Tetrahedron Vol 41 No 16 pp 3219 to 3234 1985
Printed in Great Britain

0040-4020/85 $3 00+ 00

THE PRINCIPLE OF IMPERFECT SYNCHRONIZATION
I IONIZATION OF CARBON ACIDS

Claude F Bernasconi

Contribution from the Thimann Laboratories of the
University of California, Santa Cruz, California 95064

(*Received in USA* 25 *February* 1985)

Abstract The Principle of Imperfect Synchronization (PIS) states that a product stabilizing factor will lower the intrinsic rate of a reaction if it develops late, but increase the intrinsic rate if the factor develops early It is shown in this paper that much of the structure-reactivity behavior of proton transfers involving carbon acids can be understood in the context of this principle The factors discussed include the effect of resonance near the reaction site as well as in remote substituents, the polar effect of remote substituents, and the effects of solvation of reactants and products A simple mathematical formalism is developed to describe the contribution of each factor to the intrinsic rate constant The possible reasons why there is a lack of synchronization between the various events which occur during the reaction are also discussed

Proton transfers involving carbon acids are usually slower than those involving normal acids [1] Furthermore, among the carbon acids there are large variations in reactivity Several factors are believed to be responsible for this behavior They include (a) the poor hydrogen bonding capability of carbon acids and carbanions[1a,1d,2]; (b) the need for structural reorganization in forming resonance stabilized carbanions[1,3,4]; (c) the need for solvent reorganization [3,5,6] Table I lists approximate intrinsic rate constants (k_o) and intrinsic barriers ($\Delta G_o^{\ddagger}$) for representative examples k_o and $\Delta G_o^{\ddagger}$ are defined for $\Delta G^o = 0$ (more on definitions below) and thus they allow comparisons among various systems to be made which are normalized to the same pK_a of the carbon acid

The trends in $k_o(\Delta G_o^{\ddagger})$ suggest that the decrease in k_o, or increase in $\Delta G_o^{\ddagger}$, parallels the increase in the resonance stabilization of the carbanion This has generally been understood in the context of the Principle of Least Nuclear Motion (PLNM)[4]: the intrinsic barrier increases with the increase in structural and solvational reorganization that goes along with the formation of more strongly resonance stabilized carbanions

Table I Approximate Intrinsic Rate Constants and Intrinsic Barriers for Proton Transfers from Carbon Acids

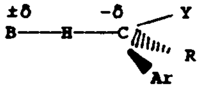
C-H acid	Base	Solvent	log k_o	$\Delta G_o^{\ddagger}$	Ref
$RCH(CN)_2$	R_2NH	H_2O	7.0	7.9	1d
$4\text{-}NO_2\text{-}C_6H_4CH_2CN$	R_2NH	50% Me_2SO-50% H_2O	3.7	12.4	7
	R_2NH	H_2O	3.1[a]	13.2	8
$CH_2(COCH_3)_2$	$RCOO^-$	H_2O	2.9	13.5	9
	R_2NH	H_2O	2.6	13.9	9
$2,4\text{-}(NO_2)_2\text{-}C_6H_3CH_2CN$	R_2NH	50% Me_2SO-50% H_2O	2.7	13.7	7
$CH_3CH(NO_2)_2$	$RCOO^-$	H_2O	1.0	16.0	10
$PhCH_2NO_2$	R_2NH	H_2O	-1.0	18.8	11
	$RCOO^-$	H_2O	-2.0	20.1	11

[a] Estimated from detritiation rates, assuming a tritium kinetic-isotope effect of 14

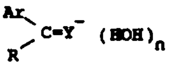
A concomitant phenomenon is that development of resonance invariably lags behind the bond changes associated with proton transfer,[12-14] a phenomenon referred to as "imbalance "[6,15] It manifests itself by an inequality between the Bronsted β_B values (variation of base)[16] and the Bronsted α_{CH} (variation of C-H acid) [16] Examples of imbalances are shown in Table II

The inequality $\alpha_{CH} > \beta_B$ [16] is usually attributed to an exalted α_{CH} value whereas β_B is assumed to be "normal" and to be an approximate measure of the degree of proton transfer in the transition state The enhanced value of α_{CH} comes about because in the transition state

(1) the negative charge is mainly on carbon while in the product ion (2) it is mainly on the Y-group



1



2

3

The effect is greatest in hydroxylic solvents as seen by comparing $\alpha_{CH} - \beta_B$ for $ArCH_2NO_2$ in water and Me_2SO (Table II) This difference can be understood in terms of greater charge dissipation in 2 by the hydrogen bonding solvent [17]

Incidentally, for the arylnitromethanes the imbalance is so strong that in water $\alpha_{CH} > 1$, a finding generally called the "nitroalkane anomaly "[18] Bordwell et al [12] have suggested that there is actually an intermediate or "virtual" intermediate (3) whose formation via 1 is rate limiting, a proposal which originally goes back to Cram [19] The recent work of Koch[20] also suggests the existence of intermediates which are hydrogen-bonded to carbon

There is one apparent exception in Table II, the 2-X-4-nitrophenylacetonitrile system for which $\alpha_{CH} < \beta_B$ The reason for this inversion is that α_{CH} has a different meaning here (called α''_{CH}) as will be discussed in a later section

The Principle of Imperfect Synchronisation; Definitions and Assumptions A major goal of this paper is to show that there exists a direct relationship between the lag in resonance development (including solvation) and the reduction in the intrinsic rate constants The consequences of this lack of synchronization may be called the "Principle of Imperfect Synchronization"[21] (PIS) This principle states that a product stabilizing factor (e g , resonance or solvation) lowers k_o if it develops late but increases k_o if it develops early By virtue of the principle of microscopic reversibility the PIS may also be defined with respect to reactants: a reactant stabilizing factor increases k_o if it is lost late but lowers k_o if it is lost early Note that for product or reactant de̲stabilizing factors the inverse relationships hold

We shall define the terms "late" and "early" in relation to the "primary process" which we take to be the proton transfer, or, probably better, the transfer of the negative charge from the base to the carbon acid Following common practice we assume that β_B (α_{BH}) is a satisfactory approximation of the progress of charge transfer in the transition state, except in some special cases to be discussed

The factors which lead to extra stabilization (destabilization) of products or reactants may be viewed as "secondary process " If the primary and secondary process occur in a single

Table II Transition State Imbalances in Proton Transfers [a]

C-H acid	Base	α_{CH}	β_B	$\alpha_{CH}-\beta_B$	Ref
$PhCH_2CH(CN)_2$	$RCOO^-$		1 0	0	13
$ArCT(CN)_2$	$ClCH_2COO^-$	0 98			13
$ArCH_2CH(COMe)COOEt$	$RCOO^-$	0 76	0 44	0 32	13
$ArCH_2NO_2$	R_2NH	1 29	0 55	0 74	12a
$ArCH_2NO_2$	$RCOO^-$	0 92[c]	0 50[c]	0 42[c]	17
$2,4\text{-}(NO_2)_2C_6H_3CH_2C_6H_3\text{-}2\text{-}X\text{-}4\text{-}NO_2$	R_2NH	0 87[b,d]	0 45[b]	0 42[b,d]	14
$2\text{-}X\text{-}4\text{-}NO_2\text{-}C_6H_3CH_2CN$	R_2NH	~0 41[b,d]	~0 62[b]	~-0 21[b,d]	7

[a] In water unless stated otherwise [b] In 50% Me_2SO-50% water [c] In Me_2SO [d] α''_{CH} instead of α_{CH}, see text under the heading "Remote Substituents B Resonance and SSAR Effects "

step, "early" and "late" refer to different extents of development within the same transition state Alternatively, if the two processes occur in separate steps "early" implies that the secondary process is a preequilibrium, "late" that it is a postequilibrium

The definition of k_o and $\Delta G_o^{\ddagger}$ to be used are the following For the general reaction

$$RR'CHY + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} RR'C\overset{-}{=}Y + BH \tag{1}$$

k_o is equal to $k_1 = k_{-1}$ when $K_1 = 1$ ($\Delta G^o = 0$) and $\Delta G_o^{\ddagger} = 2\ 3RT\ (\log k_o - \log (\bar{k}T/h))$ If B has more than one acceptor site and/or BH contains more than one equivalent proton this is sometimes taken into account by the use of statistical factors[1b] although for the broad picture to be developed in this paper these statistical corrections are of minor importance The k_o values cited in this paper were generally calculated by linear interpolation or extrapolation of Bronsted plots obtained by varying B (BH) Thus, the relationship between k_o and any point on the Bronsted plot is

$$\log k_o = \log k_1 - \beta_B \log K_1 = \log k_{-1} + \alpha_{BH} \log K_1 \tag{2}$$

