

REVIEW COMMENTARY

RATE-EQUILIBRIUM LFER CHARACTERIZATION OF TRANSITION STATES: THE INTERPRETATION OF α

EDWARD S. LEWIS

Department of Chemistry, Rice University, P.O. Box 1892, Houston, Texas 77251, U.S.A.

The effect of substituents on the rate of a reaction and the effect of the same substituents on the equilibrium can often be related by a linear free energy relation (LFER): $\log k^\ddagger = \alpha \log K^\ddagger + \text{constant}$, where k^\ddagger and K^\ddagger are the rate constant and the equilibrium constant, respectively. This review, concentrating on group transfers, adds to many studies describing the use of α to describe the transition state. Although the use of α to describe transition states is general, group transfers constitute a simple class allowing a fairly complete description yet illustrating two often neglected contributions. Group transfers can be described by the Marcus equation relating rate to an average identity rate and the equilibrium constant; a major contributor to the slope, α , of the rate-equilibrium LFER is the variation of identity rates with substituent, rather than reflecting product-like character. Substituent effect LFERs are predominantly attributable to interaction of charges with the substituent. However, α is not an exact measure of the charge on the substituent-containing group, because in a transition state, but often not in a reaction product, there are more remote centers of charge which exert a smaller attenuated effect. A simple treatment of this attenuation for group transfers is proposed. The possibility of application of these ideas to proton transfer reactions and the interpretation of the Brønsted α (or β) is proposed.

INTRODUCTION

The transition state (T.S.) is a wonderfully useful structure for describing rates through absolute reaction rate theory.¹ The T.S. is treated as a stable molecule, with its thermodynamic properties determinable from the rate. Its elemental composition and charge are found from the rate law; its structure in part from the stereochemical course; its volume, vibrational energies and solvation by effect of pressure, isotopic substitution, and solvents, respectively, on the reaction rate.²

Here the concern is the study of charge distribution in the transition state, through the use of substituent effects on the rate. The intent is to provide a framework for the interpretation of the magnitude of these effects. Substituents will be limited to those which can be expected to give linear free energy relations (LFERs) between rate constants and equilibrium constants. The primary example used for illustration will be reaction series which follow the Hammett equation, in both rates

and equilibria, but the results are more general. There are numerous sources for these ideas in addition to those specifically quoted. One which must be mentioned, although it applies to more extensive substituent changes, is the review on the 'Bema Hapothle' by Jencks;³ much of his other work is also very relevant.

SUBSTITUENT EFFECT MEASURES OF TRANSITION STATE LOCATION

If a reaction follows the Hammett equation with ρ^+ (the ρ value for the forward reaction rate) and ρ^\ddagger (the ρ value for the equilibrium with the same series of substituents), then the plot of $\log k^\ddagger$ vs $\log K^\ddagger$ will also be linear with a slope ρ^+/ρ^\ddagger . This plot is often better than the Hammett plots; it is no longer sensitive to the choice of σ scale or to solvent effects on σ . Further, this $\log k^\ddagger$ vs $\log K^\ddagger$ plot is often linear when the substituents are not included in any σ list, or even when structural

changes are well beyond limitations of Hammett substituents. The term ρ^+/ρ^- will nevertheless be used here for such substituent effects.

Implicit in the following treatments is the assumption that the substituent effect, ρ , is measuring only the change in an electrostatic interaction between the reaction center and the substituent, without consideration of the mode of transmission of this interaction. Substituent effects also arise in part from changes in hybridization, as described by Sager and Ritchie;⁴ such sources, or those arising from major conjugative interaction between reaction center and substituent, may not be covered by the treatment.

The term ρ^+/ρ^- may also be applied to reactions which follow the Taft equation. The Brønsted α and β (for general acid and general base catalysis) are also easily shown to be slopes of a $\log k^+$ vs $\log K^-$ plot for a proton transfer. Less direct but still very useful plots are those for reactions of nucleophiles, X^- , where β_{nuc} is the slope of $\log k^+$ vs $\text{p}K_a$ of XH , and for some leaving groups Y^- , where β_{lg} is again the slope of a plot of $\log k^+$ vs $\text{p}K_a$ of YH . These are equivalent to the $\log k^+$ vs $\log K^-$ plots to the extent that the substituent effect for equilibrium proton loss from YH parallels that for (for example) equilibrium carbon loss from RY , or the protonation of X^- parallels the formation of the bond to carbon or other electrophiles, an inexact but generally not very bad approximation. Bernasconi and Fornarini⁵ 'normalized' β_{nuc} to compensate for the differences in substituent effect on the equilibrium protonation vs equilibrium bond formation to carbon. Some of these corrections are found to be 10–20%. A treatment of the quality of this assumption in the gas phase was made by Brauman and Han.⁶

