{\pm} \simeq \{(f_1 - f_{12})/m_{\rm H}\}^{1/2}/2\pi)$. It corresponds roughly to the correction for a one-dimensional Eckart barrier for which $2\pi V^{\pm}/h\nu_{\rm L}^{\pm} = 6$ where V^{\pm} is the barrier height.⁴⁶ Its use in qualitative estimates of isotope effects is probably justified when no large variations in the extent of tunnelling occur.

The only difference in force constants affecting motion of isotopically substituted atoms between symmetrical transition states for C-H and hydrogen-molecule reactants was for bending at atoms flanking the reacting hydrogens, and these force constants make only a small contribution to the isotope effect. Where transition states other than symmetrical were considered, force constants and bond lengths were allowed to vary with the order z between the reacting hydrogen and attacking base, as described previously;²⁹ for nonreacting bonds values were weighted means of those in reactants and products, and for reacting bonds decreased from their reactant or product values with the square of the bond order; further details are given in footnotes to the tables.

For stretching force constants the second-power dependence upon bond order contrasts with dependence on the first power used previously.²⁹ The change is consistent with the low transition-state force constants calculated for hydrogen atom transfer reactions (e.g., Table VIII on p 245 of ref 23) and the low stretching force constant for HF_2^- relative to HF (2.3 compared with 9.7), but it has only a very minor effect upon calculated values of k_H/k_D for a reacting hydrogen.

Although experimental measurements were made at 65 $^{\circ}$ C, the calculated isotope effects are normally reported for 25 $^{\circ}$ C, the temperature at which isotope effects are most commonly quoted. The temperature dependence of the effects is considered separately.

Calculated Isotope Effects and Reaction Mechanism. The aim of the calculations was to compare isotope effects upon hydrogen transfer from a hydrogen molecule with those upon transfer from a heavy atom, typically carbon, in a polyatomic molecule, with special reference to mechanisms of hydroxide catalyzed isotope exchange of hydrogen molecules with water. Comparisons are made between calculations for "symmetrical" hydrogen and heavy-atom transition states and between the corresponding reaction equilibria, using identical or comparable force constants for the transition states where motion of an isotopically substituted hydrogen is involved. Calculated isotope effects are presented first for the stepwise mechanism of hydrogen exchange. Although this mechanism is perhaps not the most likely one, it simply illustrates the procedure and

Table V. Isotopically Sensitive Vibration Frequencies (cm^{-1}) for Symmetrical Transition States^{*a*}

Transition			Bends		
state	Stre	tches	ln pl	ane	Out of plane
С-СНОН	834i	444	1448		1344
C-CDOH	598 i	444	1065		977
H—H—OH	867i	1367	1467	606	1387
D—H—OH	857i	1006	1400	577	1303
H—D—OH	632i	1362	1143	605	1092
D—D—OH	624i	1000	1060	575	986

^a Stretching force constants of reacting bonds 1.0 mdyn/Å; stretch-stretch interaction force constant 1.2 mdyn/Å; bending force constants $f_{CCH} = 0.24$, $f_{CHO} = 0.313$, $f_{HHO} = 0.225$, $f_{HOH} = 0.175$ ergs/rad² × 10⁻¹¹. Vibrations were assigned from inspection of eigenvectors

leads on to consideration of the more probable but more complicated concerted mechanism.

A. Exchange via a Hydride Intermediate. The reaction of hydrogen with hydroxide to yield a hydride intermediate, i.e., the rate-determining step of the stepwise isotope exchange mechanism, is shown in eq 9 together with the heavy atom reaction with which it is compared. Positions of deuterium substitution for which isotope effects were calculated are denoted D.



$$D \rightarrow D + OH^{-} \rightarrow \begin{bmatrix} D - - D - - O \\ H \end{bmatrix}^{\ddagger}$$