We prefer this method over those which are based on the Marcus[22,23] equation because no theoretical assumptions are being introduced

Glossary In the equations to be developed we shall use the following symbols The site at which an effect occurs is indicated by a capital letter, either in parentheses or as subscript: Y = substituent directly attached to carbanion site; B or B^- = buffer base; BH or BH^+ = buffer acid; X = remote substituent; TS = transition state The nature of the effect to be discussed is symbolized by a lower case letter, either as superscript or subscript: r = resonance, s = solvation; r,s = combined resonance and solvation, d = desolvation; p = polar; st = steric; el = electrostatic

Resonance In keeping with Bordwell's[12] proposal we start with the simplest assumption, namely that resonance develops in a separate, postequilibrium step, as shown in eqs 3a and 3b Note that the intermediate may or may not be hydrogen bonded to BH,[12,19,20] a point taken up in the section on transition state effects The equilibrium constant K_r is a measure of resonance stabilization

$$RR'CHY + B \underset{k'_{-1}}{\overset{k'_1}{\rightleftharpoons}} RR'\bar{C}Y + BH \tag{3a}$$

$$RR'\bar{C}Y \overset{K_r(Y)}{\rightleftharpoons} RR'C\overset{-}{=}Y \tag{3b}$$

The relationship between the <u>observed</u> rate and equilibrium constants (k_1, k_{-1}, $K_1 = k_1/k_{-1}$, see eq 1) to the quantities shown in eqs 3a/3b is

$$k_1 = k'_1 \tag{4}$$

$$k_{-1} = k'_{-1}/K_r(Y) \tag{5}$$

$$K_1 = K'_1 K_r(Y) \tag{6}$$

In order to evaluate the effect of resonance stabilization on the <u>intrinsic</u> rate constant (k_o) we compare k_o for reaction 1 (equivalent to the combined eq 3a/3b) with k_o for eq 3a <u>Qualitatively</u> it is obvious that k_o for reaction 1 is lower than for reaction 3a This is because reaction 1 has a larger equilibrium constant ($K'_1 K_r(Y)$ with $K_r(Y) \gg 1$) than reaction 3a (K'_1), yet the rate constants in the forward direction are the same (eq 4), indicating that the transition state of reaction 1 is not able to benefit from the resonance stabilization of the product This is schematically shown in Fig 1A

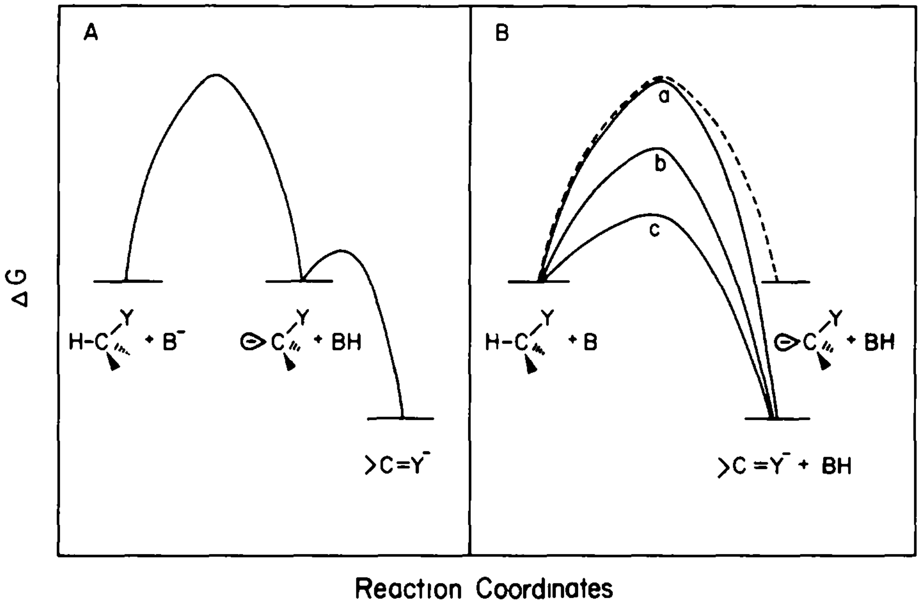


Figure 1 Schematic free energy vs reaction coordinate profiles A: refers to the situation where there is an actual tetrahedral intermediate and resonance develops in a separate postequilibrium step B: refers to situation where the tetrahedral intermediate is only hypothetical Curve a resonance development has made no progress in the transition state, ($\alpha_r^Y = 0$), curve b: resonance development is synchronous with charge transfer ($\alpha_r^Y = \beta_B$); curve c resonance is fully developed in the transition state ($\alpha_r^Y = 1\ 0$)

Quantitatively we can express the decrease in the intrinsic rate constant by

$$\delta \log k_o^r(Y) = \log k_o(\text{eq } 1) - \log k_o(\text{eq } 3a) = -\beta_B \log K_r(Y) \tag{7}$$

The relationship between the quantities of eq 7 is shown in Fig 2 The solid line represents the Bronsted plot (variation of K_1' and k_1' induced by changing pK_a^{BH}) of slope β_B for reaction 3a k_1' at $\log K_1' = 0$ corresponds to k_o for reaction 3a

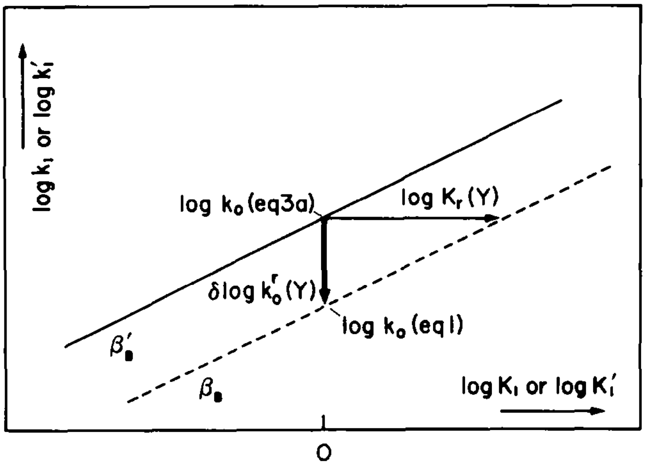


Figure 2. Effect on k_o of delayed resonance development according to eq 7 (resonance develops in postequilibrium)

The equilibrium constant for eq 3b is represented by the horizontal arrow labeled $\log K_r(Y)$ The point on the ordinate at the end of this arrow corresponds to the rate constant k_1 for reaction 1, which has the same value as k_1' The equilibrium constant for reaction 1 at this particular point is $K_r(Y)$ since we started at a point where $K_1' = 1$

The intrinsic rate constant, k_o, for reaction 1 is then found by extrapolating the actual rate constant k_1 back to the point where log $K_1 = 0$, as shown by the dashed line The dashed line represents the Bronsted plot for reaction 1; since reactant and transition state are the same for reactions 1 and 3a, the Bronsted slope β_B for reaction 1 is the same as that for reaction 3a (β'_B) Because of $\beta_B = \beta'_B$ eq 7 holds not only for $\delta\log k_o^r(Y)$ at log $K_1 = 0$ but for the difference in the rate constants of reactions 1 and 3a at any value of the equilibrium constant

The assumption that the reaction occurs in separate steps is not really necessary If the reaction occurs in a single step the effect of the delayed development of resonance k_o can be described by

$$\delta\log k_o^r(Y) = (\alpha_r^Y - \beta_B)\delta\log K_1^r(Y) \qquad (8)$$

$\delta\log k_o^r(Y)$ is defined as before except that eq 3a/3b are now hypothetical reactions For this reason log $K_r(Y)$ has been replaced by the symbol $\delta\log K_1^r(Y)$ which is a measure of the enhancement of K_1 that arises from the resonance stabilization of the product ion α_r^Y which should not be confused with the Bronsted α_{CH} or α_{BH} values, is a parameter defined as $\delta\log k_1^r(Y)/\delta\log K_1^r(Y)$; it measures what fraction of the resonance stabilization of the product ion has developed in the transition state