Following custom, we shall use α not only for Brønsted acid catalysis, but more generally for the Brønsted β , β_{nuc} , $-\beta_{\text{lg}}$ and ρ^+/ρ^- . The first general interpretation of this α was that this is a measure of how far the transition state is along the path from reagent to product, having a very small value for a reagent-like T. S. and a value near unity for a product-like T. S.⁷ In fact, if the T. S. is considered as a hybrid of reagent-like and product-like structures, α might be considered to be the weight of the product-like structure, and $1-\alpha$ would be the weight of the reagent-like structure in this hybrid.

The rationale behind this argument is that in proton transfers, in nucleophilic substitution or addition, the charge on the fragment bearing the substituent changes during the reaction. Since the charge changes, α is a measure of the charge change on going to the transition state compared with that on going to the final product. With an exception noted later, this interpretation is used here. The fragment charges so calculated in the T. S. have been called the 'apparent charges.' However, the change from reagent charge to the apparent fragment charge in the transition is not a general measure of the

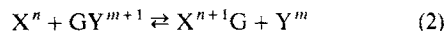
product-like character of the transition state, as will be shown below.

The Hammond postulate⁸ also bears on the question of product-like character in the T. S. The T. S. is very close to the reagent when a highly exothermic reaction has a low activation energy, and very close to the product for a highly endothermic reaction with a low activation energy for the reverse. Another expression of the fraction of product-like character, p , in equation (1) has been derived for a particular analytical form⁹ of a plot E_a vs. ΔH .

$$p = E_a / (2E_a - \Delta H) \quad (1)$$

This is roughly equivalent to the slope of a plot of $\log k^+$ vs. $\log K^+$, and has the value 1/2 for $\Delta H = 0$. We shall explore in more detail the Marcus equation¹⁰ as a relation between $\log k^+$ and $\log K^-$; it has been widely tested and found applicable to alkyl transfers,^{11,12} proton transfer¹³ and hydride transfers^{14,15} in addition to the electron transfers for which it was originally designed.

In the group transfer (2) between nucleophiles, the charge on the reagent X is n , and that on the product Y is m .

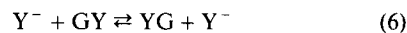
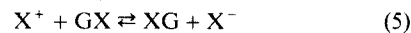


A simply treated case has $m = n$ and most results have $m = n = -1$:



The free energy of activation in the forward direction, ΔG_{YX}^\ddagger , is defined as usual, as is the overall free energy change, ΔG_{YX}° . The Marcus equation is equation (4), where ΔG_{XX}^\ddagger and ΔG_{YY}^\ddagger are the free energies of activation for the identity reactions (5) and (6):

$$\Delta G_{YX}^\ddagger = 1/2(\Delta G_{XX}^\ddagger + \Delta G_{YY}^\ddagger) + 1/2 \Delta G_{YX}^\circ + \frac{\Delta G_{YX}^\circ{}^2}{16[1/2(\Delta G_{YY}^\ddagger + \Delta G_{XX}^\ddagger) - w^R]} \quad (4)$$



and w^R is the work term to bring X^- and GY together. In this form it is assumed that w^R is the same for all X and Y , and is equal to $-w^P$, where w^P is the work to separate the immediate products into free XG and Y^- . Only for the case $m = n$ will this simplification be valid. (The work terms are subject to these assumptions, but in our work, since the term containing w^R is neglected, we can say nothing about it. The w^R can in principle only be evaluated if the $\log k^+$ vs. $\log K^-$ is concave downward.) The term $(1/2)(\Delta G_{XX}^\ddagger + \Delta G_{YY}^\ddagger) - w^R$ is called the intrinsic barrier.

