

CROSS-INTERACTION CONSTANTS. A MECHANISTIC TOOLIkchoon LEE^{1,*} and Hai Whang LEE²*Department of Chemistry, Inha University, Incheon 402-751, Korea;**e-mail: ¹ ilee@dragon.inha.ac.kr, ² hwlee@dragon.inha.ac.kr*

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This work is dedicated to Professor Otto Exner on the occasion of his 75th birthday in recognition of his outstanding contributions to the areas of physical organic chemistry and chemometrics.

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The cross-interaction constant, ρ_{ij} , is a second derivative parameter representing a change in the intensity of interaction between the two reacting partners (or fragments) i and j in a reaction. It can be either an activation or a reaction parameter. The sign and magnitude of ρ_{ij} have important mechanistic significances and are useful as a tool for the studies of organic reaction mechanism. We have presented several more important applications of the cross-interaction constants. A review with 42 references.

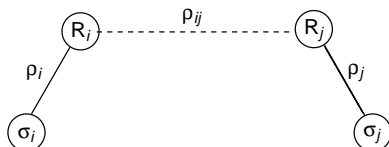
Key words: Cross-interaction constants; Transition-state structures; Mechanistic criteria; Reactivity-selectivity principle; Reaction kinetics; Nucleophilic substitutions; Review.

1. INTRODUCTION

The Hammett and Brønsted equations have been useful in characterizing transition-state (TS) structures, especially for reactions in solution¹. The slopes ρ_i and β_i which are first derivatives of $\log k$ with respect to σ_i and pK_i , respectively, provide mechanistic information such as a favored pathway

and TS structure. However, there are limitations in their application to studies of reaction mechanisms.

First, a sign reversal of ρ_i (and β_j) within a series of reaction occurs without change in the reaction mechanism or pathway. For example, isokinetic phenomena are observed with vanishing ρ_i ($= 0$) at a certain substituent of the reacting partner, $\hat{\sigma}_j$ (Scheme 1), and ρ_i changes sign at $\hat{\sigma}_j$ with different signs above ($\sigma_j > \hat{\sigma}_j$) and below ($\sigma_j < \hat{\sigma}_j$) the isokinetic point $\hat{\sigma}_j$ with no apparent change in the reaction mechanism².



SCHEME 1

Second, nonlinear changes in the magnitude of the ρ_i with TS variation for two different series of reactions are observed, *i.e.*, there is no simple linear relation between $|\rho_i|$ and r_{ij} (the distance between R_i and R_j , Scheme 1) when R_j is varied. For example, it is well known that fluoride is a much worse leaving group (LG) compared with chloride owing to the weak electron-acceptor ability of the C-F or S-F bond, and, hence, this leads to a tighter TS with a greater degree of bond formation in nucleophilic substitution reactions. However, it has been observed that the magnitude of ρ_{nuc} (or ρ_X ; X = nucleophile) is smaller for fluoride than for chloride (*e.g.*, $\rho_X(\text{F}) = -1.31$ and $\rho_X(\text{Cl}) = -2.14$ for the reactions of benzyl halides with anilines in MeOH) in contradiction to the greater magnitude of ρ_X (ρ_{nuc}) expected normally for a greater degree of bond making³. This simply indicates that, owing to less effective charge transfer to C-F or S-F bond than to C-Cl or S-Cl bond, the ρ_X value for fluoride is smaller although bond formation is actually more advanced. Thus the progress of bond-making in the TS, r_{ij} , is a function not only of ρ_i but also of R_j (which, in turn, is dependent on σ_j , Eq. (1)), so that the magnitude of ρ_i for different reaction series cannot be directly compared to deduce changes in r_{ij} unless R_j (σ_j) is held constant.

$$r_{ij} = f(\rho_i, \sigma_j) \quad (1)$$

Third, the effects of substituents in the two reacting partners, i and j , are not additive, Eq. (2), refs^{3,4}.

$$\log(k_{ij}/k_{00}) \neq \rho_i \sigma_i + \rho_j \sigma_j \quad (2)$$

These and some of other limitations inherent to the first-derivative parameters are resolved by introducing cross-interaction constants (CICs), which are second-derivative parameters.

2. THEORY³

The rate constant, k , is a function of structural and environmental factors such as σ , ρK_a , Y , N , T , P , *etc.*, where σ , ρK_a , Y , *etc.* have the usual meanings of Hammett substituent constant, basicity, ionizing power, *etc.* Let us assume that k is dependent only on the two of these rate variables, m and n , with all the rest being kept constant. A Taylor series expansion of $\log k$ around $m = n = 0$ with the assumption of negligible pure second-order⁵ and higher-order terms⁶ (Eq. (3c)) leads to a simple second-order expression, Eq. (3a). Let $k = k(m, n)$ and $k_0 = k(m = n = 0)$, where $m, n = \sigma_p, \sigma_j, \dots, \rho K_p, \rho K_j, \dots, Y, T, P, \dots$, *etc.*

Then,

$$\log(k/k_0) = M_m^0 m + N_n^0 n + Q_{mn} mn, \quad (3a)$$

where

$$M_m^0 = \left(\frac{\partial \log k}{\partial m} \right)_{n=0}, \quad N_n^0 = \left(\frac{\partial \log k}{\partial n} \right)_{m=0}$$

and

$$Q_{mn} = \left(\frac{\partial^2 \log k}{\partial m \partial n} \right) = \frac{\partial N_n}{\partial m} = \frac{\partial M_m}{\partial n} \quad (3b)$$

provided

$$Q_{mn} = Q_{mm} = Q_{nn} = \dots = 0. \quad (3c)$$

It should be noted that M_m^0 , N_n^0 and Q_{mn} are constants, whereas M_m and N_n are variables. For example, N_n^0 is the first derivative of $\log k$ with respect to n at $m = 0$, but N_n is a similar quantity at any m , *i.e.*, m can be varied and is not restricted to $m = 0$; in fact, $N_n = N_n^0 + Q_{mn}m$, (Eq. (7b), *vide infra*). Throughout this article, we adopt a convention of denoting a zero variable of the reacting partner by a superscript degree symbol.

