Stereoelectronic Origins of the Intrinsic Barrier to S_N2 Reactions

By Ikchoon Lee

DEPARTMENT OF CHEMISTRY, INHA UNIVERSITY, INCHON 402-751, KOREA

1 Introduction

The concept of the intrinsic barrier, which can be determined by means of identity reaction barriers, is very useful in allowing a better understanding of factors influencing the reactivity and thermodynamic effects on rates.

In this work, the origin of the intrinsic barrier and its significance in the transition state structures of S_N2 processes are reviewed.

The Marcus expression, equation 1, gives the kinetic barrier (ΔG^{+}) in terms of intrinsic (ΔG_0^{+}) and thermodynamic ($\Delta G°$) barriers,[1] and provides a simple

$$\Delta G^{+} = \Delta G_0^{+} + \Delta G°/2 + (\Delta G°)^2/(16\Delta G_0^{+}) \qquad (1)$$

picture of how kinetic and thermodynamic substituent effects combine to affect the overall barrier to a group-transfer reaction. Although the Marcus equation was originally derived for electron-transfer reactions in solution,[1a] it has been shown to apply to various processes including group transfers, such as methyl-transfer reactions (equation 2).[1e—i]

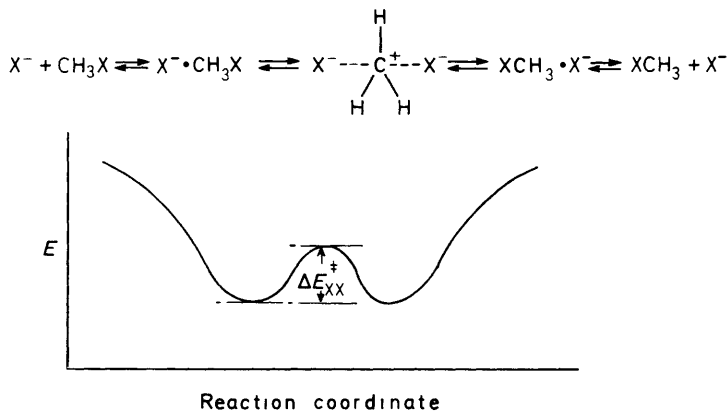$$X^- + CH_3Y \rightleftharpoons XCH_3 + Y^- \qquad (2)$$
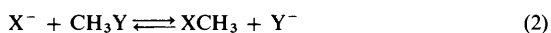
Studies of gas-phase S_N2 reactions have provided a direct means of determining experimentally the intrinsic barriers involved in the gas-phase methyl-transfer reactions.[1e—f,2] Alternatively, several elegant studies by Lewis et al.[3] involving solution-phase methyl-transfer reactions have provided kinetic data from which the intrinsic barriers can also be determined for solution-phase reactions. [The

[1] (a) R A Marcus, *Annu Rev Phys Chem*, 1964, **15**, 155, (b) R A Marcus, *J Phys Chem*, 1968, **72**, 891, (c) A O Cohen and R A Marcus, *ibid*, 1968, **72**, 4249, (d) W J Albery and M M Kreevoy, *Adv Phys Org Chem*, 1978, **16**, 87, (e) M J Pellerite and J I Brauman, *J Am Chem Soc*, 1980, **102**, 5993, (f) M J Pellerite and J I Brauman, *ibid*, 1983, **105**, 2672, (g) E S Lewis and D D Hu, *ibid*, 1984, **106**, 3992, (h) E S Lewis, *J Phys Chem*, 1986, **90**, 3756, (i) J R Murdoch, *J Am Chem Soc*, 1983, **105**, 2660, (j) E Grunwald, *ibid*, 1985, **107**, 125
[2] (a) W N Olmstead and J I Brauman, *J Am Chem Soc*, 1977, **99**, 4219, (b) J A Dodd and J I Brauman, *ibid*, 1984, **106**, 5356, (c) C -C Han, J A Dodd, and J I Brauman, *J Phys Chem*, 1986, **90**, 471
[3] (a) E S Lewis and S J Kukes, *J Am Chem Soc*, 1979, **101**, 417, (b) E S Lewis, T I Yousaf, and T A Douglas, *ibid*, 1987, **109**, 2152, (c) T I Yousaf and E S Lewis, *ibid*, 1987, **109**, 6137

$$X^- + CH_3X \rightleftharpoons X^- \cdot CH_3X \rightleftharpoons X^- --- \overset{\overset{\displaystyle H}{|}}{\underset{/ \backslash}{C}}\overset{+}{} --- X^- \rightleftharpoons XCH_3 \cdot X^- \rightleftharpoons XCH_3 + X^-$$

Reaction coordinate

Figure 1 *Double-well potential-energy surface for the gas-phase identity S_N2 reaction $X^- + CH_3X \rightleftharpoons XCH_3 + X^-$*

free-energy form of equation 1 is normally used for solution-phase reactions, but the application of the potential-energy form (1′)

$$\Delta E^+ = \Delta E_0^{\ddagger} + \Delta E^{\circ}/2 + (\Delta E^{\circ})^2/16\Delta E_0^{\ddagger} \tag{1′}$$

is more intuitive and appropriate for gas-phase and theoretical studies. Thus the free-energy ($\Delta G_0^{\ddagger}$) or the potential-energy form ($\Delta E_0^{\ddagger}$) will be used for the appropriate cases. For solution-phase reactions, the work terms, which are largely made up of solvent–solute interactions, should be included in equation 1. However, they are independent of structure throughout a series of related reactions and hence if the solvent is constant the work terms can be dropped from the Marcus equation as shown in equation 1.]

