Mechanisms of Elimination Reactions. 35. Deuterium Kinetic Isotope Effects and Tunneling in the Reaction of [2-[*p*-(Trifluoromethyl)phenyl]ethyl]trimethylammonium Ion with Hydroxide Ion in Mixtures of Water and Dimethyl Sulfoxide[1,2]

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The rates of reaction of [2-[(*p*-trifluoromethyl)phenyl]ethyl]trimethylammonium (**1h**) and [2-[(2-trifluoromethyl)phenyl]ethyl-*2,2-d*$_2$]trimethylammonium (**1d**) iodides with hydroxide ion in mixtures of dimethyl sulfoxide and water were determined as a function of temperature. A maximum in k_H/k_D (7.25 at 50 °C) is observed at 35% dimethyl sulfoxide. The Arrhenius parameters provide qualitative evidence for tunneling, and fitting the Bell theory expression for tunneling to the observed temperature dependence gives tunnel corrections, Q_{tH}/Q_{tD}, of 1.6–1.8 at 50 °C. Equations for calculating the effect of error in the Arrhenius preexponential factor, A_{aH}/A_{aD}, on the tunnel correction are derived. The error in Q_{tH}/Q_{tD} (3–18%) is less than the error in A_{aH}/A_{aD} (10–50%) but is still enough to render uncertain the significance of observed variations in Q_{tH}/Q_{tD}. These results are compared with earlier results on the (2-phenylethyl)trimethylammonium ion, and the effect of the *p*-trifluoromethyl substituent on the structure of the transition state for elimination is discussed. The application of Marcus theory to k_H/k_D variation in these reactions is considered.

Variation in the strength of the attacking base has been shown to produce k_H/k_D maxima in a number of E2 reactions.[2-4] Such maxima have generally been considered to indicate a transition state with the proton symmetrically located between the donor and acceptor atoms in the transition state.[5,6] This picture ascribes the phenomenon to zero-point energy effects, but it has also been suggested that variation in the tunnel correction could cause k_H/k_D maxima.[7] Previous work in our group on the temperature dependence of k_H/k_D in the reaction of (2-phenylethyl)trimethylammonium ion with hydroxide ion in mixtures of dimethyl sulfoxide and water showed, however, that Q_{tH}/Q_{tD} did not change signficantly and that the observed variation was due mainly or entirely to the semiclassical isotope effect, $(k_H/k_D)_s$, which reflects zero-point energy differences.[8] We undertook the present study to explore the generality of this observation, as well as the influence of an electron-withdrawing substituent on the tunnel correction and the structure of the transition state.

The [2-[(*p*-trifluoromethyl)phenyl]ethyl]trimethylammonium (**1h**) and [2-[(*p*-trifluoromethyl)phenyl]ethyl-*2,2-d*$_2$]trimethylammonium (**1d**) iodides were prepared as described in the Experimental Section. Their rates of reaction with hydroxide ion in mixtures of dimethyl sulfoxide and water were determined spectrophotometrically by following the appearance of the absorption of *p*-(trifluoromethyl)styrene. A sample set of rate data is given in Table I, and the Arrhenius parameters derived from the rate constants in 30%, 35%, 40%, and 50% Me_2SO are recorded in Table II. From these the Arrhenius parameters of the isotope effects and the k_H/k_D values in Table III were calculated.

Table I. Temperature Dependence of the Rate Constants for the Reaction of [2-[(*p*-Trifluoromethyl)phenyl]ethyl]-trimethylammonium Iodide with Hydroxide Ion in 35% Dimethyl Sulfoxide[a]

temp, °C	10^3k_H, M^{-1} s^{-1}	10^3k_D, M^{-1} s^{-1}
2.0	1.17	
11.9	4.34	
12.0	4.44	
20.6	12.9	
21.0	13.6 ± 0.4	
23.0		1.79 ± 0.00
23.2		1.82
33.0	52.5 ± 1.7	
41.0		16.3 ± 0.6
41.3	132	
42.0	145	
42.4		18.8
42.8	155	
54.0		68.8
54.2		70.9
61.5	977	
63.0	1103	
64.0		186
65.0		209 ± 1
65.4	1388	
83.7		1237
84.0		1261 ± 10

[a] Deviations are standard deviations. Numbers without deviations represent single runs.

As in our earlier work on (2-phenylethyl)trimethylammonium ion,[8] the Arrhenius parameters in Table III indicate significant tunneling through the facts that $E_{aD} - E_{aH} > 1.2$ kcal mol^{-1} and $A_{aH}/A_{aD} < 0.7$.[9] As in the previous work, the tunnel corrections were estimated by fitting the observed temperature dependence of k_H/k_D to eq 1 and utilizing expressions 2–4. The values of u_{tH} and

$$k_H/k_D = (Q_{tH}/Q_{tD}) \exp[(E_D - E_H)/RT] \quad (1)$$

$$\ln (A_{aH}/A_{aD}) = \ln (u_{tH} \sin (u_{tD}/2)/u_{tD} \sin (u_{tH}/2)) + (u_{tH}/2) \cot (u_{tH}/2) - (u_{tD}/2) \cot (u_{tD}/2) \quad (2)$$

$$E_D - E_H = (Ea_D - E_{aH}) - RT(u_{tD}/2) \cot (u_{tD}/2) - (u_{tH}/2) \cot (u_{tH}/2) \quad (3)$$

$$Q_t = (u_t/2)/\sin (u_t/2) \quad (4)$$

u_{tD} $(=u_{tH}/2^{1/2})$ in eq 2 are varied until the observed A_{aH}/A_{aD} is reproduced, and then the tunnel corrections

