constants for catalysis by lyoxide ion fall well below a linear extrapolation of the Brønsted plots in Figure 4. It is possible that these rate constants reflect the well-known lyoxide ion anomaly, which may involve a requirement for partial desolvation of the lyoxide ion.[65] The difference between these values of β and the value of $\alpha = 0.59$ for **1a–c** represents imbalance, as noted above.

The secondary solvent isotope effect of $k_{H_2O}/k_{D_2O} = 2.3 \pm 0.2$ for ^3H transfer from **1a** to water (Table IV) shows that the initial kinetic unit that is formed upon proton exchange is HOL_2^+ and, therefore, that proton transfer to water is direct. This isotope effect agrees with the value of $k_{H_2O}/k_{D_2O} = 1/l^2 = 2.1$, calculated from the fractionation factor of $l = 0.69$ for HOL_2, but is smaller than $1/l^3 = 3.0$ for L_3O^+.[64] Furthermore, the absence of strong inhibition of ^1H and ^3H exchange by D_3O^+ (Table S4) shows that the reaction does not involve initial proton transfer through water to form a hydrogen-bonded species $\gtrdot C^-{\cdot}{}^3HOH$ and H_3O^+ according to the Swain–Grunwald mechanism for hydron exchange.[66] Exchange by this mechanism is inhibited in the presence of acid because of reversal of the initial dissociation step, with return of the hydron to carbon before dissociation of $[^3H]H_2O$ into the bulk solvent.

Registry No. 1a, 116724-74-4; **1b**, 124992-84-3; **1c**, 124992-86-5; Me_2S, 75-18-3; 9-bromofluorene, 1940-57-4.

Supplementary Material Available: Tables S1–S3 summarizing rate constants for general-base catalysis for hydron exchange from **1a–c** and Table S4 showing rate constants in aqueous LCl solutions for hydron exchange (5 pages). Ordering information is given on any current masthead page.

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[65] Hupe, D.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451–464. Washabaugh, M. W.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 683–692 and references therein.

[66] Emerson, M. T.; Grunwald, E.; Kaplan, M. L.; Kromhout, R. A. *J. Am. Chem. Soc.* **1960**, *82*, 6307–6314. Grunwald, E.; Ralph, E. K. *Acc. Chem. Res.* **1971**, *4*, 107–113. The small decrease in rate observed in 1 M HCl or DCl (Table S4) was also observed with HCN[39] and may be accounted for by an acidity function effect (Paul, M. A.; Long, F. A. *Chem. Rev.* **1957**, *57*, 1–45).

The Marcus Theory of Reactions of Quinolinium Ions with BH_4^- and OH^- [1]

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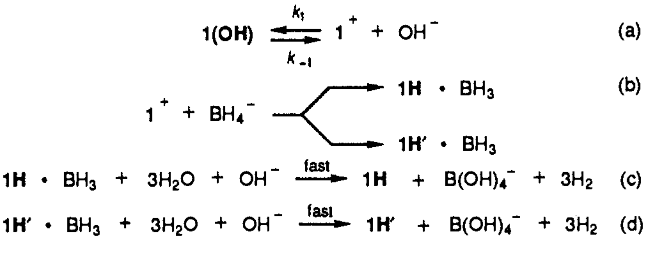
Contribution from the Chemical Dynamics Laboratory, Department of Chemistry, University of Minnesota, 207 Pleasant Street S.E., Minneapolis, Minnesota 55455. *Received July 18, 1988*

Abstract: The reactions of quinolinium ions with alkaline solutions of BH_4^- in a 4:1 mixture of 2-propanol and water were studied. Four 1-benzyl-3-cyanoquinolium ions and two 3-(aminocarbonyl)-1-benzylquinolinium ions were used. The quinolinium ions first reversibly add a nucleophile (mostly to the 4-position) and then are more slowly reduced to the 1,2- and 1,4-dihydroquinolines. The equilibrium constant for the addition of OH^- or OR^-, the rate constant for the addition, the rate constant for solvolysis of the adduct, and the rate constant for reaction of BH_4^- with the quinolinium ion were determined in each case. The quinolinium ion concentration was kept low enough so that only one of the hydridic hydrogens of BH_4^- was transferred to a quinolinium ion. Adduct formation and reduction by BH_4^- both have rates in the range 10^5–10^7 M^{-1} s^{-1}, and the Brønsted α values are similar. Both sets of rate constants can, roughly, be fitted by the Marcus theory of atom and group transfer if the intrinsic barrier is assumed to arise exclusively from the reorganization of the quinolinium ion. Since the presumptive critical complex for H^- transfer between BH_3 units, $B_2H_7^-$, is a known, stable ion, it is reasonable that the reorganization of BH_4^- does not contribute significantly to the intrinsic barrier for its reactions. The Marcus theory, and related ideas, such as the Leffler–Hammond principle, apparently can be usefully applied to reactions quite different from the original model, but the exact values of the derived parameters quite possibly do not have their apparent physical significance.