Theoretically the intrinsic barriers can be obtained by MO calculation,[4] from the energy difference between the transition state (TS) and the ion–molecule cluster, *i.e.*, the height of the central barrier in Figure 1. For an identity-exchange reaction, $X = Y$ in equation 2, $\Delta E^{\circ} = 0$ so that the activation barrier becomes equal to the intrinsic barrier, $\Delta E^+ = \Delta E_0^{\ddagger}$. Comparison of experimental and theoretical intrinsic barriers for some of the identity-exchange reactions in Table 1 shows that agreement between the two is only moderate.

However, this could be attributed to the difficulties in determining experimental values[5] and the inadequacy of the use of the 4-31G basis set for this type of calculation.[6]

[4] (*a*) S Wolfe, D J Mitchell, and H B Schlegel, *J Am Chem Soc*, 1981, **103**, 7692, 7694, (*b*) J D Mitchell, Ph D Thesis, Queen's University, 1981, (*c*) D J Mitchell, H B Schlegel, S S Shaik, and S Wolfe, *Can J Chem*, 1985, **63**, 1642, (*d*) I Lee, C K Kim, and C H Song, *Bull Korean Chem Soc*, 1986, **7**, 391

[5] Errors in $\Delta E_{XX}^{\ddagger}$ are reported to be within a few kcal/mol.[1*f*]

[6] F Keil and R Ahlrichs, *J Am Chem Soc*, 1976, **98**, 4787

Table 1 *Comparison of experimental (gas-phase) and theoretical (4-31G level) values of* $\Delta E_{XX}^{\ddagger}$ *(kcal/mol) for* $X^- + CH_3X \rightleftharpoons XCH_3 + X^-$

X	$\Delta E_{XX}^{\ddagger}$	
	Expt.	*Theoret.*
HCC	41.3	50.4
CN	35.0	43.8
NH_2	26.6	23.5
CH_3O	24.2	15.6
F	26.2	11.7
Cl	10.2	5.5
NC	—	28.5
CH_3	—	28.5
OH	—	21.2
OF	—	18.8
OOH	—	18.5

$$X^- \text{----} \overset{\displaystyle H}{\underset{\displaystyle H \quad H}{\overset{|}{C}^+}} \text{----} X^-$$
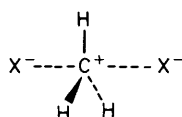
(1)

Various interpretations of the significance of the intrinsic barrier have been offered: (i) Brauman *et al.*[1f] correlated the gas-phase identity-exchange barriers, $\Delta E_{XX}^{\ddagger}$, with the methyl-cation affinity E_{mc} of the nucleophile defined as the heterolytic bond dissociation energy of the CH_3–X bond.

$$CH_3X \longrightarrow CH_3^+ + X^-$$
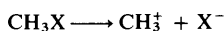
$$\Delta H° = E_{mc}(X^-) = D_0(CH_3\text{–}X) - E_{ea}(X) + E_i(CH_3)$$

where $D°$ is the bond dissociation energy, $E_{ea}(X)$ is the electron affinity of the X radical and $E_i(CH_3)$ is the methyl-radical ionization potential. They interpreted the correlation as a consequence of charge separation in the trigonal-bipyramidal penta-coordinate (TBP-5C) TS, (1), of the exchange reaction. (ii) Wolfe *et al.*,[4c] correlated their $\Delta E_{XX}^{\ddagger}$ values calculated using the 4-31G basis set with the deformation energies, ΔE_{def}, of CH_3X in the TBP-5C TS formation, especially with the C–X stretching energies ΔE_R.

Although these rationalizations are reasonable, they seem unsatisfactory since they deal with deformation energies of CH_3X only and all X's are included indiscriminately into a single correlation.

Alternatively, the intrinsic barrier in the S_N2 type processes at a carbon centre has been shown to have stereoelectronic origins.

Table 2 *Empirical parameters a_{ij} and b_{ij} from equation 3 over the Periodic Table*

	H	1	2	3	4
			a_{ij}		
H	1 18	1.46	1.74	1 82	1 96
1		1.85	2.06	2.15	2.28
2			2.36	2 45	2.62
3				2.57	2 71
4					2.87
			b_{ij}		
H	0.58	0.56	0.64	0.66	0.72
1		0.55	0.63	0.64	0.70
2			0.70	0.73	0.79
3				0 74	0.81
4					0.87

