methanol/2-propanol) are monoclinic (space group $P2_1$) with $a = 10.013$ (2) Å, $b = 12.588$ (3) Å, $c = 12.981$ (3) Å, $\alpha = 90.00°$, $\beta = 102.75$ (1)°, $\gamma = 90.00°$, $V = 1596$ (1) Å^3, and $d_{\text{calcd}} = 1.442$ g cm^{-1} for $Z = 4$. The intensity data were collected from a single crystal (0.30 × 0.60 × 0.62 mm^3) on a computer-controlled Four-Circle Nicolet Autodiffractometer with the ω scan technique at 293 K to a scattering angle of $3.0° < 2\theta < 50.7°$ by using Mo Kα radiation ($\lambda = 0.71073$ Å; graphite monochromator). Of a total of 2914 independent reflections collected, 1956 intensities greater than $3.0\sigma(I)$ were used. The structure was solved by the heavy-atom Patterson method with standard Lorentz and polarization corrections applied to the data; the hydrogen atoms were located. Structure refinement was accomplished by full-matrix least-squares methods with an anomalous dispersion correction for the bromine atom (anisotropically for nonhydrogen atoms and isotropically for hydrogen atoms). Specifically, hydrogen atoms H_O and H_{N4} were located from a difference Fourier synthesis and refined as independent isotropic atoms. The remaining hydrogen atoms were included in the structure factor calculations as idealized atoms. The final discrepancy factors were $R_1 = \sum||F_o| - |F_c||/\sum|F_o| = 0.046$ and $R_2 = \{\sum w(|F_o| - F_c|)^2/\sum w|F_o|^2\}^{1/2} = 0.045$. Besides the obvious features depicted in Figure 1, the molecular structure also has hydrogen bonds from the bromine atom to O–H_O (2.70 Å) and to N4–H_{N4} (2.43 Å), such that an O–H···Br···H–N bridge exists across the beta face of the tricyclic system. Details for this atomic arrangement are given in the microfilm supplement.[14b]

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Supplementary Material Available: Detailed data for the X-ray analysis of **5a**·HBr, including tables of bond lengths, bond angles, thermal and positional parameters, and atom contacts; experimental procedures and data for **32**, **34**, **35a**/**b**, **36a**/**b**, and **37** (11 pages). Ordering information is given on any current masthead page.

Dynamics of Hydride Transfer between NAD$^+$ Analogues[1]

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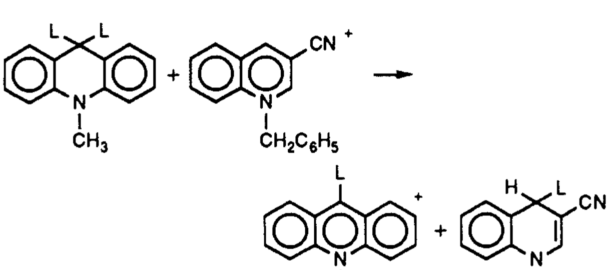
Abstract: Primary kinetic isotope effects (KIE) for hydride transfer between 10-methylacridan and 1-benzyl-3-cyanoquinolinium perchlorate have been measured in 15 different solvents. There is a reduction of the KIE from 5.2 to about 2.9 in the more viscous, nonhydroxylic solvents. Hydroxylic solvents give the larger KIE regardless of their viscosity. These results suggest a three-step process. In the first step, the heavy atoms and solvent are reorganized to a configuration intermediate between reactants and products, while the hydride retains its original attachment. In the second stage, the hydride is transferred, probably by tunneling. In the final step the products are stabilized by further solvent and heavy-atom reorganization. For nonhydroxylic solvents, translational and rotational diffusion governs the heavy-atom reorganization steps and, therefore, determines which step is rate-limiting. Only when the heavy-atom reorganizations are fast is the second step rate-limiting and the KIE maximized. The rate constant for the tunneling process is assumed to be solvent-independent. It is of the right order of magnitude to compete with solvent relaxation. Changes in rate constant, k, and equilibrium constant, K, are modest, but there is a linear correlation between ln k and ln K, with a slope of 0.87. This slope suggests that it is the third step, rather than the first, which shares rate-limiting character with the second. There is no visible trend toward a maximum isotope effect at $K = 1$.

