

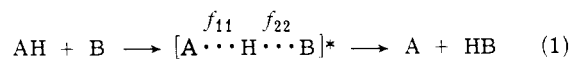
Indices of Transition State Symmetry in Proton-Transfer Reactions. Kinetic Isotope Effects and Brønsted's β in Base-Catalyzed Diazo-Coupling Reactions^{1,2}

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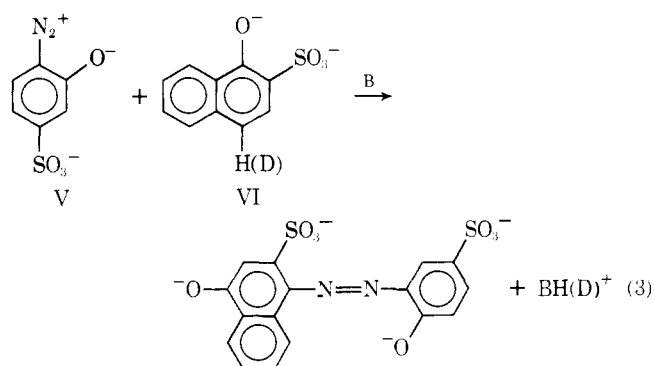
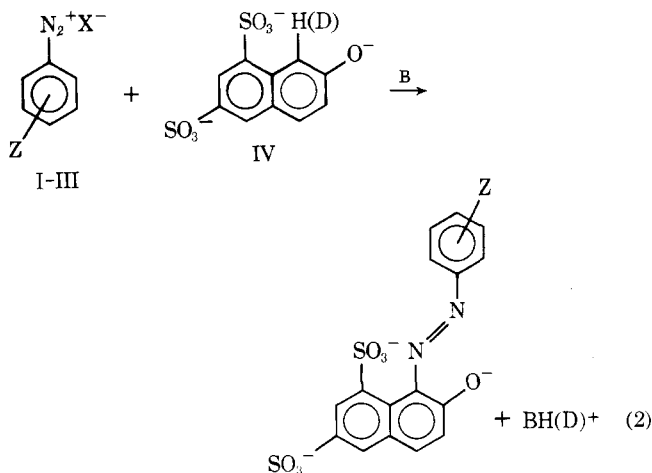
Abstract: The applicability of k_H/k_D and of Brønsted's β as indices of transition state symmetry in proton-transfer reactions has been tested in a number of base-catalyzed electrophilic aromatic substitution reactions. The data obtained from measurements involving the coupling of the diazonium salts of *m*- and *p*-chloroanilines, *p*-nitroaniline, and 4-amino-3-hydroxybenzenesulfonic acid with two naphthols and their deuterated analogs, catalyzed by 12 bases, provide ample evidence for doubting the validity of β as a measure of the degree of proton transfer at the transition state. Variations in the structure of the transition state, caused by changes in the pK_a of the catalyzing base, are more readily reflected in k_H/k_D . The origin of the observed variation of isotope effects is discussed, and the validity of k_H/k_D as an index of transition state symmetry is questioned.

Proton transfers are probably the most common chemical reactions in solution chemistry. An understanding of the mechanisms of such reactions has as its focal point a model for the transition state $[A \cdots H \cdots B]^*$. Many of the recent papers on this subject have concerned themselves mainly with the symmetry of such transition state, *i.e.*, with the degree of proton transfer between proton donor AH and proton acceptor B.⁴

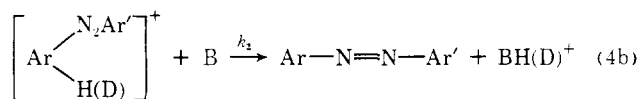
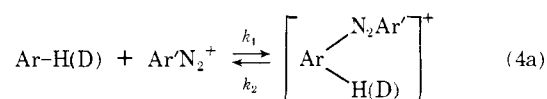


There are two main experimental approaches for studying this model: kinetic isotope effects (k_H/k_D) and Brønsted's β .⁵ In this paper, we report the results of a study designed to pinpoint the applicability and the validity of these two indices as measures of transition state symmetry in proton-transfer reactions.

Several electrophilic aromatic substitutions lend themselves to a study of the relationship between the magnitude of k_H/k_D and the parameter β of the Brønsted catalysis law. We chose the coupling of the diazonium salts of *p*- and *m*-chloroanilines and *p*-nitroaniline (I-III) with 2-naphthol-6,8-disulfonic acid (G-salt, IV) (eq 2) and of the diazonium salt of 4-amino-3-hydroxybenzenesulfonic acid (V) with 1-naphthol-2-sulfonic acid (VI) in aqueous buffer so-



lutions (eq 3). The coupling reactions depicted in both equations proceed with the formation of an intermediate σ complex from which proton transfer is rate limiting (eq 4a,b).^{4e,5} Step 4b has in essence the transition state depicted in eq 1 (AH of eq 1 being the σ complex of step 4b), and the purpose of this work is to provide information on that transition state.



Kinetic isotope effect theory predicts a maximum in k_H/k_D for proton transfers (eq 1) with a symmetrical transition state.⁶ Although tunnel corrections are ignored in these treatments, a fact which has been heavily criticized recently,⁷ the overall conclusion that a maximum in k_H/k_D is expected when the bonds A-H and B-H have equal force constants^{6d} is generally accepted. This condition is likely to be so when A and B (eq 1) are of approximately equal basicity,^{4a} *i.e.*, when $pK_{HA} \approx pK_{HB}$. Many investigators have presented data in support of a maximum k_H/k_D when $\Delta pK_A \approx 0$.⁴ Recently, however, the reality of such a maximum was questioned.⁸

The other most commonly used index for transition state symmetry in reactions represented by eq 1 is the parameter β of Brønsted's catalysis law.⁹ Leffler's hypothesis, which follows in spirit the Bell-Polanyi-Evans postulate,¹⁰ also re-

flected in the Hammond postulate,¹¹ proposes that the transition state bears the greater resemblance to the less stable of the species (reactants or products) of a chemical equilibrium, and that Bronsted's β is a measure of the degree of proton transfer from AH to B (eq 1).⁹ Cases where Bronsted's slopes are larger than one and less than zero have been reported.¹² Although such deviant Bronsted parameters have been elegantly rationalized,¹³ it is still a fact that their occurrence limits the unqualified use of Bronsted's exponents as guides for transition state structures in proton transfers. Such limitations and others have been recently presented.¹⁴

In view of these uncertainties, we present the results of our investigation with the hope of contributing to a better understanding of the usefulness and limitations of k_H/k_D and Bronsted's coefficients as indices for transition state structures in proton transfers.