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Table II. Activation Parameters for the Reaction of [2-[(*p*-Trifluoromethyl)phenyl]ethyl]trimethylammonium and [2-[(*p*-Trifluoromethyl)phenyl]ethyl-2,2-d_2]trimethylammonium Iodides with Hydroxide Ion[a]

	solvent			
	30% Me_2SO	35% Me_2SO	40% Me_2SO	50% Me_2SO
$10^{-14}A_{aH}$	0.553 ± 0.228	0.297 ± 0.023	0.0612 ± 0.0111	0.224 ± 0.096
$10^{-14}A_{aD}$	1.328 ± 0.328	0.840 ± 0.056	0.292 ± 0.082	0.650 ± 0.171
E_{aH}, kcal mol^{-1}	21.65 ± 0.26	20.65 ± 0.05	18.94 ± 0.11	18.71 ± 0.25
E_{aD}, kcal mol^{-1}	23.43 ± 0.16	22.59 ± 0.04	21.13 ± 0.18	20.52 ± 0.16
temp range, °C for H	20-75	2-65	−5 to +60	−5 to +45
temp range, °C for D	30-80	23-84	20-70	0-60

[a] From linear-regression fits to the Arrhenius equation of rate constants determined over the indicated temperature ranges. Deviations are standard deviations.

Table III. Tunnel Corrections for the Reaction of [2-[(*p*-Trifluoromethyl)phenyl]ethyl]trimethylammonium and [2-[(*p*-Trifluoromethyl)phenyl]ethyl-2,2-d_2]trimethylammonium Iodide with Hydroxide Ion[a]

	solvent			
	30% Me_2SO	35% Me_2SO	40% Me_2SO	50% Me_2SO
$E_{aD} - E_{aH}$, kcal mol^{-1}	1.78 ± 0.31	1.94 ± 0.06	2.19 ± 0.21	1.81 ± 0.29
A_{aH}/A_{aD}	0.417 ± 0.200	0.354 ± 0.036	0.210 ± 0.070	0.344 ± 0.173
k_H/k_D	6.71 ± 0.68	7.25 ± 0.18	6.39 ± 0.45	5.72 ± 0.66
Q_{tH}/Q_{tD}[b] (50 °C)	1.64 ± 0.29	1.68 ± 0.05	1.81 ± 0.13	1.58 ± 0.23
$(k_H/k_D)_s$[c] (50 °C)	4.10 ± 0.84	4.34 ± 0.17	3.59 ± 0.36	3.65 ± 0.68
Q_{tH}[b] (50 °C)	2.45 ± 0.70	2.54 ± 0.13	2.86 ± 0.31	2.31 ± 0.56

[a] Deviations are standard deviations. [b] Evaluated by fitting a temperature dependence calculated by using the first term of the Bell equation to the observed temperature dependence. See text and ref 8 for details. [c] Semiclassical isotope effect, $(k_H/k_D)/(Q_{tH}/Q_{tD})$.

can be calculated. With them and the observed isotope effect, the semiclassical isotope effect, $(k_H/k_D)_s$, can be obtained from eq 5. The results of these calculations are recorded in Table III.

$$(k_H/k_D)_{obsd} = (Q_{tH}/Q_{tD})(k_H/k_D)_s \qquad (5)$$

In our previous paper we did not comment on the effect of the uncertainty in A_{aH}/A_{aD} on Q_{tH}/Q_{tD}, for the complex functional relationship between the two did not permit any easy estimates. It is, however, important to know the uncertainty in Q_{tH}/Q_{tD} if one is to compare values from different reactions, and so we derive the necessary relations below using standard methods for estimating the propagation of errors.[10] If we let $u_{tH} = u$, $u_{tD} = u/2^{1/2}$, and $u_{tT} = u/3^{1/2}$, then $u_{t(heavy)} = u/m^{1/2}$, where m is the mass of the heavier isotope. With this relation eq 2 can be recast as eq 6, where L refers to the heavier isotope (D or T). We

$$A_{aH}/A_{aL} = [m^{1/2} \sin (u/2m^{1/2})/\sin (u/2)] \exp[(u/2) \times [\cot (u/2) - (1/m^{1/2}) \cot (u/2m^{1/2})]] \qquad (6)$$

then take the derivative of eq 6 with respect to u (eq 7) to obtain eq 8. Thus the uncertainty in u, Δu, can be

$$\partial(A_{aH}/A_{aL})/\partial u = \exp[(u/2)[\cot (u/2) - (1/m^{1/2}) \cot (u/2m^{1/2})]][(Q_{tH}/Q_{tL})[(u/4)[(1/m) \csc^2 (u/2m^{1/2}) - \csc^2 (u/2)] + \tfrac{1}{2}[\cot (u/2) - (1/m^{1/2}) \cot (u/2m^{1/2})]] + \partial(Q_{tH}/Q_{tL})/\partial u] \qquad (7)$$

$$\Delta u = (\partial(A_{aH}/A_{aL})/\partial u)^{-1}\Delta(A_{aH}/A_{aL}) \qquad (8)$$

obtained by substituting the standard deviation of A_{aH}/A_{aL} for $\Delta(A_{aH}/A_{aL})$. Differentiation of the expressions for Q_{tH} and Q_{tH}/Q_{tL} with respect to u yields eq 9 and 10. From

$$\partial Q_{tH}/\partial u = \tfrac{1}{2}[\csc (u/2) - Q_{tH} \cot (u/2)] \qquad (9)$$

$$\partial(Q_{tH}/Q_{tL})/\partial u = \tfrac{1}{2}(Q_{tH}/Q_{tL})[(1/m^{1/2}) \cot (u/2m^{1/2}) - \cot (u/2)] \qquad (10)$$

these expressions and Δu, the standard deviations of Q_{tH} and Q_{tH}/Q_{tL} are as shown in eq 11 and 12.