The purpose of this paper is to suggest that hydride transfer between NAD$^+$ analogues, A_i^+ and A_j^+, involves the prior achievement of a solvent configuration intermediate between that of ^+A_i·HA_j and that of A_iH·A_j^+. This theory requires considerably reduced primary hydrogen isotope effects for slowly relaxing solvents, and this has now been observed for a number of viscous, nonhydroxylic liquids. All hydroxylic solvents appear to give about the same, maximal isotope effect. The equilibrium constant has also been measured, in each of the solvents. It is somewhat solvent-sensitive, and the rate constant is correlated with the equilibrium constant, but these variations, in themselves, do not seem to offer a reasonable explanation for the substantial changes in the isotope effect.

We have chosen to study the reaction shown in eq 1 because previous work[2] has shown that its rate and equilibrium constant can be measured with good precision by following the appearance of the 10-methylacridinium ion absorbance around 435 nm. At this wavelength none of the other reactants or products and none of our solvents has any measurable absorption. This reaction has an equilibrium constant, K, of 22.2 in a 4:1 mixture of 2-propanol and water.[2] In all the solvents of the present study K has been large enough to ensure that a reaction mixture initiated with only reactants present, and one reactant in large excess, would go to at least 90% of completion with no more than a few percent of back-reaction, which would redistribute the isotopes. At the same time K has been small enough to be measured directly, by starting with the products, without isotopic substitution, measuring the rate of the reverse reaction, and making K consistent with the rate constant for the reverse reaction.[3] The reactants and products have the same charge type and are structurally similar, so that



(1)

(L may be either H or D)

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[1] This work was supported by the U.S. National Science Foundation through Grants 85-20903 and 89-00103.

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the form of the multidimensional potential energy function governing the system should be similar on the reactant and product sides of the surface separating reactants from products.[4] The rate constants for reactions of this type in 4:1 2-propanol–water are accurately predictable from their equilibrium constants and the rate constants for related, symmetrical reactions, by using Marcus theory of atom and group transfer.[5]

Experimental Section

9,9-Dideuterio-10-methylacridan was prepared as previously described.[6] It was freed from isotopic contamination by allowing about half of it to react with chloranil.[7,8] This reaction is highly selective for hydrogen[8] and leaves a product in which hydrogen contamination at the 9-position is undetectable by proton NMR. Recent and previous experience[6,7] suggests that 2% of 9-deuterio-10-methylacridan is detectable, so we attribute at least 98% isotopic purity to our deuterated reactant. This material had a melting point and ^{1}H NMR spectrum identical with those of the undeuterated material, apart from the absence of the band for the methylene group.

1-Benzyl-3-cyanoquinolinium perchlorate was prepared from the corresponding bromide by reduction with sodium borohydride, to give a mixture of 1-benzyl-3-cyano-1,2-dihydroquinoline and its 1,4-dihydro isomer.[9] The mixture was reoxidized by chloranil in the presence of an excess of perchloric acid[7] to give the perchlorate; mp 202 °C; ^{1}H NMR spectrum identical with that of the bromide. 10-Methylacridinium perchlorate was prepared in the same way (except that only one isomer is given by the reduction) from 10-methylacridinium iodide.

1-Benzyl-3-cyano-1,4-dihydroquinoline and 10-methylacridan were prepared as previously described.[2]

Each of the solvents was claimed by its supplier to be at least 99% pure, the most likely impurity, in most cases, being water. Sulfolane, dimethyl sulfoxide, and propylene carbonate were distilled before use. The others were used as supplied. In no case was k_{H} significantly changed by distillation. In each solvent the rate constant was also tested for sensitivity to the water content by deliberately adding 1% water. At this level, no water sensitivity was detected. Ethylene glycol, propylene carbonate, and dimethyl sulfoxide were made to be 1×10^{-4} M in $HClO_4$ to preclude hydroxylation of the quinolinium ion.