The quadratic term can be shown to allow this expression to conform to the Hammond postulate and the related reactivity–selectivity principle, RSP. It also

(in the case of a constant intrinsic barrier) makes the relation between ΔG_{YX}^\ddagger and ΔG_{YX}° non-linear, although a very large range of ΔG_{YX}° is often required to detect the curvature. However, the slope itself of an experimentally linear part of the plot is informative. For a constant intrinsic barrier, equation (4) can be differentiated with respect to ΔG_{YX}° to give this slope α :

$$\alpha = 1/2 + \Delta G_{YX}^\circ / 8 \{ 1/2(\Delta G_{XX}^\ddagger + \Delta G_{YY}^\ddagger) - w^R \} \quad (7)$$

Unfortunately, this result is not always in agreement with experiment; for several systems with ΔG_{YX}° very nearly zero, α is often different from 1/2. Some experimental values found for alkyl transfers with a changing nucleophile are as follows: for the reaction $\text{ArSO}_3^- + \text{CH}_3\text{O}_3\text{SAr}$, $\alpha = 0.38$;¹⁶ for $\text{ArS}^- + \text{CH}_3\text{SPh}$, $\alpha = 0.54$;¹⁷ for $\text{ArSeMe} + \text{Me}_2\text{Se}^+\text{Ph}$, $\alpha = 0.45$;¹² for $\text{ArSe}^- + \text{MeSePh}$, $\alpha = 0.62$;¹⁸ and for $\text{ArSO}_3^- + \text{PhCOCH}_2\text{O}_3\text{SPh}$, $\alpha = 0.74$.¹⁹ All these values, with the possible exception of the thiophenoxide–thioanisole reaction, differ from 0.5 by well over the experimental error. We must conclude that equation (7) is incorrect, even though the fit to equation (4) has been very good in several tests. The problem lies in the constant intrinsic barrier assumption. The identity rates for the methyl transfers between sulfonates were in fact directly measured, using a ³³S tracer technique.¹⁶ The identity rates for different sulfonate substituents were not constant, instead they varied considerably and fit the Hammett equation with $\rho_{ii} = 0.6$!

For these reactions with ΔG° close to zero, the quadratic term in equation (4) can be neglected, and it becomes equation (8), alternatively written as equation (9):

$$\Delta G_{YX}^\ddagger = (\Delta G_{XX}^\ddagger + \Delta G_{YY}^\ddagger) / 2 + \Delta G_{YX}^\circ / 2 \quad (8)$$

$$\ln k_{YX} = (\ln k_{XX} + \ln k_{YY}) / 2 + (\ln K_{YX}) / 2 \quad (9)$$

and with a variable nucleophile X^- and a constant leaving group we are left with the equation

$$\alpha = d \ln k_{YX} / d \ln K_{YX} = (1/2)(d \ln k_{XX} / d \ln K_{YX}) + 1/2 \quad (10)$$

which allows a value of α different from 0.5 without abandoning the Marcus equation. Equation (10) is applicable whenever the quadratic term is negligible. When the quadratic term is not negligible, the contribution of the identity rate variation can normally not be neglected either, and both the last term in equation (7) and the first term in equation (10) should be used.

The quantitative relation between α and the identity ρ has been developed for a variable Y;¹⁶ the relevant relations between the various ρ values are

$$\rho^+ = (1/2)\rho_{ii} + (1/2)\rho^\ddagger \quad (11)$$

and

$$\alpha = (1/2) + \rho_{ii} / 2\rho^\ddagger \quad (12)$$

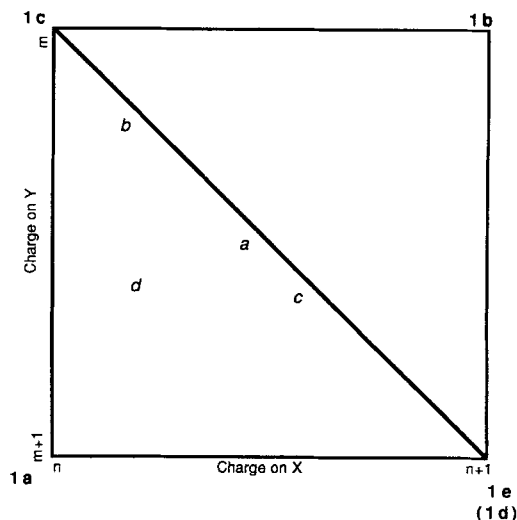


Figure 1. The More O'Ferrall–Jencks plot for a nucleophile substitution, showing the change in charge on X from n to $n+1$ and the change in the charge on Y from $m+1$ to m . The diagonal shown is the position for all one-step identity reactions, and close to that for most alkyl transfers

Hence the data on α with small ΔG_{YX}° can be fitted by a non-zero value of ρ_{ii} of the same sign as ρ^\ddagger for $\alpha > 1/2$, and of the opposite sign for $\alpha < 1/2$.