As a special case, if the two rate variables, m and n , are the substituent constants in the two reacting partners, we obtain Eqs (4):

$$\log(k/k_0) = \rho_i^0 \sigma_i + \rho_j^0 \sigma_j + \rho_{ij} \sigma_i \sigma_j, \quad (4a)$$

where

$$\rho_{ij} = \left(\frac{\partial^2 \log k}{\partial \sigma_i \partial \sigma_j} \right) = \frac{\partial \rho_j}{\partial \sigma_i} = \frac{\partial \rho_i}{\partial \sigma_j}. \quad (4b)$$

Similarly, for $m, n = \Delta pK_i$ and ΔpK_j , we get a Brønsted-type cross-interaction constant, β_{ij} , Eqs (5).

$$\log(k/k_0) = \beta_i^0 \Delta pK_i + \beta_j^0 \Delta pK_j + \beta_{ij} \Delta pK_i \Delta pK_j \quad (5a)$$

$$= \beta_i^{0'} pK_i + \beta_j^{0'} pK_j + \beta_{ij} pK_i pK_j + \text{const.}, \quad (5b)$$

where $\beta_i^{0'} = \beta_i^0 - \beta_{ij} pK_i$ etc.,

$$\beta_{ij} = \left(\frac{\partial^2 \log k}{\partial \Delta pK_i \partial \Delta pK_j} \right) = \frac{\partial \beta_j}{\partial \Delta pK_i} = \frac{\partial \beta_i}{\partial \Delta pK_j}. \quad (5c)$$

It should be noted that $\beta_i^{0'} \neq \beta_i^0$ but β_{ij} is the same in Eqs (5a) and (5b). The signs of ρ_{ij} (Eqs (4)) and β_{ij} (Eqs (5)) are the same in general, while the magnitudes of the two are related by Eqs (6) so that they are interconvertible when structural changes are due to substituents.

$$\rho_i = \beta_i \rho_i^e \quad (6a)$$

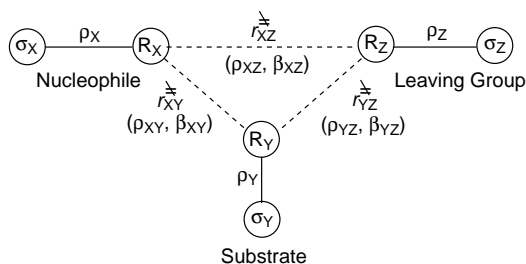
$$\rho_{ij} = \beta_{ij} \rho_i^e \rho_j^e, \quad (6b)$$

where $\rho_i^e = \Delta pK_i / \sigma_i$ etc. Some of the ρ_i^e values are^{2b}: $\text{XC}_6\text{H}_4\text{NH}_3^+$ (-2.96), $\text{XC}_6\text{H}_4\text{NH}(\text{CH}_3)_2^+$ (-3.05), $\text{XC}_6\text{H}_4\text{CH}_2\text{NH}_3^+$ (-1.06), $\text{XC}_6\text{H}_4\text{OH}$ (-2.11), $\text{XC}_6\text{H}_4\text{SH}$ (-1.82) and $\text{XC}_6\text{H}_4\text{OSO}_2\text{CH}_3$ (-2.99) for methyl cation not for proton affinity.

The $\text{S}_{\text{N}}2$ reaction is probably one of the most thoroughly studied and analyzed reactions in experimental as well as theoretical organic chemistry.

The effects of substituents on the TS structure can be most conveniently discussed using the S_N2 TS which is composed of three fragments, the nucleophile (X), substrate (Y) and leaving group (Z) (Scheme 2). Using the S_N2 TS as a prototype, discussion of the structural effects of two reacting partners can be easily extended to most of other organic reactions^{3b}, e.g., electrophilic substitution, elimination, solvolysis, etc., by a simple modification to fit the specific reaction system.

It has been shown that in the S_N2 reactions, ρ_{ij} (and β_{ij}) represents change in the intensity of interaction between two reacting partners (between two substituents σ_i and σ_j through reaction centers, R_i and R_j , for ρ_{ij} , but for β_{ij} it is between two reaction centers) on going from the initial (reactants) to transition state^{3,7}. Since in the initial state the reacting partners can be considered to be infinitely apart (no interaction), ρ_{XY} (β_{XY}) and ρ_{XZ} (β_{XZ}) represent simply the intensity of interaction in the TS, which is inversely proportional to the distance r_{XY}^\ddagger and r_{XZ}^\ddagger , respectively.



SCHEME 2

The sign and magnitude of the cross-interaction constants have important mechanistic significances and are useful as a tool for the mechanistic studies of organic reactions^{3,5}.

In the following, we will present some of the more important applications of the cross-interaction constants to the mechanistic studies of organic reactions that have been developed mainly in our laboratory for the past ten years.

3. APPLICATIONS

3.1. Isokinetic or Isoparametric Phenomena²

Within a series of reactions involving variations of two rate variables, m and n , we can define an arbitrary constant, \hat{m} (or \hat{n}) for any one of them, Eqs

(7). At this point, \hat{m} (or \hat{n}), the cross term Q_{mn} vanishes and the two rate variables, m and n , are no longer interactive, *i.e.*, *non-interactive*.

$$\begin{aligned}\log(k/k_0) &= M_m^0 m + N_n^0 n + Q_{mn} mn \\ &= M_m^0 m + (N_n^0 + Q_{mn} m)n \\ &= M_m^0 m + N_n n \\ &= M_m^0 \hat{m},\end{aligned}\tag{7a}$$

where

$$N_n = N_n^0 + Q_{mn} m\tag{7b}$$

$$N_n = 0 \quad \text{at} \quad \hat{m} = -\frac{N_n^0}{Q_{mn}}\tag{7c}$$

likewise

$$M_m = 0 \quad \text{at} \quad \hat{n} = -\frac{M_m^0}{Q_{mn}}.$$

Moreover, the reactivity becomes constant at this point and the reaction is therefore *isokinetic*. Since at \hat{m} the members of the other variables, n_1, n_2, \dots, n_n , do not incur any reactivity change and all have the same value, it can be termed as *isoparametric*. Sometimes, this has been called a *magic point*⁸.

Application of Eqs (7) to the case where m and n are the substituent constants in the two reacting partners leads to an isokinetic substituent or reactant, $\hat{\sigma}$, for which the reactant does not cause reactivity change and isokinetic condition is attained, Eqs (8).

$$\begin{aligned}\log(k/k_0) &= \rho_i^0 \sigma_i + \rho_j^0 \sigma_j + \rho_{ij} \sigma_i \sigma_j \\ &= \rho_j^0 \sigma_j + (\rho_i^0 + \rho_{ij} \sigma_j) \sigma_i \\ &= \rho_j^0 \sigma_j + \rho_i \sigma_i = \rho_j^0 \hat{\sigma}_j = -\frac{\rho_i^0 \rho_j^0}{\rho_{ij}} = -W,\end{aligned}\tag{8a}$$

where

$$\rho_i = \rho_i^0 + \rho_{ij} \sigma_j\tag{8b}$$

and

$$\rho_j = 0 \text{ at } \hat{\sigma}_i = -\frac{\rho_j^0}{\rho_{ij}} \quad (8c)$$

likewise

$$\rho_i = 0 \text{ at } \hat{\sigma}_j = -\frac{\rho_i^0}{\rho_{ij}}$$

and

$$W = \frac{\rho_i^0 \rho_j^0}{\rho_{ij}} = \text{const.} \quad (8d)$$

Since at $\hat{\sigma}_i$, $\rho_j = 0$ and ρ_j changes sign without any mechanistic change in the series of reactions, the mechanistic interpretation of the magnitude of ρ_j as a measure of the extent of bond making or bond breaking becomes difficult; an exactly opposite trend will be obtained in the regions above and below the isokinetic point $\hat{\sigma}_i$.