The dynamics of the reactions of quinolinium salts with tetrahydridoborate ion, BH_4^-, are of interest for a number of reasons. The major product of the reduction of quinolinium ions with a cyano or an aminocarbonyl group in the 3-position is the 1,2-dihydroquinoline, although, at equilibrium, about 95% of the products have the 1,4-structure.[2] An analogous discrepancy is also found in the reduction of pyridinium ions,[2] including the important enzymatic cofactor, nicotinamide adenine dinucleotide (NAD^+).[3] The formation of the 1,2-adduct precludes the use of BH_4^- as the ultimate reductant in the synthetic application of NADH-dependent enzymes.[4] The Marcus theory of atom and group transfer[5,6] provides another reason for interest. The theory contains the fundamental assumption that the potential energy surface leading from the precursor configuration to the critical configuration[7] is similar to that leading from the successor configuration to the critical configuration.[8] The formalism of the theory successfully describes a number of proton transfer rate constants, in which the structure and charge type of the reactants and products are different.[9,10] However, the intrinsic barriers, which are obtained by fitting the rate constants, sometimes differ considerably from expectations.[9,10] The present reactions are

Scheme I



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[1] This work was supported by the National Science Foundation through Grant CH85-20903 to the University of Minnesota.

[2] Roberts, R. M. G.; Ostović, D.; Kreevoy, M. M. *J. Org. Chem.* **1983**, *48*, 2053.

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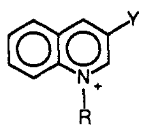
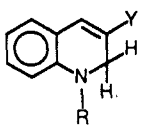
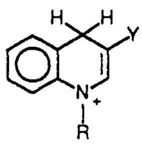
Chart I



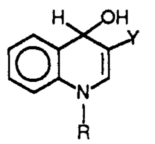
1^+



1H



1H′



1(OH)[12]

	R	Y
a:	$pCH_3–C_6H_4CH_2$	CN
b:	$C_6H_5CH_2$	CN
c:	$pBr–C_6H_4CH_2$	CN
d:	$pCN–C_6H_4CH_2$	CN
e:	$C_6H_5CH_2$	$CONH_2$
f:	$pCN–C_6H_4CH_2$	$CONH_2$

similar to the proton transfers in the dissimilarity of products and reactants, but there is independent evidence on which to base an intrinsic barrier. It is of interest to see if a successful correlation of the measured rate constants can be based on the independently estimated intrinsic barrier.

To address these questions, rate constants were determined for the reaction of six variously substituted quinolinium ions with BH_4^-, in a 4:1 2-propanol–water mixture, at 25 °C. The structures of the quinolinium ions are given in Chart I. Four of these have been reported previously by one of us (I.-S.H.L.)[11] in a paper which we designate the HLH paper. However the evaluation of rate constants has now been improved in several ways, so that we prefer the present values, and the analysis has been extended. Because BH_4^- is very rapidly hydrolyzed in neutral or acidic solution,[12] basic solutions were used for these reactions. Under these conditions the quinolinium ions were formed in situ from the corresponding 1,4-dihydro-4-hydroxyquinolines,[13] which are the predominant structures in basic solution.[14,15] The sequence of reactions is shown in Scheme I. The quinolinium concentration was adjusted to obtain 1:1 stoichiometry, so that only the first hydridic hydrogen would reduce a quinolinium ion. Both 1,2- and 1,4-dihydroquinoline are formed, and only the 1,2-product was monitored, but the form of the rate law is such that the rate constant obtained is the sum of the rate constants for the formation of the two products.[16]

The conditions of our experiments required that the equilibrium constants be available for the first reaction of Scheme I, the dehydroxylation[13] to the quinolinium ions. To get them, the K_R values of the quinolinium ions were determined by standard spectrophotometric means,[17] when they were not already available.[18] The autoprotolysis constant of the solvent, K_S was determined by measuring the pHs of dilute KOH solutions. (In the HLH paper, K_S was assumed to be the same as for methanol.[11]) The required equilibrium constants are then given by K_S/K_R. Our kinetic measurements permitted us to evaluate k_1 and k_{-1} as well as k_2. These are correlated with K_R and discussed in terms of the Marcus theory, with reference to earlier applications of this theory to ion recombination reactions.[19,20] As with k_2 values, four of the k_{-1} values have been reported before.[11] However the present values are nearly 1 order of magnitude different from the HLH values, primarily because of the newly available, measured value of K_S. The Marcus theory discussion is also taken considerably further than it was in the HLH paper.[11]

$$1^+ + H_2O \underset{}{\overset{K_R}{\rightleftharpoons}} 1(OH) + H^+ \qquad (1)$$

Experimental Section

Solutions and Materials. The solvent for all the present measurements was a mixture of 4 parts of 2-propanol with 1 part of water, by volume. The liquids were at 25.0 ± 1.0 °C when their volumes were measured. The 2-propanol was purchased from Mallinckrodt and was ChromAR HPLC grade. Both solvent components were distilled from 0.5% H_2SO_4 before use.

Low-pH buffers were prepared by adding sodium hydroxide solution to acetic acid solution. High-pH buffers were made up by adding sodium hydroxide solution to boric acid solution. The final pH values of buffers were determined electrometrically. The ionic strength was taken as the number of moles of sodium hydroxide added divided by the volume of the buffer.

Compounds 1^+a–d have been previously characterized.[17] Compound 1^+e, 3-(aminocarbonyl)-1-benzylquinolinium bromide, was prepared by the method of Shinkai and co-workers.[16,21] It had mp 223–224 °C dec (lit.[5,22] mp 224–225, 223 °C) and the expected spectroscopic characteristics.