 $\rightarrow D^{-} + D \rightarrow O_{H}$

Values of MMI_R, ZPE_R, and Q_D/Q_H needed for calculating equilibrium isotope effects are listed in Table III. Q_D/Q_H for the hydride ion was calculated assuming free translations, and insofar as H⁻ is probably strongly solvated may be a crude overestimate. Isotope effects $(k_{\rm H}/k_{\rm D})_{\rm sym}$, together with tunnelling factors and net MMI contributions obtained by combining $Q_{\rm D}/Q_{\rm H}$ for the reactants and $Q_{\rm D}^{\pm}/Q_{\rm H}^{\pm}$ for a "symmetrical" transition state, in which the force constants of the partial bonds to the reacting hydrogen are equal, are shown in Table IV. The first row of the table refers to hydrogen transfer from carbon, and the next three refer to reactions of hydrogen molecules substituted at either or both isotopic positions; the last row shows results for a hypothetical reactant X-H with the same force constant as H_2 but an atomic mass of 1000 for X. Also shown are calculated equilibrium isotope effects, and we assume that $1.0 - (k_{\rm H}/k_{\rm D})_{\rm sym} - K_{\rm H}/K_{\rm D}$ expresses the range of isotope effects available to each reaction for different degrees of hydrogen transfer in the transition state.

Force constants and isotopically sensitive vibration frequencies are collected in Table V and its footnotes. For the reacting bonds in the symmetrical transition state the force constants are $f_1 = f_2 = 1.0 \text{ mdyn}/\text{Å}$. For the hydrogen transferred between H₂ and OH⁻ as a proton the magnitudes of f_1 and f_2 only indirectly affect k_H/k_D through dependence of the tunnel correction upon $f_1 - f_{12}$, but for the hydrogen separating as a hydride ion an increase in these force constants decreases the isotope effect.

Table VI. Dependence of k_H/k_D for Hydrogen Transfer to Hydroxide upon Transition State Structure^{*a*}

z ^b	С-С-D + OH ⁻ <i>k</i> _{С-H} / <i>k</i> _{С-D}	D-H + OH ⁻ / _{kнD} с	H-D + OH ⁻ $k_{\text{H}_2}/k_{\text{HD}}^d$	$D-D + OH^{-}$ $\frac{k_{H_2}}{k_{D_2}}$
0	1.0	1.0	1.0	1.0
0.1	1.8	1.1	1.5	1.6
0.3	5.2	0.9	2.2	2.3
0.5	7.7	1.4	2.7	4.4
0.7	2.6	3.3	1.0	3.7
0.9	1.5	4.6	0.4	2.3
1.0	0.95	3.5	0.26	1.1

^a Force constant assignments for the transition state: for the reacting bonds, the stretch-stretch interaction force constant $f_{12} = \{1 + 3z^2(1-z)^2\}\sqrt{f_1f_2} \text{ mdyn/Å}$ and the bending force constant = $16z^2(1-z)^2 \times 0.212 \text{ mdyn/Å}$, where 0.212 is the bending force constant for the bifluoride ion. The transition state dependence of other force constants is as in text or ref 29. ^b z is the order of the C-H or H-H reacting bond in the transition state. ^c k_H/k_D for hydrogen separating as a hydride ion. ^d k_H/k_D for hydrogen transferred to OH- as a proton.

The isotope effects measured in this work refer to the hydrogen reacting as a hydride ion, and it is clear that for any reasonable values of stretching force constants the calculated value of $k_{\rm H}/k_{\rm D}$ for a symmetrical transition state must be close to unity (Table IV, row 2). Insofar as the hydrogen is not undergoing transfer in the usual sense and is thus not subject to the Westheimer effect this is perhaps not surprising. The equilibrium isotope effect of 3.5 for formation of the free hydride ion is considerably larger and could lead to significant isotope effects in product-like transition states, as is confirmed by the calculations of $k_{\rm H}/k_{\rm D}$ for various degrees of hydrogen transfer z in column 3 of Table VI. However, as noted above, the low value of $Q_{\rm D}/Q_{\rm H}$ for the hydride ion may be inappropriate in aqueous solution.