Results

Kinetics. The kinetics of the four coupling reactions (eq 2 and 3) were studied by monitoring the increase in the absorption maxima characteristic of the azo dyes formed. The coupling reactions, carried out in buffered media at constant ionic strength, were all subjected to catalysis by ten bases: pyridine, 2-, 3-, and 4-picolines, 2,6-lutidine, 4-cyano- and 3-nitropyridines as heteroaromatic amines, and *N*-methylmorpholine (MeMor), *N,N'*-dimethylpiperazine (DMPi), and 1,4-diazabicyclo[2.2.2]octane (Dabco) as alicyclic amines.¹⁵

The coupling reactions (eq 2 and 3) follow the kinetic law of eq 5, and nonlinear base catalysis is observed when

$$\frac{d[\text{ArN}_2\text{Ar}']}{dt} = [\text{Ar}'\text{N}_2^+][\text{ArH}] \frac{k_1(k_2[\text{B}]/k_{-1})}{1 + (k_2[\text{B}]/k_{-1})} \quad (5)$$

$k_2[\text{B}]/k_{-1} < 1$.¹⁶ Such is the case with the couplings depicted in eq 2. Here, the Bodenstein steady-state treatment is applicable, and if $k_{-1}(\text{H}) = k_{-1}(\text{D})$, the kinetic isotope effect is evaluated as $k_2(\text{H})/k_2(\text{D})$. Tables I, II, and III contain summaries of the rate data obtained in the coupling, with the G-salt, of *p*-chloro-, *m*-chloro-, and *p*-nitrobenzenediazonium salts, respectively.

Table I. pK_a Values of Bases Used, Rate Constants, and Kinetic Isotope Effects for the Coupling Reaction of *p*-Chlorobenzenediazonium Tetrafluoroborate with G-Salt and Deuterated G-Salt, 10°, $\mu = 0.25$ (KCl)

Base	pK_a	$k_1, M^{-1} \text{sec}^{-1}$	Log $k_2(\text{H})/k_{-1}$	Log $k_2(\text{D})/k_{-1}$	$k_2(\text{H})/k_2(\text{D})$
Pyridine	5.50	930	-0.097	-0.851	5.68
2-Picoline	6.37	(930) ^a	-0.296	-1.117	6.62
3-Picoline	6.12	(930) ^a	0.050	-0.678	5.35
4-Picoline	6.43	(930) ^a	0.118	-0.595	5.16
2,6-Lutidine	7.11	(930) ^a	-1.541	-2.575	10.81
4-Cyano-pyridine	1.50	(930) ^a	-1.354	-2.277	8.38
Dabco ^b	9.41	680	1.814	1.282	3.40
DMPi ^c	8.78	230	1.525	0.929	3.94
MeMor ^d	7.89	330	0.864	0.211	4.50
H ₂ O	-1.67	(930) ^a	-4.294	-5.050	5.70

^a k_1 , calculated from a series of kinetic runs with pyridine, was used for all pyridine homologs and H₂O. ^b 1,4-Diazabicyclo[2.2.2]octane. ^c *N,N'*-Dimethylpiperazine. ^d *N*-Methylmorpholine.

On the other hand, when $k_2[\text{B}]/k_{-1} \ll 1$, a linear relationship between rate and base concentration is expected. Here, it is not possible to separate the individual rate constants, and the magnitude of the isotope effect is given by

Table II. Rate Constants and Kinetic Isotope Effects for the Coupling Reaction of *m*-Chlorobenzenediazonium Tetrafluoroborate with G-Salt and Deuterated G-Salt, 10°, $\mu = 0.25$ (KCl)

Base	$k_1, M^{-1} \text{sec}^{-1}$	Log $k_2(\text{H})/k_{-1}$	Log $k_2(\text{D})/k_{-1}$	$k_2(\text{H})/k_2(\text{D})$
Pyridine	1160	0.520	-0.217	5.46
2-Picoline	(1660) ^a	0.233	-0.541	5.94
3-Picoline	1730	0.598	-0.102	5.01
4-Picoline	1615	0.753	0.070	4.82
2,6-Lutidine	(1660) ^a	-1.334	-2.347	10.30
4-Cyanopyridine	(1660) ^a	-0.592	-1.491	7.93
Dabco ^b	1435	2.776	2.262	3.27
DMPi ^c	1120	2.201	1.650	3.56
MeMor ^d	1080	1.731	1.140	3.90
H ₂ O	(1660) ^a	-3.802	-4.492	4.90

^{a-d}See corresponding footnotes in Table I.

Table III. Rate Constants and Kinetic Isotope Effects for the Coupling Reaction of *p*-Nitrobenzenediazonium Tetrafluoroborate with G-Salt and Deuterated G-Salt, 10°, $\mu = 0.25$ (KCl)

Base	$k_1, M^{-1} \text{sec}^{-1}$	Log $k_2(\text{H})/k_{-1}$	Log $k_2(\text{D})/k_{-1}$	$k_2(\text{H})/k_2(\text{D})$
Pyridine	22,880	1.657	1.018	4.36
2-Picoline	21,720	1.548	0.851	4.98
3-Picoline	21,670	1.894	1.268	4.23
4-Picoline	21,030	1.938	1.320	4.15
2,6-Lutidine	(22,880) ^a	-0.236	-1.080	6.56
4-Cyanopyridine	(22,880) ^a	0.742	0.027	5.19
Dabco ^b	20,700	3.216	2.760	2.86
DMPi ^c	17,980	2.580	2.045	3.43
MeMor ^d	15,330	2.158	1.602	3.60
H ₂ O	(22,880) ^a	-2.807	-3.485	4.76

^{a-d}See corresponding footnotes in Table I.