2 Steric Origin

Before proceeding to elaborate on the origins of the intrinsic barriers involved in the identity-exchange reaction, equation 2 with X = Y, let us first consider the correlation between the bond length, r, and the force constant, F, for the symmetric vibrational mode of the C–X bond in the TBP-5C TS, (1). It has been shown by Badger[7] that the empirical correlation shown in equation 3 holds between bond lengths and force constants of diatomic molecules, where constants

$$r = a_{ij} - b_{ij} \log F \tag{3}$$

a_{ij} and b_{ij} depend only on the rows (i and j) of the periodic table for the two atoms being bonded, *i.e.*, one atom is in row i and the other in row j. The relationship (equation 3) has been extended to loose, Lennard–Jones, noble-gas two-atom clusters, demonstrating a striking continuity of bonding between the noble-gas clusters and the usual strong chemical bonds.[8] The empirical parameters a_{ij} and b_{ij} in equation 3, including those for noble-gas clusters, are summarized in Table 2. The a_{ij} values are seen to increase slowly and smoothly as the valence shell of the atoms expands gradually along with the increase in the number of the rows of the periodic table. The parameter a_{ij} is regarded as a standard bond length for a related family of bonds between two atoms belonging to i-th and j-th rows at unit force constant, $F = 1$, *i.e.*,[8d]

$$a_{ij} = r_{(F = 1)}$$

[7] (a) R M Badger, *J Chem Phys*, 1933, **2**, 128, (b) R M Badger, *Phys Rev*, 1935, **48**, 284, (c) J Waser and L Pauling, *J Chem Phys*, 1950, **18**, 618, (d) R M Badger, *J Chem Soc*, 1934, 3, 710

[8] (a) H S Johnston, 'Gas Phase Reaction Rate Theory', The Ronald Press, New York, 1966, (b) T L Cottrell, 'The Strength of Chemical Bonds', Butterworths, London, 1958, (c) D R Herschbach and V W Laurie, *J Chem Phys*, 1961, **35**, 458, (d) H S Johnston, *J Am Chem Soc*, 1964, **86**, 1643

Table 3 *Average non-polar covalent radii, r_{ij}, over the Periodic Table*

	1	2	3	4
1	1.72	2.07	2.24	2.43
2		2.42	2.59	2.78
3			2.76	2.95
4				3.14

whereas the parameter b_{ij}, represents the degree of a bond length change in a tenfold increase of the stretching force constant:

$$r_{(F=10)} = a_{ij} - b_{ij}$$

Therefore $\qquad\qquad b_{ij} = r_{(F=1)} - r_{(F=10)}$

On the other hand, averaging the non-polar covalent bond radii (r_i) of the representative elements within the i-th row, median (or average) nonpolar covalent bond radii, $\bar{r}_{ij}$, between two atoms in the i-th and j-th rows are obtained by adding the two average covalent radii of elements, $\bar{r}_{ij} = \bar{r}_i + \bar{r}_j$, as presented in Table 3.[9] The $\bar{r}_{ij}$ values vary slowly and smoothly over the periodic table as was found for the a_{ij} value; in fact the $\bar{r}_{ij}$ values are within $\pm 10\%$ of the empirical a_{ij} values. This was taken as an indication that the a_{ij} values reflect the *median* covalent bond radii for the family of bonds between one atom in i-th and the other in j-th row.

Since equation 3 was originally derived *empirically for diatomic molecules*, it was of interest to see if one can arrive at the same correlation theoretically. The MO calculations at the 4-31[6] and 6-31G* levels [10] have indeed shown that the relationship (equation 3) holds for various diatomics which were used in the empirical correlation for 1–1, *i.e.*, $i = 1$ and $j = 1$, series. The parameters a_{11} and b_{11} obtained theoretically are 1.80 and 0.53 (4-31G),[11] and 1.80 and 0.51 (6-31G*),[10] which agree quite well with the empirical values of $a_{11} = 1.85$ and $b_{11} = 0.55$, respectively.

Moreover, it has been shown MO theoretically using the 4-31G basis set that Badgers rule, equation 3, also holds for the ion–molecule cluster, $X^- - - - CH_3X$, as well as for the TBP-5C TS, (1).[11] Using ten anionic nucleophiles (X^-) of the first row elements, a satisfactory linear correlation $(r = 0.970)$ between r and log F (equation 3) for C–X bonds in (1) was obtained with $a_{11} = 2.48$ and $b_{11} = 1.10$,[11] which are much greater than the empirical parameters $(a_{11} = 1.85$ and $b_{11} = 0.55)$ for the 1–1 series of diatomic molecules.

The results of higher level *ab initio* computations,[10] however, afforded the following conclusions:

[9] R. T. Sanderson, 'Chemical Bonds and Bond Energy', Academic Press, New York, 1971.

[10] J. K. Cho, Ph.D. Thesis, Inha University, 1989.

[11] I. Lee, J. K. Cho, and C. H. Song, *J. Chem. Soc., Faraday Trans. 2*, 1988, **84**, 1177.

(i) For anionic TS, (1), incorporation of diffuse function[12] and correlation effect[13] lowers both parameters, a_{ij} and b_{ij}.

(ii) The one-heavy-atom nucleophiles (X^- = F^-, OH^-, NH_2^-, and CH_3^-) provide excellent correlations between the bond length r and the force constant F at all levels of sophistication, and best mimic the diatomic series.