For the hydrogen transferred as a proton $k_{\rm H}/k_{\rm D}$ for the symmetrical transition state is again less than for hydrogen transfer from carbon: 2.4 compared with 7.4. The difference is less striking than for the hydride hydrogen but it is clear that the difference in Q_D/Q_H for H₂ and a hydrocarbon reactant is only in small degree compensated in the transition state. The bending vibrations of the H₂ transition state show slightly less than the normal $\sim 1/\sqrt{2}$ isotopic sensitivity but the discrepancy is smaller than for the stretching vibrations of the reactant. The reaction coordinate frequency and extent of tunnelling are practically unchanged between the two reactions and the slight difference in Q_D^{\pm}/Q_H^{\pm} stems mainly from the loss of two relatively unimportant bending force constants and a slightly more sensitive MMI term in the hydrogen case. This is consistent with the normally valid maxim that quantum contributions to isotope effects require changes in force constants.47

Thus a quite simple calculation confirms that maximum isotope effects expected from reactions of hydrogen molecules should indeed be lower by a factor of 3 than values commonly observed in other reactions because of the low isotopic partition function ratios for the reactants.

At 2.5 the isotope effect calculated for the symmetrical transition state for proton transfer is still significantly larger than the observed value of 1.3^6 . However, for product-like transition states $k_{\rm H}/k_{\rm D}$ should begin to reflect the very low equilibrium isotope effect for the reaction, $K_{\rm H}/K_{\rm D} = 0.265$ (Table V1, column 4), and insofar as formation of a hydride ion could well be expected to involve a product-like transition state an isotope effect close to unity would not be inconsistent with the mechanism.

It may be noted that the largest calculated values of k_{H2}/k_{D2} in Table VI are only about half the magnitude of isotope effects

Table VII. Isotope Effects and Tunnel Corrections at 25 °C for Nonconcerted Hydrogen Transfer^a

Transition state	У	TUN	$(k_{\rm H}/k_{\rm D})_{\rm sym}^{b}$
C-CDC-C	1.2	1.40	6.98
	1.3	1.60	7.98
	1.5	1.96	9.73
HO-HDH-OH	1.2	1.42	2.16
	1.3	1.65	2.46
	1.5	2.01	2.89
HO-DDH-OH ^d	1.2	1.42	2.42
	1.3	1.63	2.75
	1.5	1.99	3.25

^a For C with $f_1 = 1.0$, $f_2 = 2.0 \text{ mdyn/Å}$; $f_{23} = yf_1$; $f_{12} = 0$, x = 0. ^b Subscript indicates symmetrical transition state. For reactions of isotopic H₂ the measured isotope effects are indicated in footnotes c and d. ^c The calculated isotope effect is k_{H2}/k_{HD} . ^d k_{HD}/k_{D2} . This, the measured isotope effect, differs significantly from k_{H2}/k_{HD} ; cf. Q_{H2}/Q_{HD} and Q_{HD}/Q_{D2} for the reactants (Table 111).

observed for hydrogen abstraction reactions in the gas phase.⁴⁸ It is possible that the difference is in part due to lower transition-state bending vibrations for hydrogen radical than proton transfer reactions. This would be consistent with the lower electron density of the reacting bonds and the much lower force constant derived from potential surface calculations than observed for the bihalide ions.⁴⁹ An additional factor may be larger equilibrium isotope effects for the gas-phase reactions.²³

B. Concerted Mechanism of Exchange. The transition state for concerted hydrogen transfer is more complicated than that for formation of a hydride intermediate, but there is some simplification when the transition state is symmetrical, as in C. In calculating isotope effects the main additional difficulty

$$\overset{H}{\xrightarrow{f_{12}}} \begin{array}{c} f_{23} & f_{12} \\ 0 & f_{12} & f_{23} & f_{12} \\ 0 & --H & --H & --H & --H \\ f_{2} & f_{1} & f_{1} & f_{2} \\ f_{2} & f_{1} & f_{1} & f_{2} \end{array}$$

is in formulating a reaction coordinate. When there are only two reacting bonds the condition that there is an imaginary reaction coordinate frequency v_{L}^{\pm} is that in the relationship between bond stretching force constants f_1 and f_2 and their interaction force constant f_{12} ,

$$f_{12} = x\sqrt{f_1 f_2}$$

the proportionality constant x must be greater than or equal to 1.0. For more than two reacting bonds the corresponding condition has been discussed by Katz and Saunders.⁵⁰ For transition state C, if

$$f_{23} = yf_1 \text{ and } f_{12} = x\sqrt{f_1f_2}$$

 $v_{\rm L}^{\pm} = 0$ when

$$y = \pm (1 - x^2)$$

and there is a single nonzero imaginary frequency when

 $(1 + y) > x^2 > (1 - y)$

When x = 0 this condition reduces to that for two reacting bonds, and the effect of concertedness upon k_H/k_D may be examined by introducing nonzero values of x, while x and y are kept within the required limits. Outside the limits, if $(1 - y) > x^2$ there is **n**0 imaginary frequency, and if $(1 + y) < x^2$ there are two.