3-(Aminocarbonyl)-1-(*p*-cyanobenzyl)quinolinium bromide (1^+f) was prepared in the same general way. It appears never to have been characterized in spite of having been described as known compound.[6] It had the following: mp 236–239 °C dec; IR (KBr) bands (cm^{-1}) at 3294 s, 3139 vs, 3060 s, 2970 s, 1691 vs, 1632 vs, 1410 vs, 1385 s, 1369 s, and 776 vs; an appropriate ^1H NMR spectrum.[22]

Anal. Calcd for $C_{18}H_{14}BrN_3O$ (368.25): C, 58.71; H, 3.83; Br, 21.70; N, 11.41; O, 4.35. Found:[23] C, 58.52; H, 4.07; Br, 21.86; N, 11.19; O, 4.36.

Methods. Values of pH in our mixed solvent were determined with use of a Radiometer combination glass electrode and pH meter. The meter was calibrated with use of aqueous buffers of pH 7.00 and 4.00 if measurements were to be made in acidic solution or 7.00 and 10.00 if measurements were to be made in basic solution. A solvent correction of 0.17 ± 0.01 unit was determined by measuring the pHs of four $HClO_4$ solutions, of concentrations between 10^{-2} and 10^{-4} M. The true pH, estimated stoichiometrically, minus the measured pH is the correction.

The autoprotolysis constant of our solvent, K_S, was determined by measuring the pH of dilute KOH solutions. KOH was used rather than NaOH to avoid the sodium error.[24] These KOH solutions were made up by dilution from a stock solution, the concentration of which was determined by titration.

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(7) The term "critical configuration" is used for the structure that, along with the reactant structures, determines the rate constant in a generalized transition state theory calculation. We reserve the term "transition state" for the structure corresponding to the point of maximum energy on the minimum-energy path from reactants to products.[10] Because of tunneling we believe that the critical configurations for hydride transfers will generally be somewhat more expanded then the transition states: Kreevoy, M. M.; Ostovic, D.; Truhlar, D. G.; Garrett, B. C. *J. Phys. Chem.* **1986**, *90*, 3766.

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(13) The compounds may be either the hydroxy or isopropoxy adducts of the quinolinium ions. We believe they are largely the hydroxy adducts because of the steric repulsion inherent in the ethers and the steric inhibition of hydrogen bonding at the ether oxygen. We have, therefore, assumed that the adducts are the alcohols. Where this assumption is important, it is discussed in the text.

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(18) The activity coefficient was misplaced in our earlier publication,[17] with the result that all the K_R values reported are too small by a factor of 1.85. This error was carried into ref 11, as well.

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(22) Reference 16, pp 12–13.

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Table I. Rate and Equilibrium Constants

compd	K_R,[a] M	k_1,[a] s^{-1}	k_{-1},[b] $M^{-1}\,s^{-1}$	k_2,[c] $M^{-1}\,s^{-1}$
1a	6.8×10^{-6}	1.52×10^{-4}	3.7×10^{6}	1.3×10^{7}
1b	9.2×10^{-6}	1.13×10^{-4}	3.7×10^{6}	1.6×10^{7}
1c	1.9×10^{-5}	8.47×10^{-5}	5.7×10^{6}	2.1×10^{7}
1d	4.5×10^{-5}	6.37×10^{-5}	10.2×10^{6}	2.5×10^{7}
1e	9.3×10^{-10}	1.45×10^{-1}	4.8×10^{5}	8.9×10^{5}
1f	4.5×10^{-9}	8.31×10^{-2}	1.3×10^{6}	1.6×10^{6}

[a] The uncertainties in the k_1 values are about 20% of the values. [b] The uncertainties in the k_{-1} values are about 30% of the values. [c] The uncertainties in the K_R and k_2 values are about 25% of the values.

Values of K_R for $\mathbf{1^+e}$ and $\mathbf{1^+f}$ were determined spectrophotometrically, as previously described.[17] A typical set of spectra had the general appearance of Figure 2 of ref 17, with an isobestic point around 323 nm. Buffered solutions, with pH between 7.7 and 12.2, were used. The spectra of **1(OH)e** and **1(OH)f** were assumed to be those observed in the high-pH buffers, as the spectra of these substance changes with time in 10^{-3} M NaOH. These appeared to be the limiting spectra, as the pK_R values of these compounds was around 9, about 3 units below the pH of the most basic buffer. The absorbances of $\mathbf{1^+}$, A_1, were obtained from the limiting acidic solution. These and the absorbances of **1(OH)**, $A_{1(OH)}$, were obtained at several wavelengths between 280 and 330 nm. For each compound all absorbances were measured at the same initial quinolinium concentration. The limiting absorbances were combined with absorbances measured at intermediate pH values, A, according to eq 2, to get

$$K_R = \frac{(A - A_1)\,10^{-pH}}{(A_{1(OH)} - A)\gamma_\pm} \tag{2}$$

K_R values. The mean ion activity coefficient, $\gamma_\pm$, was obtained from eq 3, where I is the ionic strength.[25,26]

$$\log \gamma_\pm = \frac{-1.87I^{1/2}}{1 + 4.05I^{1/2}} \tag{3}$$

The concentration of BH_4^- was determined in solutions in which rates had been measured by adding an aliquot from each to 5 mL of aqueous solution containing 0.2 M 1-benzylnicotinamide and 0.05 M $NaHCO_3$. The resulting absorbance at 358 nm is proportional to the BH_4^- concentration,[27] with a proportionality constant that was found to be 1.254×10^3.