$$s_{Q_{tH}} = [(\partial Q_{tH}/\partial u)^2(\Delta u)^2]^{1/2} \qquad (11)$$

$$s_{Q_{tH}/Q_{tL}} = [[\partial(Q_{tH}/Q_{tL})/\partial u]^2(\Delta u)^2]^{1/2} \qquad (12)$$

The standard deviations of Q_{tH}/Q_{tD} and Q_{tH} in Table III were calculated by using these equations. The results are generally reassuring. The percentage errors in Q_{tH}/Q_{tD} average about a third of those in A_{aH}/A_{aD}; those in Q_{tH} are a little larger but still only half to two-thirds of those in A_{aH}/A_{aD}. Within the range of tunnel corrections found in this and most of our other work, it is also qualitatively obvious that the tunnel correction is not very sensitive to the precise value of A_{aH}/A_{aD}. Note, for example, that A_{aH}/A_{aD} values in Table III differ by as much as 100% (0.210–0.417), while the tunnel corrections cover a much smaller range. This will not always be true. Much larger or much smaller tunnel corrections can be expected to show a steeper dependence on A_{aH}/A_{aD}. When $Q_{tH}/Q_{tD} = 1.29$, for example, its error is more than half, and the error in Q_{tH} is equal to, the error in A_{aH}/A_{aD}. The errors in k_H/k_D quoted in Table III are computed from the standard deviations of ln k_H and ln k_D for the linear regression fits to the Arrhenius equations. Those in $(k_H/k_D)_s$ are from the combined errors of k_H/k_D and Q_{tH}/Q_{tD}.

While these results tell us nothing about the *accuracy* of the Bell theory in accounting for the temperature dependence of isotope effects, they do make it clear that the tunnel corrections computed from even moderately precise A_{aH}/A_{aL} values are meaningful within the framework of the theory. At the same time, uncommonly good experimental data are needed for really precise (say ±10% or better) values of Q_{tH} and Q_{tH}/Q_{tD}. From the results in Table III it can be seen that precision is poorer for the relatively slow reactions in 30% Me_2SO and the relatively fast reactions in 50% Me_2SO than for the two intermediate solvent mixtures.

Given the uncertainties in Table III, it is still likely that k_H/k_D reaches a maximum value at or near 35% Me_2SO. The maximum is at almost the same concentration of

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[10] Bevington, P. R. "Data Reduction and Error Analysis for the Physical Sciences"; McGraw-Hill: New York, 1969, Chapter 4.

dimethyl sulfoxide as that found for (2-phenylethyl)trimethylammonium ion, but the k_H/k_D value at the maximum is substantially larger.[2,8] The tunnel corrections are if anything somewhat smaller than those found for the unsubstituted system, but the errors are sufficient to render this conclusion less secure. Similarly, one cannot say whether the apparent maximum in Q_{tH}/Q_{tD} in 40% Me_2SO is real. If the trends in Q_{tH}/Q_{tD} and $(k_H/k_D)_s$ are real, they indicate that both contribute to the observed k_H/k_D maximum. This is in contrast to observations on the (2-phenylethyl)trimethylammonium ion, where no maximum in Q_{tH}/Q_{tD} was found. In both systems, however, the uncertainty in Q_{tH}/Q_{tD} is at least as large as the range of the values. Definitive evidence on the dependence of Q_{tH}/Q_{tD} on solvent composition must await data that are more precise and/or of a greater range than these.

The fact that k_H/k_D goes through a maximum at or near 35% Me_2SO suggests a transition state in which the proton is approximately half transferred.[5,6] Furthermore, the fact that k_H/k_D and $(k_H/k_D)_s$ at the maximum are larger with [2-[(*p*-trifluoromethyl)phenyl]ethyl]trimethylammonium ion[2] suggests a reaction coordinate with less contribution from heavy-atom motion for the former than for the latter, because model calculations have shown that heavy-atom motion depresses k_H/k_D.[8,11,12] In the present context, "heavy-atom motion" refers to the stretching of the carbon–nitrogen bond and the contraction of the developing carbon–carbon double bond that accompany the proton transfer in an E2 reaction. Although we have no direct measure of the relative extents of heavy-atom involvement in reaction coordinate motion for these two systems under the conditions of these experiments, it has been reported that the nitrogen isotope effect at 40 °C is smaller for the *p*-trifluoromethyl (1.0083) than for the unsubstituted compound (1.0133) with ethoxide in ethanol.[13] It seems reasonable to suppose that the same order would be found under our conditions. If so, the reaction coordinate could be presumed to involve less coupling of carbon–nitrogen stretching (and probably carbon–carbon contraction as well) with proton transfer for the *p*-trifluoromethyl than for the unsubstituted compound.