For x = 0 calculated isotope effects for different values of y are given in Table VII for C, and for the corresponding structure in which all atoms but the central hydrogen are

carbons, with $f_1 = 1.0$ and $f_2 = 2.0$ mdyn/Å. The positions of isotopic substitution are indicated by D in the appended transition state structures, and the second and third sets of figures refer respectively to $k_{\rm H2}/k_{\rm HD}$ and $k_{\rm HD}/k_{\rm D2}$. For y =1.2 the transition states are directly comparable with those for hydrogen transfer from carbon and H2 to hydroxide in the first and third rows of Table IV (although the reacting hydrogen is now a hydride ion rather than a proton). Additional weak bending force constants in C decrease the isotope effects slightly, and with three adjacent hydrogens there is a compensating increase in frequency and decrease in isotopic sensitivity for the bending vibrations. However, the isotope effects for the "carbon" and "hydrogen" transition states still differ by a factor of 3, reflecting the difference in Q_D/Q_H for H₂ and C-H reactants.⁵¹ As expected, increasing y increases isotope effects by increasing tunnelling but leaves the difference unaffected.

Increasing x from zero introduces the additional interaction force constants f_{12} into the transition state. An increase in f_{12} relative to f_{23} decreases motion of the central hydrogen in the reaction coordinate and causes it to move in a real stretching mode. This leads to isotopically sensitive zero point energy in the stretching vibrations and, under constraint of the product rule, diminished isotopic sensitivity for the reaction coordinate. As shown in Table VIII for y = 1.2, $k_{\rm H}/k_{\rm D}$ decreases, despite the increase in the calculated tunnelling corrections (TUN) due to an increase in magnitude of the reaction coordinate frequency.⁵² The effect is greater for the transition state in which the flanking atoms are hydrogens, and the decrease in $k_{\rm H}/k_{\rm D}$ from 2.2 to 1.0 as x increases from 0 to 1.4 in this case compares with a decrease of 7.0 to 5.4 for the carbon transition state.

For the flanking hydrogens the effect of increasing x upon isotopic substitution complements that for the central atom. Motion in the reaction coordinate increases and, as shown in Table VII1, $k_{\rm H}/k_{\rm D}$ increases. When x = 0 there is no hydrogenic motion in the reaction coordinate and the low value of $Q_{\rm D}/Q_{\rm H}$ for the reactants gives a substantial inverse isotope effect, $k_{\rm H}/k_{\rm D} = 0.36$, irrespective of y. Thus the effect of a large value of x is to convert an inverse isotope effect into a normal one, although even for large values of $x k_{\rm H}/k_{\rm D}$ remains close to 1.0.

Thus as anticipated by Bell⁵³ and confirmed by Katz and Saunders' calculations,⁵⁰ concerting motion of a reacting hydrogen with that of other atoms is a potent factor moderating isotope effects. For a nonreacting hydrogen the isotope effect is correspondingly enhanced. Interestingly, in the hydroxide catalyzed isotope exchange the small isotope effect measured for the central hydrogen (1.2-1.65) and "large" effect for a flanking hydrogen (1.3) are both consistent with strongly concerted hydrogen transfers.

There is therefore qualitative agreement between experiment and calculations, and it is worth considering to what extent the calculated results depend upon the specific force constants and symmetrical structure assigned to the transition state, and also whether they can account for the distinctive maximum in $k_{\rm H}/k_{\rm D}$ observed with changing hydroxide basicity (Figure 2).

As discussed in more detail below the greater sensitivity of the reaction to base than acid catalysis^{6.16} may indicate that the OH⁻ groups in the transition state are strongly bound to their adjacent hydrogens. The values of 1.0 and 2.0 mdyn/Å used for f_1 and f_2 , respectively, are consistent with this, but $k_{\rm H}/k_{\rm D}$ is little affected by increasing f_2 to 5.0 mdyn/Å or indeed by using equal values of f_1 and f_2 .