To determine the stoichiometry of the reduction of quinolinium ions by BH_4^-, varying amounts of BH_4^- were added to a fixed amount of quinolinium ion under conditions approximating those of a rate measurement. The solution was allowed to stand for a time equal to 7 half-lives of the reaction at the given pH and the initial quinolinium concentration. Then the absorbance was determined at 450 and/or 400 nm. The stoichiometry was determined from a plot of absorbance as a function of the BH_4^-/quinolinium ion ratio.

Pseudo-first-order rate constants, k_{obsd} were determined spectrophotometrically, by eq 4.[28] For reactions with half-lives of several minutes or more, the absorbances were measured in a conventional spectrophotometer. Solutions were brought to the proper temperature before mixing, and the temperature of the cell compartment was held at 25.0 ± 0.2 °C by circulating water at the temperature through jackets. When reactions had half-lives between 0.2 and 200 s, absorbance was monitored by a light-pipe device which has been previously described,[29] which had a mixing time of ~0.1 s. In that case the reaction was carried out in a cell that was immersed in a thermostat at the appropriate temperature.

$$k_{obsd} = t^{-1}[\ln (A_0 - A_\infty)/(A_t - A_\infty)] \tag{4}$$

Results

K_S. Eleven determinations of K_S with KOH solutions ranging in concentration from 2×10^{-4} to 4×10^{-4} M gave an average value of 2.8×10^{-16} M^{-2} with an average deviation from the mean of 2.0×10^{-16}. The probable error of the mean is 0.4×10^{-16}. This value of K_S may be compared with K_S for methanol, 2×10^{-17},[30] which was used for the mixed solvent in the HLH paper.[11]

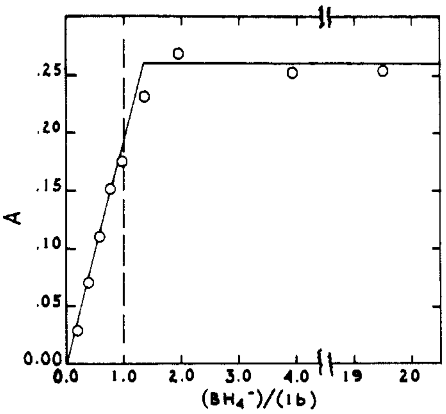

Figure 1. The infinite-time absorbance, A, at 450 nm, of solutions originally containing 2.0×10^{-4} M **1b**, as a function of the initial $(BH_4^-)/(\mathbf{1b})$ concentration ratio. The circles are the experimental points. The solid lines are straight lines drawn through points which are well removed from the equivalence point. The vertical dashed line indicates the theoretical equivalent point.

K_R. Values of K_R were determined for $\mathbf{1^+e}$ and $\mathbf{1^+f}$, as described in the Experimental Section. These are given in Table I, along with the values for $\mathbf{1^+a{-}d}$, which were available from earlier work.[17,18] The scatter in the measured K_R values leads to a probable error of ~15%.[31] When we add possible systematic errors to this, we estimate the uncertainty of the K_R values as ±25%. This is somewhat worse than the 15% uncertainty of the K_R values reported earlier.[17] The added uncertainty may be due to the high-pH side reaction, noted in the Experimental Section.

Reaction Stoichiometry. Under the conditions of our kinetic studies the quinolinium ion is formed by solvolysis of the 4-hydroxy-1,4-dihydroquinoline, and is either reduced or reverts to the reactant by reaction with OH^-.[13] Thus only the steady-state concentration of quinolinium ion is present. The reaction solutions were basic enough to keep the hydrolysis of BH_4^- insignificant, but the second, third, and fourth hydride of BH_4^- hydrolyze much more rapidly than the first in water,[12] and probably in our mixed solvent, as well. Our rate law becomes considerably simpler if only the first hydride from each BH_4^- reacts with a quinolinium ion. This should be realized if the initial 4-hydroxyl-1,4-dihydroquinoline concentration is sufficiently low, because then the small, steady-state concentration of quinolinium ion will fail to compete with hydrolysis for the second, third, and fourth hydride. Figure 1 shows that this condition has approximately been achieved by $\mathbf{1^+b}$ at the quinolinium ion concentration preferred for kinetic studies. Presumably this is also true for the other 3-cyanoquinolinium ions, as their K_{R^+} values are similar, so the steady-state concentrations of the free ions should be also. In the HLH paper all four hydrogens of BH_4^- were assumed to be transferred to quinolinium ions, but there was no compelling evidence for this, and it is now shown to be untrue. This assumption was responsible for the factor of four in the denominator of the first term on the right hand side of eq 8 of the HLH paper.[11] Otherwise eq 5 of the present paper is identical with eq 8 of the HLH paper. Since, in fact, much less than four hydrogens per BH_4^- unit are used, the factor of 4 is in error. Actually, somewhat *more* than 1 mol of BH_4^-/mol of 3-cyanoquinolinium ion appears to be required. This may reflect the loss of some BH_4^- to hydrolysis during the several hours that these reactions require, or may simply be due to experimental error. If, in fact, Figure 1 shows the loss of some BH_4^-, this will not cause a serious error in rate constants, because those were determined from measurements made over the first 1–2 half-lives of reactions, while stoichiometric experiments ex-