For $\alpha_r^Y < \beta_B$, $\delta\log k_o^r(Y)$ is negative, and for the limiting case $\alpha_r^Y = 0$ equations 7 and 8 are equivalent, with $\delta\log K_1(Y) = \log K_r(Y)$ This limiting case is represented in Fig 1B by curve a For $\alpha_r^Y = \beta_B$, which implies perfect synchronization between charge transfer and resonance development (Fig 1B, curve b), there is no change in k_o, while for the (unrealistic) case $\alpha_r^Y > \beta_B$ (Fig 1B, curve c) the intrinsic rate constant would be enhanced by the resonance effect

The quantities of eq 8 are illustrated in Fig 3 for the case $\alpha_r^Y < \beta_B$ but with $\alpha_r^Y > 0$ Just as in Fig 2 the solid sloping line labeled β'_B represents the Bronsted plot for reaction 3a which however now is a hypothetical reaction Thus the rate constant k_1 at log $K_1 = 0$ on the solid line is equal to k_o for the hypothetical reaction 3a

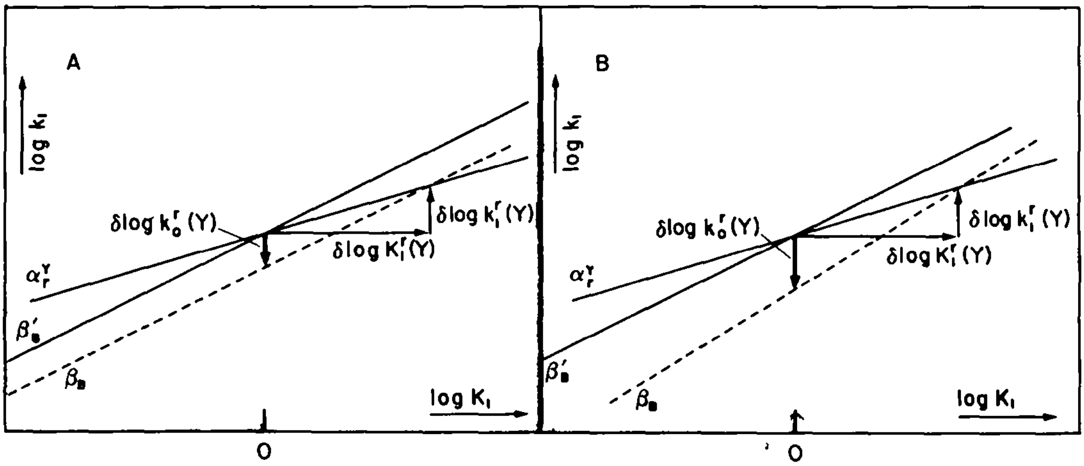


Figure 3. Effect on k_o of delayed resonance development according to eq 8 A $\beta_B = \beta'_B$ B $\beta_B > \beta'_B$ Note that $\delta\log k_1^r(Y) = \alpha_r^Y\delta\log K_1^r(Y)$

The horizontal arrow ($\delta\log K_1^r(Y)$) represents the increase in K_1 which comes from the resonance effect, the vertical arrow ($\delta\log k_1^r(Y) = \alpha_r^Y\ \delta\log K_1^r(Y)$) the increase in k_1 which goes along with it Thus the point at the end of the $\delta\log k_1^r(Y)$-arrow corresponds to the rate constant k_1 of the (actual) reaction 1 for the situation where the log of the equilibrium constant has the value $\delta\log K_1$ The intrinsic rate constant, k_o, for reaction 1 is then found by extrapolating back to the point where log $K_1 = 0$, as shown by the dashed line

It should be noted that Fig 3A is based on the implicit assumption that β_B' for the hypothetical reaction 3a (solid line) is the same as β_B for the actual reaction 1 (dashed line) When this is the case eq 8 not only holds for $\delta\log k_o^r(Y)$ but for $\delta\log k_1$ at any value of K_1, just as with eq 7 On the other hand, if β_B and β_B' are different, as shown in Fig 3B, eq 8 is still valid but only for $\delta\log k_o^r(Y)$ (i e , when $\log K_1 = 0$) with β_B referring to the experimental Bronsted slope

Solvation of Carbanion For simplicity we shall assume that solvation occurs mainly at the site of negative charge development on the Y-group Other possible solvation effects will be discussed below

We shall first assume that solvation of the product ion occurs in a separate postequilibrium step, as shown in eqs 9a/9b [24]

$$\mathrm{RR'CHY} + \mathrm{B} \underset{k_{-1}''}{\overset{k_1''}{\rightleftharpoons}} \mathrm{RR'C}\overset{-}{\cdots}\mathrm{Y} + \mathrm{BH} \qquad (9a)$$

$$\mathrm{RR'C}\overset{-}{\cdots}\mathrm{Y} + \mathrm{sol} \overset{K_s(Y)}{\rightleftharpoons} \mathrm{RR'C}\overset{-}{\cdots}\mathrm{Y\ sol} \qquad (9b)$$

The effect of solvation on k_o can then be described by

$$\delta\log k_o^s(Y) = -\beta_B\log K_s(Y) \qquad (10)$$

which is completely analogous to eq 7 Alternatively, if solvation occurs in the same step as proton transfer we have, in analogy to eq 8,

$$\delta\log k_o^s(Y) = (\alpha_s^Y - \beta_B)\delta\log K_1^s(Y) \qquad (11)$$

where α_s^Y measures the progress of product solvation at the transition state

The combined effects of delayed resonance and delayed solvation are thus given by

$$\delta\log k_o^r(Y) + \delta\log k_o^s(Y) = (\alpha_r^Y - \beta_B)\delta\log K_1^r(Y) + (\alpha_s^Y - \beta_B)\delta\log K_1^s(Y) \qquad (12)$$

It should be realized that resonance and solvation are not easily separated in practice because differences in the solvation of Y (e g , hydrogen bonding) are expected to change the relative weight of the canonical form $\mathrm{RR'C{=}Y^-}$ within the resonance hybrid Hence one expects that $\delta\log K_1^s(Y)$ and $\delta\log K_1^r(Y)$ are interdependent

If the progress of solvation were strictly coupled to the degree of resonance development, i e , if $\alpha_s^Y = \alpha_r^Y$, eq 12 would simplify to

$$\delta\log k_o^{r,s}(Y) = (\alpha_{r,s}^Y - \beta_B)\delta\log K_1^{r,s}(Y) \qquad (13)$$

with

$$\delta\log k_o^{r,s}(Y) = \delta\log k_o^r(Y) + \delta\log k_o^s(Y) \qquad (14)$$

$$\delta\log K_1^{r,s}(Y) = \delta\log K_1^r(Y) + \delta\log K_1^s(Y) \qquad (15)$$

$$\alpha_{r,s}^Y = \alpha_r^Y = \alpha_s^Y \qquad (16)$$

In a later section we shall show that it is more likely that $\alpha_s^Y < \alpha_r^Y$ Nevertheless, if one prefers to express the combined effects of delayed resonance and delayed solvation by a single equation, eq 13 can still be used, with

$$\alpha_{r,s}^Y = \frac{\alpha_r^Y\delta\log K_1^r(Y) + \alpha_s^Y\delta\log K_1^s(Y)}{\delta\log K_1^r(Y) + \delta\log K_1^s(Y)} \qquad (17)$$

We shall mainly adopt eq 13 in our further discussion

The combined effects of delayed resonance and delayed solvation of the Y-group can adequately explain the trend in k_o shown in Table I Assuming that $\alpha_{r,s}^Y - \beta_B$ does not vary dramatically from one system to another, this trend just reflects the increase in $\delta\log K_1^{r,s}(Y)$ (see eq 13) as we go down the list

There are other PIS effects, though, which can play a significant role, they are now discussed

(De)Solvation of Anionic Base (B^-) The frequently reported negative deviation of the hydroxide ion point from Bronsted plots[23] is most likely the result of such desolvation which is ahead of proton transfer in the transition state The strong curvature in the Bronsted plots observed with highly basic oxyanions in proton transfers and nucleophilic reactions has been attributed to the same phenomenon [9,25]