(iii) The best values of a_{11} (2.19) and b_{11} (0.69) obtained with the four one-heavy-atom nucleophiles at the MP2/6-31 + G*//6-31 + G* level of computation[10] suggested that the carbon centre in the TBP-5C TS, (1), has a covalent bond radius corresponding to a 3rd row element; this should originate in the drastic extension of the C–X bonds which is required in order to accommodate five ligands in the rather small sized first row element C. Dewar *et al.*[14] have pointed out that the drastic bond extension in forming the S_N2 TS is *mainly of a steric origin*, i.e., the C–X bonds must be extended in the TS in order to accommodate five ligands *sterically* at the small central carbon atom.[14]

In the identity reactions (X = Y in equation 2) the energy needed to form a TBP-5C TS constitutes the intrinsic barrier, $\Delta E_0^{\ddagger}$, since the reactions are thermoneutral; the expansion of the covalent bond radius from that of the 1st row to that corresponding to the 3rd row requires energy for the reaction centre, carbon, so that the origin of this barrier lies in the expansion of the covalent bond radius.[15] The median covalent bond length of the central carbon in the TBP-5C TS corresponding to that of a 3rd row element ($r_{13} = a_{13} = r_0$) therefore means that substantial median activation barrier, $\Delta E_{00}^{\ddagger}$, is required for the reaction series (2) with X = Y. Thus, the expansion of covalent bond radius to a median value of r_0 provides a *median intrinsic barrier, $\Delta E_{00}^{\ddagger}$*, for the reaction series, which originates really in the steric repulsion between the two (entering and leaving) groups (X) bonding at the relatively small-sized carbon atom in a 5-coordinated TS.[14,15]

This was also clear in a recent theoretical study of energy barrier involved in the S_N2 reactions by Sand *et al.*;[15a] they found that the activation barrier originates primarily from the long bond length in the TS. There is also an interesting approach to the energy barrier which is also concerned with the bond stretching in the TS.[15b]
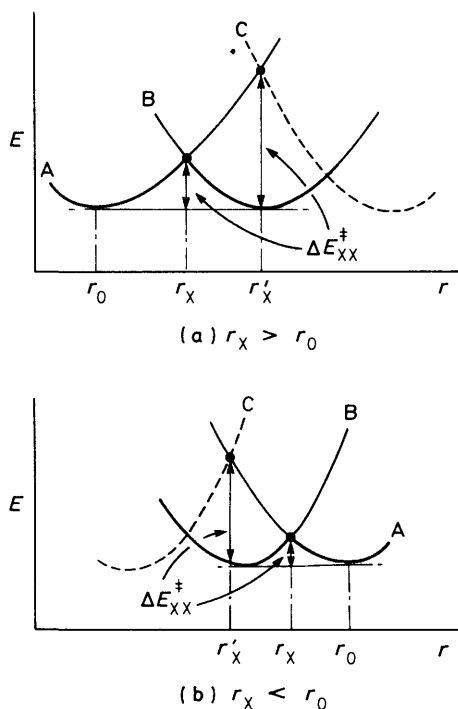
3 Electronic Origin

Since a median covalent bond length r_0 provides a median intrinsic barrier, $\Delta E_{00}^{\ddagger}$, for a family of closely related reactions, a small variation, $\Delta r = r_X - r_0$, from the median bond length r_0 for the individual nucleophile (or LG) X leads to a small variation in the intrinsic barrier, $\delta\Delta E_{XX}^{\ddagger} = \Delta E_{XX}^{\ddagger} - \Delta E_{00}^{\ddagger}$. It has been

[12] (a) T Clark, J Chandrasekhar, G W Spitznagel, and P v R Schleyer, *J Comput Chem*, 1983, **4**, 294, (b) M J Frisch, J A Pople, and J S Binkley, *J Chem Phys*, 1984, **80**, 3265, (c) Z Latajka and S Scheiner, *Chem Phys Lett*, 1984, **105**, 435

[13] (a) C Moller and M S Plesset, *Phys Rev*, 1934, **46**, 618, (b) J S Binkley and J A Pople, *Int J Quant Chem*, 1975, **9**, 229

[14] F Carrion and M J S Dewar, *J Am Chem Soc*, 1984, **106**, 3531

[15] (a) P Sand, J Bergmann, and E Lindholm, *J Phys Chem*, 1988, **92**, 2039, (b) S S Shaik, *J Am Chem Soc*, 1988, **110**, 1127

Figure 2 *Coupling of the two harmonic oscillators. Oscillators, B and C, cross oscillator A at r_X and r'_X giving barriers, $\Delta E^{\ddagger}_{XX}$, between them*

shown that this variation within a series originates in the *electronic state of the nucleophile X.*

A simple harmonic oscillator treatment of the variation in the intrinsic barrier within a reaction series (Figure 2) gave equation 4.[16]

$$\delta \Delta E^{\ddagger}_{XX} = 1/2 \, F \, (r_X - r_0)^2 \qquad (4)$$

According to this equation the intrinsic barrier to the identity $S_N 2$ reaction 2 with a particular X ($= Y$) can be represented by a point on a parabolic curve for a harmonic oscillator, A, in Figure 2. If the stretching, r_X, in the TBP-5C TS, (1), is greater than r_0, the barrier will be represented as a point on the right-hand branch of the curve; this intrinsic barrier originates in the stretching or expanding beyond r_0 (E region). Alternatively if $r_X < r_0$, then the barrier will be represented by a point on the left-hand branch of the curve; the intrinsic energy in this case corresponds to the compression energy (C region). However, near the