In fact, we can use any two rate variables, m and n , in Eqs (3) and define such an isokinetic or isoparametric point. A well-known example is the case when $m, n = \sigma$ and T . Since at isokinetic temperature \hat{T} , ρ changes sign, the mechanistic interpretation of ρ becomes exactly opposite above and below \hat{T} (ref.⁹).

$$\rho = 0 \text{ at } \hat{T} \text{ isokinetic temperature.}$$

Likewise,

$$\rho = 0 \text{ at } \hat{P} \text{ isokinetic pressure}$$

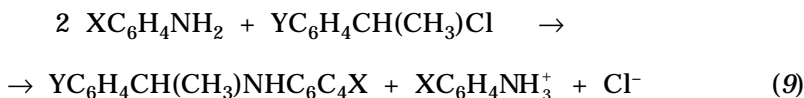
$$\rho = 0 \text{ at } \hat{Y} \text{ isokinetic medium, or solvent, etc.}$$

Most interesting cases are, however, *experimental determination of $\hat{\sigma}_i$ at which $\rho_j = 0$ as theoretically predicted by Eqs (8)*.

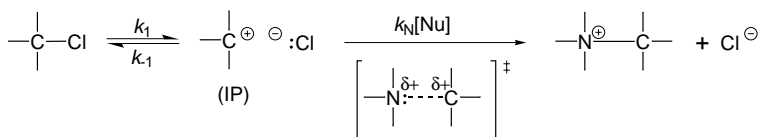
We will give three typical examples:

$$1) \rho_X = 0 \text{ at } \hat{\sigma}_Y^+$$

The reactions of 1-phenylethyl chlorides (1-PEC) with anilines in methanol at 35.0 °C, Eq. (9), are found to proceed by an ion-pair (IP) mechanism (Scheme 3)^{2b,10}.



For this reaction series, ρ_X was found to vanish experimentally at $\hat{\sigma}_Y^+ \approx -0.23$. Applying Eq. (8c), it is predicted that $\rho_X = 0$ at $\hat{\sigma}_Y^+ = -(-0.47/-2.05) = -0.23$, in agreement with the experimental results.



SCHEME 3

Similarly, the reactions of benzhydryl chlorides ($\text{YC}_6\text{H}_4\text{CH}(\text{C}_6\text{H}_5)\text{Cl}$) and $\text{XC}_6\text{H}_4\text{NH}_2$ in MeOH at 35.0 °C gave $\rho_X = 0$ at $\sigma_Y^+ = +0.22$ (ref.¹¹). The experimentally observed isokinetic points, $\hat{\sigma}_Y^+$, were exactly as predicted by Eqs (8). Observation of $\hat{\sigma}_Y^+$, at which ρ_X changes sign, indicates that the reaction series does not react by a simple classical $\text{S}_{\text{N}}1$ (for which non-zero ρ_X is not possible) or by a direct displacement, $\text{S}_{\text{N}}2$, mechanism (for which ρ_X should be always negative). It has been suggested that at $\hat{\sigma}_Y^+$, a repulsive electronic interaction between C_{α} and N (at $\sigma_Y^+ < \hat{\sigma}_Y^+$) reverses to an attractive interaction (at $\sigma_Y^+ > \hat{\sigma}_Y^+$) in the TS (ref.²⁶). This is possible due to interaction of a high-electron-density reaction center of the nucleophile with fully resonance developed π -orbital charge at C_{α} by the relatively strong resonance electron donors at the *para* position ($\sigma_p^+ < \hat{\sigma}_p^+$) of the carbocation, and larger fraction of this resonance effect is expressed in the TS than the polar effect, *i.e.*, the imbalanced TS (refs^{2b,12}).

$$2) \rho_Y = 0 \text{ at } \hat{\sigma}_X$$

Sign reversal of ρ_Y is rather common and many examples belonging to this category are reported. For the reactions of Y-substituted benzyl and benzoyl halides with anilines in suitable solvents, the isokinetic points, $\hat{\sigma}_X$ at which $\rho_Y = 0$, were observed experimentally as predicted by Eqs (8) (Table I, ref.¹³). For example, the reaction series A becomes isokinetic, $\rho_Y = 0$, with 3,5-dinitroaniline ($\hat{\sigma}_X = 2 \times \sigma(3\text{-NO}_2) = 2 \times 0.71 = 1.41$). The sign reversal simply indicates that C_{α} of the substrate changes from positively charged ($\rho_Y < 0$ at $\sigma_X > \hat{\sigma}_X$) to negatively charged ($\rho_Y > 0$ at $\sigma_X < \hat{\sigma}_X$) in the TS, which in turn suggests changes in bond cleavage of halides from more advanced to less advanced than bond making by anilines in the TS.

$$3) \rho_Z = 0 \text{ at } \hat{\sigma}_X$$

Sign reversal of ρ_Z is rare. For the reactions of cumyl arenesulfonates, $C_6H_5C(CH_3)_2OSO_2C_6H_4Z$, with anilines ($XC_6H_4NH_2$) in acetonitrile at 55.0 °C, ρ_Z was found to vanish experimentally at the predicted $\hat{\sigma}_X$ (≈ 0.8 by interpolation) by Eq. (8); $\rho_Z = 0$ at $\hat{\sigma}_X = -(\rho_Z^0 / \rho_{XZ}) = -(0.62 / -0.75) = 0.83$ (ref.¹⁴). Cumyl derivatives always react normally by the limiting S_N1 mechanism in ionizing solvent, for which ρ_Z is zero *i.e.*, nucleophile (aniline) has no effect on the rate¹⁵, in contrast to the large effect of aniline nucleophiles on the rate in the above reaction series. Again if the reaction were a direct backside displacement (S_N2) type, ρ_Z should be positive and cannot have negative value, in contrast to a negative ρ_Z value observed. These and the fact that ρ_{XZ} is large negative have been interpreted to indicate a front-side attack S_N2 mechanism for this reaction series.

There are many other examples of the observable isokinetic or isoparametric phenomena, ($N_n = 0$ or $\rho_i = 0$), at the predicted value (\hat{m} or $\hat{\sigma}_j$) by Eqs (7) and (8) (refs^{2a,16}).

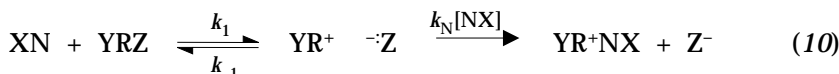
3.2. Ion-Pair Mechanism: S_N1 vs S_N2C^+

Both S_N1 and S_N2C^+ reactions proceed through an ion-pair (IP) intermediate. In the former, the leaving group (Z^-) departure is the rate-determining step (k_1) and the ion-pair reacts with nucleophiles (XN) (or solvent, SOH) in a subsequent fast step (Fig. 1a), whereas in the latter cation within the ion-pair which is formed in a fast pre-equilibrium step ($K = k_1/k_{-1}$) reacts with nucleophiles (XN) in the rate-limiting step (Fig. 1b), $k_{obs} = (k_1/k_{-1})k_N = Kk_N$, (see Scheme 3). *In the classic S_N1 mechanism, the nucleophile does not par-*

TABLE I
The $\hat{\sigma}_X$ values at which $\rho_Y = 0$ (ref.¹³)