This conclusion leads to several interesting corollaries. The fact that k_H/k_D for the reaction of (2-arylethyl)trimethylammonium ions with ethoxide in ethanol increases in the order unsubstituted < *p*-Cl < *p*-CF_3 was interpreted as indicating a decrease in the extent of proton transfer in the transition state from more than to close to half-transfer.[12] Our results suggest that the observed trend may reflect a decreasing contribution of heavy-atom motion to the motion along the reaction coordinate rather than changes in the extent of proton transfer in the transition state.

The consistently somewhat smaller tunnel corrections for the *p*-trifluoromethyl than for the unsubstituted[8] compound seem at first sight to argue against this conclusion, for decreased heavy-atom motion should lead to a smaller effective mass along the reaction coordinate and hence a larger tunnel correction because the effective mass, *m*, appears in the denominator of the expression for the tunneling frequency derived by Bell (eq 13).[14] The *p*-trifluoromethyl substituent, however, also lowers the apparent activation energy of the reaction (E_{aH} = 18.7–21.6 kcal mol^{-1} for the *p*-trifluoromethyl and 19.7–24.9 kcal mol^{-1} for the unsubstituted compound). This should be reflected in a similar difference in barrier heights, *E*, and so a smaller *m* for the reaction of the *p*-trifluoromethyl compound may be counterbalanced by a smaller *E*. There is no reason to expect any significant effect of substitution on the half-width of the barrier (*a* in eq 13).

$$\nu_t = E^{1/2}/\pi a(2m)^{1/2} \qquad (13)$$

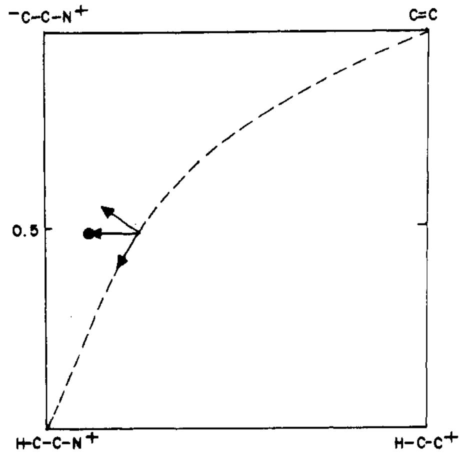

Figure 1. More O'Ferrall–Jencks diagram for the reaction of (2-arylethyl)trimethylammonium ions with hydroxide ion in Me_2SO–H_2O. The dashed line indicates the approximate path for the unsubstituted reactant. The arrows indicate the perpendicular and parallel shifts expected for the *p*-trifluoromethyl substituent. The arrow terminating in a dot represents the resultant or observed shift.

Our conclusion concerning the nature of the transition state can be expressed in terms of a More O'Ferrall–Jencks diagram[15,16] and the Thornton rules.[17,18] In figure 1 the dashed line represents the path for the unsubstituted compound. Its transition state is carbanion-like,[2] which places it on the left side of the diagram and, in 35% Me_2SO, at 0.5 on the vertical (proton transfer) axis. The *p*-trifluoromethyl substituent is expected to lower the free energy of the carbanion (upper left corner). According to Thornton's rules.[17,18] this should produce a shift toward the carbanion in the direction perpendicular to the reaction coordinate (upper arrow) and away from it in the direction parallel to the reaction coordinate (lower arrow). The vector sum or resultant of these two shifts is given by the central arrow. The transition state for the *p*-trifluoromethyl compound is thus predicted to have less C–N cleavage than for the unsubstituted compound but about the same extent of proton transfer, in agreement with the facts outlined above. These conclusions are essentially the same as those of Alunni and Jencks[35] on the effect of a *p*-nitro substituent on the transition state for elimination from 2-phenylethyl quanternary ammonium salts in water.

The Marcus theory of proton-transfer reactions predicts the sort of k_H/k_D maxima we discussed above,[19-21] and it is of the interest to see whether the theory gives a reasonable quantitative as well as qualitative description of our results. The theory breaks the overall process down into three steps: formation of an encounter complex between substrate and base (eq 14), the actual proton transfer

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$$\mathrm{B + SH} \xrightleftharpoons{w_r} \mathrm{B{\cdots}SH} \qquad (14)$$

$$\mathrm{B{\cdots}SH} \xrightleftharpoons{\Delta G_R^{0'}} \mathrm{BH{\cdots}S} \qquad (15)$$

$$\mathrm{BH{\cdots}S} \xrightleftharpoons{-w_p} \mathrm{BH + S} \qquad (16)$$

(eq 15), and separation of the products (eq 16). Charges are omitted for simplicity. The observed free energy of the overall reaction is then given by eq 17. The predicted

$$\Delta G_R{}^0 = \Delta G_R{}^{0'} + w_r - w_p \qquad (17)$$

relation between k_H/k_D and $\Delta G_R{}^{0'}$, the free energy change for reaction within the encounter complex, can be written as in eq 18. We have simplified the usual form of the

$$\ln (k_H/k_D) = \ln (k_H/k_D)_{max}[1 - (\Delta G_R{}^{0'}/4\Delta G^{\ddagger}{}_0)^2] \qquad (18)$$

equation somewhat by letting $\Delta G^{\ddagger}{}_0 = (\Delta G^{\ddagger}{}_{0,H}\Delta G^{\ddagger}{}_{0,D})^{1/2}$, where $\Delta G^{\ddagger}{}_0$ is the free energy of activation for the step represented by eq 15 when $\Delta G_R{}^{0'} = 0$.[22]