The effect of asymmetry in the transition state may be seen by calculating equilibrium isotope effects, K_H/K_D , and considering that $1.0 - (k_H/k_D)_{sym} - K_H/K_D$ represents the limits to variation of k_H/k_D with degree of hydrogen transfer in the

Table VIII. Isotope Effects and Tunnel Corrections at 25 °C for Concerted and Nonlinear Transition States^a

Transition state	x	TUN	$(k_{\rm H}/k_{\rm D})$ sym
	0	1.40	6.98
CCDCC	1.0	1.64	5.78
	0	1.42	2.16
OHDHO ^{b,c}	1.0	1.60	1.21
	1.4	1.61	0.96
	0	1.01	0.36
ODHHO ^{b,d}	1.0	1.34	0.96
	1.4	1.37	1.35
, D	0	1.20	1.21
, H H	1.0	1.45	0.71
0 ^e	1.4	1.37	0.57

 ${}^{a}f_{12} = x\sqrt{f_{1}f_{2}}$ in C; y = 1.2; other force constants as in Table VII. b Reaction coordinate frequences ($\nu_{L} \neq (H) \text{ cm}^{-1}$) and isotopic sensitivities (in brackets) for x = 0, 1.0, and 1.4, respectively: 865 (${}^{b}1.39, {}^{c}1.01$), 2206 (${}^{c}1.15, {}^{d}1.09$), 2760 (${}^{c}1.12, {}^{d}1.10$). ${}^{e}y = 1.2$, H-D-H angle is 90°. Force constants unchanged from linear transition state.

transition state. Only if $K_{\rm H}/K_{\rm D}$ is large are large values of $k_{\rm H}/k_{\rm D}$ likely, for product-like transition states. Neglecting symmetry numbers as usual, for the central hydrogen, for which $k_{\rm HD}/k_{\rm D2}$ is the kinetic isotope effect determined experimentally, we have from eq 3

$$\frac{K_{\rm HD}}{K_{\rm D_2}} = \frac{Q_{\rm H_2}Q_{\rm D_2}}{Q_{\rm HD}^2} = 1.21 \tag{10}$$

and it is clear that the value is too close to 1.0 to cause significant variation from the small effect calculated for symmetrical transition states. However, for the flanking hydrogens, for which $k_{\rm H2}/k_{\rm HD}$ is measured,

$$\frac{K_{\rm H_2}}{K_{\rm HD}} = \frac{Q_{\rm HD}Q_{\rm H_2O}}{Q_{\rm H_2}Q_{\rm HDO}} = 0.26 \tag{11}$$

and $K_{\rm H}/K_{\rm D}$ is substantially inverse. The calculation is for 25 °C and at the temperature of measurement, 100 °C, the value is closer to unity (0.4 rather than 0.26) but it is still small enough that for a sufficiently product-like transition state the kinetic isotope effect might be expected to be inverse.

The significant feature of the isotope maximum in Figure 2 is that the observed variation in $k_{\rm H}/k_{\rm D}$ (1.2–1.65) is small. It is possible therefore that it results from quite a small variation in force constants, and if so its origin could not easily be determined from model calculations since these distinguish only gross features of isotope effects. Interestingly, however, the calculations indicate that quite large changes in force constants and transition state structure, of the magnitude that might well be expected of the large variations in basicity of the hydroxide ion with changing Me₂SO content of the medium, lead to changes in isotope effect quite small enough to be consistent with those observed. While the calculations do not require an isotope maximum they are fully compatible with it, and the situation contrasts nicely with the Westheimer effect³² for simple hydrogen transfers where experiment and calculations involving comparable changes in force constant show an isotope maximum with large changes in $k_{\rm H}/k_{\rm D}$.

Transfer of hydrogen as a hydride ion could lead to a transition state with a nonlinear arrangement of the reacting bonds. This is usually regarded as a further factor reducing isotope effects^{34,36} and additional calculations in which structure C was modified to give an angle of 90° at the central hydrogen confirmed that this was so irrespective of the magnitude of bending forces constants and despite an increase in f_{23} to maintain the same contribution from tunnelling as in the linear transition state (Table VIII).