Solvent	Reactants, °C	ρ_X^0	ρ_Y^0	ρ_{XY}	$\hat{\sigma}_X$
A $C_6H_5Cl-C_6H_{12}$ (1 : 1, v/v)	$YC_6H_4COCl +$ $XC_6H_4NH_2$ (25)	-3.35	1.09	-0.77	1.41
B $C_6H_5Cl-C_6H_{12}$ (1 : 1, v/v)	$YC_6H_4COBr +$ $XC_6H_4NH_2$ (25)	-3.16	0.58	-0.62	0.94
C $C_6H_5NO_2$	$YC_6H_4CH_2Br +$ $XC_6H_4NH_2$ (40)	-1.82	-0.29	-0.42	-0.69
D 1M Me_2SO in $C_6H_5NO_2$	$YC_6H_4CH_2Br +$ $XC_6H_4NH_2$ (40)	-1.40	0.22	-0.57	0.39

participate in the TS so that any interaction which involves the nucleophile in the TS is zero; thus $\rho_{XY} = \rho_{XZ} = 0$ and only non-zero interaction is that between the substrate (RY) and leaving group, Z^- , $\rho_{YZ} (\neq 0)$, which is normally large positive¹⁷. On the other hand in the S_N2C^+ mechanism, the nucleophile participates in the TS by attacking the preformed cation within the IP (Eq. (10)); the nucleophile therefore interacts with the substrate, cation YR^+ , but does not interact with the leaving group, Z^- , which is no longer bonded covalently to YR^+ in the IP.



Thus, ρ_{XY} is nonzero (normally large negative) but ρ_{XZ} is zero. Here again, ρ_{YZ} has a nonzero value.

The distinction between the two is clear: ρ_{XY} is zero for S_N1 , whereas for S_N2C^+ it has nonzero value, $\rho_{XY} \neq 0$. Moreover, in the latter, an isokinetic behavior is likely to be observed.

We have given examples of S_N2C^+ mechanism above in Section 1. The reactions of 1-PEC (ref.¹⁰) and benzhydryl chlorides¹¹ with anilines gave $\rho_{XY} = -2.05$ and -1.46 , respectively. Another example is the reactions of cumyl chlorides with anilines in MeOH at 35.0 °C, for which ρ_{XY} was -0.54 and $\hat{\sigma}_Y^+ = 0.39$ (extrapolated) at which $\rho_X = 0$ (ref.¹⁸).

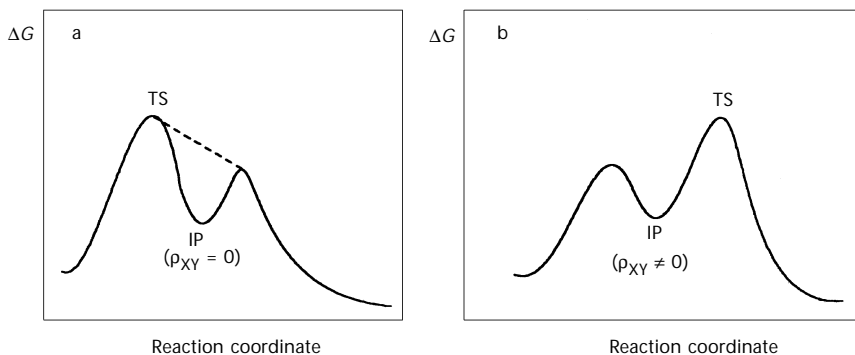


FIG. 1

Gibbs energy profiles for reactions involving ion-pair intermediate. Leaving group departure is the rate-determining step (a), and cation within the ion-pair which is formed in a fast pre-equilibrium step reacts with nucleophiles in the rate-limiting step (b)

The most important features of the above examples of the S_N2C^+ mechanism are observation of a large negative ρ_{XY} , and of a region where the thermodynamically more stable derivatives ($\delta\sigma_X > 0$) are kinetically more reactive ($\delta \log k_{XY} > 0$) so that ρ_X is positive. In such a region, an inverse thermodynamic stability–reactivity relationship holds^{2b}. Clearly, for the classic S_N1 and S_N2 mechanisms, the positive ρ_X value is not observable.

Many examples of S_N1 reactions can be found in the literature. We give here only two of them where ρ_{XY} and ρ_{XZ} values are tested explicitly. For the reactions of *tert*-butyl(phenyl)methyl arenesulfonates ($YC_6H_4CHC(CH_3)_3 \cdot OSO_2C_6H_4Z$) in methanol–acetonitrile mixtures at 65.0 °C (ref.¹⁷), added aniline nucleophiles ($XC_6H_4NH_2$) had no effect on the rate, *i.e.*, $\rho_{XY} = \rho_{XZ} = 0$. In contrast the ρ_{YZ} values were large and positive, $\rho_{YZ} = 0.6$ – 1.0 . For the reactions of 1-adamantyl arenesulfonates in MeOH–MeCN mixtures at 65.0 °C, aniline nucleophiles had no effect on the rate indicating that $\rho_{XY} = \rho_{XZ} = 0$ (ref.¹⁹).

However, for the nucleophilic substitution reactions of *exo*- and *endo*-norbornyl arenesulfonates with anilines in methanol and acetonitrile, the ρ_{XZ} values were very small but distinctly nonzero (≥ 0.01) as expected from a very loose, open or “exploded” type S_N2 TS (ref.²⁰).

It is therefore possible to distinguish between S_N1 ($\rho_{XY} = 0$) and S_N2C^+ ($\rho_{XY} \neq 0$) although both mechanisms involve ion-pair intermediate.

3.3. Tightness of the S_N2 Transition State

The sign and magnitude of ρ_{XZ} are useful for predictions of TS variation with substituent in the nucleophile (X) and leaving group (Z) and TS tightness of the S_N2 TSs. The definition of ρ_{XZ} , Eq. (11), requires that a stronger nucleophile ($\delta\sigma_X < 0$) and/or a stronger nucleofuge ($\delta\sigma_Z > 0$) leads to an earlier TS on the reaction coordinate with a lower degree of bond-making ($\delta|\rho_X| < 0 \rightarrow \delta\rho_X > 0$) and bond-breaking ($\delta\rho_Z < 0$) when ρ_{XZ} is positive. Conversely, a later TS is obtained when ρ_{XZ} is negative. Experimental results are entirely consistent with this prediction³.

$$\rho_{XZ} = \frac{\partial^2 \log k_{XZ}}{\partial \sigma_X \partial \sigma_Z} = \frac{\partial \rho_Z}{\partial \sigma_X} = \frac{\partial \rho_X}{\partial \sigma_Z} \quad (11)$$

On the other hand, *the magnitude of ρ_{XZ} is inversely proportional to the TS tightness, i.e., the distance between R_X and R_Z , r_{XZ}^\ddagger (Scheme 2) is shorter for the greater magnitude of ρ_{XZ} (refs^{7,21}).* Moreover, the magnitude of ρ_{XZ} has been

found to be a relatively large constant value at a primary carbon (average value of 0.33 in MeCN or MeOH at 45–65 °C), whereas it is a smaller constant at a secondary carbon center (average of 0.12 in MeCN at 65 °C), irrespective of the size of the group attached to the reaction center²¹ (Table II). These constant ρ_{XZ} values suggest that the TS is tight or loose (r_{XZ}^\ddagger in Scheme 2 is short or long) depending on whether the reaction center (R_Y) carbon is primary or secondary, but the TS tightness varies very little with regard to the group attached to the reaction center, R_Y . This constancy of the TS tightness has been confirmed by high-level *ab initio* MO calculations