Table IV. Rate Constants and Kinetic Isotope Effects for the Coupling Reaction of *p*-Diazo-*m*-hydroxybenzenesulfonic Acid with 1-Naphthol-2-sulfonic Acid and 4-Deuterio-1-naphthol-2-sulfonic Acid, 0°, $\mu = 0.45$ (KCl)

Base	Log $k_1(\text{H})k_2(\text{H})/k_{-1}(\text{H})$	Log $k_1(\text{D})k_2(\text{D})/k_{-1}(\text{D})$	$[k_1(\text{H})k_2(\text{H})/k_{-1}(\text{H})]/[k_1(\text{D})k_2(\text{D})/k_{-1}(\text{D})]$
Pyridine	-1.680	-2.292	4.09
2-Picoline	-1.134	-1.756	4.19
3-Picoline	-1.233	-1.865	4.29
4-Picoline	-1.208	-1.792	3.84
2,6-Lutidine	-1.814	-2.449	4.35
4-Cyanopyridine	-1.540	-2.257	5.22
Dabco ^a	0.078	-0.211	1.95
DMPi ^b	0.219	-0.170	2.45
MeMor ^c	-0.330	-0.788	2.87
H ₂ O	-4.510	-5.140	4.75
OH ⁻	-0.358	-0.858	3-16

^a 1,4-Diazabicyclo[2.2.2]octane. ^b *N,N'*-Dimethylpiperazine. ^c *N*-Methylmorpholine.

$[k_1(\text{H})k_2(\text{H})/k_{-1}(\text{H})]/[k_1(\text{D})k_2(\text{D})/k_{-1}(\text{D})]$. Such is the case in the coupling reaction of eq 3, for which the rate data are given in Table IV.

Bronsted Relations. The catalytic rate constants determined in this work for seven heteroaromatic amines and three alicyclic amines are correlated, by least-squares analysis, with the pK_a 's of the corresponding amines. A summary of the separate and collective values for the Bronsted exponent β , the preexponential term, $\log G$, and the correlation coefficient r is given in Table V. The strong deviation of hydroxide ion in the Bronsted plot (Figure 1) of the reaction of eq 3 seems to be a specific effect due primarily to electrostatic repulsion between the negatively charged catalyzing

Table V. Summary of Brønsted Coefficients for Azo Coupling Reactions

Reaction	Fig	Type of amine	β_{H}^a	β_{D}^a	Log G_{H}^b	Log G_{D}^b	r_{H}^c	r_{D}^c
I + IV	1	Heteroaromatic	0.30	0.35	-1.80	-2.79	0.99	0.99
		Alicyclic	0.52	0.61	-3.21	-4.62	0.99	0.99
		Combination of all	0.49	0.52	-2.90	-3.75	0.97	0.98
II + IV	2	Heteroaromatic	0.27	0.31	-0.99	-1.96	0.99	0.99
		Alicyclic	0.60	0.66	-3.11	-4.14	0.96	0.97
		Combination of all	0.52	0.54	-2.35	-3.14	0.97	0.98
III + IV	3	Heteroaromatic	0.24	0.26	0.36	-0.37	0.99	0.99
		Alicyclic	0.60	0.69	-2.71	-3.98	0.94	0.94
		Combination of all	0.45	0.47	-1.11	-1.81	0.94	0.95
V + VI	4	Heteroaromatic	0.072	0.097	-1.70	-2.46	0.56	0.69
		Alicyclic	0.079	0.26	-0.86	-2.74	0.30	0.71
		Combination of all	0.37	0.40	-3.24	-3.95	0.93	0.94

^a Brønsted exponent β for the undeuterated and deuterated substrates. ^b Preexponential term for the undeuterated and deuterated substrates. ^c Correlation coefficients for the respective plots.

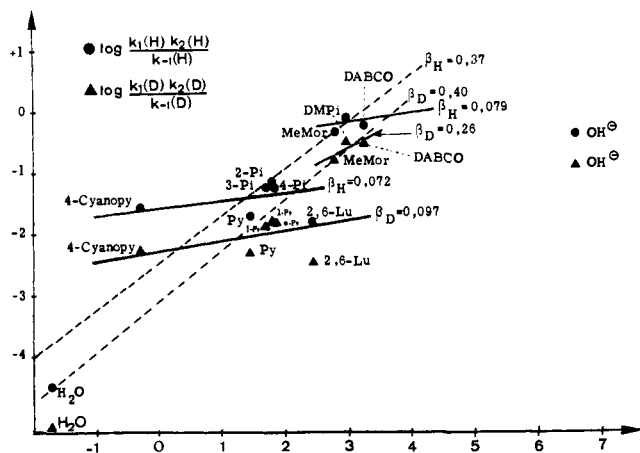
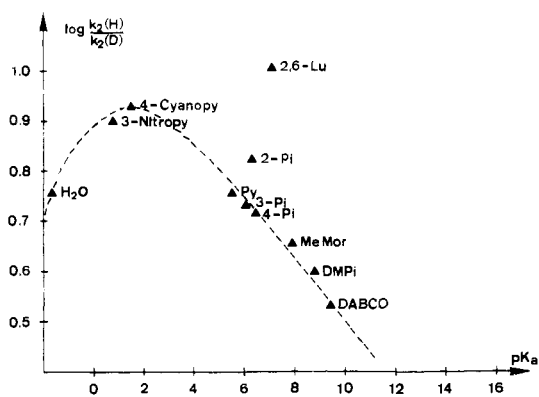


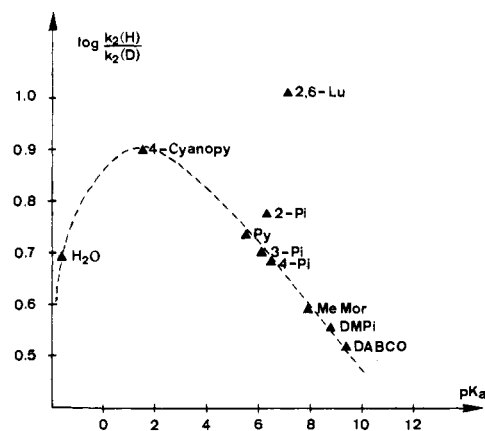
Figure 1. Brønsted plot for the coupling reaction of V + VI.