The situation is analogous to the solvation of the product ion, except that the direction of the reaction is reversed and no interdependence with a resonance effect exists Thus, it is a reactant which is being partially desolvated, a process which again might be described as a preequilibrium[25d] (eqs 18a/18b),

$$B^- \,\text{sol} \overset{K_d(B^-)}{\rightleftharpoons} B^- + \text{sol} \qquad (18a)$$

$$B^- + RR'CHY \underset{k_{-1}''}{\overset{k_1''}{\rightleftharpoons}} RR'\bar{C}{-}Y\,\text{sol} \qquad (18b)$$

or as an event which is concerted with the proton transfer

If desolvation is a preequilibrium we have, as shown by Jencks,[25d]

$$\delta\log k_o^d(B^-) = (1-\beta_B)\log K_d(B^-) \qquad (19)$$

$K_d(B^-)$ is the equilibrium constant for partial desolvation of the base Since desolvation is energetically expensive, $\log K_d(B^-)$ is negative and hence $\delta\log k_o^d(B^-)$ is also negative

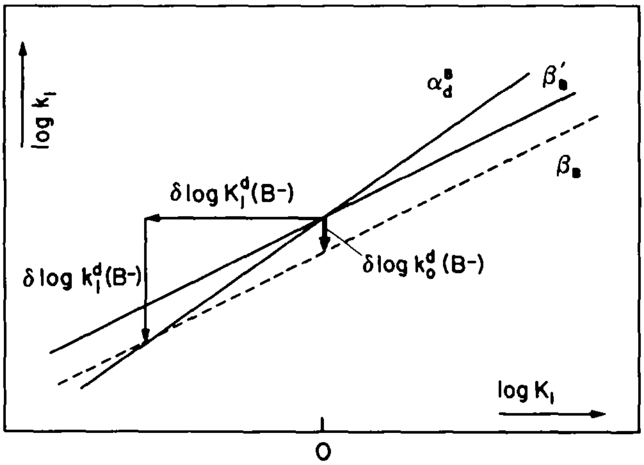


Figure 4. Effect on k_o of desolvation of the base which is ahead of proton transfer according to eq 20, for case where $\beta_B = \beta'_B$ Note that $\delta\log k_1^d(B^-) = \alpha_d^{B^-}\,\delta\log K_1^d(B^-)$

If desolvation occurs in the same step as proton transfer, we have

$$\delta\log k_o^d(B^-) = (\alpha_d^{B^-} - \beta_B)\delta\log K_1^d(B^-) \qquad (20)$$

$\delta\log K_1^d(B^-)$ measures the reduction in K_1 which is due to the solvation of B^- while $\alpha_d^{B^-} = \delta\log k_1^d(B^-)/\delta\log K_1^d(B^-)$ measures the progress of the desolvation in the transition state For $\alpha_d^{B^-} > \beta_B$ eq 20 predicts a decrease in k_o The situation is shown in Fig 4 for $\beta_B = \beta'_B$

Solvation of Cationic Acid (BH^+) When the base is neutral and the acid cationic as with amines the solvation of the developing cation may affect k_o This manifests itself, e g , in the frequent observation that at the same pK_a^{BH} the reactivity of amines is in the order 3° >

2° > 1° > NH_3 [1b,7,9,26] This trend has been attributed to a decrease in hydrogen bonding solvation of the protonated amine in the order NH_3 > 1° > 2° > 3°, coupled with a lag in the development of this solvation in the transition state [1b,26a] This is of course just another PIS effect which can be described by

$$\delta\log k_o^s(BH^+) = (\alpha_s^{BH^+} - \beta_B)\delta\log K_1^s(BH^+) \qquad (21)$$

Inasmuch as $\delta\log K_1^s(BH^+)$ decreases in the order NH_3 > 1° > 2° > 3°, $\delta\log k_o^s(BH^+)$ becomes less negative for a given $\alpha_s^{BH^+} - \beta_B$, provided that $\alpha_s^{BH^+} < \beta_B$

Solvation of Neutrals. In principle, the solvation of the carbon acid, of B if it is neutral, and of BH if it is neutral, may contribute their own PIS effects However, since the solvation energy of these neutrals is relatively small, effects on k_o are likely to be small and we shall ignore them

Table III Solvent Effect on log k_o upon Transfer from Water to Me_2SO, or to Me_2SO–H_2O Mixtures

Reaction	% Me_2SO[a] (χ_{Me_2SO})[b]	$\delta\log {}^{W}k_o^{D}$	Ref
$ArCH_2NO_2$ + $RCOO^-$	100(1 0)	−4 5	11,12,17
$CH_3CH_2NO_2$ + ArO^-	50(0 20)	−1 15	27
	71(0 39)	−2 15	27
$CH_3CH(NO_2)_2$ + $RCOO^-$,ArO^-	50(0 20)	−1 0	10,28
$CH_2(COCH_3)_2$ + $RCOO^-$	90% (0 69)	−2 4	9
+ R_2NH	90% (0 69)	−1 04	9
+ RNH_2	90% (0 69)	−1 01	9
$CH_3COCH(CH_3)COOC_2H_5$ + AcO^-	50 (0 20)	−0 4	27
	71 (0 39)	−0 9	27

[a] % by volume [b] Mole fraction

Change of Solvent Intrinsic rates of proton transfer depend strongly on the solvent Examples are shown in Table III These solvent effects can be understood along similar lines as the solvation effects discussed in the previous sections Again neglecting solvation effects of neutrals, we can express the change in k_o upon transfer from water (W) to Me_2SO or to a Me_2SO–water mixture (D) as the sum of three major contributions:

$$\delta\log {}^{W}k_o^{D} = \delta\log {}^{W}k_o^{D}(Y) + \delta\log {}^{W}k_o^{D}(B^-) + \delta\log {}^{W}k_o^{D}(BH^+) \qquad (22)$$

The contribution from the carbanion is given by

$$\delta\log {}^{W}k_o^{D}(Y) = (\alpha_{r,s}^{Y} - \beta_B)(-\log {}^{W}\gamma_Y^{D}) \qquad (23)$$

${}^{W}\gamma_Y^{D}$ is the solvent activity coefficient[29] for the transfer of the carbanion from W to D $\alpha_{r,s}^{Y}$ is defined as before but since eq 23 refers to a change in solvent the numerical value of $\alpha_{r,s}^{Y}$ may well be different from that in eq 13

According to eq 23 $\delta\log {}^{W}k_o^{D}(Y)$ will be positive if $\alpha_{r,s}^{Y} < \beta_B$ since $\log {}^{W}\gamma_Y^{D}$ is positive [30] Examples of solvent activity coefficients are given in Table IV Some of the entries in Table IV were obtained indirectly by applying one of the following equations and solving for the unknown quantity, as explained in the footnotes of the table

$$\Delta p {}^{W}K_{CH}^{D} = \log {}^{W}\gamma_Y^{D} + \log {}^{W}\gamma_{H^+}^{D} - \log {}^{W}\gamma_{CH}^{D} \qquad (24)$$

$$\Delta p {}^{W}K_{BH}^{D} = \log {}^{W}\gamma_B^{D} + \log {}^{W}\gamma_{H^+}^{D} - \log {}^{W}\gamma_{BH}^{D} \qquad (25)$$

As the data in Table III show, k_o always increases upon transfer from W to a D, irrespective of the charge type of B/BH This indicates that the $\delta\log {}^{W}k_o^{D}(Y)$ term makes the largest contribution to the solvent effect

Table IV Representative Solvent Activity Coefficients for Transfer from Water to Me_2SO or Me_2SO-Water Mixtures

Compound	% Me_2SO	$\log{}^W\gamma^D$	Remarks
$CH_2(COCH_3)_2$	50	0 14	Ref 31
	81	-0 10	Ref 31
	90	~-0 5	estimated
$\overline{C}H(COCH_3)_2$	50	~2 07	a
	81	~3 73	a
	90	~4 5	a
AcOH	50	~-0 06	b
	90	~-1 5	estimated
	100	-2 15	b
AcO^-	50	3 08	Ref 32
	90	6 5	c
	100	8 16	Ref 33
$CH_3CH_2CH_2NH_2$	50	-0 35	d
	90	~-0 09	estimated
$CH_3CH_2CH_2NH_3^+$	50	-1 81	Ref 32
	90	~-2 8	c
H^+	50	-1 93	Ref 32
	90	~-3 05	e
	100	-3 31	Ref 33

[a] From ${}^W\gamma^D_{CH}$, ${}^W\gamma^D_{H^+}$, $\Delta p{}^WK^D_{CH}$ via eq 24 [b] From ${}^W\gamma^D_{B}$, ${}^W\gamma^D_{H^+}$, $\Delta p{}^WK^D_{BH}$ via eq 25 [c] From estimated ${}^W\gamma^D_{BH}$, and from ${}^W\gamma^W_{H^+}$ and $\Delta p{}^WK^D_{BH}$ via eq 25 [d] From ${}^W\gamma^D_{BH^+}$, ${}^W\gamma^D_{H^+}$ and $\Delta p{}^WK^D_{BH}$ via eq 25 [e] Extrapolated from data in Ref 32