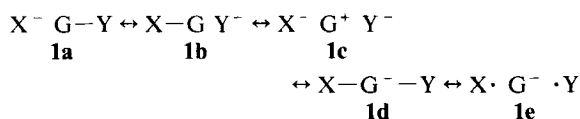
The reason why $\rho_{ii} \neq 0$ is not very subtle, and is immediately obvious when the More O'Ferrall–Jencks two-dimensional diagram²⁰ for a substitution reaction is noted. Figure 1 shows such a diagram for a group transfer. In this plot the reagent is shown at the lower left and the product at the upper right. The vertical axis is shown as the charge on Y, varying from $m+1$ in the reagent to m in the product, and the horizontal axis is the charge on X, varying from n in the reagent to $n+1$ in the product. Alternatively, they might have been labelled $-\beta_{lg}$ and β_{nuc} , respectively. The extreme upper left obviously corresponds to the structure $[\text{X}^n \text{G}^+ \text{Y}^m]^{m+n+1}$, the lower right is for $\text{G} = \text{alkyl}$, best represented as $[\text{X} \cdot^{n+1} \text{G}^- \cdot \text{Y}^{m+1}]^{m+n+1}$.

The location of the transition state along the identity reaction diagonal, here described in terms of non-zero values of ρ_{ii} , is alternatively described by Albery and Kreevoy¹¹ as the tightness parameter, τ . This is unity when $\rho_{ii} = 0$ and can vary from 0 to 2. The two notations do not have an essential difference. A more general treatment by Grunwald²¹ describes the position in terms of 'disparity', referring to motion perpendicular to the reaction coordinate.²² The hypothetical disparity reaction, which has a minimum energy at the transition state for the parent reaction, is the conversion of the species at the upper left of a More O'Ferrall–Jencks diagram such as Figure 1 to the

species at the lower right. Both species can be hypothetical. For alkyl transfers (with $m = n = -1$) the disparity reaction is presemably reaction (13):



Any point on the top left to bottom right diagonal is a potential identity reaction transition state, for it is the line for which the charge on X and that on Y are identical, a requirement for the identity transition state. However, at point *a* these charges are exactly $-1/2$, at point *b* the absolute value of the charges on X and Y are each greater than $1/2$ and at points *c* they are less, the remainder of the total charge resides on G, thus for *b* the charge on G is positive and for *c* G is negatively charged. For many group transfers, notably alkyl transfers between nucleophiles, there is very little deviation from this identity reaction line, because the intrinsic barriers are large, and the range of ΔG_{YX}^\ddagger is not large. The absence of significant selectivity changes with large rate changes²³ is a manifestation of the unimportance of the Marcus quadratic term. Hence for these reactions α differs from 0.5 principally because ρ_{ii} differs from zero. No case of a transition state exactly at *a* has been found. While cases may be found of this perfectly central transition state, it is now clear that it is at best an exceptional model for the transition state for alkyl transfers. The transition state consistent with this More O'Ferrall-Jencks diagram is the resonance hybrid **1**:



thus the transition state at point *a* has equal contributions of **1a** and **1b**, and a combination of **1c**, **1d** and **1e** so that X and Y each have a $1/2$ negative charge. Similarly, the T.S. marked *b* has equal **1a** and **1b**, but a predominance of **1c**, and *c* has an excess of **1d** or **1e**. A transition state not generally found for alkyl transfer, although possible for some faster group transfers, might be *d* with a substantial excess of both **1a** and **1c**.

Transition states near the upper left corner with major contributions of **1c** have been described as 'loose,' 'exploded' or having 'bond breaking before bond making.' In alkyl transfers these pose no problems; they have also been described as borderline S_N1 , and are widely understood. The α -arylethyl transfers between nucleophiles and of methoxymethyl transfers between amines are an extreme example, where the identification of nucleophilic participation is far from trivial.²⁴ Examples with SO_3 or phosphonyl transfer with 'exploded' transition states are also known.²⁵

Transition states near the lower right corner have been described as 'tight' or with 'bond making before bond breaking.' However, with some substituted benzyl and phenacyl transfers, this description requires a con-

tribution of hypervalent carbon, which appears unlikely. The explanation in terms of structure **1e** appears more attractive for carbon transfer, although transfers of groups centered around atoms of higher atomic number can easily have hypervalent contributions; indeed, the hypervalent structure may be a real intermediate.