Figure 2. Coupling reaction of I + IV. Correlation of isotope effect with pK_a of catalyzing base.

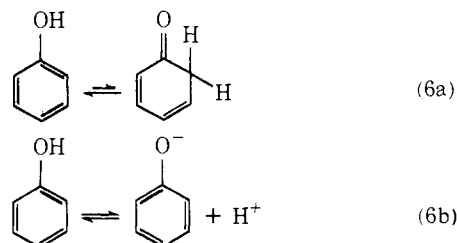
base and the intermediate σ complex with three anionic charges.^{4c}

Discussion

Kinetic Isotope Effects. Sensitivity to Strength and Structure of Catalyzing Bases. It is readily apparent from inspection of Figures 2–5 that the isotope effects for the four coupling reactions (eq 2 and 3) exhibit maxima in their variation with the pK_a of the catalysts. Based on accepted interpretation for variation of $k_{\text{H}}/k_{\text{D}}$ with systematic variations in pK_a ,^{4a,6d} we expected the largest primary isotope effects, in each case, to be associated with the most symmetrical transition states (eq 4b) which are expected when the conjugate acid HB of the catalyzing base has the same acidity as the substrate (σ complex) which is undergoing deproto-

Figure 3. Coupling reaction between II + IV. Correlation of isotope effect with pK_a of catalyzing base.

nation. The pK_a values of these ketone-like σ complexes (eq 4b) can be derived from the constant K_{T} for the tautomeric equilibrium (eq 6a) and the acid dissociation constant K_a (eq 6b) for phenol. For eq 6a, $\Delta F^\circ = 13 \text{ kcal mol}^{-1}$ and for eq 6b, $K_a \approx 10^{-10}$ which leads to $K_{\text{T}} \approx 3 \times 10^{-10}$,¹⁷ and a



corresponding $pK_{\text{a}(\text{keto})} \approx 1$. Figures 2–5 show clearly defined maxima at $\Delta pK_a \approx -0.5$ which support the predictions of Westheimer,^{6b} Bell and Goodall,^{4a} and Schowen,^{6d} about a maximum $k_{\text{H}}/k_{\text{D}}$ when $f_{11} = f_{22}$ (eq 1), a condition which is realizable when $pK_{\text{HA}} \approx pK_{\text{HB}}$. This finding is analogous to earlier reports.^{4,6} One could object, of course, that in our data, with the exception of the diazo coupling between *p*-chlorobenzenediazonium fluoroborate, I (eq 2), and the G-salt, only one point, that of H_2O , lies to the left side of the maxima. This shortcoming of our investigation was realized only when the experimental work was finished. We therefore investigated the effect of an even weaker base than 4-cyanopyridine, namely 3-nitropyridine ($pK_a = 0.81$),¹⁸ in the reaction of *p*-chlorobenzenediazonium salt (I) with G-salt. At the same time, the results obtained with pyridine were repeated. The measured isotope effect for 3-nitropyridine, $k_2(\text{H})/k_2(\text{D}) = 7.92$, included in Figure 2 makes it quite evident that the observed maximum is not an

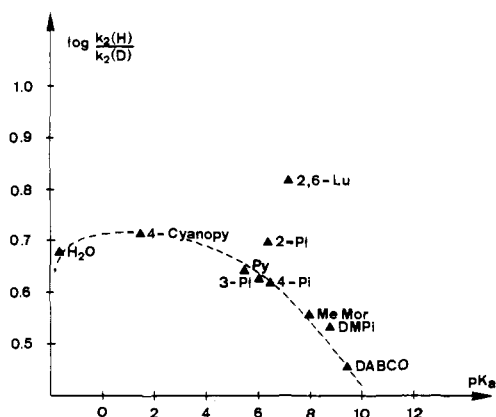


Figure 4. Coupling reaction between III + IV. Correlation of isotope effect with pK_a of catalyzing base.

artifact, but a reality, even if one considers only 3- and 4-substituted pyridines.

From the thermodynamic point of view, negative values for ΔpK_a ($pK_a(\sigma \text{ complex}) - pK_a(\text{base})$) correspond to reactions with the equilibrium on the side of the products, *i.e.*, to a negative value for ΔF° . In the symbolism of eq 1, these are reactions where $pK_{BH} > pK_{AH}$, *i.e.*, exergonic, where increasing basicity (larger pK_{BH}) brings about increased asymmetry in the reaction coordinate and a corresponding decrease in the magnitude of the primary kinetic isotope effect. On the other side, *i.e.*, where ΔpK_a and, correspondingly, ΔF° are positive, the equilibrium is in favor of the reactants ($AH + B$), and k_H/k_D increases with increasing basicity of B. Here, the stronger the proton acceptor, the more symmetric the reaction coordinate becomes. This expectation is confirmed by our experiments (Figures 2–5) except for the sterically hindered 2-picoline and 2,6-lutidine, and one is tempted to conclude that the magnitude of the isotope effects is a reliable measure of the symmetry of the transition state in the studied proton transfer reactions.