For the contribution of the two other factors we can write

$$\delta\log{}^Wk^D_o(B^-) = (\alpha^{B^-}_d - \beta_B)\log{}^W\gamma^D_B \qquad (26)$$

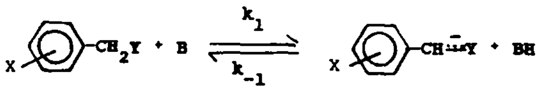
$$\delta\log{}^Wk^D_o(BH^+) = (\alpha^{BH^+}_s - \beta_B)(-\log{}^W\gamma^D_{BH^+}) \qquad (27)$$

Again, the meaning of $\alpha^{B^-}_d$ and $\alpha^{BH^+}_s$ is the same as before but the numerical values may be different than in eqs 20 and 21, respectively

For anionic bases $\log{}^W\gamma^D_{B^-}$ is strongly positive (Table IV) and thus $\delta\log{}^Wk^D_o(B^-)$ is positive if desolvation is ahead of proton transfer ($\alpha^{B^-}_d > \beta_B$) For a cationic acid $\log{}^W\gamma^D_{BH^+}$ is typically negative (Table IV) which leads to a negative $\delta\log{}^Wk^D_o(BH^+)$ when solvation lags behind ($\alpha^{BH^+}_s < \beta_B$)

From this we see that with anionic bases the two solvent effects reenforce each other ($\delta\log{}^Wk^D_o(Y)$ and $\delta\log{}^Wk^D_o(B^-)$ are both positive), with neutral bases they counteract each other This is borne out by the data on the deprotonation of acetylacetone (Table III)

Remote Substituents A Polar Effects Let us consider a reaction of the type



(28)

where X is a remote substituent exerting a polar effect only If α_{CH} which is obtained by varying X is different from β_B this is tantamount to k_o being dependent on X [34]

The extent of this substituent dependence of k_o is directly related to the imbalance, $\alpha_{CH} - \beta_B$, by

$$\delta\log k^P_o(X) = (\alpha_{CH} - \beta_B)\delta\log K^P_1(X) \qquad (29)$$

where $\delta\log K_1^p(X)$ is the change in K_1 brought about by a change in X If β_B is independent of X, eq 29 holds not only for $\delta\log k_o^p(X)$ (at $\log K_1 = 0$) but for any base, i e , for any value of $\log K_1$ This situation is illustrated in Fig 5A (with $\beta_B = \beta'_B$)

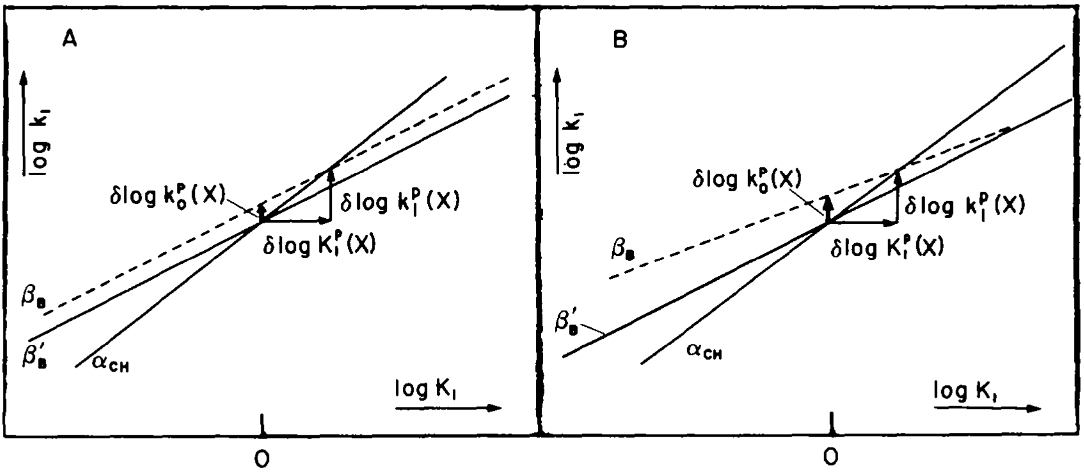


Figure 5. Effect on k_o of polar remote substituent that is more electron withdrawing, according to eq 29 A $\beta_B = \beta'_B$ B $\beta_B < \beta'_B$ Note that $\delta\log k_1^p(X) = \alpha_{CH}\delta\log K_1^p(X)$

From eq 29 we see that for $\alpha_{CH} > \beta_B$ (Table II) k_o increases when X becomes more electron withdrawing since $\delta\log K_1^p(X) > 0$ In principle, one could understand this increase in the context of the PIS: the product stabilizing factor develops early in the transition state and hence k_o is increased It is important to realize, though, that this increase is mainly a transition state effect as further discussed in a later section In other words it has nothing to do with any special characteristics of the remote substituent; rather, it is a consequence of the imbalance, i e , of the fact that the negative charge is mainly localized on carbon in the transition state (1), a phenomenon caused by the Y group, not by X

One should also note that, although significant, the effects of X on k_o are relatively minor compared to the effects discussed in the preceding sections A numerical example will serve to illustrate this point The deprotonation of a series of 1-arylnitromethanes by morpholine in water affords $\alpha_{CH} = 1\ 29$,[12a] the deprotonation of the five arylnitromethanes with X = H, m-CH_3, m-Cl, m-OCH_3 and m-NO_2 by the three bases piperidine, piperazine and morpholine yields $\beta_B = 0\ 56 \pm 0\ 06$ for m-OCH_3 and $0\ 55 \pm 0\ 06$ for all the others,[12a] showing that β_B is independent of X (case of Fig 5A)

For the change from X = H ($pK_a^{CH} = 7\ 39$) to say X = m-NO_2 ($pK_a^{CH} = 6\ 67$) eq 29 affords $\delta\log k_o^p(X) = (1\ 29-0\ 55)\times 0\ 72 = 0\ 53$ Compared to the effect of changing Y (Table I) this is a rather small effect Furthermore, since for all other systems $\alpha_{CH} - \beta_B$ is smaller than for the arylnitromethanes (Table II), the substituent effect on k_o will be correspondingly reduced[35]

If β_B depends on X the situation is as shown in Fig 5B Equation 29 still holds with β_B referring to the compound with $\log K_1 = \delta\log K_1^p(X)$ β_B now depends on the size (and sign) of $\delta\log K_1^p(X)$ For example, in Fig 5B β_B is assumed to decrease with increasing electron withdrawing strength of X which has the effect of increasing $\alpha_{CH} - \beta_B$ and thus to magnify the effect of $\delta\log K_1^p(X)$ on $\delta\log k_o^p(X)$ Since the substituent effects on k_o are relatively small to begin with, the small variations which are introduced by a substituent dependence of β_B will be smaller still, and hence will not concern us any further

Remote Substituents. B. Resonance and SSAR Effects. π-acceptor substituents which stabilize the charge by resonance may influence k_o though a PIS effect of their own The deprotonation of arylnitromethanes by benzoate ion in Me_2SO is a case in point The rate constants for X = p-CN and p-NO_2 show marked negative deviations from the Bronsted plot defined by X =

H, p-CH_3, p-Br, m-NO_2 and 3,5-$(NO_2)_2$.[17a] This deviation can be understood by a delayed development of resonance and solvation of the p-NO_2 (4b) (p-CN) group in the transition state, just as for the β-nitro group.

That appreciable solvation of π-acceptor substituents indeed occurs has been shown in comparisons between solution and gas phase acidities.[36] The phenomenon has been called the SSAR (substituent-solvation-assisted-resonance) effect.[36]

The retarding effect on k_o can be described by an equation similar to eq 13, namely

$$\delta\log k_o^{r,s}(X) = (\alpha_{r,s}^{X} - \beta_B)\delta\log K_1^{r,s}(X) \qquad (30)$$

Alternatively, since the weight of the canonical form 2 is likely to depend on the presence of a π-acceptor substituent in the aryl group, all PIS effects related to delayed resonance and solvation at both Y and X might be expressed with a single equation

$$\delta\log k_o^{r,s}(Y,X) = (\alpha_{r,s}^{Y,X} - \beta_B)\delta\log K_1^{r,s}(Y,X) \qquad (31)$$

Mathematically the PIS effect induced by the p-CN and p-NO_2 groups can be described in several different ways. The ones used in the preceding discussion treat it either as an essentially independent factor which affects k_o (eq 30), or all PIS effects which have to do with delayed resonance and solvation of the carbanion are lumped together (eq 31).

