

Is the Transition State Indeed Intermediate between Reactants and Products? The Michael Addition Reaction as a Case Study

SHMARYAHU HOZ

Department of Chemistry, Bar-Ilan University, Ramat Gan 52900, Israel

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A chemist's *wissendurst* is rarely quenched by the discovery of a new synthetic route or transformation. Greater insight into chemical processes requires an elucidation of the more fundamental mechanistic details. Reaction intermediates, if such exist in a given process, denote local energy minima and can oftentimes be observed directly or trapped. Transition states, on the other hand, are located at energy maxima, and their accurate description has traditionally represented a substantially more formidable challenge. In an attempt to obtain greater insight into the nature of these elusive species, physical organic chemists have utilized a variety of linear free energy relationships (LFERs), of which the Bronsted and Hammett equations are perhaps the best known examples.

The conversion of the LFER data into transition state (TS) structural information has been traditionally based on a few simple, interrelated and seemingly sound assumptions:

1. The first premise is that the activated complex has a structure which is intermediate between, and hence bears a considerable resemblance to, the reactants and products.

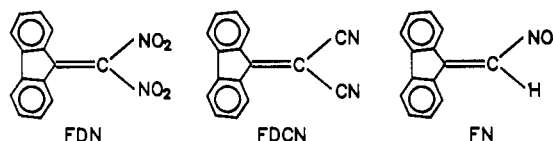
2. As a corollary to this first assumption, it is further posited that the effect of a given perturbation (such as a variation of substituents, solvent, etc.) on the activation free energy (ΔG^\ddagger) will be a fraction of the effect of the same perturbation on the equilibrium free energy (ΔG°). Technically, this fraction is obtained as the slope of a plot of ΔG^\ddagger vs ΔG° or any related quantities.

3. Finally, it is argued that this fraction corresponds to the extent to which the transition state has progressed along the reaction coordinate.¹ Thus, if the aforementioned fraction is close to unity, it indicates that the transition state has a product-like response to the perturbation and, presumably, a product-like structure. On the other hand, if the fraction is close to zero, the transition state has not progressed significantly toward products and, therefore, resembles the reactants.

LFERs of various types have played an important role in the study of nucleophilic reactivity. The S_N2 reaction is perhaps the most thoroughly studied reaction in this regard. Nevertheless, little progress has been made in "understanding" nucleophilicity. As a result, Ritchie suggested two decades ago that S_N2 processes

are not suitable as model reactions for the investigation of nucleophilicity since the nucleophilic component is accompanied by a rupture of a bond to the leaving group.^{2a} Nucleophilicity itself can be better understood from an investigation of nucleophilic reactions where no leaving group departure takes place at the transition state. Examples of such cases are the anion-cation combination reactions.^{2b,c} Indeed, the nucleophilicity scale (N_+), which was determined by Ritchie in these reactions, differed significantly from the Swain-Scott scale (n).³ Following this line of logic, we have initiated a study of the Michael addition reaction, a nucleophilic process which is uncoupled with an expulsion of a leaving group. In addition to giving us some very interesting insight into this area, our studies of these reactions have led us to an antitraditional perception of LFERs¹ as mechanistic probes.

The first three systems we looked at (FDN, FDCN, and FN), obeyed the Ritchie equation:² $\log k/k_0 = N_+$.



The most remarkable correlation was obtained with FDN, where the reactivity range extended over 10 orders of magnitude with a correlation coefficient of 0.998.^{4,5} One difference was observed, however, between our results and those of Ritchie. While the slope of the plot of $\log k$ vs N_+ in Ritchie's anion-cation combination reactions was unity, the slope in the case of the three olefins was shown to be nonunity (ca. 1.2). We suggested, therefore, that the Ritchie equation should be modified by the addition of a nonunity selectivity parameter (S_+). However, in the best tradition of studies on nucleophilic reactions,⁶ we could not attach unequivocally any mechanistic meaning to either the unity or nonunity values of S_+ .

(1) Lefler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963.

(2) (a) Ritchie, C. D. *Acc. Chem. Res.* 1972, 5, 348. (b) Ritchie, C. D. *Pure Appl. Chem.* 1978, 50, 1281. (c) Ritchie, C. D. *Can. J. Chem.* 1986, 64, 2239.

(3) Swain, G. C.; Scott, C. B. *J. Am. Chem. Soc.* 1953, 75, 141.