The question of whether the proton (or deuteron) is closer to the σ complex or to the base catalyst may, likewise, be answered in the light of the Bell–Polanyi–Evans–(Hammond) postulates,^{10,11} which imply that exergonic reactions involve reactant-like transition states while endergonic reactions have product-like transition states. When applied to our coupling reactions, the implication is that, except for catalysis by water, and in the I–IV coupling reaction (eq 2), catalysis by 3-nitropyridine (Figure 2), the proton undergoing transfer is closer to the intermediate σ complex than to the catalyst. With 4-cyanopyridine, the transition state is almost symmetrical.

More subtle differences in the position of the proton in the transition state, reflected in k_H/k_D , are apparent from inspecting the change in the magnitude of the isotope effect as the acidity of the σ complex is varied. This was accomplished by conducting the coupling reaction (eq 2) between the G-salt (IV) and the series *p*-chloro-, *m*-chloro-, and *p*-nitrobenzenediazonium salts where the change in the substituent Z (eq 2) is expected to induce changes in the acidity of the proton (or deuteron) being transferred. The magnitude of k_H/k_D decreases regularly in the series; with pyridine as base, $k_H/k_D = 5.68, 5.46,$ and 4.36 for the *p*-Cl, *m*-Cl, and *p*-NO₂ compounds, respectively. This is in line with the expectation that as $pK_a(\sigma \text{ complex})$ decreases, the asymmetry of the reaction coordinate increases (for exergonic reactions), and k_H/k_D decreases accordingly. Zollinger has already shown that electron-attracting substituents increase the acidity of the σ complex and lower the isotope effect.¹⁹

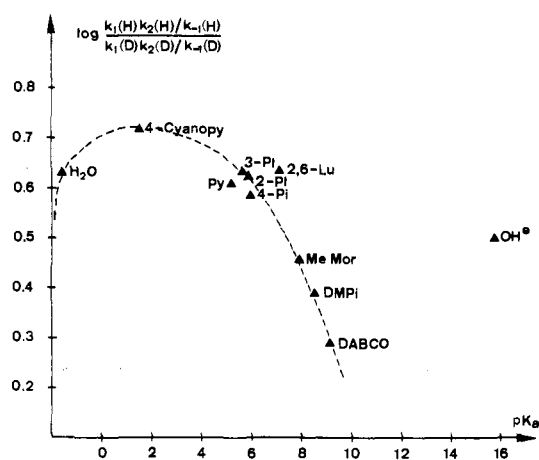


Figure 5. Coupling reaction of V + VI. Correlation of isotope effect with pK_a of catalyzing base.

In all four reactions, the points for 2,6-lutidine lie markedly above the curves in the $\log [k_1(H)k_2(H)/k_{-1}(H)]/[k_1(D)k_2(D)/k_{-1}(D)]$ vs. ΔpK_a and $\log [k_2(H)/k_2(D)]$ vs. ΔpK_a diagrams (Figures 2–5). For 2-picoline, the same holds true, but only in the runs with the G-salt where steric hindrance is afforded by the sulfonic acid group in the peri position. These two large isotope effects may be caused by the methyl groups neighboring the basic centers which make the approach to the proton in the σ complex more difficult. The steric interaction between the methyl group(s) and the peri-sulfonic acid group triggers repulsive forces which lead, especially with 2,6-lutidine, and to a lesser degree with 2-picoline, to a relatively high and steep ascent of the energy barrier along the reaction coordinate. Such narrow potential barriers favor tunneling,²⁰ which is known to be responsible for larger k_H/k_D than is encountered in the absence of tunneling.

Even in the absence of tunneling, large k_H/k_D values can be accommodated. For an $A \cdots H \cdots B$ particle, the simplest way to emerge from the repulsive forces between A and B is to stretch, and thus to weaken, the A–H bond. This behavior may be coupled with a considerable loss in the zero-point energy of the degenerate bending vibrations in the transition state, and the resulting isotope effect can, in extreme cases, reach a k_H/k_D value of *ca.* 18 as calculated by Bigeleisen for a bond-free transition state.²¹

The Magnitude of β and the Degree of Proton Transfer. If the Bronsted exponent β is smaller or larger than 0.5, then the activated complex has, after Leffler,⁹ a reactant-like or a product-like structure, respectively. Consequently, β should be smaller than 0.5 in reactions exhibiting negative ΔpK_a differences and larger than 0.5 when ΔpK_a is positive. Bell and coworkers confirmed this expectation experimentally for several endergonic reactions.^{4a,22}

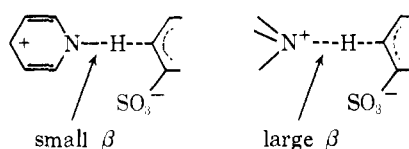
The coupling reactions with the G-salt catalyzed by bases which give negative ΔpK_a values agree with Leffler's hypothesis only when catalysis is accomplished by pyridine and its homologs (*p*-Cl: $\beta_H = 0.30, \beta_D = 0.35$; *m*-Cl: $\beta_H = 0.27, \beta_D = 0.31$; *p*-NO₂: $\beta_H = 0.24, \beta_D = 0.26$). On the other hand, the β values for the alicyclic amines all lie above 0.5, showing, by comparison with the pyridine bases, a higher catalytic efficiency, and in Leffler's language, a higher degree of proton transfer. The reason for the observation that alicyclic amines are better catalysts²³ than the pyridine bases for proton transfer may be that the free electron pair on the nitrogen occupies an orbital with a larger spatial extension (sp^3) in the alicyclic amines than in the heteroaromatic amines where the nitrogen is sp^2 . The higher degree of proton transfer with the alicyclic amines may

Table VI. Temperature Dependence of the Kinetic Isotope Effect of the Reaction of *p*-Chlorobenzenediazonium Tetrafluoroborate with G-Salt, Catalyzed by Pyridine, $\mu = 0.25$ (KCl)^a

Temp, °C	(1/T) × 10 ³ , °K ⁻¹	k ₂ (H)/k ₂ (D)
11.41	3.514	5.44 ± 0.32
20.88	3.401	5.25 ± 0.33
30.09	3.298	4.83 ± 0.40
48.92	3.105	4.58 ± 0.24