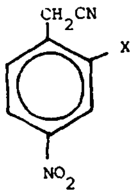
A third approach is to view the PIS effect induced by the p-CN and p-NO_2 groups as a factor which modifies the polar substituent effect, and to use an equation such as[37]

$$\delta\log k_o^{p,r}(X) = (\alpha''_{CH} - \beta_B)\delta\log K_1^{p,r}(X) \qquad (32)$$

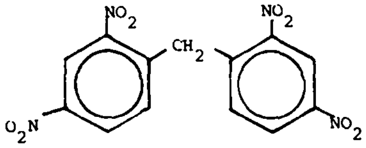
α''_{CH} is the Bronsted α_{CH}-value defined by the two points X = H and X = p-NO_2 (or p-CN). For example in the deprotonation of arylnitromethanes by benzoate ion in Me_2SO[17] one obtains $\alpha''_{CH} = 0.61$ for the pair H and p-NO_2, $\alpha''_{CH} = 0.75$ for the pair H and p-CN, which compare with $\alpha_{CH} = 0.92$. The reduced values of α''_{CH} compared to α_{CH} mean that the polar effect of the π-acceptor substituents is attenuated by the delayed resonance (and solvation).

The *physical* interpretation of $\alpha''_{CH} < \alpha_{CH}$ becomes clear if we recall why α_{CH} is high to begin with: it is because the *non* π-acceptor substituents are close to the center of negative charge in the transition state (1) but less so in the product (2). For the π-acceptors which carry a significant amount of charge in the *product ion* this is no longer true.

As long as a Bronsted plot defined by non π-acceptors is available there is no need to use eq 32. One simply equates the deviation from the Bronsted plot with $\delta\log k_o^{r,s}(X)$ as given by eq 30. On the other hand, if no such Bronsted plot is available, the use of eq 32 is the only practical choice. An example is the deprotonation of 2-X-4-nitrophenylacetonitriles where only data for X = H and X = NO_2 have been obtained thus far (last entry in Table II).[7]



4a (X = H)
4b (X = NO_2)



5a (X = H)
5a (X = NO_2)

In this study α''_{CH} was actually found to be *smaller* than β_B which means that there is a sign change in eq 32, i.e., it is the less acidic compound which has the higher k_o value (Table I). The small α''_{CH} value indicates that in this example the PIS effect of the π-acceptor substituent overpowers its polar effect. This is not surprising since the cyano group in the phenylacetonitrile anion carries less negative charge than the β-nitro group in the phenylnitromethane anion, and thus there is a correspondingly greater charge on the phenyl substituent

Another interesting case is the pair 5a/5b,[14b] for which β_B = 0 45 and α''_{CH} = 0 87 (Table II) The fact that α''_{CH} exceeds β_B by a substantial amount indicates that the PIS effect of the 2,4-dinitrophenyl group (right hand side of 5a/5b) dominates and that the PIS effect of the X-substituent cannot be very large in this system

Why is There Imperfect Synchronization? Since one of the basic laws of Nature is to minimize Gibbs free energy, and since, in principle, intrinsic barriers could be lowered by perfect synchronization, or better yet, by having product stabilizing factors develop early, one wonders why transition states are typically imbalanced in the "wrong" direction Basically the answer must of course be rooted in the laws of quantum mechanics The quantum mechanical principles involved are likely to be the same which make it energetically more advantageous for many chemical reactions to occur in separate steps rather than by concerted mechanisms [38,39]

Some specific ideas which bear on this question have appeared in the recent literature With respect to the deprotonation of arylnitroalkanes, Kresge[18] has suggested that the fraction of negative charge shifted to the oxygens of the nitro groups in the transition state may be related (proportional?) to the π-order of the C-N bond Since the π-order in turn may depend on the fraction of negative charge which has been transferred from the base to the nitroalkane, the charge on the oxygens will only be a fraction of a fraction and hence quite small For example, if the fraction of transferred negative charge and with it the π-order is equal to β_B = 0 56,[12a] and the shift of negative charge to the oxygen is proportional to the π-order, we have ≈0 56 × 0 56 ≈ 0 31 for the charge on the oxygens [40]

The nitroalkanes have also been discussed in the context of the valence bond configuration mixing model developed by Shaik and Pross [41] In their terminology the product configuration (negative charge on oxygen) is a diexcited configuration which is of high energy in the early phases of the reaction In contrast, the intermediate configuration (negative charge on carbon) is monoexcited and of lesser energy in the early phases of the reaction Hence the intermediate configuration makes a larger contribution to the transition state than the product configuration In the late phases of the reaction coordinate the relative energies of intermediate and product configurations are reversed and the product configuration becomes dominant

Kresge's view, and Pross and Shaik's proposal are really quite similar However, the latter treatment offers a more detailed rationale as to why the shift of the negative charge to the oxygen is delayed

It is interesting that the picture which emerges from the valence bond model is that the mixing of the intermediate configuration into the transition state actually lowers its energy and hence reduces the intrinsic barrier In other words, if the intermediate configuration did not exist, or were of higher energy than the product configuration even in the early phases of the reaction, the intrinsic barrier would be even higher This seems to be a contradiction of the premise of the PIS which states that the intrinsic barrier is increased by the delayed development of the resonance (the "product configuration")

The contradiction is only an apparent one, though It arises from the use of different reference states In formulating the PIS we implicitly assume that the transition state has its optimal configuration as determined by the laws of quantum mechanics We then use this transition state as our reference in dealing with how the intrinsic barrier is affected by changes in the energy levels of reactants and products In the valence bond approach the reference state is a hypothetical high energy transition state which does not have the intermediate configuration mixed in

How can we understand the lag in the solvation of the products or the early desolvation of reactants? The lag in the solvation of π-acceptors used either as the Y-group or as remote substituents must of course, in part, be a direct consequence of the lag in the development of resonance, and thus of the lag in the shift of the negative charge to the peripheral atoms of these groups But the fact that solvation of the developing positive charge on BH^+ is also retarded, or that desolvation of B^- is ahead of proton transfer, suggests that there is an additional lack of synchronization which has nothing to do with the delayed shift of the charge

A likely factor is the entropy loss (gain) which accompanies solvation (desolvation) Once a charge is being solvated, the restriction of the solvent molecules, and with it the entropy, may remain relatively independent of the amount of charge on the solute On the other hand, the *enthalpy* should strongly depend on the amount of charge Because of these different sensitivities of entropy and enthalpy to the amount of charge, the gain in Gibbs free energy from the solvation of a *partial* charge will therefore be disproportionately small compared to that of a full charge, since essentially all of the entropy has to be paid while only a fraction of the enthalpy is being released [42]

This state of affairs may have either of two consequences (a) The solvent molecules fail to arrange themselves around the developing charge in the transition state, i e , there is a "physical lag" in the solvation (b) The solvent molecules do arrange themselves around the developing charge but the benefit in free energy is minimal, i e, there is an "energy lag " It should be noted that the notions developed above are quite similar to suggestions made by Richard and Jencks[43] in a different context

An additional factor which might contribute to non-synchronous solvation or desolvation is a *dynamic* solvent effect caused by a certain "inertia" of the solvent in its response to shifts in charges or dipole moments which occur along the reaction coordinate [44]

Effects on Transition States and Intermediates All effects discussed so far are factors which are predominantly present in the reactants or products (resonance and solvation) and only poorly developed in the transition state There are factors, however, which operate predominantly or exclusively in the transition state and have nothing to do with the PIS They also affect the intrinsic rate They are now briefly discussed

A. Steric and Electrostatic Effects. Both of these effects operate in the transition state only Steric effects always lead to rate reductions ($\delta\log k_o^{st} < 0$); the size of the steric effect is relatively easily evaluated from reaction series involving bases of varying bulk [26d,45]

Electrostatic effects[46] may lead to rate enhancements if there is Coulombic attraction (with neutral B), or to rate reductions if there is repulsion (with anionic B) The size of the electrostatic effects ($\delta\log k_o^{el}$) is more difficult to assess than steric effects because the different base charge types have also different PIS effects for desolvation of B^- and solvation of BH^+, respectively An example where a separation between electrostatic and solvation effects was attempted has been reported recently [46b]