TABLE II
The ρ_{XZ} values for the reactions of $ROSO_2C_6H_4Z$ with $XC_6H_4NH_2$ (refs^{21c,22})

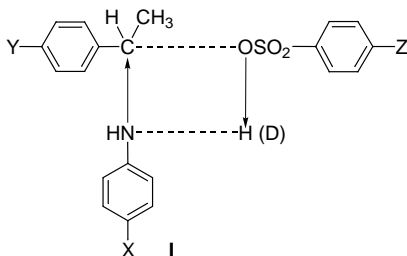
Alkyls	R	Solvent	T, °C	ρ_{XZ}
Primary	CH ₃	MeCN	65.0	0.32
		MeOH	65.0	0.30
	CH ₂ H ₅	MeCN	65.0	0.34
		MeOH	65.0	0.33
	CH ₂ =CHCH ₂	MeCN	45.0	0.37
	CH ₂ =C(CH ₃)CH ₂	MeCN	45.0	0.40
	CH≡CCH ₂	MeCN	45.0	0.29
	(CH ₃) ₃ CCH ₂	MeCN	55.0	0.31
	(CH ₃) ₃ SiCH ₂	MeCN	65.0	0.33
		MeOH	65.0	0.31
Secondary	(CH ₃) ₂ CH	MeCN	65.0	0.10
	CH ₃ CHCH ₂ CH ₃	MeCN	65.0	0.12
	CH ₃ CH(CH ₂) ₂ CH ₃	MeCN	65.0	0.13
	CH ₃ CH(CH ₂) ₃ CH ₃	MeCN	65.0	0.13
	(CH ₃ CH ₂) ₂ CH	MeCN	65.0	0.12
	CH ₃ CH ₂ CH(CH ₂) ₂ CH ₃	MeCN	65.0	0.12
	[-CH ₂ CHCH ₂ CH ₂ -]	MeCN	65.0	0.11
	[-CH ₂ CH(CH ₂) ₂ CH ₂ -]	MeCN	65.0	0.11
	[-CH ₂ CH(CH ₂) ₃ CH ₂ -]	MeCN	65.0	0.11
[-CH ₂ CH(CH ₂) ₄ CH ₂ -]	MeCN	65.0	0.11	

at the MP2/6-31+G*//MP2/6-31+G* level of theory on the reactions of $X^- + RX \rightleftharpoons XR + X^-$ with various primary and secondary R groups for $X = F$ and Cl (ref.²²).

The overall tightness, $r_{X\dots X}^\ddagger$, was indeed constant for each nucleophile, $X = F$ and Cl . For $X = Cl$ the constant values were $r_{Cl\dots Cl}^\ddagger = 4.67 \pm 0.02$ and 4.80 ± 0.02 Å for primary (average of seven values) and secondary (average of nine values) carbon centers, respectively²². The theoretical difference in the tightness of ca 0.1 Å for $X = Cl$ corresponds to the experimental difference in ρ_{XZ} of ca 0.2 Å. This theoretical analysis lends credence and reliability to the mechanistic significances of the cross-interaction constants and in particular to the inverse proportionality established experimentally between the magnitude of ρ_{XZ} and the overall TS tightness. The results of secondary kinetic isotope effect (SKIE) studies involving deuterated nucleophiles (e.g. $XC_6H_4ND_2$) as well as α -deuterated substrates (e.g. $YC_6H_4CD_2Cl$) were consistent with the predicted tightness based on the magnitude of ρ_{XZ} (ref.^{21c}).

3.4. Front-Side Attack S_N2 Mechanism

The reaction of 1-phenylethyl arenesulfonates, $YC_6H_4CH(CH_3)OSO_2C_6H_4Z$, with anilines, $XC_6H_4NH_2$ (Scheme 4), gave a large negative ρ_{XZ} ($= -0.56$) suggesting that the two, nucleophile (X) and leaving group (Z), are in close



SCHEME 4

proximity in the TS (ref.²³). Based on various experimental results, the TS is believed to involve a four-center hydrogen-bonded type, I, which is a result of frontal attack. The k_H/k_D values in Table III are in accord with this proposal^{21c,24}. The size of k_H/k_D is large, exceeding the limit of secondary KIEs ($k_H/k_D \leq 1.41$) and the magnitude suggests that a stronger hydrogen bond is formed by a weaker nucleophile ($\delta\sigma_X > 0$) and/or nucleofuge ($\delta\sigma_Z < 0$). This is consistent with the greater deprotonation occurring when aniline has an electron-acceptor substituent which makes the amine hydrogen more acidic, and when leaving group has an electron-donor substituent which lo-

calizes more electronic charge on the reaction center oxygen leading to a stronger electrostatic attraction of the proton.

The interpretation of the magnitude is complicated by the increased out-of-plane bending vibrational frequencies of the other N-H(D) bond due to steric hindrance in the closer approach of the nucleophile toward C_α which leads to an inverse effect ($k_H/k_D < 1.0$). When the nucleophile is changed to *N,N*-dimethylaniline, the size of ρ_{XZ} decreases to -0.24 (ref.²⁵), which is still somewhat high because of closer approach of the nucleophile towards the leaving group in the partial front-side attack, but without the deprotonation involved in the four-center type TS. The optical rotation measurements for the reaction of 3-nitroaniline and 1-phenylethyl 4-nitrobenzenesulfonate in acetonitrile at 25 °C indicated that approximately 55% retention of the original reactant stereochemistry in the product. Thus the fraction of frontal attack S_N2 is slightly over 50% of the total reaction²⁶.

A large negative ρ_{XZ} ($\rho_{XZ} \leq -0.4$, $\beta_{XZ} \leq -0.2$) suggests the partial front-side attack S_N2 mechanism. Similar larger negative ρ_{XZ} values were also found for the reactions of 2-phenylethyl arenesulfonates ($\rho_{XZ} \approx -0.45$)²⁷, 1- and 2-(1- or 2-naphthyl)ethyl arenesulfonates ($\rho_{XZ} = -0.4$, $\beta_{XZ} \approx -0.2$)²⁸, 2- and 3-thienylethyl arenesulfonates with anilines ($\rho_{XZ} = -0.5$, $\beta_{XZ} = -0.3$)²⁹, and anilino thioethers ($C_6H_5N(CH_3)CH_2SC_6H_4Z$) with anilines ($\rho_{XZ} = -1.7$, $\beta_{XZ} = -0.27$)³⁰. A similar mechanism has been suggested to apply to these reactions.

Another interesting case is the reactions of cumyl arenesulfonates with anilines, discussed above in Section 3.1., for this case, ρ_{XZ} was -0.75 so that the front-side attack S_N2 mechanism was proposed to apply¹⁴.