^a $A_{k_2(\text{H})}/A_{k_2(\text{D})} = 1.16 \pm 0.13$ ($r = 0.98$), $E_{k_2(\text{D})} - E_{k_2(\text{H})} = 0.88$ kcal mol⁻¹ = 3.63 kJ mol⁻¹.

be explained as follows. In the transition state of the coupling reaction of eq 2, there is a negative charge very close to the catalyst, and the positive charge developing in the base catalyst is delocalized away from the reaction site in the pyridine bases but not so in the alicyclic amines. The electrostatic attraction of the negative and positive charges in the latter case will shorten the bonds to the proton and cause β to be larger for the alicyclic amines



Specific effects such as these seem not to be common in Bronsted relations. However, recently, Kresge *et al.*,^{14a} have discussed specific effects in the hydrolysis of vinyl ethers.

It is interesting to note that a “back of the envelope”^{6d} calculation of the isotopic β^{25} leads to estimates of *ca.* 0.25 and *ca.* 0.8 corresponding to experimental values of 5.7 and 3.4 for $k_{\text{H}}/k_{\text{D}}$ for catalysis by pyridine and by Dabco, respectively, in the coupling of I with IV (eq 2). These values of *ca.* 0.25 and *ca.* 0.8 are to be compared, within the framework of approximations involved,^{6d} with the values of β found experimentally, *viz.*, 0.3 and 0.52 for the pyridine bases and the alicyclic amines, respectively, in the coupling of I with IV.

Experiments aiming at finding a correlation between the isotope effect and the β value usually encompass a $\text{p}K_{\text{a}}$ range of *ca.* 10 units. Within this limited range, the Bronsted relation does not deviate significantly from a linear behavior. On the other hand, the isotope effects usually change in response to changing the $\text{p}K_{\text{a}}$ of the catalyst, and more often than not a maximum is observed. The dilemma is obvious. A linear behavior for β , coupled with Leffler’s hypothesis, suggests the same degree of proton transfer which according to isotope effect theory should yield a constant value for $k_{\text{H}}/k_{\text{D}}$. Clearly, this is not the case in our work, and one is left with a few alternatives. First, the Bronsted exponents, even if evaluated from measurements involving similarly structured catalysts, are rather insensitive to variations in $\text{p}K_{\text{a}}$ and, therefore, are imprecise indices for transition state symmetry in proton-transfer reactions. Alternatively, it is conceivable that the degree of proton transfer for reactions exemplified by eq 1 varies but little over wide $\Delta\text{p}K$ ranges. This latter view is stressed in the recent calculations of Bell, Sachs, and Tranter⁷ whose model predicts that the position of the proton in the transition state $\text{A} \cdots \text{H} \cdots \text{B}$ (eq 1) is “never more than 0.15 Å distant from the center.” This then raises the question whether the variations in $k_{\text{H}}/k_{\text{D}}$ which accompany variations in $\Delta\text{p}K$ are truly reflections of changes in the symmetry of the transition state $\text{A} \cdots \text{H} \cdots \text{B}$. According to the model of Bell, Sachs, and Tranter,⁷ the ratio of the force constants, f_{11}/f_{22} , is insensitive to variations in the charge

Table VII. Temperature Dependence of the Kinetic Isotope Effect of the Reaction of *p*-Chlorobenzenediazonium Tetrafluoroborate with G-Salt, Catalyzed by 2,6-Lutidine, $\mu = 0.25$ (KCl)^a

Temp, °C	(1/T) × 10 ³ , °K ⁻¹	k ₂ (H)/k ₂ (D)
11.48	3.513	9.67 ± 1.38
21.08	3.399	8.91 ± 1.33
30.08	3.298	8.75 ± 1.05
39.56	3.198	8.08 ± 1.05
48.81	3.106	7.10 ± 0.74

^a $A_{k_2(\text{H})}/A_{k_2(\text{D})} = 0.84 \pm 0.22$ ($r = 0.96$), $E_{k_2(\text{D})} - E_{k_2(\text{H})} = 1.39$ kcal mol⁻¹ = 5.74 kJ mol⁻¹.

produced or neutralized in the proton-transfer processes. As a consequence of the small differences between f_{11} and f_{22} , the frequency of the “symmetrical” stretching vibration is the same for A–H and A–D throughout the extreme values for f_{11}/f_{22} , and therefore “contributes nothing to the isotope effect, and the explanation of variable isotope effects in terms of this vibration fails completely”⁷ for their model. The model, however, shows a pronounced maximum close to the point where $\Delta F^\circ = 0$, *i.e.*, where $\Delta\text{p}K = 0$. The calculated maximum, which agrees with several experimental observations⁴ including the ones reported here, is attained by taking into account a quantum mechanical tunnel correction.

In comparing the two indices, β and $k_{\text{H}}/k_{\text{D}}$, we can finally conclude that while kinetic isotope effects are much more sensitive than Bronsted exponents to variations in $\text{p}K_{\text{a}}$, the use of either quantity as an index of transition state “symmetry” may be doubtful.