Reactions proceeding from left to right (eq 1) were initiated with 10-methylacridan concentrations $\sim 10^{-4}$ M and with 1-benzyl-3-cyanoquinolinium perchlorate in at least 20-fold excess. Rate constants, k_+, were evaluated from eq 2.[10a] An absorbance is A, measured at a time,

$$k_+ = t^{-1} \ln (A_\infty - A_0)/(A_\infty - A_t) \qquad (2)$$

t. Subscripts on the As indicate the time to which they pertain. All H-transfer and a few D-transfer reactions were monitored to at least 75% of completion. For these a computer was used to simultaneously optimize k_+ and A_∞, by minimizing the sum of the squares of the differences between measured values of A and those calculated from eq 2 with the parameters in question. For the slower D-transfer reactions A_∞ was calculated from the known, initial concentrations and the equilibrium constant. The measurement of the equilibrium constants is described below. They were assumed to be isotopically insensitive. Values of k_{H} or k_{D} were given by k_+/C_{O}, where C_{O} is the concentration of the oxidizing agent, which was in excess. Each reported k_{H} is the average of at least four determinations, with an overall average deviation from the mean of $\sim$4% and standard error of $\sim$1.4%.[11a] To minimize the impact of imperfections in temperature control, isotope effects, $k_{\mathrm{H}}/k_{\mathrm{D}}$, were evaluated from parameters measured at the same time, in adjacent cells in the spectrophotometer. Each $k_{\mathrm{H}}/k_{\mathrm{D}}$ value reported is the average of at least four determinations, with an overall average deviation from the mean of 7% and a standard error of 3%. This is significantly better than the 6% standard error which might be expected[11b] from the individual standard errors of k_{H} and k_{D}, suggesting that the strategy of simultaneous measurement has merit.

Extensive ion pairing was found for 1-benzyl-3-cyanoquinolinium bromide in benzonitrile and even in acetonitrile at concentrations between 10^{-3} and 10^{-2} M. The ion pair has a charge-transfer absorption around 420 nm; the unpaired ions do not. This was used to estimate the extent of ion-pair formation. In acetonitrile, there was a linear relation between the mole fraction of ion pairs and k_{H}, with the k_{H} for free ions being larger than that for ion pairs by the factor of 4.4. Since we wanted to avoid the added complication of ion pairing in our $k_{\mathrm{H}}/k_{\mathrm{D}}$ values, these were all determined with the perchlorate, which should be much less prone to ion pairing than the bromide. In addition, solvents with dielectric constants below 25 were not used. With these measures neither k_{H} itself nor $k_{\mathrm{H}}/k_{\mathrm{D}}$ showed any systematic concentration dependence in any of the solvents, and we believe that the reported results are substantially free of effects due to ion pairing.

Equilibrium constants were evaluated as previously described.[3] The decay of absorbance was monitored at 435 nm, for solutions initially containing $\sim 10^{-4}$ M 10-methylacridinium perchlorate and $\sim 10^{-2}$ M 1-benzyl-3-cyano-1,4-dihydroquinoline. This decay is describable by eq 3,[10b] in which k_- is the rate constant of eq 1, right to left, and other

$$k_{-1} = t^{-1}\left[\frac{A_0 - A_\infty}{A_0 + A_\infty}\right] \ln \left[\frac{A_0^2 - A_t A_\infty}{A_0 A_t - A_0 A_\infty}\right] \qquad (3)$$

symbols have the same significance as they have in eq 2. K is linked to k_+ through eq 4, in which C_{H} is the concentration of 1-benzyl-3-cyano-1,4-dihydroquinoline in the given experiment. It is linked to A through eq 5 and the Beer–Lambert law. (C_{Ac} is a concentration of 10-methylacridinium ion. A subscript 0 indicates an initial concentration and a subscript ∞ indicates a concentration at equilibrium.) A computer program calculates k_- from an initial estimate of A_∞ and the decay of absorbance data. From k_- and the previously available k_{H}, K is calculated and used to make a second estimate of A_∞. Then k_- is recalculated. The whole procedure is repeated until k_- is no longer changed by recalculation. Because the equilibrium constants were modest in the present instance, A_∞ values were less than a tenth of the corresponding A_0 values, and reactions could be followed to over 50% of completion. We, therefore, believe that the k_- values obtained are nearly as reliable as the k_+ values, and the K values are uncertain by $\sim$6%. Each K value was replicated at least four times, and the scatter would appear to support this estimate.

$$K = k_{\mathrm{H}} C_{\mathrm{H}}/k_- \qquad (4)$$

$$K = \frac{C_{\mathrm{H},\infty} C_{\mathrm{Ac},\infty}}{(C_{\mathrm{Ac},0} - C_{\mathrm{Ac},\infty})^2} \qquad (5)$$