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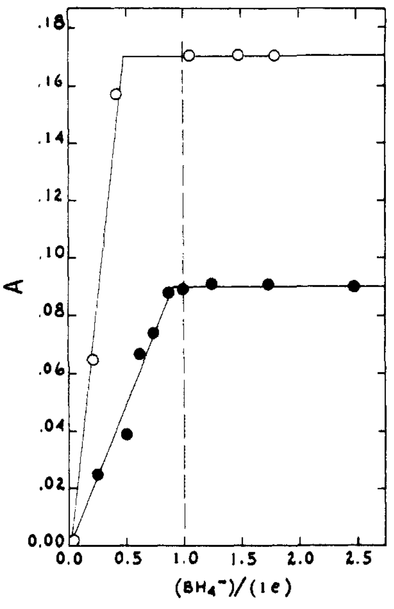

Figure 2. The infinite-time absorbance, A, of solutions originally containing 1.85×10^{-4} M **1e** (open circles; 450 nm) and 4.75×10^{-5} M **1e** (filled circles; 400 nm) as a function of the initial (BH_4^-)/(**1e**) concentration ratio. The solid lines are straight lines drawn through points which are well removed from the equivalence point. The vertical dashed line indicates the theoretical equivalence point.

tended over 7 half-lives of reaction.

The (aminocarbonyl)quinolinium ions, however, have much lower K_R values and higher steady-state concentrations of free ions. Under the conditions originally preferred for the kinetic studies, they were more successful competitors for the hydridic hydrogens. As the reaction proceeded, the reactant was consumed, and the steady-state concentration of quinolinium ion was diminished. This led to a steady diminution of the apparent first-order rate constant as the reaction proceeded, a condition not conducive to the determination of accurate rate constants. Stoichiometry close to one to one was restored by a reduction in reactant concentration, as shown in Figure 2.

Rate Constants. All rates were measured at initial quinolinium ion concentrations between 5×10^{-5} and 2×10^{-4} M. The concentration of BH_4^- was always at least 10 times the quinolinium concentration and usually 20 times. The lower quinolinium ion concentrations were used to avoid transferring more than one hydride per BH_4^- to quinolinium ion. Under these conditions the growth of absorbance was a simple, exponential function of time. Pseudo-first-order rate constants, k_{obsd} were evaluated by using eq 4. Applying the Bodenstein steady-state approximation to 1^+, Scheme I yields eq 5,[11,32] where the rate constants are defined

$$\frac{1}{k_{obsd}} = \frac{k_{-1}}{k_1 k_2} \frac{[OH^-]}{[BH_4^-]} + \frac{1}{k_1} \qquad (5)$$

in the scheme, and the quantities in brackets are concentrations. Equation 5 predicts that $1/k_{obsd}$ will be a linear function of $[OH^-]/[BH_4^-]$, will intercept, $1/k_1$ and slope, k_{-1}/k_1k_2. As shown by Figure 3, such plots were reasonably linear. Another example is shown in the HLH paper.[11] Their slopes and intercepts were evaluated by the method of least squares.[33] In one case—the one shown in Figure 3—the point for the highest $[OH^-]/[BH_4^-]$ and $1/k_{obsd}$ was excluded from the least-squares calculation because its inclusion causes the "best" line to miss the lowest $1/k_{obsd}$ points by a considerable fraction of their value. Since we believe these points to be the best indicators of the true value of the intercept and since this intercept also plays a key role in the calculation of k_{-1}, we thought it was best to exclude the highest point. Since k_{-1}/k_1 is given by K_R/K_S, which were measured, all three rate constants were available. They are given in Table I.

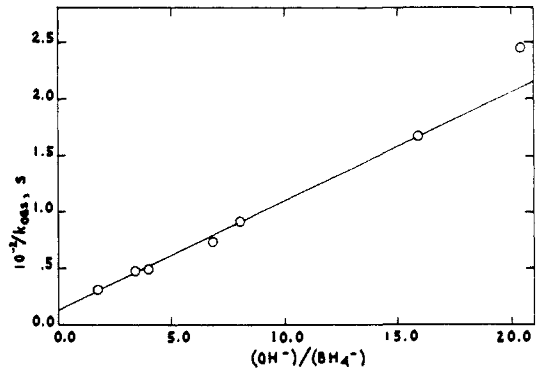

Figure 3. A typical plot of $1/k_{obsd}$ as a function of (OH^-)/(BH_4^-). The solid line is the least-squares fit, omitting the point furthest to the right, for reasons that are discussed in the text. The substrate is **1f**.