Temperature Dependence of $k_{\text{H}}/k_{\text{D}}$. In the coupling of I with IV (eq 2), the calculated $k_{2\text{H}}/k_{2\text{D}} = 5.68$ for catalysis by pyridine and 10.80 for catalysis by 2,6-lutidine at 10°. The possibility of tunneling in the latter case led us to carry out the pyridine-catalyzed and the 2,6-lutidine-catalyzed reactions at five different temperatures, between 11 and 49°. The temperature dependence of the reactions with deuterated and nondeuterated compounds allows us to determine the ratio of the frequency factors $A_{\text{H}}/A_{\text{D}}$ as well as the difference in activation energies $E_{\text{D}} - E_{\text{H}}$ by using the Arrhenius equation. If the $A_{\text{H}}/A_{\text{D}}$ ratio is smaller than 0.5 given by the transition state theory, or if $E_{\text{D}} - E_{\text{H}}$ is considerably higher than the ZPE difference for the C–H and C–D stretching vibrations, then the possibility of tunneling exists.^{21b,27}

In our experiments, we calculated for the two bases, at the corresponding temperatures, the $k_2(\text{H})/k_{-1}(\text{H})$ and $k_2(\text{D})/k_{-1}(\text{D})$ values from the k_1 values obtained with eq. 5 and the $k_2(\text{H})/k_2(\text{D})$ values assuming that $k_{-1}(\text{H}) = k_{-1}(\text{D})$. The ratio $A_{k_2(\text{H})}/A_{k_2(\text{D})}$ and the difference $E_{k_2(\text{D})} - E_{k_2(\text{H})}$ were calculated by regression analysis of the log [$k_2(\text{H})/k_2(\text{D})$] vs. $1/T$ values (Tables VI and VII).

The value for $A_{\text{H}}/A_{\text{D}}$ for the pyridine-catalyzed runs is slightly higher than the normal value of 1. However, in extrapolating toward $1/T = 0$, small deviations influence the results strongly. For example, a reduction of the isotope effect at 48.92° by 1.5% (to 4.50), which is within the limit of error, is enough to give $A_{\text{H}}/A_{\text{D}}$ the theoretical value of 1, a correlation coefficient of 0.99, and $E_{\text{D}} - E_{\text{H}} = 4.04$ kJ mol⁻¹. The difference in activation energies of 3.63 kJ mol⁻¹ is below the ZPE difference (*ca.* 5 kJ mol⁻¹).

In the measurements with 2,6-lutidine, the ratio $A_{\text{H}}/A_{\text{D}} = 0.84$. This value is not low enough to suggest tunneling. Values of 0.15 and 0.17 for $A_{\text{H}}/A_{\text{D}}$, indicative of tunneling, were found in the ionization of 2-nitropropane by 2,4,6-collidine²⁷ and in the base-catalyzed bromination of acetone,²⁸ respectively. As in the case of pyridine, a ratio of $A_{\text{H}}/A_{\text{D}} =$

Table VIII. k_1 Values for the Reaction of *p*-Nitrobenzenediazonium Tetrafluoroborate with G-Salt, Catalyzed by Pyridine, 10°, $\mu = 0.25$ (KCl)

$k_1(\text{H}), M^{-1} \text{sec}^{-1}$	$k_1(\text{D}), M^{-1} \text{sec}^{-1}$	$k_1(\text{H})/k_1(\text{D})$
22,880	22,240	1.0288
22,693	21,665	1.0475
23,034	22,291	1.0333
23,529	21,023	1.1192
Mean \pm std	Mean \pm std	Mean \pm std
23034	21805	1.057
± 358	± 593	± 0.042

I can be obtained for 2,6-lutidine by raising the $k_2(\text{H})/k_2(\text{D})$ value at 48.81° by 3% to 7.30. The correlation coefficient is then 0.97, and $E_{\text{D}} - E_{\text{H}} = 5.29 \text{ kJ mol}^{-1}$. The difference in activation energies in this series is 5.74 kJ mol⁻¹, i.e., 60% larger than in the runs with pyridine. This difference, however, should lie between 10.3 and 12.4 kJ mol⁻¹ to provide a reliable proof for tunneling.^{27,28}

Secondary Isotope Effects. In the couplings of I and II with IV, the nonlinear dependence on the base concentration was not marked enough for calculating the $k_1(\text{D})$ values in the deuterated G-salt experiments. However, this was possible in the coupling reaction of *p*-nitrobenzenediazonium salt (III) catalyzed by pyridine. These measurements, therefore, were repeated four times to see whether a ratio of $k_1(\text{H})/k_1(\text{D})$ different from unity could be obtained. According to Streitwieser and coworkers,²⁹ no significant secondary isotope effect can be expected in electrophilic aromatic substitutions, because the two effects responsible for it—the sp^2 - sp^3 change in hybridization and hyperconjugation—compensate one another. In the literature, however, one finds data showing $k_{\text{H}}/k_{\text{D}} < 1$, as in the chlorination³⁰ and nitration³¹ of benzene and in the nitration of toluene³¹ and fluorobenzene.³² The opposite trend is shown by results on bromination of benzene³³ and biphenyl.³⁴

The results of our calculations are summarized in Table VIII. The *t*-test³⁵ shows that, at the 98% confidence level, $k_1(\text{H})/k_1(\text{D}) > 1$. This is probably due to hyperconjugation in the σ complex which is not fully compensated for by the sp^2 - sp^3 change in hybridization at the reaction center.

Experimental Section

Preparation of Reagents. Aryldiazonium tetrafluoroborates were prepared from the respective anilines.³⁶ *p*-Amino-*m*-hydroxybenzenesulfonic acid (Fluka) was first crystallized from hot water in the presence of activated charcoal and then diazotized *in situ* with NaNO₂ at 0°. Aliquots of this solution were used to start a kinetic run.

Procedures described by Zollinger were followed to deuterate 1-naphthol-2-sulfonic acid³⁷ and G-salt.³⁸

The apparent molecular weights of the deuterated and similarly treated undeuterated compounds were determined by potentiometric acid-base titration.

Bases, commercially available products, were purified by crystallization or distillation. Dabco was purified by sublimation. 3-Nitropyridine was prepared from 3-aminopyridine³⁹ and purified by sublimation.

Buffer Solutions. Phosphate buffer was used for the coupling reactions with 1-naphthol-2-sulfonic acid. This consisted of 0.1 mol of Na₂HPO₄ · 12H₂O, 64 ml of 1 M NaOH, and 29.0 g of KCl per liter. For the coupling reactions with G-salt, a borax buffer was used which consisted of 0.1 mol of Na₂B₄O₇ · 10H₂O and 16 ml of 1 N HCl per liter.

Aliquots of 25 ml of these buffer solutions were used for each kinetic run; the desired ionic strength was adjusted with solid KCl, and the pH of each solution was measured at the end of reaction.