[16] I. Lee, *J. Chem. Soc., Perkin Trans. 2*, 1989, 943.
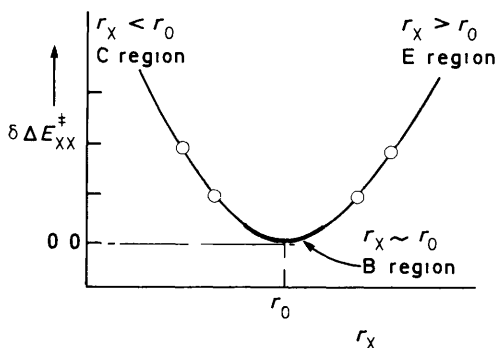
Figure 3 *A parabolic curve representing three regions Two points on each region of the curve correspond to the two crossing points given in Figures* 2(a) *and* 2(b) *respectively*

bottom of the well, *i e*, $r_X \sim r_0$ (B region), the relation 4 will be more accurate since the harmonic oscillator model of the potential-energy function is better applicable near the bottom of the well In fact, application of equation 4 to all members of X within a series tacitly assumes that *the force constants F_X are nearly invariant within a particular reaction series i e*,

$$F_1 \sim F_2 \sim \qquad F_X \sim F$$

Thus, if for a series, r_X values were greater than r_0, the intrinsic barriers $\Delta E^{\ddagger}_{XX}$, will be given by points in the E region of a curve similar to that in Figure 3 and will form an approximately straight line provided the range covered by $\delta\Delta E^{\ddagger}_{XX}$ or Δr is sufficiently small, *i e*, equation 5 will apply and have a positive slope, α [16]

$$\delta\Delta E^{\ddagger}_{XX} = \alpha(r_X - r_0) \qquad (5)$$

Similarly, if for a series $r_X < r_0$, the $\Delta E^{\ddagger}_{XX}$ values will be linearly related to Δr with a negative slope α in the C region When, however, r_X values are not much different from r_0, $r_X \sim r_0$, *i e*, in the B region, no such linearity will be expected but parabolic behaviour will be observed in accordance with equation 4 Therefore, for any series of identity-exchange reactions, the intrinsic barriers should belong to one of the regions, E, C, or B, provided the range covered by the series is sufficiently small

Applications of the simple harmonic oscillator model of the intrinsic barrier to series of symmetrical methyl-transfer reactions, *i e* X = Y in equation 2 have provided evidence in support of the electronic origin of the variations in barrier from a median value, $\Delta E^{\ddagger}_{\infty}$ [16] The identity S_N2 reactions 2 (X = Y) with anionic nucleophiles (or nucleofuges) X^- of the first-row elements, X = F, OH *etc* have been studied both experimentally [2] and theoretically [4] The *ab initio* MO theoretical results with the 4-31G basis set on r_X, F_X, and $\Delta E^{\ddagger}_{XX}$ given in Table 4 have shown that plots of $\Delta E^{\ddagger}_{XX}$

Table 4 *The distance, r_X/Å, force constants, F_X/mdyne Å^{-1}, of the C–X bond in the TS, (1), and the intrinsic barrier, $\Delta E^{\ddagger}_{XX}$/kcal mol^{-1}, calculated using 4-31G basis set for reaction: X$^-$ + CH$_3$X $\rightleftharpoons$ XCH$_3$ + X$^-$ (mdyne Å^{-1} = 10^2 N m^{-1}; 1 kcal = 4.184 kJ)*

X$^-$	r_X	F_X	$\Delta E^{\ddagger}_{XX}$
CH$_3$	2.161	1.998	—
CCH	2.124	1.913	50.4
CN	2.112	2.417	43.8
NC	2.014	2.702	28.5
NH$_2$	2.008	2.795	—
OF	1.932	3.194	18.8
OCH$_3$	1.924	3.232	23.5
OOH	1.920	3.281	18.5
OH	1.909	2.317	21.2
F	1.827	2.674	11.7

versus r_X are linear with a positive slope, $\alpha > 0$ in equation 5, and correlation coefficient of 0.973. Thus the series belongs to the E region covering a relatively wide range, $\delta\Delta E^{\ddagger}_{XX} \sim 40$ kcal/mol. Analysis involving changes in r_X and F_X indicated that the total contribution from the increase in r_X to the increase in the intrinsic barrier, $\Delta E^{\ddagger}_{XX}$, is more than 3 times greater than that from the change (decrease) in F_X, and hence $\delta\Delta E^{\ddagger}_{XX}$ is relatively insensitive to the variation in F_X, supporting the invariance assumption of F used in equation 4. Moreover, the reactivity follows the order of leaving group (LG) ability; a better LG has a lower barrier and hence is more reactive. Thus the degree of C–X bond breaking is substantially greater than that of X–C bond formation so that the TBP-5C TS has a loose structure with a positive charge on the reaction centre carbon, as in (1). In addition, a worse LG has a higher LUMO, σ^*_{CX}, and in order to lower the LUMO so that a smaller inter-frontier level gap ($\Delta\varepsilon_{FMO}$) is obtained for a greater charge-transfer stabilization in the TS,[17] a greater degree of bond breaking is required as the reaction progresses, which results in a greater deformation energy of the TS giving a net increase in the intrinsic barrier.