(4) Hoz, S.; Speizman, D. *Tetrahedron Lett.* 1978, 1775.

(5) Hoz, S.; Speizman, D. *J. Org. Chem.* 1983, 48, 2904.

(6) The frustration in the attempts to "really" understand nucleophilicity was nicely phrased by a referee who was quoted by Ritchie (2nd Conference on Physical Organic Chemistry, Brazil, 1983) as saying that "...the search for an understanding of nucleophilic reactivity [is comparable] to the search for the Holy Grail".

(7) Hoz, S. In *Nucleophilicity*; Harris, J. M., McManus, S. P., Eds.; Advances in Chemistry Series; American Chemical Society: Washington, DC, 1987; Chapter 12.

Shmaryahu Hoz was born on Mount Scopus, Jerusalem, in 1945. He received his B.Sc. in chemistry and physics and M.Sc. in chemistry from the Hebrew University in Jerusalem. After obtaining his Ph.D. from Bar-Ilan University in 1974, he spent a year as a postdoc with Joe Bunnett at UCSC and then rejoined the Department of Chemistry at Bar-Ilan University, where he is now a Professor of Chemistry. His research interests include reaction mechanisms, focusing in particular on the chemistry of bicyclobutane and nucleophilic attacks on low-LUMO compounds. In recent years, he has started drifting toward computational chemistry, guided by the maxim, "If you can't beat 'em, join 'em."

Our results seem to corroborate Ritchie's basic assumption that the differences between the Swain-Scott n and the N_+ scales stem from the presence or the absence of leaving group departure. However, we have noticed that an additional difference exists between the two groups of substrates, those which obey the Ritchie equation and those which exhibit Swain-Scott behavior. The first group is characterized by low-lying (LL) LUMO (usually low π^* orbitals), i.e., high electrophilicity, whereas the second features high LUMOs (HL; usually σ^* orbitals), i.e., low electrophilicity. Clearly, any classification on its own is of limited merit. However, since the electrophile's LUMO energy largely controls its reactivity in nucleophilic reactions, it is reasonable to assume that this LUMO-based classification has more mechanistic significance than the presence or absence of a leaving group.

In a very qualitative manner, one can see that a different chemical pattern is obtained in the two extreme cases of nucleophilic reactions. In the case of substrates of low electrophilicity (HL; e.g., MeBr), covalent bonding takes place at the transition state. On the other hand, when substrates of very high electrophilicity (LL) react with nucleophiles, very frequently *electron transfer* is encountered. The important question is, therefore, What would be the nature of the reaction of nucleophiles with substrates of intermediate electrophilicity? Our assumption was that there is a continuous behavior between the two ends. That is, in all TSs, both covalent bonding and diradical character are present but are mixed in varying proportions. The diradicaloid character which is due to the electron-transfer component is more pronounced with LL substrates, whereas covalent bonding dominates the transition state of reactions of substrate with lower electrophilicity. (A theoretical substantiation of this hypothesis using the Shaik-Pröss curve-crossing model will be presented later on.)

We present two cases which demonstrate the diradicaloid nature of the transition state. One case relates to the radicaloid character of the nucleophile, while the other relates to the radical character of the substrate.

The first case relates to the α -effect.⁸ In a normal nucleophilic reaction, a plot of $\log k$ vs the basicity ($\log K_B$) of the nucleophile is usually linear with a positive slope. However, a positive deviation from this line is observed with nucleophiles such as HOO^- , ClO^- , and NH_2OH . The latter all carry a lone pair of electrons at a position α to the nucleophilic atom and are, hence, dubbed α -nucleophiles, while the aforementioned positive deviation is referred to as the α -effect. Needless to say, the literature is replete with explanations for this effect.⁸ It is well-known that the α -effect is exhibited almost solely in nucleophilic reactions with unsaturated substrates. In our terminology these compounds are LL substrates, and therefore, both the nucleophile and the substrate may acquire a relatively large radical character at the TS. We suggest that the α -effect, at least in part, is a straightforward consequence of the radical character of the nucleophile. In the case of an α -effect nucleophile, this will lead to energy lowering of the TS by virtue of the well-known stabilizing effect of a radical center by a neighboring lone pair. In terms of molecular orbitals, the stabili-