B. Intermediate Configuration. As discussed earlier, one can view the imbalanced transition states as arising from a strong contribution of the "intermediate configuration,"[41] which has the negative charge localized on carbon Hence, any factor which stabilizes this configuration should also stabilize the transition state, thereby lowering the intrinsic barrier or increasing k_o

The polar effect of remote substituents on k_o can be viewed in this light, as suggested earlier The intermediate configuration is also likely to have different solvation characteristics than the product configuration This may lead to solvent effects which are on top of the PIS effects discussed before For example, the transition state may be subject to special stabilization or destabilization by dipolar non-hydroxylic solvents, as has been suggested for certain S_N2 reactions,[29] or by special solvent reorientation effects as envisioned by Ritchie [3] We believe, though, that these transition state solvent effects are relatively small compared to the PIS effects

Finally, if there is a discrete hydrogen-bonded intermediate (3) along the reaction coordinate, the stabilization of 3 which arises from such hydrogen bonding is likely to be reflected in some stabilization of the transition state, too

A Numerical Example The following example illustrates how some of the formalism developed in this paper may be used quantitatively, or at least semiquantitatively The example refers to the solvent effect on k_o in the deprotonation of acetylacetone by carboxylate ions and primary amines [9] The effect of changing the solvent from water to 90% aqueous Me_2SO can be described by

$$\delta\log {}^{W}k_{o}^{D} = \delta\log {}^{W}k_{o}^{D}(Y) + \delta\log {}^{W}k_{o}^{D}(B^{-}) + \delta\log {}^{W}k_{o}^{D}(BH^{+}) + \delta\log {}^{W}k_{o}^{D}(TS) \qquad (33)$$

The first term is given by eq 23, the second by eq 26 (only important for carboxylate ions), the third by eq 27 (only important for amines), while the fourth term includes all possible transition state solvent effects Experimentally known quantities include $\beta_B = 0\ 83^{47}$ and $\delta\log {}^{W}k_{o}^{D} = 2\ 38$ for $RCOO^{-}$, $\beta_B = 0\ 53^{47}$ and $\delta\log {}^{W}k_{o}^{D} = 1\ 01$ for RNH_2 Estimates of solvent activity coefficients can be taken from Table IV $\log {}^{W}\gamma_{Y}^{D} \approx 4\ 5$, $\log {}^{W}\gamma_{B^{-}}^{D} \approx 6\ 5$, $\log {}^{W}\gamma_{BH^{+}}^{D} \approx -2\ 8$

For the carboxylate reactions eq 33 becomes

$$2\ 38 = (\alpha_{r,s}^{Y} - \beta_B)(-\log {}^{W}\gamma_{Y}^{D}) + (\alpha_{d}^{B^{-}} - \beta_B)\log {}^{W}\gamma_{B^{-}}^{D} + \delta\log {}^{W}k_{o}^{D}(TS)$$

$$\approx (\alpha_{r,s}^{Y} - 0\ 83)(-4\ 5) + (\alpha_{d}^{B^{-}} - 0\ 83)6\ 5 + \delta\log {}^{W}k_{o}^{D}(TS) \qquad (34)$$

while for the amine reactions we have

$$1\ 01 = (\alpha_{r,s}^{Y} - \beta_B)(-\log {}^{W}\gamma_{Y}^{D}) + (\alpha_{s}^{BH^{+}} - \beta_B)(-\log {}^{W}\gamma_{BH^{+}}^{D}) + \delta\log {}^{W}k_{o}^{D}(TS)$$

$$\approx (\alpha_{r,s}^{Y} - 0\ 53)(-4\ 5) + (\alpha_{s}^{BH^{+}} - 0\ 53)(4\ 0) + \delta\log {}^{W}k_{o}^{D}(TS) \qquad (35)$$

How can we estimate the various unknown parameters in eqs 34 and 35? In the case of the carboxylate ion reactions we can take advantage of the fact that $\beta_B = 0\ 83$ is so high that the choice of $\alpha_{d}^{B^{-}}$ is quite restricted Assuming the maximum possible value for $\alpha_{d}^{B^{-}}$ (1 0) and assuming that $\delta\log {}^{W}k_{o}^{D}(TS)$ is negligible, affords $\alpha_{r,s}^{Y} \approx 0\ 55$ via eq 34 A value of 0 55 for $\alpha_{r,s}^{Y}$ seems quite reasonable it meets the expectation that there should be less synchronization in the solvation (coupled with resonance) of the Y group than in the desolvation of the base ($|\alpha_{r,s}^{Y} - \beta_B| > |\alpha_{d}^{B^{-}} - \beta_B|$), and that $\alpha_{r,s}^{Y} < (\beta_B)^2 = 0\ 69$ (Kresge's[18] assumption)

Note that the assumption of a $\alpha_{d}^{B^{-}} < 1\ 0$ would lower $\alpha_{r,s}^{Y}$ while the assumption of $\delta\log {}^{W}k_{o}^{D}(TS) > 0$ would increase $\alpha_{r,s}^{Y}$ For example, if $\alpha_{d}^{B^{-}} = 0\ 83 = \beta_B$ (and $\delta\log {}^{W}k_{o}^{D}(TS) = 0$) one obtains $\alpha_{r,s}^{Y} \approx 0\ 30$ both of these $\alpha_{d}^{B^{-}}$ and $\alpha_{r,s}^{Y}$ values seem unrealistic Or, if $\delta\log {}^{W}k_{o}^{D}(TS) = 0\ 7$ (and $\alpha_{d}^{B^{-}} = 1\ 0$) one calculates $\alpha_{r,s}^{Y} \approx 0\ 70$ which seems much too high

For the amine reactions we again assume that $\delta\log {}^{W}k_{o}^{D}(TS)$ is negligible As with the carboxylate ion reactions one expects $\alpha_{r,s}^{Y} < (\beta_B)^2$ With $\beta_B = 0\ 53$ we have $(\beta_B)^2 = 0\ 28$ On this basis we may assume $\alpha_{r,s}^{Y} \approx 0\ 20$; solving eq 35 for $\alpha_{s}^{BH^{+}}$ then affords a value of 0 36 for $\alpha_{s}^{BH^{+}}$ This is a "reasonable" value since it is lower than $\beta_B = 0\ 53$

At this point it is difficult to assess how much physical reality should be associated with the numbers obtained in these calculations As more quantitative experimental data become available, a test for the validity of these calculations and concomitant assumptions will be the emergence, or absence, of internal consistency of the conclusions drawn from a large number of systems

Conclusions We have discussed a number a factors which affect the intrinsic rates of proton transfers They can be put into two main categories: PIS effects and transition state effects

The PIS effects associated with delayed development of resonance stabilization by the Y-group and the concomitant lag in solvation of the negative charge are the dominant factors which determine the rank order in k_o for the different carbon acids (Table I) Other PIS effects include delayed resonance and solvation of π-acceptors used as remote substituents, delayed solvation of the positive charge on the base (neutral bases) and advanced desolvation of the base (anionic bases)

In other types of reactions, e g , nucleophilic addition to olefins, many of the same PIS effects are operative as well as additional ones, as discussed elsewhere[48] *It would appear then that the PIS is, quite generally, the mechanism by which the PLNM manifests itself*

The mathematical formalism used to describe the various PIS effects is most directly applicable to polar substituent and solvent effects on k_o For substituent effects (eq 29) the three quantities α_{CH}, β_B and $\delta\log K_1^P(X)$ are all experimentally accessible and thus $\delta\log k_o^P(X)$ is easily obtained For solvent effects (eq 33, coupled with eqs 23, 26, 27) the quantities ${}^{W}\gamma_{Y}^{D}$, ${}^{W}\gamma_{B^-}^{D}$, ${}^{W}\gamma_{BH^+}^{D}$, $\delta\log {}^{W}k_o^{D}$ and β_B are experimentally accessible By making some assumptions about the relationship of $\alpha_{r,s}^{Y}$, $\alpha_{d}^{B^-}$ and $\alpha_{s}^{BH^+}$ to β_B, and/or about $\delta\log {}^{W}k_o^{D}(TS)$, various parameters can be estimated as illustrated with an example in the previous section The other equations (eqs 8, 11-13, 20, 21) are mainly useful in a qualitative sense