The predictions of the hybrid **1** lead to an understanding of the deviations from point *a*. Very stable anions (such as sulfonates) lead to an emphasis on structure **1c**, groups G well able to tolerate a positive charge likewise emphasize **1c**, G beyond the first row of the Periodic Table can stabilize **1d**, and X^- and Y^- easily oxidized to $X \cdot$ and $Y \cdot$ will favor the structure **1e** (an electron paired structure with a 'formal' XY bond). The contribution of **1e** accounts for the often observed correlation between rate of attack of a nucleophile and its oxidation potential.²⁶

This introduction of a second dimension in the reaction coordinate diagram constitutes a considerable improvement in the interpretation of α . We no longer require that the total charge be divided only between the leaving group and the attacking group. Hence the transferring group can carry charge of either sign. It should be noted that the variation of the charge on the transferring group is not a modification or an extra term on the Marcus equation; it is contained within the equation as a variable intrinsic barrier present even with modest structural changes.

The charge distributions, calculated in this way and called 'effective charges,' will in this paper hereafter be called 'infinite attenuation charges.' The charge transition state distributions, calculated very simply from α , are not quite correct, even with the assumptions that ρ^+ is sensitive only to electrostatic interactions of substituents with the rest of the molecule, because there are more remote centers of charge in the transition state.

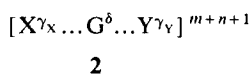
The estimation of transition state 'effective charges' from substituent effects is of course not limited to group transfers, which have clearly defined identity reactions and the Marcus equation is applicable. 'Effective charges' can also be calculated for reactions for which no identity reactions can exist, such as eliminations or additions to multiple bonds. Bernasconi²⁷ has suggested an intrinsic barrier as well as a thermodynamic driving force for such reactions; the intrinsic barrier is that for a reaction in a series having zero free energy change within the collision complex.

Evidence points in many such reactions to different extents of forming or breaking the various bonds in the transition state, described by Sayers and Jencks²⁸ as an 'imbalance' and by Bernasconi²⁷ as the operation of the 'principle of non-perfect synchronization.' It is not possible to attempt to describe the entire charge distribution in such reactions with a single substituent effect study. There are examples where multiple substituents have been fruitfully varied.

The work on alkyl transfers was nearly all done in dipolar aprotic solvents. In these solvents the anions are certainly solvated, but not by the rather specific hydrogen bonds that characterize protic solvents. Work in protic solvents can introduce substituent-dependent solvation which can deform β_{nuc} or β_{lg} . An example by Jencks²⁹ has a negative β_{nuc} , presumed to arise from a necessary prior reversible cleavage of a hydrogen bond to a nucleophile, which is followed by attack with a very small dependence on basicity.

REMOTE CHARGE EFFECTS

The transition state for the group transfer (2) between nucleophiles may be represented by the structure 2, where γ_X is the charge on X, δ is the charge on G and γ_Y is the charge on Y.



In the following approach, we divide these charges sharply and localize them within the fragments X, G and Y. In this way the fragment charges add up to the total charge:

$$\gamma_X + \gamma_Y + \delta = m + n + 1 \quad (14)$$

In relating ρ^+/ρ^- for a variable Y to the charge distribution in the transition state, clearly the largest contributor will be the charge γ_Y . However, we should not neglect the interaction of the more remote charge, δ , with the substituent in Y, or even that of the still more remote charge γ_X with the substituent in Y. We can allow for these interactions by introducing an attenuation factor a to allow for the effect of introducing an extra (partial) bond between δ and Y, and a further attenuation of a^2 for the interactions of γ_X with the substituent in Y. In dealing with normal single bonds an attenuation of a factor of 2–2.5 per CH_2 group introduced between the reaction site and the fragment bearing the substituent has generally been accepted.³⁰ The partial bonds in a transition state are longer than those in stable molecules; we shall use a value of $a = 3$ as a working value, but this is still considered an adjustable parameter, with the constraint $2 < a < \infty$.

The relation between the various charges and α for a variable leaving group becomes equation (15). The value of α can be approximated in this case by $-\beta_{\text{lg}}$.

$$\alpha = m + 1 - (\gamma_Y + \delta/a + \gamma_X/a^2) \quad (15)$$

For the particular case of nucleophilic substitution with $\text{G} = \text{alkyl}$ and $m = n$, it has been noted that there is little difference between identity reactions and unsymmetrical reactions except for the ΔG° term in the Marcus equation. Hence we can carry over the necessary feature of the identity reactions which have $\gamma_Y = \gamma_X$ to the unsymmetric reactions. With this restriction,

Table 1. Transferring group charges, δ , from equation (15) for $a = 3$ and ∞

Reaction	α	$\delta(a = \infty)^a$	$\delta(a = 3)$
$\text{PhSO}_3^- + \text{MeO}_3\text{SAr}$	0.64	-0.28	-0.4
$\text{PhS}^- + \text{MeSAr}$	0.46	-0.08	-0.44
$\text{PhSe}^- + \text{MeSeAr}$	0.38	-0.24	-0.8
$\text{PhSO}_3^- + \text{PhCOCH}_2\text{O}_3\text{SAr}$	0.26	-0.48	-0.58 ^b
$\text{PhSeMe} + \text{Me}_2\text{Se}^+\text{Ar}$	0.46	-0.08	0.00

^aThis value is the 'effective charge'.