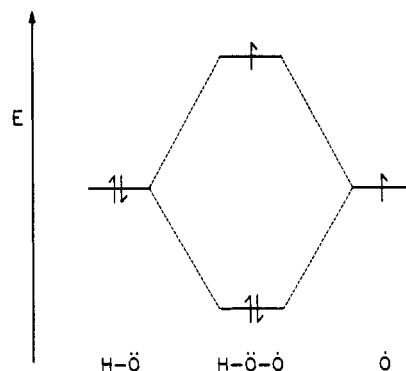
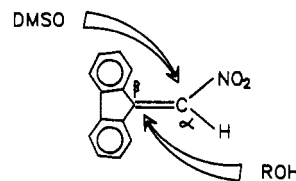


Figure 1. MO diagram for the stabilization of a radical center by a neighboring lone pair.

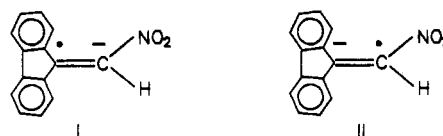
zation of the nucleophile stems from the partial manifestation of the constructive $2e^- + 1e^-$ interaction⁹ (Figure 1) at the TS. Thus an α -nucleophile has a mechanism for lowering the energy of the TS in its reactions with LL substrates, which is unavailable to a normal nucleophile, thereby giving rise to the α -effect.¹⁰

The second example is associated with the radical character of the substrate. One of the fluorenyl-derived substrates (FN) displays a variable regioselectivity in its reactions with nucleophiles. In hydrogen bond donating solvents like water and methanol, the attack takes place on the β -carbon, whereas in DMSO the nucleophile binds to the α -carbon.⁵



Traditionally, a key factor in the determination of the site of attack is the stability of the incipient carbanion at the transition state. Thus, the acidity of nitromethane and that of fluorene may serve as criteria for the relative stabilities of the TSs for the β - and α -attacks, respectively. Analysis along this line did not justify the observed variation in the regioselectivity.⁵ In light of the above discussion, it is clear that the radical anion of FN rather than the anionic adduct should serve as a model for the transition state. It was suggested by Kochi¹¹ that, in electrophilic aromatic substitution, the transition state is also diradicaloid and the positional selectivity (ortho, meta, para) is controlled by the spin density at these positions. Namely, radical combination will be more favored at positions of higher spin density.

In the case of the radical anion of FN, two of the contributing resonance structures are I and II. If the



spin resides mainly on $C\beta$ (I), "normal" attack will be

(9) Albright, T. A.; Burdett, J. K.; Whangbo, M.-H. *Orbital Interactions in Chemistry*; Wiley: New York, 1985; p 17.

(10) Hoz, S. *J. Org. Chem.* 1982, 47, 3545.

(11) Fukuzumi, S.; Kochi, J. K. *J. Am. Chem. Soc.* 1981, 103, 7240.

(8) Hoz, S.; Buncel, E. *Isr. J. Chem.* 1985, 24, 313.

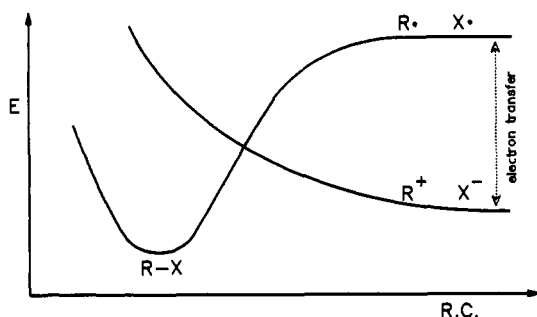


Figure 2. Curve-crossing diagram for the cleavage of a C-X bond in R-X.

observed; whereas, if the second structure dominates, the nucleophile will combine with the α -carbon. We have, therefore, calculated the spin density of the radical anion of FN using MNDO with and without two water molecules, each with its hydrogen 2.0 Å away from the nitro oxygens. It was found that in the MNDO calculations of the radical anion, as well as in the STO-3G calculations performed on the MNDO-optimized geometry, the addition of the two water molecules caused a shift in the spin density from the α -carbon to the β -carbon. Hence, the variation in spin densities as a function of the medium corresponds with the variation in the regioselectivity.