Theory

Our model for the reaction is based on the idea that the covalency change of a hydride transfer is a tunneling process.[12] However, only a small fraction of the barrier is evaded in this way, and the tunneling process only displaces the hydrogen by 0.1–0.2 Å.[13] Prior to this the reactants approach each other, passing successively through configurations which might be described as an encounter pair, a precursor configuration, and finally reaching a configuration appropriate for tunneling. In this pretunneling configuration the interaction between the hydrogen to be transferred and the acceptor carbon is already substantially attractive, and the existing C–H bond somewhat stretched, so that the force constant for hydrogenic motion along the line of the two carbons is substantially reduced (as in the formation of a strong hydrogen bond[14]). Since tunneling requires the same energy in beginning and ending configurations, the solvent is brought to a configuration intermediate between that of reactants, and that of the products. This is not the minimum-energy solvation for the pretunneling configuration, and contributes to the observed free energy of activation. The most probable pretunneling configuration, thus, does not lie on the nontunneling minimum-energy path from reactants to products because it has a solvent arrangement which minimizes the energy when the hydride is partially transferred,

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Scheme I

$$\mathrm{A_i}^+ + \mathrm{A_jH} \xrightleftharpoons[k_{-1}]{k_1} {}^+\mathrm{A_i}\cdot\mathrm{HA_j} \xrightleftharpoons[k_{-2}]{k_2} \mathrm{A_iH}\cdot\mathrm{A_j}^+ \xrightleftharpoons[k_{-3}]{k_3} \mathrm{A_iH} + \mathrm{A_j}^+$$

rather than minimizing the energy of the pretunneling configuration itself. Tunneling occurs because it permits the hydrogen transfer to occur at larger donor–acceptor separations, thereby reducing the concomitant nonbonded repulsions. A large part of the free energy of activation is solvent-related. Gas-phase hydride transfers have much lower energy barriers.[15] However, the structure of the highly shielded cations and the nature of the solvents (all having dielectric constants between 25 and 65) should (and does) minimize the solvent effect on rate and equilibrium constants.

This general approach seems to have been first suggested by Libby, for electron-transfer reactions.[16] On this basis, Marcus developed a simple formalism, first for electron transfer rate constants,[17a–c] and then for atom and group transfers.[17d] These have been hugely successful in systematizing rate constants, but they are based on conventional, quasi-thermodynamic transition-state theory and, thus, avoid all questions about dynamics.[4] Recently, Hynes and co-workers have examined the dynamics of solvation during heterolytic transformations from the same point of view.[18] Their work is the direct antecedent of our present treatment.

To quantify our treatment we assign rate constants as shown in Scheme I. In this scheme $^+\mathrm{A_i}\cdot\mathrm{HA_j}$ is the pretunneling configuration and $\mathrm{A_iH}\cdot\mathrm{A_j}^+$ is the posttunneling configuration. In a first approximation we assume that every $\mathrm{A_iH}\cdot\mathrm{A_j}^+$ which is formed goes on to products, $\mathrm{A_iH}$ and $\mathrm{A_j}^+$. This makes it unnecessary to consider, explicitly, the rate constants governing the fate of $\mathrm{A_iH}\cdot\mathrm{A_j}^+$. By making the steady-state approximation for $^+\mathrm{A_i}\cdot\mathrm{HA_j}$, eq 6 is readily obtained for the single observable rate constant,

$$k = \frac{k_1 k_2}{k_{-1} + k_2} \tag{6}$$

k. Equation 6 illustrates the familiar fact that the rate-limiting step in a two-step sequence is determined by competition between the second step and the *reversion* of the first step.

If our tunneling model for the second step is accepted, an order-of-magnitude estimate of k_2 can be made. It is approximated as the product of the C–H vibration frequency in $^+\mathrm{A_i}\cdot\mathrm{HA_j}$ times the tunneling probability on each vibration against the barrier.[19,20] In the reactant, $\mathrm{A_jH}$, the vibration frequency is close to 3000 cm^{-1}, but this should be considerably reduced in $^+\mathrm{A_i}\cdot\mathrm{HA_j}$, for the reasons given above. A value of 1000 cm^{-1} (3×10^{13} s^{-1}), corresponding roughly to the lowest known vibration frequencies in strongly hydrogen bonded species,[21] will be used. An internal check of this frequency will presently be provided. The tunneling probability, $G(V)$, can be estimated by means of eq 7.[22] In eq 7, V_B