A second application involved solution-phase methyl-transfer reactions between substituted (X) benzenesulphonates, reaction 6.[1g,16] The normalized

$$XC_6H_4O_2SO^- + CH_3OSO_2C_6H_4X \rightleftharpoons XC_6H_4O_2SOCH_3 + {}^-OSO_2C_6H_4X \qquad (6)$$

Brönsted coefficients, $\beta_N = 0.37$ and $\beta_L = -0.63$, were used to assign $+0.25$ electronic charge unit (e.u.) at the reaction centre carbon and -0.63 e.u. on both sulphonate oxygens.[18] Here again a better LG with a more electron-withdrawing substituent gave a lower barrier, $\Delta G^{\ddagger}_{XX}$, indicating that the reactivity trend is in the order of LG ability. Thus the TBP-5C TS for this reaction series with X

[17] (a) N. D. Epiotis, W. R. Cherry, S. S. Shaik, R. L. Yates, and F. Bernardi, 'Structural Theory of Organic Chemistry', *Top. Curr. Chem.*, 1977, **70**, Part 1; (b) A. Pross and S. S. Shaik, *J. Am. Chem. Soc.*, 1981, **103**, 3702; (c) K. Fukui, H. Fujimoto, and S. Yamabe, *J. Phys. Chem.*, 1972, **76**, 232.
[18] This is true only when the normalized coefficients are used. See also: E. S. Lewis, *J. Phys. Org. Chem.*, 1990, **3**, 1.

varying from *p*-CH$_3$O to 3,4-dichloro is loose and bond breaking greatly exceeds bond formation. Moreover the range of $\delta\Delta G_{XX}^{\ddagger}$ covered in this series was very small with only $\delta\Delta G_{XX}^{\ddagger} = 0.9$ kcal/mol. Therefore, $\delta\Delta G_{XX}^{\ddagger}$, should be linearly related to r_X, by equation 5, with a positive slope, $\alpha > 0$. On the other hand, plots of $\Delta G_{XX}^{\ddagger}$ *versus* Hammett substituent constants σ gave an excellent linear correlation (equation 7) with negative slope and correlation coefficient of 0.993.
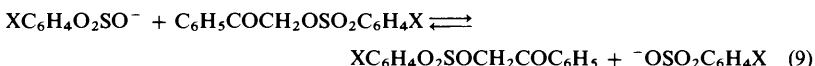
$$\delta\Delta G_{XX}^{\ddagger} = -1.02\,\sigma \qquad (7)$$

Comparison of equations 5 and 7 thus led to

$$\left.\begin{array}{l} r_X = \lambda\sigma + r_0 \\ \Delta r = \lambda\sigma \qquad \lambda < 0 \end{array}\right\} \qquad (8)$$

where λ is a negative constant. This relation shows that the C–X bond stretch beyond r_0, $\Delta r = r_X - r_0$, in the TS is linearly related to σ, and hence the variation of the intrinsic barrier, $\delta\Delta G_{XX}^{\ddagger}$, is related to the electron-donating or -withdrawing power of the substituent in the nucleophile. This clearly shows that $\delta\Delta G_{XX}^{\ddagger}$ is of an electronic origin.

Solution-phase phenacyl-group transfer reactions, (equation 9),[3c] indicated

$$XC_6H_4O_2SO^- + C_6H_5COCH_2OSO_2C_6H_4X \rightleftharpoons$$
$$XC_6H_4O_2SOCH_2COC_6H_5 + {}^-OSO_2C_6H_4X \quad (9)$$

that the reaction centre carbon is, in this case, negatively (-0.48 e.u.) charged in the TBP-5C TS, and the reactivity trend follows the order of nucleophilicity. This reactivity trend as well as the large negative charge on the reaction centre carbon in the TS is exactly opposite to those found for the examples belonging to the E region, and indicates that in this reaction series bond formation is ahead of bond breaking and the TS is relatively tight so that the bond length r_X is shorter than r_0, $r_X < r_0$. Thus the reaction series belongs to the C region, in which a linear correlation (equation 5) between $\Delta G_{XX}^{\ddagger}$ and Δr should hold with a negative slope, $\alpha < 0$. The range covered by $\delta\Delta G_{XX}^{\ddagger}$ was small, *ca.* 1.10 kcal/mol. Alternatively, plots of $\Delta G_{XX}^{\ddagger}$ *versus* σ gave a good linearities with a positive slope and a correlation coefficient of 0.988, equation 10. Comparison of equations 5 and 10 yielded

$$\delta\Delta G_{XX}^{\ddagger} = 1.89\,\sigma \qquad (10)$$

again equation 8 which is exactly the same relation as that obtained for reactions belonging to the E region.