Acknowledgement Financial support by NSF grant No CHE-8315374 is gratefully acknowledged I wish to thank Professor Richard D Gandour for criticism of the manuscript

References and Notes

(1) For recent reviews, see (a) Eigen, M , *Angew Chem Int Ed Engl* 1964, *3*, 1 (b) Bell, R P "The Proton in Chemistry," Cornell University Press: Ithaca, N Y , second ed , 1973; Chapter 10 (c) Crooks, J E In "Proton Transfer Reactions," Caldin, E , Gold, V , Eds , Wiley: New York, 1975; p 153 (d) Hibbert, F *Compr Chem Kin* 1977, *8*, 97

(2) (a) Bell, R P "The Proton in Chemistry," Cornell University Press: Ithaca, N Y , first edition, 1959, p 155 (b) Ritchie, C D *J Am Chem Soc* 1969, *91*, 6749

(3) Ritchie, C D In "Solute-Solvent Interactions," Coetzee, J F ; Ritchie, C D , Eds ; Dekker New York; 1969; p 219 (c) Ritchie, C D *Ibid* 1969, *91*, 6749

(4) Hine, J *Adv Phys Org Chem* 1977, *15*, 1

(5) (a) Ogg, R A ; Polyani, M *Trans Farad Soc* 1935, *31*, 604 (b) Caldin, E F *J Chem Soc* 1959, 3345

(6) For a recent review, see Bernasconi, C F *Pure Appl Chem* 1982, *54*, 2335

(7) Bernasconi, C F , Hibdon, S A *J Am Chem Soc* 1983, *105*, 4343

(8) Hibbert, F ; Long, F A *J Am Chem Soc* 1972, *94*, 2647

(9) Bernasconi, C F ; Bunnell, R D *Isr J Chem* in press

(10) Bell, R P ; Tranter, R L *Proc R Soc London, Ser A* 1974, *337*, 518

(11) Keeffe, J R , Munderloh, N H *J Chem Soc Chem Commun* 1974, 17

(12) (a) Bordwell, F G ; Boyle, W J , Jr *J Am Chem Soc* 1972, *94*, 3907; 1975, *97*, 3447 (b) Bordwell, F G ; Bartmess, J E , Hautala, J A *J Org Chem* 1978, *43*, 3107

(13) Bell, R P , Grainger, S *J Chem Soc , Perkin Trans 2* 1976, 1367

(14) (a) Terrier, F ; Farrell, P G ; Lelievre, J ; Chatrousse, A P *J Chem Soc Perkin 2*, in press

(15) Jencks, D A ; Jencks, W P *J Am Chem Soc* 1977, *99*, 7948

(16) In the reverse direction β_B corresponds to α_{BH}, and α_{CH} to β_{C^-} We shall use these symbols throughout this paper, mainly to distinguish them from other types of α or β values as developed below An inequality such as $\alpha_{CH} > \beta_B$ corresponds to $\beta_{C^-} < \alpha_{BH}$ in the reverse direction

(17) (a) Keeffe, J R ; Morey, J ; Palmer, C A ; Lee, J C *J Am Chem Soc* 1979, *101*, 1295 (b) Keeffe, J R , personal communication

(18) Kresge, A J *Can J Chem* 1975, *52*, 1897

(19) Cram, D J "Fundamentals of Carbanion Chemistry," Academic Press: New York, 1965, Chapters I, III and V

(20) Koch, H F *Acc Chem Res* 1984, *17*, 157

(21) Hine[4] appears to be the first to have used this expression, but without developing the concept in any detail

(22) Cohen, A O ; Marcus, R A *J Phys Chem* 1968, *72* 4249

(23) Kresge, A J *Chem Soc Rev* 1973, *2*, 475

(24) Such a possibility has been suggested by Murdoch, J R , Bryson, J A ; McMillen, D F ; Brauman, J I *J Am Chem Soc* 1982, *104*, 600

(25) (a) Hupe, D J ; Jencks, W P J Am Chem Soc 1977, 99, 451 (b) Hupe, D J , Wu, D Ibid 1977, 99, 7653 (c) Pohl, E R ; Wu, D ; Hupe, D J Ibid 1980, 102, 2759 (d) Jencks, W P ; Brant, S R ; Gandler, J R ; Fendrich, G , Nakamura, C Ibid 1982, 104, 7045

(26) (a) Jencks, W P "Catalysis in Chemistry and Enzymology," McGraw-Hill: New York, 1969; p 178 (b) Bell, R P ; Trotman-Dickenson, A F J Chem Soc 1949, 1288 (c) Spencer, T A ; Kendall, M C R ; Reingold, I D J Am Chem Soc 1972, 94, 1250 (d) Hine, J ; Houston, J G ; Jensen, J H ; Mulders, J Ibid 1965, 87, 5050 (e) Hine, J ; Mulders, J ; Houston, J G ; Idoux, J P J Org Chem 1967, 32, 2205

(27) Cox, B G ; Gibson, A J Chem Soc , Chem Commun 1974, 638

(28) Bernasconi, C F ; Kanavarioti, A J Org Chem 1979, 44, 4829

(29) Parker, A J Chem Rev 1969, 69, 1

(30) The negative sign for $\log {}^{W}\gamma_{Y}^{D}$ in eq 23 arises from the definition of $\log {}^{W}\gamma^{D} = {}^{W}\Delta^{D}G^{o}/RT$ with ${}^{W}\Delta^{D}G^{o}$ being the free energy of transfer from W to D [29]

(31) Watarai, H Bull Chem Soc Jpn 1980, 53, 3019

(32) Wells, C F In "Thermodynamic Behavior of Electrolytes in Mixed Solvents-II," Furter, W F , Ed ; Adv Chem Ser 1979, 177, 53

(33) Cox, B G ; Hedwig, G R ; Parker, A J ; Watts, D W Aust J Chem 1974, 77, 477

(34) (a) Marcus, R A J Am Chem Soc 1969, 91, 7274 (b) Bernasconi, C F ; Leonarduzzi, G D Ibid 1982, 104, 5133

(35) A larger sensitivity of pK_a^{CH} to a given substituent may, however, compensate or even overcompensate for the reduced $\alpha_{CH} - \beta_B$ E g , for the arylnitromethanes in Me_2SO, $pK_a^{CH} = 12\ 03$ for X=H, $pK_a^{CH} = 10\ 04$ for X = m-NO_2 With $\alpha_{CH} - \beta_B = 0\ 42$ this yields $\delta \log k_o^{p}(X) = 0\ 42 \times 1\ 99 = 0\ 83$

(36) (a) Fujio, M ; McIver, P I ; Taft, R W J Am Chem Soc 1981, 103, 4017 (b) Mashima, M ; McIver, R I ; Taft, R W ; Bordwell, F G ; Olmstead, W N Ibid 1984, 106, 2717 (c) Bordwell, F G ; Cripe, T A , Mashima, M ; Taft, R W Ibid 1985, 107, 0000

(37) In order to simplify the symbols, r in eq 32 is meant to include solvation of the π-acceptor

(38) (a) Jencks, W P Chem Soc Rev 1981, 10, 345 (b) Jencks, W P Acc Chem Res 1980, 13, 161

(39) Dewar, M J S J Am Chem Soc 1984, 106, 209

(40) On the basis of kinetic deuterium isotope effects Kresge[18] prefers a value of 0 4 for the degree of proton transfer and thus for the π-order With this assumption the negative charge on oxygen is calculated as $\approx 0\ 4 \times 0\ 4 \approx 0\ 16$

(41) (a) Pross, A ; Shaik, S S J Am Chem Soc 1982, 104, 1129 (b) Pross, A Adv Phys Org Chem in press

(42) For the early desolvation of the base the loss in free energy will be small because the loss of enthalpy is made up by the large gain in entropy

(43) Richard, J P ; Jencks, W P J Am Chem Soc 1984, 106, 1373

(44) (a) Kurz, J L ; Kurz, L C J Am Chem Soc 1972, 94, 4451 (b) Van der Zwan, G , Hynes, J T J Chem Phys 1982, 76, 2993 (c) Truhlar, D G ; Hase, W L ; Hynes, J T J Phys Chem 1983, 87, 2664

(45) Feather, J A ; Gold, V ; J Chem Soc 1965, 1752

(46) (a) Kresge, A J , Chiang, Y J A Chem Soc 1973, 95, 803 (b) Thibblin, A Ibid 1984, 106, 183

(47) In 90% Me_2SO-10% water

(48) Bernasconi, C F , in preparation