^bBecause of the delocalization of the charge in the phenacyl group, with most of the charge on oxygen, the term δ/a^3 was substituted for δ/a in equation (15). This is why the attenuation correction is smaller than the example immediately above.

equation (15) together with equation (14) allow (for any value of a) a solution of γ_Y and δ from an experimental α .

These values (for $a = 3$) differ from the earlier 'infinite approximation' values. The values for some reactions given before are presented in the Table 1.

The use of equation (15) to calculate the charge distribution is, of course, only a first approximation to the effect of remote charges. The direction of the effect when the attenuation is finite can be estimated by considering the limit for $a = 1$. In this case equation (15) reduces to

$$\alpha = m + 1 - (m + n + 1) = -n \quad (16)$$

and when the substituent containing group is anionic, $\alpha = 1$, and only the charge on the attacking group is relevant. Similarly, when the attacking nucleophile is neutral, regardless of the charge on GY , $\alpha = 0$. No information on the charge distribution is now contained in α . While this limit is meaningless, these limits point to the direction that finite a can change α for a particular charge distribution. The precision of calculation of the charge distribution falls with a , and even the $a = 3$ values of δ in Table 1 are less precise than the $a = \infty$ values.

A similar equation can be derived when the changing reagent is the nucleophile X in reaction (2):

$$\alpha = (\gamma_X + \delta/a + \gamma_Y/a^2) - n \quad (17)$$

In this case α can be approximately measured as β_{nuc} . The same assumption for $\text{G} = \text{alkyl}$ of $\gamma_X = \gamma_Y$ can be applied if $m = n$, and the two equations (14) and (17) can be solved for γ_X and δ , given α . Again, the limits for $a = 1$ are $\alpha = 1$ if $m = 0$, corresponding to +1 net charge on the transition state, and $\alpha = 0$ if the transition state has a net charge of -1, $m = -1$.

Equations (15) and (17) also apply to cases where $m \neq n$. In this case, for example the Menschutkin reaction, γ_X most likely is of the opposite sign from γ_Y , and the assumption that they are equal is clearly wrong.

The Menshutkin reaction has been extensively studied from many aspects; many are quoted by Ando *et al.*,³¹ Arnett and Reich,³² Matsui and Tokura³³ and Abraham³⁴. Thus equation (15) or (17), which now have three unknowns, can no longer be solved with equation (14) for the charge distribution. Yet the effect is still present, and the changes can be significant. It is still possible to solve the $a = \infty$ case, where α for the leaving group variation is $\alpha = m + 1 - \gamma_Y$, or for a varying nucleophile, where $\alpha = \gamma_X - n$, but a solution for δ requires both. For any particular charge distribution, α may come closer to zero, because of the influence of remote charges, regardless of whether the attacking neutral nucleophile or the leaving group contains the substituents.

There are few data on the Menshutkin reaction in which both the leaving group and the attacking nucleophile can be varied to establish α at both ends in the same system, but the work of Ando and co-workers^{31,35} is a distinct exception. Although this work on substituted dimethylanilines with various substituted benzenesulfonate esters was designed to study the carbon and hydrogen isotope effects on the transferring group, it also yields substituent effects on the rates summarized in Table 2. The ρ^+ values are newly calculated.

There are no comparable data on the equilibrium; we can find several measures of ρ^- for protonation of substituted dimethylanilines in protic solvents and they fall in the range -2.5 to -4 . The value used ($\rho^- = -4.2$) may be more reliable since it is in the solvent dimethylformamide but it is for the unmethylated anilines.³⁶ The value of β_{nuc} so estimated is about 0.55. The probable benzyl group positive charge is likely delocalized enough so that the infinite attenuation approximation is almost adequate.