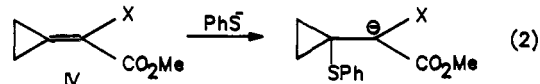
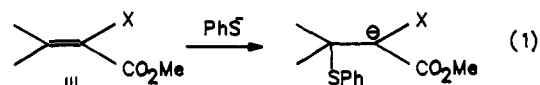
Using the anion-cation combination reaction, we can substantiate theoretically the existence of an electron-transfer component at the transition state. A cross section in the potential surface for the homolytic C-X bond cleavage of R-X in the gas phase yields the well-known Morse curve (Figure 2). In order for R-X to undergo solvolysis, this compound must at some point depart from its covalent-leading-to-diradical surface to an ionic one. In the gas phase, the ionic curve is much higher in energy than the Morse curve, so the two surfaces never cross. However, in polar media, the ionic state is dramatically stabilized. As a result, when R-X acquires enough energy, it may cross over from the ascending Morse curve to the descending ionic one to give R^+ and X^- (Figure 2). In the reverse direction, this reaction is nothing other than the anion-cation combination reaction of the type studied by Ritchie. We note that we begin this reaction with ionic reactants and, along the way to the products, the system shifts to the diradical-covalent surface. It is clear that such a shift necessitates an electron transfer from X^- to R^+ to produce R^{\cdot} and X^{\cdot} . The actual degree of radical character of the nucleophile and the substrate will depend on the position of the transition state along the Morse curve. Since descending along this curve involves a trade-off between the diradical and the covalent character, in an early TS, the system will be largely diradicaloid; whereas, in a late TS, the diradicaloid moiety will largely "collapse" into a more covalent configuration.

The aforementioned treatment has been based on the curve-crossing model of Shaik and Pross.¹² Analysis of a two-configuration model led these authors to an additional insight into the nature of the TS. They concluded that the amount of charge that had been transferred from the nucleophile to the substrate, as

the TS was reached, is ca. half an electron.¹³ The reasoning behind this is rather straightforward. If the TS is located right below the crossing point, then its electronic configuration is a mixture of equal amounts (50% of each) of the two configurations: that of the reactants and that of the products. Since the two differ from each other by a single electron transfer and since, at the reactant stage, the system begins with 100% of the ionic configuration, half an electron must have been transferred in order to reach the 50-50 configuration of the TS. This conclusion obviously contradicts the traditional intuitive approach which assumes that the amount of charge transferred correlates with the progression of the TS along the reaction coordinate. It should be emphasized that although the intuitive approach may, under certain circumstances, properly describe the physical reality, it is not enforced by any theoretical rule. Clearly, as the system proceeds toward the TS, the overlap increases and, at the same time, the energy gap decreases. Therefore, one would expect that more charge would be gradually transferred from the nucleophile to the substrate as the system moves from right to left. However, at the TS itself, half a unit of charge has been transferred from X^- to R^+ .¹⁴

It is important to note that the addition of a third low-energy configuration may shift the position of the TS from the avoided crossing zone sidewise and alter the above analysis. However, in the absence of specific information regarding the nature of this configuration, it is impossible to predict the effect it may have on the charge distribution at the TS. Another factor which may also shift the TS sidewise is the skewing effect, which will be discussed later on in this Account.

Various examples can be cited which demonstrate that there may not necessarily be any connection between the reaction coordinate and charge variations in a given reaction. For the purpose of brevity, we cite only three. The first is the Michael addition reaction shown in eqs 1 and 2.¹⁵ The difference in strain energy



Relative Rate		
X	H	SPh
III	1	
IV	18	5160

in the two substrates (III and IV) amounts to about 14 kcal/mol.¹⁶ This value corresponds to a rate enhancement of ca. 11 orders of magnitude. The fact that the experimental rate enhancement was only 18 indicates a very early TS. Traditionally, one would expect a negligible rate enhancement by electron-withdrawing groups on the substrate, since very little charge is

(13) Pross, A.; Shaik, S. S. *Tetrahedron Lett.* 1982, 23, 5467.

(14) In order to distinguish between this and a complete electron transfer, Shaik and Pross (*Acc. Chem. Res.* 1983, 16, 363) have introduced the term electron shift.

(15) Seyed-Mahdvi, F.; Tiechmann, S.; de Meijre, A. *Tetrahedron Lett.* 1986, 27, 6185. de Meijre, A. *Chem. Br.* 1987, 865.

(16) This is the strain caused by grafting a double bond onto a cyclopropyl moiety: Greenberg, A.; Liebman, J. F. *Strained Organic Molecules*; Academic Press: New York, 1978.