Solution-phase methyl-transfer reactions between thiophenoxides, equation 11,[3a] is reported to give negligibly small (negative) charge, (-0.08 e.u.) on the

$$XC_6H_4S^- + CH_3SC_6H_4X \rightleftharpoons XC_6H_4SCH_3 + {}^-SC_6H_4X \qquad (11)$$
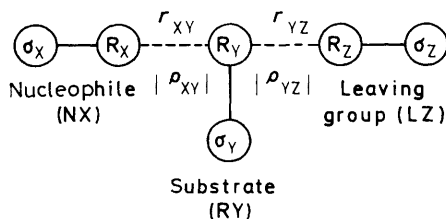
Scheme 1 σ_i *and* R_i *are substituent and reaction centre, respectively, where* $i =$ X, Y, *or* Z

reaction centre carbon in the TS; this reaction shows no trend in the reactivity *versus* nucleophilicity or LG ability as a whole so that there is no linearity between $\delta\Delta G^{\ddagger}_{XX}$ and Δr. This series in fact belongs to the B region, for which the equation 4 applies well. Moreover the $G^{\ddagger}_{XX}$ values were not linearly related to σ but were a quadratic function of σ, equation 12, which suggested the same quadratic

$$\delta\Delta G^{\ddagger}_{XX} = \beta\sigma^2 \qquad \beta > 0 \qquad (12)$$

correlation between $\delta\Delta G^{\ddagger}_{XX}$ and Δr as equation 4. Comparison of equations 4 and 12 again led to equation 8.
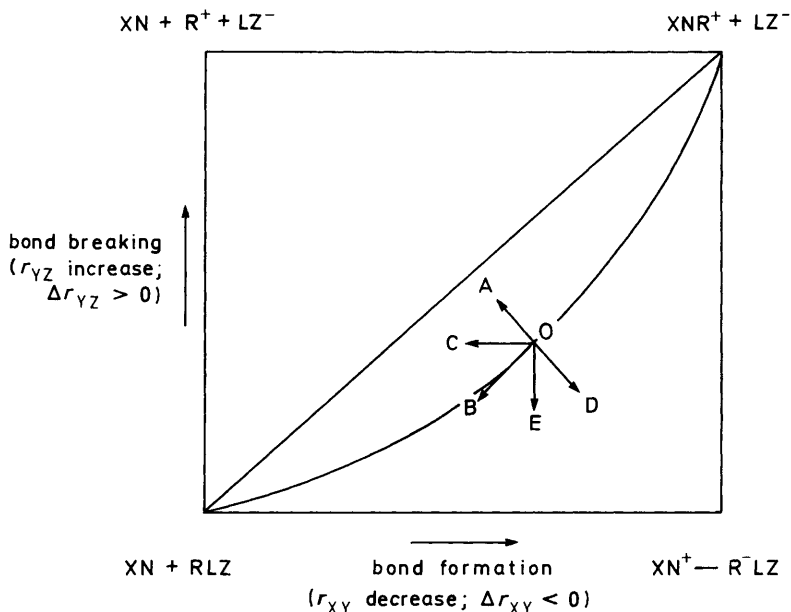
Thus the relation (equation 8) is a fundamental one for the thermoneutral reactions, $\Delta G^\circ = 0$ in equation 1, *i.e.*, the intrinsic-controlled reaction series;[16,19] for a more electron-withdrawing substituent in the LG ($\delta\sigma_Z > 0$), *i.e.*, a better LG, a greater degree of bond formation ($\Delta r_{XY} < 0$), is obtained whereas for a more electron-donating substituent ($\delta\sigma_X < 0$) in the nucleophile, *i.e.*, a stronger nucleophile, a greater degree of bond breaking ($\Delta r_{YZ} > 0$) is obtained, equation 13 (see Scheme 1). These predictions of the TS variation are shown to be consistent with those by the quantum-mechanical (QM) model.[18,19]

$$\left.\begin{array}{l} \Delta r_{XY} = a\sigma_Z \\ \Delta r_{YZ} = b\sigma_X \qquad a,b < 0 \end{array}\right\} \qquad (13)$$

It has been shown that for a thermodynamic-controlled reaction[19] series, *i.e.*, $\delta\Delta G^\circ \gg \delta\Delta G^{\ddagger}_{XX}$ and hence $\delta\Delta G^{+} \propto \delta\Delta G^\circ$ in equation 1, the sign of λ in equation 8 reverses to positive, $\lambda > 0$, which results in the relationships of equation 14. The TS variation can be predicted by the potential energy surface (PES) diagram,[4c,19,20] Figure 4, for this type of reaction series. These relations indicate that a more electron-withdrawing substituent in the LG ($\delta\sigma_Z > 0$) gives a greater bond distance r_{XY}, *i.e.*, less bond formation, $\Delta r_{XY} > 0$. This corresponds to a TS

[19] (a) A. Pross and S. S. Shaik, *J. Am. Chem. Soc.*, 1981, **103**, 3702; (b) I. Lee and C. H. Song, *Bull. Korean Chem. Soc.*, 1986, **7**, 186.