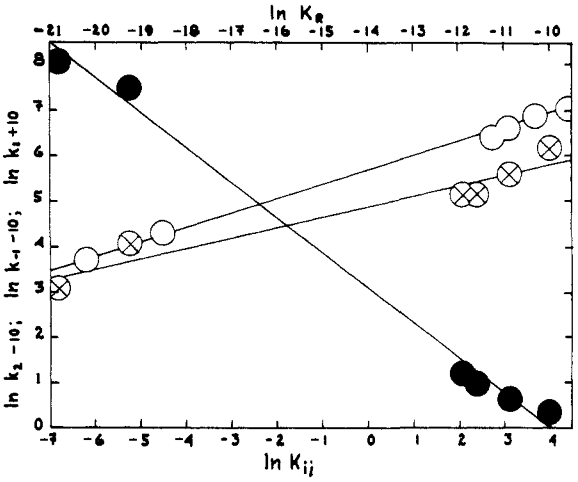

Figure 4. The correlation of rate constants with equilibrium constant. The open circles represent the correlation of ln k_2 with ln $K_{ij}°$, on the lower abscissa. They give a slope of 0.31 ± 0.03 and a correlation coefficient of 0.999. The filled points represent the correlation of ln k_1 with ln K_R. They give a slope of −0.78 ± 0.03 and a correlation coefficient of 0.996. The crossed points represent the correlation of ln k_{-1} with ln K_R. They give a slope of 0.23 ± 0.03 and a correlation coefficient of 0.96.

The uncertainties (root-mean-square errors) in the intercepts, and, therefore, the uncertainties in the k_1 values, are about 20% of the values themselves.[33] $(K_R/K_S)k_1$ gives k_{-1}, so the uncertainties in all three of the former parameters contribute to the uncertainties in the latter.[34] The resulting uncertainties in the k_{-1} values are around 30% of their values. This declines to around 25% if the contribution from K_S is neglected. This is the uncertainty if the *relative* values of k_{-1}. Similarly,[34] the uncertainties in the k_2 values are around 25% of the values themselves, the largest part being due to the uncertainties in the K_R values.

Discussion

Brønsted plots[35-37] can be made for all three sets of rate constants. For k_1 and k_{-1} the relevant equilibrium constant is K_R. For k_2 it is $K_{ij}°$; the equilibrium constant for reduction of quinolinium ions by acridan.[6,17] The $K_{ij}°$ are proportional to the equilibrium constants for the reduction of the quinolinium ions by BH_4^- if the **1H**·BH_3 dissociation constants are structure-in-

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(32) Reference 16, pp 64–65.

(33) Reference 31, pp 101–106.

(34) Livingtonn, R. *Physico Chemical Experiments*, 3rd ed.; The MacMillan Co.: New York, 1957.

(35) Brønsted, J. N.; Pedersen, K. J. *Z. Phys. Chem.* **1923**, *108*, 185.

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(37) Brønsted originally proposed this relation to correlate rate and equilibrium constants for proton transfer reactions,[35,36] but it has since been applied to a wide range of reaction types. The term "Brønsted relation" is used, here, in a general sense.

variant within the present series of compounds. Since Brønsted plots are log-log plots, they will differ from those involving their own equilibrium constants only in their intercepts. The plots are shown in Figure 4.

The plots do not provide serious tests of the linearity of the Brønsted relations, because of the small number of points, their distribution, and their rather large uncertainties. However, hydride transfers from acridan to quinolinium ions give an accurately linear Brønsted plot,[17] as do the reaction of quinolinium ions with hydroxide in aqueous solution.[15,38] If linearity can be assumed, these plots do provide reasonably well determined slopes (α values): $\alpha_2 = 0.31 \pm 0.01$, $\alpha_{-1} = 0.23 \pm 0.03$, and $\alpha_1 = -0.78 \pm 0.03$, with the α values given the subscripts of the corresponding k values.

In additin to their statistical uncertainty, all three α values have some further uncertainty due to ambiguities in the reactions. Either OH^- or 2-PrO^- may add to the quinolinium ions, and they may add at either the 2- or the 4-position. Hydride may be transferred from BH_4^- to either the 2- or the 4-position. As a worst case example of the difficulties this may cause, if the fraction of OH^- addition (as opposed to 2-PrO^- addition) were 0.75 for cyanoquinolinium ions and 0.25 for carbonylquinolinium ions the α_{-1} for OH^- addition would be 0.35 instead of 0.23. As noted, however, we believe that 2-propoxide addition is relatively minor in all cases, because of steric constraints. We also do not believe that the fraction of OH^- addition is likely to vary very much over this limited range of structures. For hydride transfer the fraction of 1,4-addition is 0.45 for **1⁺b** and 0.57 for **1e** under somewhat different conditions from those used in the kinetic study.[2] If these fractions are typical of the cyanoquinolinium ions and (aminocarbonyl)quinolinium ions respectively, α_2, for hydride addition to the 4-position, would be reduced by only 0.03. Taking into account both random systematic errors, we consider it reasonable to assign an uncertainty of ±0.05 to α_2 and 0.1 to α_{-1} and α_1.

The values of k_{-1} are smaller by nearly 1 order of magnitude than those given in the HLH paper.[11] For **1⁺b**, k_1 and k_{-1} were obtained by HLH[11] in the same way we now get them, but K_R and K_S are used in this process, and as noted above, we have now improved both of these. HLH[11] obtained the values of k_1 and k_{-1} for compounds other than **1⁺b** by assuming that α_{-1} has the same value in our mixed solvent as in water, 0.47.[15] This is now shown not to be the case and adds further error to the values of k_{-1} in the HLH paper.[11] Both α_1 and α_{-1} are, of course, quite different from the values that were assumed or implied in the HLH paper.[11]

The Marcus theory,[5,6] as modified to take account of the effect of transition-state tightness on α,[6,17] is capable of accommodating α_2 and the k_2 values reported in Table I. The theory as adapted for the particulars of the present case is summarized in eqs 6–12.