In order to evaluate the "intrinsic barrier", $\Delta G^{\ddagger}{}_0$, it is necessary to know $\Delta G_R{}^{0'}$ and k_H/k_D at each experimental point. Unfortunately we cannot obtain absolute values because we do not know w_r and w_p. Even if we did, we could not evaluate $\Delta G_R{}^0$ because $\Delta G_R{}^0 = 2.3RT(\mathrm{p}K_{SH} - \mathrm{p}K_{BH})$, and the conjugate base of SH has no independent existence in an E2 reaction, thereby precluding the determination of $\mathrm{p}K_{SH}$. Relative values of $\Delta G_R{}^0$ and $\Delta G_R{}^{0'}$ can, however, be calculated if we assume that w_r, w_p, and $\mathrm{p}K_{SH}$ are constant. Bell and Cox[23] have shown that $\Delta\mathrm{p}K$ can be evaluated for proton transfers to hydroxide ion in Me_2SO–water mixtures by means of its relation to the H_- acidity function (eq 19).

$$\Delta \mathrm{p}K = \mathrm{p}K_{SH}{}^0 - H_- - \log ([\mathrm{H_2O}]/[\mathrm{OH^-}]) \qquad (19)$$

The problem of evaluating $\Delta\mathrm{p}K$ without knowledge of $\mathrm{p}K_{SH}{}^0$ can be sidestepped either by letting $\Delta\mathrm{p}K = 0$ at the observed k_H/k_D maximum and fitting the data to eq 18 or by letting $\Delta\mathrm{p}K = 0$ at that Me_2SO–H_2O mixture which gives the best least-squares fit of the data to eq 18. We chose the latter course, and list in Table IV the results obtained by using the present data, along with results on (2-phenylethyl)trimethylammonium ion[2] and (2-phenylethyl)dimethylsulfonium ion.[3]

The most striking feature of the results is the low values found for the intrinsic barriers, $\Delta G^{\ddagger}{}_0$. The overall free energy of activation in Marcus theory is given by eq 20.

$$(\Delta G^{\ddagger})_{obsd} = \Delta G^{\ddagger} + w_r \qquad (20)$$

From the rate constants, $(\Delta G^{\ddagger})_{obsd}$ can be calculated to be 20 kcal mol^{-1} at the k_H/k_D maximum, where $\Delta G^{\ddagger}$ and $\Delta G^{\ddagger}{}_0$ should be the same. The two sets of data from the literature on the unsubstituted ammonium and sulfonium salts (lines 2 and 3 in Table IV) have a $(\Delta G^{\ddagger})_{obsd}$ under the same conditions of 23 and 21 kcal mol^{-1}, respectively. Thus, w_r for the three reactions is in the range 17–22 kcal mol^{-1}, much larger than the intrinsic barriers.

These w_r values are significantly larger than those of 8–16 kcal mol^{-1} summarized in Kresge's review.[24] The w_r term represents the free energy required to form the encounter complex, which would include free energies of desolvating and orienting the reactants so that the proton transfer can occur. There is no general agreement on what constitutes a reasonable value of w_r, but 2.5–6 kcal mol^{-1} has been estimated for reactions in aqueous solution.[24,25]

Table IV. Fits to Marcus Theory of k_H/k_D Values for E2 Reactions of Onium Salts with Hydroxide Ion in Mixtures of Dimethyl Sulfoxide and Water at 50 °C

reactant	calcd $(k_H/k_D)_{max}$	%Me_2SO at max	$\Delta G^{\ddagger}{}_O$,[b] kcal mol^{-1}
p-$CF_3C_6H_4CH_2CH_2NMe_3{}^+$	6.9	34	1.4 ± 0.2
$PhCH_2CH_2NMe_3{}^+$ [c,d]	5.0	37	1.4 ± 0.1
$PhCH_2CH_2SMe_2{}^+$ [e]	5.7	32	4.0 ± 0.6

[a] From a least-squares fit to $\ln (k_H/k_D) = a + b(\Delta G^{0'}{}_R)_{rel}{}^2$, where $a = \ln (k_H/k_D)_{max}$ and $b = -\ln (k_H/k_D)_{max}/(4\Delta G^{\ddagger}{}_0)^2$, letting $(\Delta G^{0'}{}_R)_{rel} = 0$ at that Me_2SO concentration which gives the best fit. [b] Deviations are from the standard deviations of the coefficients, b. [c] At 60 °C. [d] Data from ref 2. [e] Data from ref 3.

In the present reactions, it seems likely that removal of a solvating water molecule from hydroxide ion would be the major component of w_r. ΔG for removal of one water molecule from $OH^-(H_2O)_3$ in the gas phase is 7.5 kcal mol^{-1} at 300 K according to the data of Payzant, Yamdagni, and Kebarle.[36] It is likely to be considerably smaller in solution, particularly in the presence of a good hydrogen bond acceptor such as dimethyl sulfoxide. It is hard to imagine that bringing the desolvated hydroxide ion up to the β-hydrogen of the substrate would cost much free energy. The loss of translational and rotational entropy should be compensated at least partially by the electrostatic attraction of the oppositely charged reactants. All in all, it seems difficult to justify more than a quarter to a third (6–8 kcal mol^{-1}) of the apparent w_r terms. It has been suggested that Marcus theory may systematically underestimate intrinsic barriers,[24] but nearly order-of-magnitude increases in $\Delta G^{\ddagger}{}_0$ would be needed to bring w_r into a more reasonable range.