(12) Shaik, S. S. *Prog. Phys. Org. Chem.* 1985, 15, 197. Pross, A.; Shaik, S. S. *Acc. Chem. Res.* 1983, 16, 363. Pross, A. *Adv. Phys. Org. Chem.* 1985, 15, 99; *Acc. Chem. Res.* 1985, 18, 212.

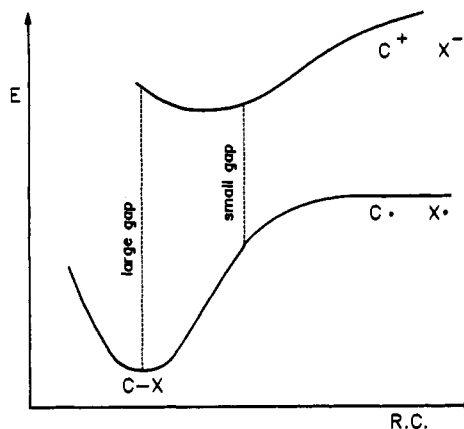
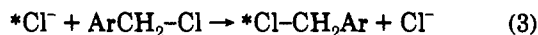


Figure 3. Valence bond diagram for the ionic and covalent configurations of Me-X.

expected to be transferred from the nucleophile to the substrate at such an early TS. Contrary to this expectation, a very mildly negative charge-stabilizing group (X = SPh) induced a significant rate enhancement.¹⁵ Thus, in spite of the extreme earliness of the TS, a relatively large amount of charge was transferred from the nucleophile to the substrate.

The second example is the identity S_N2 reaction in a benzylic system, e.g., eq 3. The rate of this reaction



is sensitive to ring substituents. However, since the reaction is degenerate, the initial and the final charges on the substituent are identical. This sharply demonstrates that the charge sensed by a ring substituent at the TS cannot be described as a linear combination of the charges in the reactants and products and, therefore, charge cannot be used as an indication to the position of the TS along the reaction coordinate.¹⁷

The last example is a computational one. In Me-X, where X = F, OH, N₃, etc., the Me and the X group bear partial charges owing to the electronegativity of X. Homolyzing the C-X bond leads to the formation of the corresponding uncharged radicals. According to the traditional understanding, the positive charge on the Me group, for example, is expected to decrease gradually as the system proceeds toward the neutral products. Again, contrary to that traditional intuition, high-level ab-initio calculations have shown¹⁸ that as the C-X bond is stretched, *more* positive charge is accumulated on the Me group. Only at relatively large C-X separation does the charge start to gradually vanish. This seemingly odd phenomenon can be easily rationalized in terms of the valence bond theory.¹⁹ In Figure 3 the pure ionic and covalent configurations of a C-X bond are arbitrarily depicted. The C-X bond is polar in its equilibrium geometry because of the mixing of the ionic configuration into the covalent one. However, the degree of mixing largely depends on the energy gap between the two configurations.¹⁹ This gap is evidently smaller at C-X separations larger than that of the equilibrium geometry (see Figure 3), and hence, stretching of the bond gives rise to higher partial charges

(17) Pross, A. *Tetrahedron Lett.* 1983, 24, 835.

(18) Hoz, S.; Basch, H.; Goldberg, M. *J. Am. Chem. Soc.* 1992, 114, 4364.

(19) Pauling, L. *The nature of the chemical bond*, 3rd ed.; Cornell University Press: New York, 1960; Chapter 3.

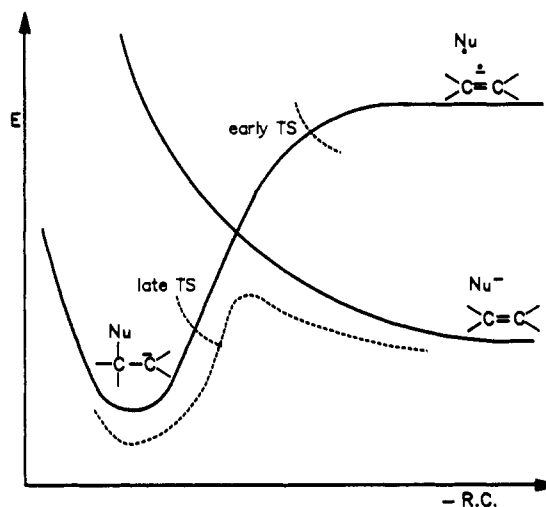
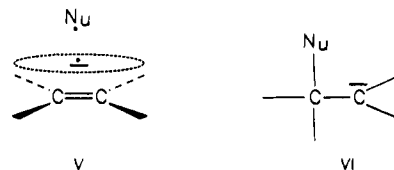