$$[G(V)]^{-1} = 1 + \exp[2\pi(V_B - V)/h\upsilon_B] \tag{7}$$

is the potential energy at the top of the one-dimensional barrier separating the pretunneling configuration from the posttunneling configuration; V is the potential energy of the pretunneling configuration; and υ_B is the frequency that would be associated with the negative of the curvature at the top of the barrier at the point where it separates the pre- from the posttunneling configuration. A value of 8 kJ mol^{-1} (1.3×10^{-20} J molecule^{-1}) was taken for $(V_B - V)$, and 1000 cm^{-1} (3×10^{13} s^{-1}) for υ_B. These values are arbitrary, but they lead to about the right isotope effect in a colinear, three-atom-model calculation. They give a $G(V)$ of 1.5×10^{-2}. When this is combined with a 1000 cm^{-1} vibration frequency, a value of 4×10^{11} s^{-1} is obtained for $k_{2,\mathrm{H}}$, which is just about the right magnitude to compete with solvent relaxation.[23–25] The model for which eq 7 is derived is rather different than the one we now propose, but the result should not be very model-specific, since the tunneling probability is approximately determined by the cross section of the barrier above the tunneling path.[22]

In eq 6, k_1 and k_2 will be isotopically sensitive: the former because a substantial change in force constant and frequency is assumed to accompany the formation of the pretunneling configuration from reactants; the latter because it is the rate constant for a tunneling process.[22] However, the isotope effects on k_1 and k_2, $k_{1,\mathrm{H}}/k_{1,\mathrm{D}}$ and $k_{2,\mathrm{H}}/k_{2,\mathrm{D}}$, may be reasonably expected to be solvent-independent, since we suggest that they are determined by the structural characteristics of the reactants. The rate constant for disabling the pretunneling configuration, k_{-1}, will be much less isotopically sensitive, because quite small displacements from the ideal configuration are probably sufficient to make tunneling inefficient.[26] Thus, k_{-1} was assumed to be the same in the H and D variants of the reaction, but solvent-sensitive. Equation 6 then gives eq 8 for the observable isotope effect, $k_\mathrm{H}/k_\mathrm{D}$.

$$\frac{k_\mathrm{H}}{k_\mathrm{D}} = \frac{k_{1,\mathrm{H}} k_{2,\mathrm{H}} (k_{-1} + k_{2,\mathrm{D}})}{k_{1,\mathrm{D}} k_{2,\mathrm{D}} (k_{-1} + k_{2,\mathrm{H}})} \tag{8}$$

If $k_{-1} \gg k_2$ (fast-solvent relaxation), eq 8 can be reduced to eq 9; if $k_{-1} \ll k_2$ (slow-solvent relaxation), eq 10 can be obtained. Thus a group of "fast" solvents which give an upper limiting isotope effect of θ is expected. Another group, of "slow" solvents, should give a lower limiting isotope effect of ϕ. For intermediate solvents the isotope effect is related to $k_{-1}/k_{2,\mathrm{H}}$ by eq 11.

$$\frac{k_\mathrm{H}}{k_\mathrm{D}}\ (\text{fast}) = \frac{k_{1,\mathrm{H}} k_{2,\mathrm{H}}}{k_{1,\mathrm{D}} k_{2,\mathrm{D}}} \tag{9}$$

$$\frac{k_\mathrm{H}}{k_\mathrm{D}}\ (\text{slow}) = \frac{k_{1,\mathrm{H}}}{k_{1,\mathrm{D}}} \tag{10}$$

$$\frac{k_{-1}}{k_{2,\mathrm{H}}} = \frac{(k_\mathrm{H}/k_\mathrm{D}) - \phi}{\theta - (k_\mathrm{H}/k_\mathrm{D})} \tag{11}$$

Similar results are obtained if the first step is assumed to be fast and reversion of the second step competes with the third step in Scheme I. In this and all subsequent development we assume that $k_{-2} = k_2$. Equation 7 gives the same $G(V)$ for the forward and reverse reactions. The C–H vibration frequencies in $^+\mathrm{A_i}\cdot\mathrm{HA_j}$ and $\mathrm{A_iH}\cdot\mathrm{A_j}^+$ should be *very* similar in view of the general symmetry of the reaction, which has been pointed out. With these assumptions the kinetic isotope effect is given by eq 12, in which

$$\frac{k_\mathrm{H}}{k_\mathrm{D}} = \frac{K_{1,\mathrm{H}} k_{2,\mathrm{H}} (k_{2,\mathrm{D}} + k_3)}{K_{1,\mathrm{D}} k_{2,\mathrm{D}} (k_{2,\mathrm{H}} + k_3)} \tag{12}$$