We prefer to believe that, for a number of reasons, Marcus theory is inapplicable to the present results and is of doubtful applicability in many other cases where maxima in k_H/k_D are discernible over a relatively narrow range of $\Delta\mathrm{p}K$ values. Perhaps the most vulnerable aspect of the results summarized in Table IV is the assumption that w_r and w_p remain constant as the solvent composition changes. This can hardly be true, and, if it is not, the $(\Delta G_R{}^{0'})_{rel}$ values are in error to an unknown extent.

On a more fundamental point, the implicit assumption that $\mathrm{p}K_{SH}$ remains constant with changing solvent composition is debatable. As we have noted above, $\mathrm{p}K_{SH}{}^0$ is unknowable because S^- does not have any significant lifetime for these 2-arylethyl derivatives. It thus has only the status of an apparent or effective pK and may not be the same for transition states with different extents of proton transfer. The $\mathrm{p}K_{SH}{}^0$ in 35% Me_2SO calculated from eq 19 by assuming $\Delta\mathrm{p}K = 0$ is about 19, far smaller than the pK of 37 estimated for the (2-phenylethyl)dimethylsulfonium ion by McLennan and Wong[4] from linear free-energy relationships and the pK of toluene. A roughly similar estimated value should apply to the quaternary ammonium salts.

The difference between the "experimental" value of 19 and the estimated value of 37 is obviously the result of a driving force from the concerted cleavage of the carbon–nitrogen (or carbon–sulfur) bond and the formation of the carbon–carbon double bond. The magnitude of such a driving force should depend on the concertedness of the reaction, and so the "experimental" $\mathrm{p}K_{SH}$ is unlikely to have the constant value assumed in our treatment.

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Even with these cogent reasons for doubting the quantitative significance of the intrinsic barriers derived from fitting these isotope effects in E2 reactions to Marcus theory, a more general residue of skepticism still remains. It arises in part from the fact that really major errors from the sources mentioned would be needed to make the values derived from Marcus theory plausible, and errors of that magnitude do not seem likely. An equally important source of worry is the very form of eq 18, which ensures that only unusually small values of $\Delta G^{\ddagger}_0$ will allow a significant k_H/k_D maximum to be observed. The range of $\Delta G_R{}^0$ values covered in most experimental examples of k_H/k_D maxima is not wide. In our case, the widest range of $(\Delta G_R{}^{0\prime})_{\mathrm{rel}}$ values is ca. 9 kcal mol^{-1} for the data in line 3 of Table IV. Even the much wider range of ΔpK values covered by a collection of ketones and nitroalkanes with various bases[26] amounts to barely more than 30 kcal mol^{-1} (roughly −15 to +15 kcal mol^{-1}) in $\Delta G_R{}^0$. The k_H/k_D values at the extremes amount to at least one-third those at the maximum. From eq 18, it is easy to show that $\Delta G^{\ddagger}_0$ cannot be much more than 5 kcal mol^{-1}. Even allowing for likely variations in $w_r - w_p$ and the probability that a single $\Delta G^{\ddagger}_0$ can be valid only for a more closely related set of substrates than is found in this miscellaneous collection, it is difficult to conceive of a combination of errors that could make really substantial intrinsic barriers appear so small.

While Marcus theory provides a convenient qualitative rationale for k_H/k_D maxima, rather sweeping changes in our present views of slow proton transfers would be required to accomodate intrinsic barriers of 5 kcal mol^{-1} or less. We believe it is more prudent to reserve judgment on the physical significance of the intrinsic barriers obtained from eq 18. It is still reasonable to suppose that the solvent reorganization and orientation process of eq 14 may not be entirely distinct from the proton transfer of eq 15 in reactions such as the present ones. When there is coupling of the proton transfer with internal heavy-atom reorganization, as seems likely for these E2 processes,[4] there is no reason for excluding coupling with solvent reorganization as well. In such a case, the shape of the energy surface in the vicinity of the transition state may be quite different from that assumed in the intersecting-parabolas model of simple Marcus theory and may respond to perturbation in a fashion that is quantitatively if not qualitatively different. The same reservation should apply to any slow proton transfer such as ketone enolization or proton abstraction from aliphatic nitro compounds, where heavy-atom reorganization is part of the rate-determining step.

Experimental Section

Solvents. Distilled water was redistilled from potassium permanganate. Dimethyl sulfoxide was stirred over calcium hydride for at least 2 days and distilled under reduced pressure to give material of melting point mp 18.0–18.5 °C (lit.[27] mp 18.5 °C). Mixtures of dimethyl sulfoxide and water were prepared gravimetrically.

***p*-(Trifluoromethyl)benzyl alcohol** was obtained from the reduction of *p*-(trifluoromethyl)benzoic acid (25.6 g, 0.14 mol) with lithium aluminum hydride (5.21 g, 0.14 mol) in 96% yield by the method of Nystrom;[28] bp 78–79 °C (4 mm) [lit.[29] bp 78.5–80 °C (4 mm)].