Kinetic Measurements. A solution of naphthol, base, and appropriate amounts of buffer and KCl to adjust the ionic strength was made up to a volume of 49.0 ml. The solution was thermostated

Table IX. Sample Data for the Calculation of the Rate Constant for the Reaction of *p*-Diazo-*m*-hydrobenzenesulfonic Acid (D) with 1-Naphthol-2-sulfonic Acid (N), Catalyzed by Pyridine^a

<i>t</i> , sec	$[\text{Az}]_t \times 10^3, M$	$k_k \times 10^5, \text{sec}^{-1}$
8,330	2.00	2.88
10,890	2.45	2.83
14,145	2.90	2.73
16,990	3.25	2.71
19,080	3.60	2.77
24,360	4.23	2.83
∞	6.40	

^a At 0°, $\mu = 0.45$ (KCl), $[\text{N}] = 1 \times 10^{-2} M$, $[\text{D}]_0 = 1 \times 10^{-4} M$.

and the reaction started by adding 1.0 ml of diazonium salt solution kept at the same temperature.

The formation of the G-salt dye was followed by observing the increase in optical density in the spectrophotometer cell. In the reactions with 1-naphthol-2-sulfonic acid, the reactions were followed by removing samples and quenching with 2 N HCl. The concentration of the dyes formed was followed by monitoring the optical density at the following wavelengths: 480, 478, and 496 nm for the reactions of I, II, and III, respectively, with IV, and 460 nm for the coupling of V with VI.

When half-lives were longer than ca. 30 sec, measurements were made with a conventional spectrometer (Beckman Models DB or DBG). For the faster reactions (*m*-chlorobenzenediazonium fluoroborate with G-salt), a Durrum-Gibson stopped-flow spectrophotometer which has a mixing time of 2 msec was used. Constant temperature was provided by circulating thermostated water through the reservoir containing the driving syringes and through the mixing and observation block. When mixing was activated, the changes in transmittance at 478 nm were recorded on a Tektronix oscilloscope. A permanent record was obtained on a Polaroid film which allowed for better reading of the change in transmittance with time.

Data Treatment. All kinetic measurements were carried out in the presence of excess coupling component. Thus pseudo-first-order kinetics were observed

$$d[\text{Az}]/dt = k[\text{D}][\text{N}] = k_k[\text{D}] \quad (7)$$

where $[\text{Az}]$, $[\text{D}]$, and $[\text{N}]$ are the concentrations of the formed azo dye, diazonium salt, and the coupling component (naphthol), respectively, k_k is the pseudo-first-order rate constant, and k is the second-order rate constant.

The decomposition of diazonium salts, which runs parallel to the coupling reaction, is also first order with respect to the salt and is allowed for. Thus, k_k is given by

$$k_k = \frac{1}{t(1+q)} \ln \frac{[\text{D}]_0}{[\text{D}]_0 - [\text{Az}]_t(1+q)} \quad (8)$$

$[\text{D}]_0$ is the initial diazonium salt concentration, $[\text{Az}]_t$ is the concentration of azo dye at time *t*, and

$$q = ([\text{D}]_0 - [\text{Az}]_{\infty})/[\text{Az}]_{\infty}$$

Table IX shows data for a sample calculation. All calculations were carried out on a CDC 6400/6500 computer at the computer center of the ETH.

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Ozonation of Hindered Vinyl Alcohols. Production of Free Radicals by Ozonation

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Abstract: Details concerning the formation of an oxy radical by ozonation of trimesitylvinyl alcohol are given. Evidence is presented for a mechanism by which the radical is produced, involving a π complex at one of the mesityl groups of trimesitylvinyl alcohol. Ozonation of 2,2-dimesitylvinyl alcohol at -150° also produces an oxy radical in good yield. The radical is isolated in the form of its dimer. Ozonation of 2,2-dimesitylvinyl alcohol at -78° affords no appreciable amount of the dimer. In contrast to these results, ozonation of 2-mesityl-2-phenylvinyl alcohol gave no sign of a radical or its dimer even at -150° .

In earlier communications, the first production of a stable radical *via* ozonation was reported.^{1,2} The radical was characterized as the oxy radical (VII) of trimesitylvinyl alcohol (I). In this paper, the experimental details of this work are reported, evidence is given for the probable mechanism by which the radical is produced, and the formation of the analogous, but less stable, radical from 2,2-dimesitylvinyl alcohol is described.

The discovery of the oxy radical VII and its formation *via* ozonation came from an extension of our studies of the competition between ozonolysis and epoxide formation during ozonation of hindered olefins.³ We had found that 1,1-dimesitylethylene gave at least 95% epoxide and wanted to study the effect of placing one or two more mesityl groups at the double bond.² Since trimesitylethylene was not known, we studied trimesitylvinyl alcohol, which had previously been synthesized by Fuson.⁴

Upon ozonation of a methylene chloride-methanol solution of trimesitylvinyl alcohol with an equivalent of ozone at

-78° , a black solution was produced which exhibited a strong epr signal, a broad singlet 7–8 G in width, with a g value of 2.004. When the reaction mixture was allowed to come to room temperature, it lost its color and epr signal after a short time. The recovery of trimesitylvinyl alcohol was 55–60%. When the above ozonation was repeated, after which an equivalent of hydroquinone was added to the cold reaction mixture, the color immediately disappeared. The recovery of the vinyl alcohol was 63%. In a third experiment, an equivalent of the efficient radical scavenger, galvinoxyl,⁵ was added to the cold reaction mixture containing the radical. At about -35° , the color and epr signals of both radicals disappeared, and a less than 10% recovery of I was obtained. It was shown that the radical could not be produced by oxygen alone, and that galvinoxyl did not react with the vinyl alcohol (I) at -35° . These data show that the radical was produced by ozone, it must have been present in the reaction mixture to the extent of more than 50%, and the most likely structure of the radical is VII, produced by