K is the equilibrium constant for the process indicated by its subscripts. In our model k_{-1} is isotopically insensitive, so $K_{1,\mathrm{H}}/K_{1,\mathrm{D}} = k_{1,\mathrm{H}}/k_{1,\mathrm{D}}$. The process for which k_3 is the rate constant (solvent and heavy atom relaxation) is entirely analogous to the process for which k_{-1} is the rate constant. Thus, equations just like 9–11 would still apply to the case in which the second and third step, among them, are rate-limiting, and the conclusions reached previously would still apply.

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Table I. Solvent Effects on Various Aspects of the Reaction Shown in Eq 1

solvent	k_H, M^{-1} s^{-1}	K	k_H',^{a} M^{-1} s^{-1}	k_H/k_D	τ_s,^{b} ps	τ_L,^{c} ps	τ_D,^{d} ps	viscosity^e	density^f
IPA–H_2O (4:1)^c	4.51×10^{-2}	22.2	1.43×10^{-2}	5.22				2.65^f	0.829^g
ethylene glycol	5.30×10^{-2}	31.7	1.48×10^{-2}	5.20	100^h	86^h	813^h	17.4	1.113
methanol	2.78×10^{-2}	20.6	9.08×10^{-3}	5.09	88^h	8.2^i	48^i	0.545	0.791
acetonitrile	1.38×10^{-2}	6.7	6.83×10^{-3}	5.20	0.4–0.9^j	0.2^i	3.3^i	0.345	0.786
acetonitrile–triacetin (9:1)	1.31×10^{-2}	6.98	6.38×10^{-3}	4.14				0.405^f	0.823^g
acetonitrile–triacetin (4:1)	1.35×10^{-2}	7.54	6.39×10^{-3}	4.49				0.505^f	0.860^g
acetonitrile–triacetin (7:3)	1.25×10^{-2}	6.59	6.22×10^{-3}	4.02				0.638^f	0.897^g
acetonitrile–triacetin (3:2)	1.39×10^{-2}	6.94	6.78×10^{-3}	4.46				0.828^f	0.934^g
acetonitrile–triacetin (1:1)	1.43×10^{-2}	6.88	7.01×10^{-3}	4.15				1.140^f	0.971^g
benzonitrile	1.22×10^{-2}	16.9	4.29×10^{-3}	4.01		5.8^j	38^i	1.24	1.010
propylene carbonate	9.46×10^{-3}	3.1	6.22×10^{-3}	3.54	4.9^j	5.1^j	43^i	2.24	1.189
sulfolane^k	6.36×10^{-3}	4.0	3.81×10^{-3}	3.31				9.87	1.261
sulfolane–triacetin (4:1)^l	5.81×10^{-3}	3.8	3.55×10^{-3}	2.88				13.50^g	1.24^g
sulfolane–triacetin (3:2)^l	7.02×10^{-3}	3.7	4.33×10^{-3}	3.43				17.12^g	1.22^g
dimethyl sulfoxide	3.69×10^{-3}	1.8	2.97×10^{-3}	2.64	3.1^j	2.4^i	19.5^i	1.98	1.10

[a] k_H' is the intrinsic k_H, obtained from $\log k_H' = \log k_H - 0.37 \log K$. [b] Solvent relaxation time measured with various probes; see refs 24 and 25. [c] Longitudinal relaxation time calculated from $\tau_L = (\epsilon/\epsilon_s)\tau_D$; ref 29. [d] Debye relaxation time; ref 28. [e] Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; Wiley, New York, 1972; pp 3–13, unless indicated otherwise. [f] Measured at 25 °C with an Ostwald viscosimeter. [g] Assuming that these are linear in volume fractions. [h] Reference 25. [i] Reference 23. [j] Reference 24. [k] Measured at 30 °C. [l] By volume.