Table IA, Temperature Dependence of isotobe Effects	Table IX.	Temperature	Dependence of	lsotope	Effects ^a
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Transition		$(k_{\rm H}/k_{\rm D})_{\rm sym}$			
state	MMI	x	25 °C	-65 °C	100 °C
С-СНС-С	1.07	0	6.98	5.31	4.46
		1.4	5.37	4.35	3.78
0HDHO	2.35	0	2.16	2.07	2.02
		1.4	0.96	1.09	1.18
0DHHO	2.33	0	0.36	0.45	0.52
		1.4	1.35	1.45	1.53

^a Transition state C: force constants as in Table V111.

C. Temperature Dependence of Isotope Effects. So far calculated isotope effects at 25 °C only have been considered, whereas the experimental measurements were made at 65 or 100 °C. Normally isotope effects decrease (become closer to 1.0) with increasing temperature, but in the present instance, because of the isotopic sensitivity of the partition function ratios for hydrogen molecules, and the corresponding lack of sensitivity for the transition states, MMI contributions to $k_{\rm H}/k_{\rm D}$ are large, especially for concerted transition states (2.35 for $k_{\rm H2}/k_{\rm HD}$ and 2.21 for $k_{\rm HD}/k_{\rm D2}$), and for small isotope effects zero point energy contributions are inverse. This means that there is an inverse temperature dependence with larger isotope effects at higher temperatures. The effect is small so that $k_{\rm H}/k_{\rm D}$ at 100 °C differs little from that at 25 °C, but it is clearly seen from the calculated values at different temperatures in Table IX. Insofar as a mechanism involving ratedetermining diffusion would not be expected to show inverse temperature behavior the calculations suggest that experimental measurement of $k_{\rm H}/k_{\rm D}$ as a function of temperature might provide a criterion of mechanism.

D. Solvent Isotope Effect. Strictly speaking, calculations of solvent isotope effects, upon changing catalyst and solvent from OH^- and H_2O to OD^- and D_2O without isotopic substitution of the hydrogen molecule, cannot be made. Nevertheless, qualitative estimates of isotope effects for the different exchange mechanisms are possible.

Measurements of solvent isotope effects for hydrogen transfer to hydroxide in other reactions^{54,55} and studies of isotopic fractionation in the solvation shell of the hydroxide ion itself^{54,56} leave little doubt that both rate-determining desolvation of the hydroxide ion and formation of a hydride intermediate would be subject to an inverse secondary solvent isotope effect. For the concerted mechanism, on the other hand, the solvent isotope effect would be combined with a primary effect for the proton transferred from a water molecule (eq 12).

$$DO^{-} + H_{2} + D_{2}O \longrightarrow [DO^{-}H^{-}H^{-}D^{-}OD]^{\ddagger} (12)$$

$$\uparrow \qquad \uparrow \qquad \uparrow \qquad \uparrow$$

$$2ry \qquad 1ry \quad 2ry$$

If we assume that the hydrogens flanking the central atom of the transition state are equivalent (see below) and, less importantly, that isotopic substitution at one position is independent of that at another³⁰ we can estimate the primary contribution from $k_{\rm H2}/k_{\rm HD} = 1.3$ for exchange of H₂ and HD (eq 3) by allowing for the change in isotopic reactants from H₂ and HD to H₂O and D₂O, i.e.

$$\frac{k_{\rm H}}{k_{\rm D}} = 1.3 \left(\frac{Q_{\rm D_2O}}{Q_{\rm H_2O}}\right)^{1/2} \frac{Q_{\rm HD}}{Q_{\rm H_2}} = 5.1$$

Despite the assumptions and combination of $k_{\rm H2}/k_{\rm HD}$ measured at 100 °C with partition function ratios for 25 °C it seems likely that the primary effect should be large enough to override any solvent isotope effect of normal magnitude to give $k_{\rm H}/k_{\rm D} > 1$.

As already noted a satisfactory measurement of a solvent isotope effect does not exist. However, combination of Wilmarth's measurement⁶ of the rate of para to ortho hydrogen conversion in H₂O with earlier measurements by Wirtz and Bonhoeffer¹⁵ and by Abe¹⁶ of H₂ exchange in D₂O gives values of $k_{\rm H_2O}/k_{\rm D_2O}$ of ~1.4 and 2.2 at 100 °C which would be consistent with the concerted mechanism.