$$\Delta G^* = W^r + \lambda/4 + \Delta G^{\circ\prime}/2 + (\Delta G^{\circ\prime})^2/4\lambda \tag{6}$$

$$\Delta G^* = -RT \ln (kh/\tilde{k}T) \tag{7}$$

$$\Delta G^{\circ\prime} = \Delta G^\circ - W^r \tag{8}$$

$$\Delta G^\circ = -RT \ln K_{eq} \tag{9}$$

$$\lambda = (\lambda_i + \lambda_j)/2 \tag{10}$$

$$d\lambda/d(\Delta G^\circ) = 2(\tau - 1) \tag{11}$$

$$d(\Delta G^*)/d(\Delta G^\circ) = C_0' + C_1'\Delta G^\circ + C_2'(\Delta G^\circ)^2 \tag{12}$$

$$C_0' = (\tau - 1)/2 - W^r/2\lambda + W^{r2}(\tau - 1)/2\lambda^2 + \tfrac{1}{2}$$

$$C_1' = \tfrac{1}{2}\lambda + W^r(\tau - 1)/\lambda^2$$

$$C_2' = -(\tau - 1)/2\lambda^2$$

W^r is the standard free energy for bringing the reactants into a precursor configuration—that is, a configuration suitable for the covalency changes. In the present case W^r has been assumed not to be a function of ΔG°.[39] ΔG° is the standard free energy for the converion of reactants to products. Ordinarily this theory contains a parameter, W^p, which is the standard free energy for forming the successor complex from the separated products, and thus is analogous to W^r for the reverse reaction. Since BH_3 associates spontaneously with Lewis bases, including olefins and tertiary amines,[40] it is reasonable to suppose that the primary product of the rate-limiting step is a dihydroquinoline–BH_3 complex and that W^p is zero. For the reaction of OH^- with a quinolinium ion there is also only one product and we have again taken zero for W^p. Equations 6–12 have been modified accordingly.

For the hypthetical reaction with $\Delta G^{\circ\prime}$ equal to zero, λ is the energy required to deform the precursor configuration into the successor configuration (including the accompanying solvent (reorganization) *without* the covalency changes that occur in the actual reaction. λ values for reactions of the donor and acceptor which are structurally symmetrical as well as energetically symmetrical are λ_i and λ_j. Thus, for the reduction of quinolinium ions by BH_4^-, λ_i is the λ for the reaction shown in eq 13 and λ_j is the λ for that shown in eq 14. For atom-transfer reactions λ

$$\mathbf{1}^+ + \mathbf{1H}^* \rightarrow \mathbf{1H} + \mathbf{1}^{+*} \tag{13}$$

$$BH_3 + BH_4^{-*} \rightarrow BH_4^- + BH_3^* \tag{14}$$

is obtained by averaging λ_i and λ_j (eq 10). For ion-combination reactions like the reaction of OH^- with quinoliniuim ions, λ has to be evaluated in some other way. In the present case it was adjusted to fit the results. The tightness parameter, τ, is the total bond order to the in-flight atom or group in the critical configuration of the transfer reaction.[41] In an ion-combination reaction it has no obvious physical meaning and takes the formal value of unity.[9] Other symbols have their customary significance.[10] The Bronsted α is $d(\Delta G^*)/d(\Delta G^\circ)$. In the theory, α is not a partial derivative, as W^r and λ may be functions of ΔG°.[17]

For reduction of quinolinium ions by BH_4^-, λ_i (eq 13) has been determined. It is 389 kJ mol^{-1}.[6] We can assume that λ_j is not far from zero, because $BH_3 \cdot HBH_3^-$ is a known ion;[42] its structure is nearly symmetrical,[43] and the estimated energy required to symmetrize it is less than 5 kJ mol^{-1}.[44] A value of τ (0.81) is available for hydride transfer between quinolinium ions.[6] It may not be exactly appropriate for hydride transfer from BH_4^- to quinolinium ions, but the true value is likely to be slightly less than unity, since this is an activated process, probably reflecting some loss of binding energy by the in-flight hydride. We have, therefore, used $\tau = 0.81$. That leaves W^r and $\Delta G^{\circ\prime}$ unevaluated, and we have two pieces of experimental information to be fitted; $\alpha = 0.31$ and $\Delta G^* = 34$ kJ mol^{-1} (central value). Equations 6–12 reproduce the experimental values of α and ΔG^* if W^r is 3 kJ mol^{-1} and $\Delta G^{\circ\prime} = -39$ kJ mol^{-1} for a typical reaction. The ΔG° value, -36 kJ mol^{-1}, is reasonable, but there is not much to compare it to. No reliable reduction potential appears to be available for BH_3.[45] The W^r value seems a little too positive but it is hard to say anything definitive because of the substantial uncertainty in α.

Qualitatively, our results suggest an explanation for the failure of the kinetically controlled ratio of 1,2- to 1,4-product to correspond to the equilibrium product distribution.[2] The equilibrium product distribution probably reflects primarily the difference in covalent bond energy between the 1,2- and 1,4-isomers. However, χ is only about 0.4 in the critical complexes, so these covalent bond

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[39] In a previous study of reactions of NAD^+ analogues with an anionic reducing agent, a weak functional relation between W^r and ΔG° was inferred.[29] In the present case, however, there is insufficient data on which to base any further adjustable parameters.