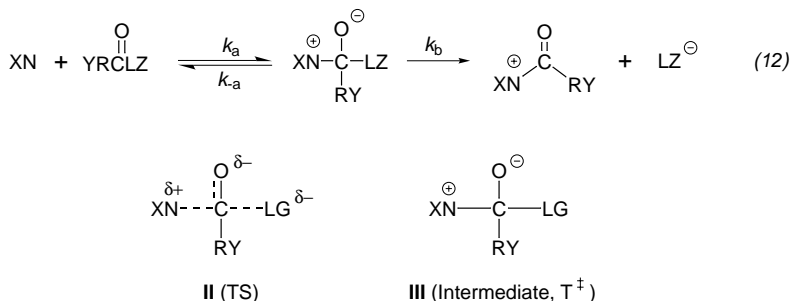
TABLE III

Kinetic isotope effects (k_H/k_D) for the reactions of 1-phenylethyl arenesulfonates with deuterated anilines²⁴ in MeCN at 35 °C

X	Y	Z	k_H/k_D
4-CH ₃ O	H	4-NO ₂	1.703
4-CH ₃ O	H	4-CH ₃	1.964
3-NO ₂	H	4-NO ₂	2.348
3-NO ₂	H	4-CH ₃	2.583 (2.341 at 65 °C)

3.5. Acyl Transfer Reaction Mechanism

Two distinct reaction pathways have been proposed for nucleophilic substitution at a carbonyl carbon, Eq. (12).



One-step concerted mechanism proceeds through a tetrahedral TS, **II**, the rate-determining step being k_a , whereas two-step addition-elimination processes occur *via* a tetrahedral intermediate, **III** ($k_a \gg k_b$). In the stepwise pathway, a mechanistic changeover can take place from rate-limiting breakdown ($k_N = K k_b = (k_a/k_{-a})k_b$) to formation (k_a) of the intermediate depending on (i) relative basicities (pK_a) of the nucleophile (NX) and nucleofuge (LZ), and (ii) electron-donating or electron-withdrawing power of the nonleaving group (RY). When the nucleophile is strongly basic, $k_{-a} \ll k_b$, so that $k_N = k_a$, whereas when the nucleophile is weakly basic, $k_{-a} \gg k_b$, and $k_N = K k_b$ and the second is the rate-determining step. The energy profiles are similar to those of Figs 1a and 1b in Section 3.2., respectively. Furthermore, experimental results indicated that an electron donor Y ($\delta\sigma_Y < 0$) favors leaving group (or basic group) expulsion ($\delta\sigma_Z > 0$), or conversely disfavors amine (or weakly basic group) expulsion ($\delta\rho_X < 0$) in the stepwise mechanism with rate-limiting departure of the leaving group³¹. Thus $\rho_{XY} = \delta\rho_X/\delta\sigma_Y = (-)/(-) > 0$ and $\rho_{YZ} = \delta\rho_Z/\delta\sigma_Y = (+)/(-) < 0$. On the other hand, weakly basic nucleophile ($\delta\sigma_X > 0$) was found to favour leaving group expulsion³¹ $\delta\rho_Z > 0$ so that $\rho_{XZ} = \delta\rho_Z/\delta\sigma_X = (+)/(+) > 0$. *The signs of ρ_{XY} (> 0) and ρ_{YZ} (< 0) for the rate-limiting breakdown of the tetrahedral intermediate are exactly opposite to those for S_N2 reactions^{3,32}, $\rho_{XY} < 0$ and $\rho_{YZ} > 0$. Therefore, for the concerted acyl transfer (or rate-limiting formation of the intermediate, for which $\rho_{YZ} = 0$) in which k_a is the rate-determining step, the signs of ρ_{XY} and ρ_{YZ} are reversed from those of the rate-limiting breakdown of the intermediate. These sign reversals were confirmed by MO theoretical studies³³. The sign of ρ_{XZ} is always positive for the rate-limiting breakdown of the in-*

intermediate, but it can be either positive or negative for the concerted, one-step reactions³². For example, in the reactions of Z-thiophenyl 4-nitrobenzoates with X-pyridines, the ρ_{XZ} changed from a large positive (+1.41) for the weakly basic pyridines to a small negative (-0.32) value for the strongly basic pyridines at $pK_a^0 \approx 5.0$. This was attributed to a change in the rate-limiting step from breakdown to formation of a tetrahedral intermediate³⁴.

The magnitudes of the cross-interaction constants for the rate-limiting breakdown are in general large compared to those for the concerted mechanism since the observed k_N value for the former is a complex quantity, $k_{\text{obs}} = k_N = K k_b$, whereas that for the latter is simply $k_a (= k_{\text{obs}})$. For example, $\rho_{XY}(k_N) = \rho_{XY}(K) + \rho_{XY}(k_b) = (++) + (\approx 0) = (++)$ (refs^{32,33}) since there is a strong interaction within the intermediate, *i.e.*, $\rho_{XY}(K)$ is large positive.

3.6. Reactivity-Selectivity Principle^{33,35} (RSP)

Let us consider changes in reactivity, δR_j^0 , and selectivity, δS_i^j , which are defined as Eqs (13) and (14). δR_j^0 , Eq. (13), represents the change of reactivity by substituting $\sigma_j (\neq 0)$ for $\sigma_j = 0$ when σ_i is kept constant to $\sigma_i = 0$, and δS_i^j , Eq. (14), represents the change in selectivity for i by substituting $\sigma_j (\neq 0)$ for $\sigma_j = 0$. Here division by ρ_i^0 assures that

$$\delta R_j^0 = \log k_{0j} - \log k_{00} = \log \left(\frac{k_{0j}}{k_{00}} \right) = \rho_j^0 \sigma_j, \quad (13)$$

$$\delta S_i^j = \frac{\rho_i}{\rho_i^0} - \frac{\rho_i^0}{\rho_i^0} = \frac{\rho_i - \rho_i^0}{\rho_i^0}. \quad (14)$$

We are comparing two relative selectivities, which are the magnitude of ρ irrespective of the sign; we are tacitly assuming that there is no sign change of ρ within the set of substituents j (σ_j) considered. Here ρ_i^0 and ρ_i (or ρ_i^j) denote selectivity for i with $j = 0$ and with any other $j (\neq 0)$, respectively (Table IV).

Substituting Eq. (8b) into Eq. (14) leads to Eq. (15).

$$\delta S_i^j = \frac{\rho_{ij} \sigma_j}{\rho_i^0} \quad (15)$$

Finally substituting σ_j from Eq. (13) into Eq. (15), we obtain Eq. (16)

$$\delta S_i^j = \frac{\rho_{ij}}{\rho_i^0 \rho_j^0} \delta R_j^0 \quad (16)$$

or alternatively,

$$\delta R_j^0 = \frac{\rho_i^0 \rho_j^0}{\rho_{ij}} \delta S_i^j = W \delta S_i^j. \quad (17)$$

It is clear from Eq. (17) that increasing reactivity of reactant j ($\delta R_j^0 > 0$) leads to decreasing selectivity ($\delta S_i^j < 0$) only when W is negative, *i.e.*, RSP is valid only when $W < 0$. The fact that sign of W determines the sign relationship between changes in δR_j^0 and δS_i^j is evident from Eqs (13) and (15); the sign of δR_j^0 is determined by ρ_j^0 (Eq. (13)) whereas that of δS_i^j is determined by ρ_{ij}/ρ_i^0 (Eq. (15)), and hence combination of both by eliminating σ_j from the two equations, *i.e.*, W , represents the sign correlation of the two changes. Equation (8a) shows that at a noninteractive (or magic) point, $\hat{\sigma}_j$, the reaction becomes isokinetic (irrespective of the substituent i), $\rho_i = 0$ and the sign of ρ_i (Eq. (8b)) reverses. This means that the validity of RSP can also reverse at this point.