[*p*-(Trifluoromethyl)phenyl]acetonitrile. *p*-(Trifluoromethyl)benzyl alcohol (22.7 g, 0.13 mol) was stirred and heated for 12 h with 70 mL of 48% hydrobromic acid. The mixture was extracted with ether, and the extract was washed with water and 10% sodium bicarbonate solution and dried over anhydrous potassium carbonate. The ether was removed on a rotary evaporator and the resulting crude bromide dissolved in 50 mL of methylene chloride. The solution was stirred and refluxed with a solution of 100 g (2.0 mol) of sodium cyanide in 140 mL of water in the presence of a catalytic amount of tetrabutylammonium bromide for 12 h.[30] The mixture was extracted with ether and the extract dried over anhydrous magnesium sulfate. Concentration on a rotary evaporator followed by distillation yielded 68% of product, bp 134 °C (20 mm) [lit.[29] bp 131–132 °C (20 mm)].

2-[*p*-(Trifluoromethyl)phenyl]ethylamine was prepared by a modification of the procedure of Nystrom.[31] To a stirred solution of 16.6 g (0.091 mol) [*p*-(trifluoromethyl)phenyl]acetonitrile in 170 mL of ether was added dropwise a mixture of 4.3 g (0.11 mol) of lithium aluminum hydride and 15.0 g of aluminum chloride in 225 mL of ether. The mixture was refluxed for 8 h and cooled to 0 °C, and water was added with stirring followed by the cautious additon of 300 mL of 30 M potassium hydroxide. The mixture was extracted with ether in a continuous extractor for 10 h and the ether extract dried over anhydrous potassium carbonate. The ether was removed on a rotary evaporator and the product distilled to give 53% of the amine, bp 89–90 °C (10 mm) [lit.[29] bp 105.5–6.0 °C (22 mm)].

[2-[*p*-(Trifluoromethyl)phenyl]ethyl]trimethylammonium iodide was obtained by adding 53.5 g (0.38 mol) of methyl iodide dropwise with stirring to a mixture of 8.9 g (0.047 mol) of 2-[*p*-(trifluoromethyl)phenyl]ethylamine and 17.4 g (0.094 mol) of tri-*n*-butylamine in 100 mL of dimethylformamide.[32] After 3 h, ether was added to precipitate the product which was removed by filtration and recrystallized from ether and ethanol to give a 25% yield of product, mp 230–231 °C. Anal. Calcd for $C_{12}H_{17}NF_3I$: C, 40.11; H, 4.74; Found: C, 40.59; H, 4.79. The two-step methylation procedure described below for the corresponding deuterated amine gives better overall yields.

[*p*-(Trifluoromethyl)phenyl]acetonitrile-*α,α-d*$_2$ was obtained by stirring for 5 h 7.7 g (0.041 mol) of [*p*-(trifluoromethyl)phenyl]acetonitrile in 15 mL of methylene chloride with 5.0 mL of 99.8% deuterium oxide in the presence of a few milligrams of tetramethylammonium bromide and anhydrous potassium carbonate. After five successive exchanges with fresh deuterium oxide the product was isolated in 70% yield and shown by NMR to contain less than 5% of residual protium in the *α*-position; bp 133–134 °C (20 mm) [lit.[29] bp 131–132 °C (20 mm)].

2-[(*p*-(Trifluoromethyl)phenyl]ethylamine-*2,2-d*$_2$ was obtained by reducing [*p*-(trifluoromethyl)phenyl]acetonitrile-*α,α-d*$_2$ with lithium aluminum hydride by the procedure described above for the corresponding undeuterated nitrile. A 61% yield of product was obtained; bp 89–90 °C (10 mm) (lit.[29] bp 105.5–106.0 °C (22 mm)].

[2-[*p*-(Trifluoromethyl)phenyl]ethyl-*2,2-d*$_2$]dimethylamine was prepared from the corresponding primary amine (above) by the Eschweiler–Clarke reaction by following the procedure of Icke and Wisegarver.[33] The product was obtained in 62% yield; bp 99–100 °C (15 mm) [lit.[29] bp 108–108.5 °C (23 mm)].

[2-[*p*-(Trifluoromethyl)phenyl]ethyl-*2,2-d*$_2$]trimethylammonium iodide was obtained by treatment of 2.5 g (0.011 mol) of [2-[*p*-(trifluoromethyl)phenyl]ethyl-*2,2-d*$_2$]dimethylamine with 3.2 g (0.023 mol) of methyl iodide in 25 mL of nitromethane for 5 h at room temperature.[34] The solution was concentrated on a rotary evaporator and the residue recrystallized from ethanol and ether to obtain 79% of product, mp 230–231 °C.

Kinetics. A stock solution of the quaternary ammonium salt was made by dissolving 1.4×10^{-4} mol of the salt in 50 mL of the appropriate Me_2SO–water solvent mixture. A 1.0-mL aliquot was

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placed in a 25-mL volumetric flask and diluted with 20.0 mL of the solvent mixture, and the resulting solution was equilibrated in a constant-temperature bath and diluted to the mark with the solvent mixture. The solution was then transferred to a 50-mL volumetric flask and allowed to equilibrate once more. A 0.1-mL aliquot of sodium hydroxide solution was added and the flask swirled vigorously. The sodium hydroxide was of a known molarity which was chosen to give the desired final concentration, which was at least 10 times the concentration of substrate for reactions run under pseudo-first-order conditions and approximately 2 times the concentration of the substrate for reactions run under second-order conditions. The latter method was used for the undeuterated substrate from 75 °C and up in 30% Me_2SO, 60 °C and up in 40% Me_2SO, and 45 °C and up in 50% Me_2SO.