The situation becomes somewhat more complicated if there is a comparable flux through all three steps, and the rate constant is given by eq 13 if the steady-state approximation is applied to both $^+A_i{\cdot}HA_j$ and $A_iH{\cdot}A_j^+$. However, if $k_{-2} = k_2$ is maintained

$$k = \frac{k_1 k_2 k_3}{k_{-1}k_{-2} + k_{-1}k_3 + k_2 k_3} \qquad (13)$$

and the approximation, $k_{-1} = k_3$, is made, eq 13 gives eq 8 for the kinetic isotope effect, except that the second term in each of the parentheses is multiplied by a factor of 2. Thus, it is likely that eqs 9–11 and the conclusions which follow from them are reasonable approximations quite generally. Equation 11 permits the evaluation of a parameter proportional to solvent relaxation rates from modest, easily measured rate constants.

There is, furthermore, a good prospect that $k_{2,H}$ can be evaluated with useful reliability from model calculations, now under way, in which a potential energy hypersurface will be fitted to the substantial body of data available for this type of reaction.[27] In that case, numerical values of k_{-1} itself will become available.

Results

Isotope effects on the reaction shown in eq 1 have been measured for a number of solvents, and they do, indeed, approximate, the anticipated pattern. There is one group of high isotope effects, with values centering around 5.2, another group of low isotope effects, centering around 2.9, and one or two examples of intermediate values. The scatter of the experimental values about these two central values is ~0.2. The results are given in Table I.

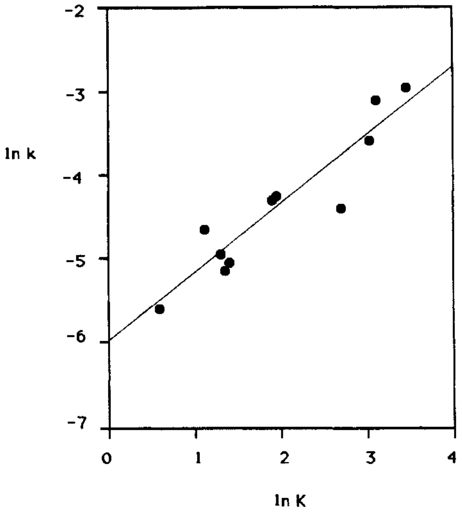

Figure 1. The relation between ln k_H and ln K. The line is the least-squares-correlation line,[11c] with slope of 0.87 and correlation coefficient of 0.95.

Equilibrium constants, K, have also been measured in each solvent, and these are also shown in Table I. Compared to the changes in K required to produce substantial changes in k_H/k_D[6] the solvent effects on K are small. There is no indication that k_H/k_D approaches a maximum as K approaches 1.0,[28] although the reaction is structurally quite symmetrical. There is, however, a linear correlation between ln k_H (or k_D), individually, and ln K_H[29] shown in Figure 1. The least-squares slope is 0.87, and the correlation coefficient is 0.95.[11c] There is no comprehensive relation between k_H/k_D and either dielectric relaxation time[30,31] or relaxation times measured after electron-transfer reactions.[24,25] All hydroxylic solvents appear to be "fast", giving the upper limiting value of k_H/k_D, θ, ~5.2, regardless of their other characteristics. Among nonhydroxylic solvents, higher viscosity appears to lead to lower k_H/k_D values, with a number of solvents giving the lower limiting value, ϕ, ~2.9. There is also a general correlation between k_H/k_D and k_H. There is somewhat better correlation with the intrinsic rate constant, k_H', which is k_H with a small, Marcus theoretical[5] correction for the effect of the equilibrium constant on k_H. However, the range of k_H and k_H' is small. There is a general tendency for solvent density to be correlated with solvent viscosity and, thus, for k_H/k_D in nonhydroxylic solvents to be correlated with density.

Discussion

The value of 1000 cm^{-1}, which was used for the pretunneling C–H stretching frequency, ν_{PT}, in arriving at the conclusion that k_2 was of the same order of magnitude as k_{-1}, can be tested by using it to make a one-frequency, zero-point energy estimation of $k_{1,H}/k_{1,D}$ (eq 14).[32] The reactant C–H stretching frequency,

$$\frac{k_{1,H}}{k_{1,D}} = \exp\left[\frac{0.293hc}{2kT}(\nu_R - \nu_{PT})\right] \qquad (14)$$

ν_R, was assumed to be 2800 cm^{-1}. Equation 8 gives a value of 3.6 for $k_{1,H}/k_{1,D}$, which is in reasonable agreement with the apparent value of ϕ, 2.9.