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energies are very incompletely expressed. On the other hand, the critical complexes still have considerable charge separation. The residual negative charge of the BH_4^- unit is much closer to the positive charge on N in the critical complex for 1,2-addition than in that for 1,4-addition.

The value of α_{-1}, for the hydroxylation of the quinolinium ions, is also in reasonable accord with the Marcus theory. W^r and W^p were both assumed to be zero, and τ was taken as 1. Then, using central values of ΔG° and ΔG^* ($\Delta G^\circ = -50.6$ kJ mol^{-1}; $\Delta G^* = 36.8$ kJ mol^{-1}) eq 6[46] gave a value of 238 kJ mol^{-1} for λ. This is a very satisfactory outcome, because it is a little over half of the well-determined λ_i for hydride transfer between quinolinium ions, 389 kJ mol^{-1}.[6] The quinolinium reactant in that reaction is undergoing changes very analogous to those in the present reaction. A covalent bond is being formed at C-4, and the positive charge is being neutralized. However, the "donor", instead of being a dihydroquinoline, which would match the contributions of the acceptor to λ, is simply OH^-, which probably contributes only a little desolvation energy to λ. Thus λ for hydroxide addition to quinolinium ions is expected to be a little over half of 389 kJ mol^{-1}.

Using this value of λ and the other parameters already selected, eq 12 gives 0.39 for α_{-1}. This is in qualitative agreement with the experimental value (0.23) in that both are substantially less than 0.5 and indicates a critical configuration closer to reactants that to products. There is a substantial quantitative gap between them, but the uncertainty in α may account for a good deal of it. It may be significant that a similar treatment of an α value for a similar reaction in aqueous solution *underestimates* α.[10]

As we have already concluded for the reaction with BH_4^-, the Marcus theory can be applied reactions which depart widely from the model for which it was derived. The qualitative conclusions which are reached seem reasonable. In particular, the idea that the intrinsic barrier can be approximated by adding independent contributions from each of the reactants, embodied in eq 10, seems to be strongly supported. This was anticipated by Hine[19] some time ago. However, too much physical significance should not be given to the numerical values of the parameters, as these values may well be compensating for the inadequacies of the model. These conclusions are probably applicable to proton transfer as well.[47]

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(46) Equation 6 was rearranged to give an explicit solution for λ; $\lambda = 2[\Delta G^* - \Delta G^{\circ\prime}/2 + (\Delta G^{*2} - \Delta G^*\Delta G^{\circ\prime})^{1/2}]$.

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Solvent Dependence of Oxygen Isotope Effects on the Decarboxylation of 4-Pyridylacetic Acid

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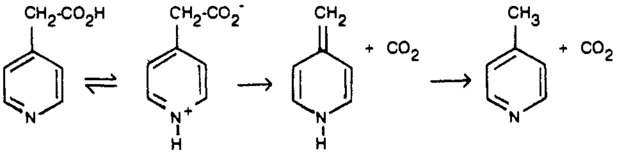
Abstract: Oxygen isotope effects on the decarboxylation of 4-pyridylacetic acid have been measured by the remote-label technique. The isotope effect varies from $k^{16}/k^{18} = 0.995$ per oxygen in 25% dioxane to 1.003 in 75% dioxane. The isotope effect reflects three contributions: An inverse isotope effect of 0.98–0.99 due to the change in carbon–oxygen bond order on going from ground state to transition state, an effect of 1.01–1.02 due to desolvation of the carboxyl group, and an effect of approximately 1.01 due to the acid–base equilibrium of the carboxyl group. Thus, oxygen isotope effects on decarboxylation should be a useful probe for carboxyl desolvation in enzymatic decarboxylations.

In its simplest form, decarboxylation involves the cleavage of a carbon–carbon bond of a carboxylic acid or, more commonly, a carboxylate anion, forming carbon dioxide and leaving behind an organic residue with an unshared pair of electrons. In general, the organic product stabilizes this electron pair, usually by delocalization. Such delocalization is particularly important in enzymatic reactions, where an "electron sink" is generally provided by a coenzyme (e.g., pyridoxal 5′-phosphate, thiamine pyrophosphate), by an enzyme-bound metal ion (various oxidative decarboxylases), or by a prosthetic group (lysine amino group, covalently bound pyruvate).

Rates of decarboxylations are also influenced by the polarity of the medium within which the reaction occurs. In most decarboxylations the transition state is less polar than the ground state (i.e., the negative charge is more delocalized), and consequently decarboxylations proceed more rapidly in less polar solvents. A particularly dramatic example of this effect is the decarboxylation of the pyruvate–thiamine complex studied by Crosby, Stone, and Lienhard,[1] in which the rate increases 9000-fold on going from water to ethanol. Kemp and collaborators have shown that decarboxylation of benzisoxazole-3-carboxylic acids also shows very large medium effects.[2] Rate differences as large as 900 000-fold are observed on going from water to hexamethylphosphoramide. The decarboxylation of 4-pyridylacetic acid (eq 1) also shows large medium effects,[3] with the rate increasing 4000-fold on going from water to 75% dioxane.



(1)

In addition to the general polarity effect, a specific effect of carboxyl group solvation is also important. The starting carboxylate ion, being charged and polar, is extensively solvated. The product of the decarboxylation, CO_2, being nonpolar, is not ex-

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