Table 2. Estimated α and ρ values for $\text{YC}_6\text{H}_4\text{NMe}_2 + \text{GO}_3\text{SC}_6\text{H}_4\text{X}$ from refs 29 and 33

Y	G	X	ρ^+	ρ^- (est.)	α^a
<i>p</i> -CH ₃	<i>p</i> -Bromobenzyl	Variable	+2.06 ^b	> +2.94 ^c	<0.70
<i>p</i> -OCH ₃	Benzyl	Variable	+2.17 ^b	> +2.94 ^c	<0.74
<i>p</i> -CH ₃	Benzyl	Variable	+2.10 ^b	> +2.94 ^c	<0.71
H	Benzyl	Variable	+2.04 ^b	> +2.94 ^c	<0.69
Variable	<i>p</i> -Bromobenzyl	<i>p</i> -Cl	-2.3 ^b	-(>4.2) ^d	<0.55
Variable	Benzyl	<i>p</i> -Cl	-2.33 ^b	-(>4.2) ^d	<0.55
Variable	CH ₃	<i>p</i> -Br	-2.45 ^c	-4.2 ^f	0.58

^a This is ρ^+/ρ^- for the sulfonate leaving groups and β_{nuc} for the amines.
^b In acetone.

^c This is the value for equilibrium loss of sulfonate groups in sulfolane; the corresponding value in acetone would presumably be larger.

^d This is the value for acidity of substituted anilinium ions in the higher dielectric solvent dimethylformamide³⁶

^e In acetonitrile.

^f As in footnote d except there is no significant dielectric constant correction in this acetonitrile solvent.

The α for the leaving group variation may be estimated using ρ for the equilibrium loss of substituted sulfonates ($\rho = +2.94$) from methyl arenesulfonates in sulfolane;¹⁶ it may be higher in the lower dielectric acetone. Neglecting this solvent change on ρ^- , $\alpha = 2.1/2.94 = 0.7$. Such a value appears to indicate a product-like transition state. However, assuming an identity rate variation similar to that for the methyl transfer case, the corresponding infinite attenuation charge development on the sulfonate might be nearly this large for a transition state with little bonding to the nucleophile. With all the uncertainties, an α for the leaving group appears reasonable for a rather central T.S. with nearly equal product-like and reagent-like character.

In sum, these substituent effects are not entirely incompatible with having about equal contributions of reagent-like and product-like character, as has been found for the negatively charged transition states for methyl transfer, but the very rough β_{nuc} estimates of α do appear to be large. The variation of ρ^+ for variation of either group for changes in the other group fall in a systematic order and might therefore be suitable for analysis by Jenck's method,^{3,37} but it is not clear how significant these variations are.

To the extent that the infinite attenuation is a good approximation, the information on the charge distribution is given by $\delta = -(\beta_{\text{lg}} + \beta_{\text{nuc}}) \approx +0.2$, when the charge on the attacking amine is β_{nuc} and that on the leaving group is β_{lg} (a negative number). Unfortunately, the large uncertainties on ρ for the amine $\text{p}K_{\text{a}}$ values and the imperfect correlation between ρ^+/ρ^- and β_{nuc} or $-\beta_{\text{lg}}$ is too great to give this estimate of δ much credibility, even if it is plausible.

A further possibly major problem in dealing with the Menshutkin reaction within the context of the Marcus equation is the work term w^{R} . Because w^{R} involves the formation of a neutral complex, where w^{P} resembles an intimate ion-pair dissociation, it is unreasonable to assume that $w^{\text{R}} = -w^{\text{P}}$. Hence the measured equilibrium constant differs from that for conversion of the reagent complex to the product complex.

THE BRØNSTED CATALYSIS LAW

The most deeply rooted notion of measuring the extent of product-like character from substituent effects is in the interpretation of the Brønsted catalysis law. We can now ask if the special effects attributed to variable identity rates and to the effects of remote charges can influence the interpretation of structural change on proton transfer rates.

In alkyl transfers the value of α was shown not to represent the amount of product-like character when in the More O'Ferrall-Jencks diagram the transition state lies well off the diagonal from reagent to product. The question then to be asked is whether or not there is a corresponding effect on the Brønsted coefficients.