Immediately after the addition of base and mixing, a portion of the contents of the flask was transferred to a quartz cell in a thermostatically controlled, insulated cell compartment of a Beckman DB-GT spectrophotometer. The temperature was monitored by an iron–constantan thermocouple in the cell compartment. The increase in absorbance vs. time was recorded at the λ_{max} of *p*-(trifluoromethyl)styrene (approximately 260 nm, but dependent on the solvent composition and, to a small extent, the temperature). Rate constants were obtained from the slopes of least-squares fits of the data to the appropriate integrated rate equation. Arrhenius parameters were evaluated from least-squares fits of the data to a plot of ln *k* *vs.* $1/T$.

Control Experiments. Analysis of the product mixture by GLPC on a 12 ft × 0.125 in. column of 5% SF-96 on Chromosorb W at 50 °C and on a 6 ft × 0.125 in. column of 25% didecyl phthalate on 60–80-mesh firebrick at 150 °C showed no products other than *p*-(trifluoromethyl)styrene and trimethylamine. Solutions of [2-[*p*-(trifluoromethyl)phenyl]ethyl]trimethylammonium iodide in 30%, 35%, 40%, and 50% Me_2SO in the absence of base showed no detectable increase in ultraviolet absorption when kept at 80 °C for up to 24 h.

Registry No. **1d**·I^-, 78698-15-4; **1h**·I^-, 77207-67-1; *p*-(trifluoromethyl)benzyl alcohol, 349-95-1; *p*-(trifluoromethyl)benzoic acid, 455-24-3; [*p*-(trifluoromethyl)phenyl]acetonitrile, 2338-75-2; 2-[*p*-(trifluoromethyl)phenyl]ethylamine, 775-00-8; [*p*-(trifluoromethyl)phenyl]acetonitrile-α,α-d_2, 78698-16-5; 2-[(*p*-(trifluoromethyl)phenyl]ethylamine-2,2-d_2, 78698-17-6; [2-[*p*-(trifluoromethyl)phenyl]ethyl-2,2-d_2]dimethylamine, 78698-18-7; hydroxide ion, 3352-57-6.

Photochemical and Thermal Reactions of Aromatic Schiff Bases

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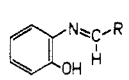
The photochemical and thermal reactions of aromatic Schiff bases (SB) prepared from *o*-aminophenol and aldehydes and from *o*-aminophenol and ketones are compared. All SB's are converted by light into the corresponding benzoxazolines. For the SB's derived from aldehydes, benzoxazoline formation is a prerequisite to convert them by a second photon into benzoxazoles. In some cases oxygen is not required for this second reaction step. SB's derived from ketones are converted into benzoxazoles by the absorption of just one photon, but only in the presence of oxygen and only if the aliphatic residue R_1 of the $N{=}C(R_1R_2)$ bridge contains at least two carbon atoms. A radical mechanism is proposed for this reaction. Benzoxazine formation is observed in some cases as a thermal side reaction. The photochemical reactions of the latter were also investigated.

The condensation products of *o*-aminophenol and certain aldehydes or ketones (Schiff bases, SB) are readily converted into 2-substituted benzoxazoles if they are illuminated in inert solvents like methylcyclohexane (MCH). The photoconversion of *N*-benzylidene-*o*-aminophenol (**1a**)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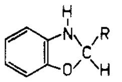
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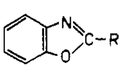
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(R = Ph; cf. Table I) into 2-phenylbenzoxazole (**3a**) has been investigated by us in some detail.[1] We showed that **1a** is first converted into 2-phenylbenzoxazoline (**2a**) and that a second photon is required to convert **2a** into **3a**. In addition, light-induced trans → cis and thermal- and light-induced cis → trans isomerizations of **1a** take place. Competing with the photodehydrogenation **2a** → **3a** is the thermal and photolytic back-reaction **2a** → **1a**. Due to this back reaction the lifetime of **2a** is about 200 s in the dark at room temperature (cf. Table I). The oxazole **3a** is also formed in degassed solutions of **1a**. In this case molecular hydrogen is evolved, but both the chemical yield and the relative quantum yield are considerably lower than in air-saturated solutions.

Table I. Long-Wavelength Absorption (λ_{max}) of Schiff Base 1, Lifetimes (τ) of the Corresponding Oxazolines 2[a], and Chemical Yields of Formation of the Oxazoles 3[b]

compd	R	λ_{max}, nm	τ, s	% chemical yield: air saturated	% chemical yield: degassed
1a	C_6H_5	368	200	80	10
b	*o*-C_6H_5OH	357	50	25	20
c	*p*-C_6H_5OH	350	4800	30	dec
d	*o*-$C_6H_5OCH_3$	357	9	30	dec
e	*p*-$C_6H_5OCH_3$	351	15	45	traces
f	α-$C_{10}H_7$	367	600	50	20
g	β-$C_{10}H_7$	363	240	75	60
h	9-anthryl	407	780	80	dec
i	$CH{=}CHC_6H_5$	366	12	25	dec
k	2-furanyl	365	15	35	25
l	2-thiophenyl	363	45	45	15
m	ferrocenyl	348	10	70	dec
n	$C(CH_3)_3$	315	9000	80	65

[a] At room temperature in air-saturated solutions. [b] The solvent was methylcyclohexane.

The course of the reaction can easily be followed by spectroscopic means because the UV absorption spectra of **1a**–**3a** differ characteristically from each other. Due to resonance interaction between the two phenyl rings across the C=N double bond linkage, **1a** has a broad structureless

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