For S_N1 , $\rho_X = 0$, $\rho_Y^0 < 0$, $\rho_Z^0 > 0$ and $\rho_{YZ} > 0$ so that W is negative and RSP is valid with respect to substituents Y and Z only¹⁷. For S_N2 (dissociative, $\rho_Y^0 < 0$) $\rho_X^0 < 0$, $\rho_Y^0 < 0$, $\rho_Z^0 > 0$, and in general $\rho_{XY} < 0$, $\rho_{YZ} > 0$ and $\rho_{XZ} < 0$ (ref.³). Thus W is negative for the set of (X,Y) and (Y,Z) but it is positive for (X,Z) set. Thus the RSP is valid for the sets (X,Y) and (Y,Z), but is not valid for (X,Z) set. Likewise for S_N2 (associative, $\rho_Y^0 > 0$), W is negative and hence RSP

TABLE IV
Schematic presentation of $\log k_{ij}$ as a function of σ_i and σ_j

$i \setminus j$	$\sigma_j < 0$	$\sigma_j = 0$	$\sigma_j > 0$
$\sigma_i < 0$	$\log k_{ij}$	$\log k_{i_0}$	$\log k_{ij}$
$\sigma_i = 0$	$\log k_{0j}$	$\log k_{00}$	$\log k_{0j}$
$\sigma_i > 0$	$\log k_{ij}$	$\log k_{i_0}$	$\log k_{ij}$
ρ_i	ρ_i^j	ρ_i^0	ρ_i^j
(ρ_i/ρ_i^0)			

(δR_j^0) is accompanied by (δS_i^j)

For this reaction, $k_{\text{obs}} = K k_2$ where $K = k_1 / k_{-1}$ in Eq. (18). The AM1 MO results showed that while the $\rho(k_{\text{obs}})$ values differ greatly ($\rho(k_{\text{obs}}) = 14.7$ and 6.7 for $X = Y$ in the gas phase and in water, respectively), the magnitude of ρ_{XY} was found to be similar in the gas phase ($\rho_{XY} = -0.58$) and in water ($\rho_{XY} = -0.55$). The experimental value of $\rho(k_{\text{obs}})$ in 70% (v/v) aqueous DMSO in the temperature range of 30–60 °C was 5.70 (for $X = Y$)⁴⁰. The corresponding theoretical value in water ($\rho(k_{\text{obs}}) = 6.7$) is again in satisfactory agreement with the experimental value in aqueous DMSO solution. Thus here again, the ρ value in the gas phase is considerably larger than that in aqueous solution, but the magnitude of ρ_{XY} is quite similar in the gas phase and in water.

Thus, the magnitudes of the first-derivative parameters in the gas phase and in solution differ greatly, whereas the magnitudes of cross-interaction constants remain virtually constant in the gas phase and in solution. This agreement in the ρ_{XY} value, despite a large difference in the magnitude of ρ_Y (and ρ_X) found in the gas phase and in solution suggests that *cross-interaction constants (ρ_{XY}) may be independent of the environmental effects and constitute an intrinsic property of a reaction*³⁷.

The cross-interaction constants for equilibrium processes are in general large when in the product state the two fragments interacting are covalently bonded, and especially when a positive charge center is involved. Examples are (i) equilibrium cross-interaction constant involved in the reactions of *Y*-benzyl bromide with *X*-*N,N*-dimethyl anilines in acetonitrile ($\rho_{XY} = -1.45$)⁴¹ and (ii) cross-interactions involved in the protonation equilibria of diaryl (*X,Z*) ketones in the gas phase for which *ab initio* calculations gave $\rho_{XZ} = -1.39, -1.66$ and -1.40 for *X*-phenyl-*Y*-hetaryl- (5-membered) (*Z*) ketones with *Y* = NH, O and S, respectively, at the MP2/6-31G*//HF/6-31G* level⁴².

4. SUMMARY AND OUTLOOK

In the past decade, significant advances in the applications of the cross-interaction constants, ρ_{ij} (and β_{ij}), to the mechanistic studies of organic reactions have been made. The sign and magnitude of the cross-interaction constants have made it possible to correctly interpret some of the isokinetic (or isoparametric) phenomena, ion-pair mechanism, tightness of the S_N2 TS and front-side attack S_N2 mechanism. They have also provided us with additional mechanistic criteria for acyl transfer reaction mechanism and validity of the RSP. Parallel theoretical studies on gas-phase reactions have proved to be valuable in unrevelling the intrinsic nature of the cross-

interaction constants. Further investigations of the MO theoretical gas-phase reactions should give insight into intrinsic features of the transition states through the cross-interaction constants and lead to much wider applications of them to the studies of the organic reaction mechanism.

The mechanistic criteria discussed in this article are summarized in Table V.

TABLE V
Summary of qualitative mechanistic criteria using the cross-interaction constants (CIC)

Reaction type	$\rho_{XY} (\beta_{XY})$	$\rho_{YZ} (\beta_{YZ})$	$\rho_{XZ} (\beta_{XZ})$
S_N1	0	++ ^a	0
S_N2C^+	--	+	0
S_N2	-	+	\pm^b
Front-side attack S_N2	-	+	--
Acyl transfer: rate-limiting breakdown of $T^\pm (T^-)$	++	--	++
Acyl transfer: rate-limiting formation of $T^\pm (T^-)$	-	0	\pm

^a Double plus or minus denotes relatively large positive or negative value. ^b (\pm) Denotes that the sign can be either positive or negative.

We look forward to establishing more quantitative mechanistic applications of the cross-interaction constants, especially in the fields of acyl transfer reaction and front-side attack S_N2 mechanisms. Applications to base-catalyzed elimination reactions and the imbalanced TS problems are the promising areas of future extension.

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REFERENCES

1. a) Lowry T. H., Richardson K. S.: *Mechanism and Theory in Organic Chemistry*, 3rd ed., Chaps 2 and 3. Harper and Row, New York 1987; b) Isaacs N. S.: *Physical Organic Chemistry*, Chaps 4 and 9. Longman, Harlow 1987.
2. a) Lee I. in: *Organic Reactivity: Physical and Biological Aspects*, Spec. Publ. No. 148, p. 361. R. Soc. Chem., Cambridge 1995; b) Lee I.: *J. Phys. Org. Chem.* **1996**, *9*, 661.
3. a) Lee I.: *Chem. Soc. Rev.* **1990**, *19*, 317; b) Lee I.: *Adv. Phys. Org. Chem.* **1992**, *27*, 57.