The discussion is limited to variable oxygen and

nitrogen acids and bases, and is within the context of the Marcus equation. It will avoid carbon acids and bases such as the 'anomalous' nitro compounds, which have been extensively discussed and are now fairly well understood.³⁸

The transition states for alkyl transfers that are off the diagonal in the More O'Ferrall-Jencks diagram are characterized by having varying identity rates. Using the same arguments for proton transfers brings up the question of the magnitude of identity rates for oxygen or nitrogen acid-base pairs. Since a large fraction of known proton transfer rates between oxygen or nitrogen have been shown to be nearly diffusion controlled, it has been generally accepted that all these reactions have low and essentially the same barriers. Eigen³⁹ has described normal acid-base reactions as those which are diffusion controlled in the thermodynamically favourable direction. Nevertheless, in his review, most of his examples are one or two orders of magnitude slower than the diffusion-controlled limit for the thermodynamically neutral cases; thus we are not forced to assume that identity reactions involving oxygen or nitrogen acid-base pairs are necessarily diffusion controlled. The diffusion control is not related formally to the Marcus equation, which is concerned with the barrier to be overcome after a collision complex is formed. It is therefore essentially a unimolecular process with a barrier less than about 5 kcal mol⁻¹. We can reproduce the Eigen curves with a barrier of as high as 7 kcal mol⁻¹.

We can ask whether a barrier can vary within this limit of 5-7 kcal that is correlated with acid strength. For generality, we should stay well within that limit, with perhaps a range of $\Delta G_{\ddagger}^{\ddagger}$ of 2 kcal mol⁻¹ for a range of free energies of 8 kcal mol⁻¹ corresponding to a range of K_a values of about 10⁶. In the range near $\Delta G^{\circ} = 0$, equation (10) then gives

$$\alpha = \pm 1/2 \times 2/8 + 1/2 = 0.5 \pm 1.25 = 0.375 - 0.625 \quad (18)$$

This range is plausible even for diffusion-controlled identity reactions resulting from a correlation of the identity rate with acid strength.

It has been customary to attribute the variation of α from 1/2 to represent the derivative of the quadratic term as shown in equation (7). Since in alkyl transfer this interpretation is almost always wrong, we must ask whether the neglect of the quadratic term is also justifiable for proton transfers. Clearly this depends on the intrinsic barrier, and also on work terms. For reactions with rate constants less than 1 l mol⁻¹, and with equilibrium constants within 5-6 powers of ten of unity, the quadratic term contributes very little, unless w^R is large.⁴⁰ It is of interest that the Marcus equation has been fitted to some curved Brønsted plots for slow reactions, but the fits usually require a very large w^R . When the Brønsted plot for slow reactions is experimentally linear, and the equilibrium constant is either near unity or covers a

wide range, we may assume that there is no significant contribution of the quadratic term, and we are *not* measuring fraction of product-like character when α is determined. Here then we suggest two other sources of $\alpha \neq 0.5$.

Chiang *et al.*⁴¹ have perhaps found an example of the varying identity barrier in their discussion of the peculiar behavior of calculated work terms in fitting ketonization of enols to the Marcus equation. They use instead a variable Albery-Kreevoy¹¹ τ value and write, following Kreevoy and Lee:

$$\alpha = 0.5(1 + \Delta G/\Delta G_0^{\ddagger}) + 0.5(1 - \tau) \quad (19)$$

However, writing this is compatible with the Marcus equation only if it is recognized that $\tau \neq 0$ corresponds to a variable identity rate, which is unquestioned in the hydride transfers of ref. 14, 15, but has not previously been recognized for proton transfers. The $1 - \tau$ term corresponds exactly to the first term of equation (10).

The remote charge effect must also contribute, although the formal treatment represented by equations (15) and (17) may be inadequate. Let us consider several cases in which the acid or base represented as HA or B is the one of variable structure.

As in the case of alkyl transfer, for a transfer, for a transition state charge on the A fragment of 0.5 less than the charge on HA in a reaction with a neutral substrate, α will be less than 1/2 because of the finite attenuation, it will be less than 1/2 if a cationic substrate is being protonated and more than 1/2 if an anionic substrate is being attacked.

Similarly, if the charge on B in the transition state is 0.5 more than B, α will be more than 1/2 for proton abstraction from a cationic species and less than 1/2 for a neutral or anionic species.

No matter what the charge type, the finite attenuation will deform the observed α in the direction determined mostly by the charge on the substrate. The finite attenuation makes α different from the charge change at the variable structure fragment. At present, there seems to be no basis for selecting a value of a to allow a quantitative measure of this effect. However, the usual Brønsted relations for a variety of bases with a single substrate will all be deformed in the same direction. Only differences in α influenced by a change in charge of the substrate will have an effect. There seem to be few data of this sort, so the opportunity to compare the data with experiment appears to be lacking.

We conclude that many slow proton transfers, in addition to slow alkyl transfers, may have transition states as close to reagents as to products, and yet have a value of α significantly different from 1/2.

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