The observations summarized in Table I can be rationalized in terms of the suggested model as follows. The reversion of the pretunneling configuration (the first step in Scheme I, right to left) and the stabilization of the posttunneling configuration (the third step in Scheme I, left to right) both compete in rate with

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the tunneling step (the second step). The correlation of ln k_H with ln K suggests that it is the third step which mainly shares rate-limiting character with the second, rather than the first. In the nonhydroxylic solvents translational and rotational solvent motions, which are responsive to bulk viscosity,[33] are important components of the heavy atom reorganization steps. We suggest that the hydroxylic solvents disable the pretunneling configuration or stabilize the posttunneling configuration, by hydrogenic motions which are faster than molecular rotation and unrelated to bulk viscosity.[34] In the theoretical section we have shown that the observed pattern of isotope effects could be produced by the competition of the tunneling step with either or both of the spontaneous heavy atom reorganization steps.

Other things being equal, eq 2 anticipates that high-viscosity solvents, which give lower limit values for k_H/k_D, should also give lower values of k_H' than solvents which give upper limit values of k_H/k_D. In the lower limit cases an additional bottleneck has appeared. We recognize, of course, that the solvents might also influence k in more conventional, quasi-thermodynamic ways.[4] Some of those influences are also reflected in K. Those may be removed by using k_H' instead of k_H. In fact, all the lower limit solvents give significantly smaller values of k_H' than do solvents which give larger values of k_H/k_D although the differences are not large.

Since solvent viscosity, in general, is correlated with solvent density, the isotope effects and rates cited in Table I correlate with the latter to about the same degree as they do with the former. This raises the possibility that the kinetic quantities are responding to internal pressure, a quasi-thermodynamic solvent property,[35] rather than to viscosity, a dynamic property. At the moment we see no rigorous way to exclude this possibility. However, it seems unattractive because it seems likely that an increase in internal pressure would increase the rate of our reaction, since it almost certainly has a negative volume of activation.[36] Similarly, the present results do not require that the second stage be a tunneling process. They strongly suggest only some sort of two- or three-stage process, in which solvent characteristics determine the rate-limiting stage. Without this we see no way that two very different sets of isotope effects could be generated with such small ranges of K and k_H. The suggested model accounts for the observations and seems to be in general accord with theory and previous work on this reaction. Further tests are in progress.

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Inclusion by Cyclodextrins To Control Dye Aggregation Equilibria in Aqueous Solution[†]

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Abstract: Oxazine 1 perchlorate (A) and oxazine 170 perchlorate (D) were selected to investigate the influence of cyclodextrins (CDs) on the dyes' aqueous solution aggregation equilibria. Through equilibrium processes, these days form inclusion complexes with β- and γ-CD. The amphiphile hexane sulfonate can be coincluded with D in γ-CD. We report determination of the stoichiometries of all inclusion complexes and measurement of all equilibrium constants; temperature effect data on some of the latter are also included. This study clearly demonstrates that proper size matching between the guest and the host's cavity leads to substantially larger equilibrium constants. All experimental measurements for each dye rely on changes in absorption intensities of the individual long wavelength monomer and dimer absorption bands. Because H-dimers are formed, the dimer absorption bands are blue-shifted relative to the monomer bands and only the monomers fluoresce. Although, in the absence of CDs, A is mostly monomer and D is mostly dimer or larger aggregate, the intercession of CDs can be used to force A to mostly dimer and D to mostly monomer.

In recent years, there has been considerable interest in cyclodextrin (CD) inclusion complexes, as they can alter the physical properties and chemical reactivities of guest molecules.[1-6] Many organic compounds can be included in the cavities of these cyclic oligosaccharides because of the hydrophobic attraction of their interiors. In aqueous solutions, equilibria are established between uncomplexed molecules and inclusion complexes; frequently, guest and host combine to form two or more complexes that differ in their stoichiometries and degree of stabilization. The stoichiometries, the magnitude of the equilibrium constants, and the degree of protection afforded the included compounds depend to a large extent on the fit of the guest molecules into the cavities of the cyclodextrins. The three common CDs, designated α, β, and γ, consist of six, seven, and eight glucose units, respectively. Instead of cylinders, truncated cones provide a better approximation to CD shapes. The internal diameter range is 4.2–8.8 Å in α-CD, 5.6–10.8 Å in β-CD, and 6.8–12.0 Å in γ-CD; the height of each CD is 7.8 Å.[7]

The ability to alter dye solubilities and to shift equilibria among dye monomer, dimer, and higher aggregate forms makes CD

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