Mechanistic Conclusions. The principal conclusion to be drawn from the calculations is that the small isotope effects observed for isotopic substitution of the hydrogen molecule are indeed consistent with rate-determining hydrogen transfer. Arguably the occurrence of effects close to 1.0 for substitution at both isotopic positions for reaction via a hydride intermediate (eq 1) would be fortuitous, but this mechanism seems less likely than concerted hydrogen transfer (transition state A). For the concerted mechanism the low value of $Q_{\rm HD}/Q_{\rm H_2}$ in the reactants, together with the coupling of hydrogen motion and possibility of a nonlinear configuration in the transition state, make isotope effects larger than those observed very unlikely.

The calculations do not rule out a mechanism in which desolvation of an encounter complex between hydrogen and hydroxide is rate determining¹⁴ (eq 2) but they dispose of the main argument in its favor, that the magnitudes of the observed isotope effects require it. Moreover, an objection to this mechanism is its apparent implication that the measured activation energy should be a minimum for reactions of the hydroxide ion with other nonpolar hydrogens. For hydrogens attached to carbon this does not appear to be the case.⁵⁷ Although little reliance can be placed on the crudely measured solvent isotope effects, their magnitudes also tell against the mechanism, as they do against reaction via a hydride intermediate.

The concerted reaction, with a transition state of the type shown in A or C, appears therefore to give the most satisfactory account of the isotope measurements; but what of other evidence? The objection raised by Wilmarth⁶ and Abe¹⁶ that the mechanism implies acid as well as base catalysis is met by a symmetrical transition state in which changes in bonding are not fully in step and there is weak bonding to and charge localization at the central hydrogen, i.e., a transition state possessing some "hydride character" (D). The strong bonding

$$\delta^{-} (1-2\delta)^{-} \delta^{-}$$
HO---H---H---OH
D

implied for the hydroxide ion then diminishes the importance of the water molecule acting as an acid and hence susceptibility to catalysis by stronger acids. Nonsynchronous bond breaking is now a familiar feature of other concerted reactions.⁵⁸

Of course it is possible that the transition state is not symmetrical as depicted in C and D, but by the principle of microscopic reversibility any departure from a symmetrical structure implies parallel reaction paths and enantiomeric transition states.⁵⁹ Asymmetry due to weakened binding of one of the OH groups should increase proneness to acid catalysis and presumably would not be pronounced. As noted above, variations in $k_{\rm H}/k_{\rm D}$ with changing hydroxide basicity can as well be accounted for by variations of force constants within a symmetrical transition state as by introduction of asymmetry.

A point against strong hydride character in the transition state is the implication of eq 11 that for the consequently extensive proton transfer to hydroxide k_{HD}/k_{H_2} for the proton might be expected to reflect the large inverse equilibrium isotope effect for its reaction. A further difficulty is the implication of the weak acidity dependence of exchange and of the enthalpy of transfer data in H₂O-Me₂SO mixtures,^{1,9,60} emphasized above, that for a concerted mechanism the major charge localization in the transition state is not upon the hydride hydrogen as in D but upon the hydroxyl groups.¹ In extenuation one may argue that the greater accessibility to solvating molecules of two hydroxyl groups in the transition state compared with one in the reactants perhaps compensates for the delocalization of charge.¹ However, an alternative explanation of the lack of acid catalysis is that the ion H-H-OHproposed by Ritchie¹⁴ is formed as an intermediate; that is, that the reaction is as shown in Figure 1 but with transition state A the highest point on the potential energy profile. Although not required by the concerted mechanism, the presence of the H-H-OH⁻ ion would remove the necessity of postulating pronounced hydride character in the transition state. It would also account for the dominance of specific hydroxide over general base catalysis,¹ a further experimental point established by Wilmarth,¹³ and would remove the necessity of supposing that the concerted transition state is formed in a termolecular collision. This is an unsatisfactory feature of the simpler mechanism notwithstanding the fact that one of the molecules is a solvent molecule.

It seems that the available results are consistent with a concerted mechanism but that details of the transition state and reaction intermediates remain uncertain. If such a conclusion seems vague in relation to the extensive studies carried out, this is due at least in part to the lack of analogy with more familiar organic or inorganic reactions and to the quite limited structural variations permitted by the reactants.

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