4. Lee I., Lee D., Lee J. K., Kim C. K., Lee B.-S.: *J. Chem. Soc., Perkin Trans. 2* **1996**, 2519.
5. Similar second-order cross-interaction constants are reported with different notations:
a) Dubois J. E., Ruasse M. F., Argile A.: *J. Am. Chem. Soc.* **1984**, 106, 4840; b) Jencks W. P.: *Chem. Rev.* **1985**, 85, 511; c) Yoh S. D., Cheong D. Y.: *J. Phys. Org. Chem.* **1996**, 9, 701.
6. Kevill D. N., D'Souza M. J.: *J. Chem. Soc., Perkin Trans. 2* **1994**, 2427.
7. Lee I.: *J. Phys. Org. Chem.* **1992**, 5, 736.
8. Exner O.: *J. Chem. Soc., Perkin Trans. 2* **1993**, 973.
9. a) Leffler J. E., Grunwald E.: *Rates and Equilibria of Organic Reactions*. Wiley, New York 1963; b) Exner O.: *Collect. Czech. Chem. Commun.* **1964**, 29, 1094.
10. Lee I., Lee W. H., Bentley T. W.: *J. Chem. Soc., Perkin Trans. 2* **1993**, 141.
11. Chang S., Koh H. J., Lee B.-S., Lee I.: *J. Org. Chem.* **1995**, 60, 7760.
12. Amyes T. L., Stevens I. W., Richard J. P.: *J. Org. Chem.* **1993**, 58, 6057.
13. Shpanko I. V.: *Mendeleev Commun.* **1991**, 119.
14. Koh H. J., Lee H. W., Lee I.: *J. Chem. Soc., Perkin Trans. 1* **1994**, 125.
15. Brown H. C., Okamoto Y.: *J. Am. Chem. Soc.* **1958**, 80, 4979.
16. a) Shpanko I. V., Serebryakov I. U., Korostylev A. P.: *Zh. Org. Khim.* **1988**, 26, 1358; b) Shpanko I. V., Goncharov A. N., Litvinenko L. M.: *Zh. Org. Khim.* **1979**, 15, 1648; c) Shpanko I. V., Litvinenko L. M., Goncharov A. N., Korzhilova O. I.: *Zh. Org. Khim.* **1981**, 17, 965; d) Shpanko I. V., Goncharov A. N.: *Zh. Org. Khim.* **1987**, 23, 2591.
17. Lee I., Choi M. S., Lee H. W.: *J. Chem. Res., Miniprint* **1994**, 0568.
18. Lee I., Koh H. J., Hong S. N., Lee B.-S.: *Gazz. Chim. Ital.* **1995**, 125, 347.
19. Oh H. K., Kwon Y. B., Koh H. J., Lee I.: *New J. Chem.* **1996**, 20, 579.
20. Oh H. K., Joung E.-M., Ch I. H., Park Y. S., Lee I.: *J. Chem. Soc., Perkin Trans. 2* **1998**, 2027.
21. a) Koh H. J., Lee H. W., Lee I.: *J. Chem. Soc., Perkin Trans. 2* **1994**, 253; b) Oh H. K., Kwon Y. B., Cho I. H., Lee I.: *J. Chem. Soc., Perkin Trans. 2* **1994**, 1697; c) Lee I.: *Chem. Soc. Rev.* **1995**, 24, 223.
22. a) Lee I., Kim C. K., Chung D. S., Lee B.-S.: *J. Org. Chem.* **1994**, 59, 4490; b) Oh H. K., Kwon Y. B., Chung D. S., Lee I.: *Bull. Korean Chem. Soc.* **1995**, 16, 827.
23. Lee I., Kim H. Y., Kang H. K., Lee H. W.: *J. Org. Chem.* **1998**, 53, 2678.
24. Lee I., Koh H. J., Lee H. W.: *J. Chem. Res., Miniprint* **1990**, 2177.
25. Lee I., Kim H. Y., Lee H. W., Kim I. C.: *J. Phys. Org. Chem.* **1989**, 2, 35.
26. Lee I., Shim C. S., Lee H. W., Lee B.-S.: *Bull. Korean Chem. Soc.* **1991**, 12, 255.
27. Lee I., Choi Y. H., Lee H. W., Lee B.-S.: *J. Chem. Soc., Perkin Trans. 2* **1988**, 1537.
28. Oh H. K., Song S. J., Cho I. H., Lee I.: *Bull. Korean Chem. Soc.* **1996**, 17, 254.
29. Oh H. K., Yun J. H., Cho I. H., Lee I.: *Bull. Korean Chem. Soc.* **1997**, 18, 390.
30. Oh H. K., Yang J. H., Lee I.: Unpublished results.
31. a) Gresser M. T., Jencks W. P.: *J. Am. Chem. Soc.* **1997**, 99, 6963; b) Gresser M. T., Jencks W. P.: *J. Am. Chem. Soc.* **1977**, 99, 6970; c) Castro E. A., Santander C. L.: *J. Org. Chem.* **1985**, 50, 3595; d) Oh H. K., Shin C. H., Lee I.: *J. Chem. Soc., Perkin Trans. 2* **1995**, 1169; e) Oh H. K., Lee H. C., Lee I.: *Bull. Korean Chem. Soc.* **1995**, 16, 839; f) Lee I., Koh H. J.: *New J. Chem.* **1996**, 20, 131; g) Kim T.-H., Huh C., Lee B.-S., Lee I.: *J. Chem. Soc., Perkin Trans. 2* **1995**, 2257.
32. Lee I.: *Bull. Korean Chem. Soc.* **1994**, 15, 985.
33. a) Lee D., Kim C. K., Lee B.-S., Lee I.: *Bull. Korean Chem. Soc.* **1995**, 16, 1203; b) Lee I., Lee D., Kim C. K.: *J. Phys. Chem. A* **1997**, 101, 879.

34. Koh H. J., Ham K. L., Lee H. W., Lee I.: Unpublished results.
35. a) Pross A.: *Adv. Phys. Org. Chem.* **1977**, *14*, 69; b) Buncl E., Wilson H. J.: *J. Chem. Educ.* **1987**, *64*, 475.
36. Lee I., Lee B.-S., Koh H. J., Chang B. D.: *Bull. Korean Chem. Soc.* **1995**, *16*, 277.
37. Kim W. K., Ryu W. S., Han I. S., Kim C. K., Lee I.: *J. Phys. Org. Chem.* **1998**, *11*, 115.
38. Władkowski B. D., Wilbur J. L., Brauman J. I.: *J. Am. Chem. Soc.* **1994**, *116*, 1994.
39. Waszczylo Z., Westaway K. C.: *Tetrahedron Lett.* **1982**, *23*, 143.
40. a) Bowden K., Williams K. D.: *J. Chem. Soc., Perkin Trans. 2* **1994**, 77; b) Bowden K.: *Org. Reactiv.* **1994**, 19.
41. Lee I., Park Y. K., Huh C., Lee H. W.: *J. Phys. Org. Chem.* **1994**, *7*, 555.
42. Lee I., Kim C. K., Kim C.-K., Chung D. S.: *J. Chem. Soc., Perkin Trans. 2*, in press.