[20] (a) I. Lee and H. S. Seo, *Bull. Korean Chem. Soc.*, 1986, **7**, 448; (b) I. Lee, C. S. Shim, S. Y. Chung, and H. W. Lee, *J. Chem. Soc., Perkin Trans. 2*, 1988, 975; (c) I. Lee, Y. H. Choi, and H. W. Lee, *J. Chem. Soc., Perkin Trans. 2*, 1988, 1537; (d) For this type of series, the reactivity–selectivity principle is known to apply in general: E. Buncel and H. Wilson, *J. Chem. Educ.*, 1987, **64**, 475 and references cited therein.

$$XN + R^+ + LZ^-$$ $$XNR^+ + LZ^-$$

bond breaking
(r_{YZ} increase;
$\Delta r_{YZ} > 0$)

$$XN + RLZ$$ $$\text{bond formation}$$ $$XN^+ - R^-LZ$$

$$(r_{XY} \text{ decrease}; \Delta r_{XY} < 0)$$

Figure 4 *Potential energy surface diagram of an associative* S_N2 *reaction. X and Z represent substituents in the nucleophile and leaving group, respectively*

shift from point O toward C as a result of Hammond (O ⟶ B) and anti-Hammond (or Thornton) shifts (O ⟶ A) in the PES diagram. A more electron-donating substituent in the nucleophile ($\delta\sigma_X < 0$) gives a less bond breaking *i.e.*, a smaller r_{YZ} ($\Delta r_{YZ} < 0$), which corresponds to a TS shift to point E as a result of the sum of two vectors OB and OD. These TS variations of the PES model are shown to apply to the thermodynamically controlled reaction series.[19]

$$\left.\begin{array}{l} \Delta r_{XY} = a'\sigma_Z \\ \Delta r_{YZ} = b'\,\sigma_X \qquad a',b' > 0 \end{array}\right\} \tag{14}$$

The important features can be recapitulated as follows.

(i) The major component of the intrinsic barrier originates in the steric effect of the two, entering and leaving, groups; this component provides a median barrier height, $\Delta E_{00}^{\ddagger}$, at a median bond length, r_0, in the TBP-5C TS, for a particular family of closely related reactions.

(ii) The minor component of the intrinsic barrier originates in the electronic state of the reactants, nucleophile or leaving group and/or substrate. This component determines small variations in the intrinsic barrier, $\delta\Delta E_{XX}^{\ddagger}$ from the median value, $\Delta E_{00}^{\ddagger}$, due to small variations in the bond length from the median length, $\Delta r = r_X - r_0$, within a reaction series.

(iii) The variations, $\delta\Delta E_{XX}^{\ddagger}$, can be grouped in three categories: expansion

$(r_X > r_-)$, compression $(r_X < r_0)$, and borderline $(r_X \cong r_0)$ regions of a harmonic oscillator potential energy curve, when $\delta\Delta E^{\ddagger}_{XX}$ covered is relatively small.

(iv) There is a fundamental correlation between the bond length change Δr in the TS and the Hammett's constant σ of a substituent in the nucleophile or LG *i.e.*, $\Delta r = \lambda\sigma$ with a negative constant λ for the thermoneutral reactions, the reactivities of which are controlled by the intrinsic barrier (intrinsic-controlled reaction series).

4 Concluding Remarks

We have dealt here with applications to only the most simple and clear-cut cases of thermoneutral S_N2 reactions. However, in reality non-identity reactions with $X \neq Y$ in equation 2 will be more general. Although the TS will not be of the symmetrical TBP-5C type, (1), classification of such reactions may still be possible into the intrinsic- and thermodynamic-controlled reaction series in many cases, so that the effects of substituents on the degree of bond formation and cleavage (equations 13 and 14) can be very useful in characterizing the TS. In this respect, the use of experimentally determinable cross-interaction constants[22] ρ_{XY} and ρ_{YZ} are helpful, since changes in the logarithms of the magnitude of such constants (Scheme 1) are similarly related to substituent constants with opposite slopes,

$$\Delta \log |\rho_{XY}| = A\sigma_Z$$
$$\Delta \log |\rho_{YZ}| = B\sigma_X$$

where the constants A and B are now positive for the intrinsic-controlled series, whereas they are negative for the thermodynamic-controlled reaction series.

[21] (a) R. A. More O'Ferrall, *J. Chem. Soc., B*, 1970, 274; (b) W. P. Jencks, *Chem. Rev.*, 1985, **85**, 511.

[22] (a) I. Lee and S. C. Sohn, *J. Chem. Soc., Chem. Commun.*, 1986, 1055; (b) I. Lee, H. Y. Kim, and H. K. Kang, *J. Chem. Soc., Chem. Commun.*, 1987, 1216; (c) I. Lee, H. K. Kang, and H. W. Lee, *J. Am. Chem. Soc.*, 1987, **109**, 7472; (d) I. Lee, H. Y. Kim, H. K. Kang, and H. W. Lee, *J. Org. Chem.*, 1988, **53**, 2678; (e) I. Lee, C. S. Shim, S. Y. Chung, H. Y. Kim, and H. W. Lee, *J. Chem. Soc., Perkin Trans. 2*, 1988, 1919; (f) I. Lee, H. Y. Kim, H. W. Lee, and I. C. Kim, *J. Phys. Org. Chem.*, 1989, **2**, 35.