Figure 4. Curve-crossing diagram for the Michael addition reaction.

on C and X. In longer distances, the overlap term becomes dominant, actuating a charge flow in the opposite direction to nullify the partial charges. This third example further demonstrates that the actual progression of charge variations in a chemical process does not follow the long, intuitively based, traditional expectation.

Putting all these pieces together directed us toward a different perspective on the interpretation of LFER in general and on the Michael addition reaction in particular. Figure 4 shows the curve-crossing diagram for the Michael addition reactions. As we move along the Morse type curve, we proceed from the ionic adduct at the left to a homolytic dissociation of the C-Nu bond and the formation of the radical anion of the substrate. This corresponds to an unusual reaction since two electrons are used to expel an odd electron residue. It is worth noting that such a reaction was indeed observed by Cram in the pyrolysis of 1,1,2-triphenyl-2-methoxypropoxide.²⁰ For a "normal" β -elimination to occur, the system has first to move along the Morse curve and then to cross over to the reactant ("ionic") configuration. If the TS of the Michael addition reaction (motion from right to left in Figure 4) is achieved early on, the contribution of the product configuration will be in the form of a radical on the nucleophile and a radical anion on the substrate (as in V). As the TS occurs later, the degree of coupling between the two radicaloid moieties increases and the radical anionic character of the substrate is replaced by an adduct-like anionic character (as in VI).

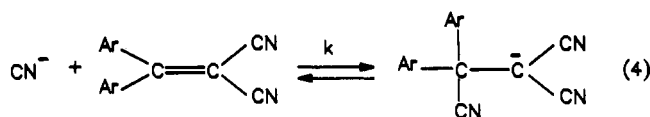


The question to be asked at this stage is, Since the same amount of charge is transferred to the substrate at the TS, regardless of its position, why isn't ρ a universal constant reflecting the fact that always half an electron is transferred at the TS? In other words,

(20) Cram, D. J.; Langemann, A.; Lwowski, W.; Kopecky, K. R. *J. Am. Chem. Soc.* 1959, 81, 5760.

is there a difference in substituent response to the dissimilar electronic distribution in an early and a late TS? Focusing our attention on substituents at the β -position,²¹ it is clear that, in an early TS (V), the negative charge can be delocalized over the whole molecule including the substituents. However, in a late TS (VI), this delocalization is disrupted by the formation of the covalent bond, which in turn locks the negative charge at a position remote from the substituent. Hence, it is clear that the substituents will see more of the negative charge in an early TS than in a late one. Thus, a relatively large ρ value will be obtained for an early TS and a small one for a late TS. This conclusion is obviously at odds with the traditional intuitive understanding.

Several experimental observations made in our laboratory seem to be in accordance with the above conclusion. The first one is the reaction of 1,1-diaryl-2,2-dicyanoethylene with CN^- (eq 4).²² For electron-



donating substituents we were able to measure both the rate and the equilibrium constants for the addition reaction. It was found that the kinetic ρ value (1.46) is larger than that of the equilibrium value (1.07). If the TS in this case is indeed reached early on, the substrate acquires a relatively large radical anionic character, which enables effective charge delocalization onto the substituents. On the other hand, in the product, the charge is localized on the malononitrile moiety and is largely removed from the substituents. Therefore, although more negative charge is accommodated by the substrate at the product stage than at the TS, the equilibrium ρ value is smaller than the kinetic one.

Another example is the reaction of 1,1-diaryl-2-nitroethylene with CN^- in water and in DMSO.²³ Due to the higher reactivity of cyanide in DMSO, an earlier TS is expected in DMSO than in water.²⁴ In accordance with the present model the observed ρ value in DMSO was 5-fold larger than in water.²⁵

The third example comes from the analysis of the ^{13}C NMR data, in combination with ρ values, for the nucleophilic addition of CN^- to 1,1-diaryl-2,2-dinitroethylene in four different solvent systems.²⁶ The $^{13}\text{C}_\beta$ chemical shift was found to correlate better with $\log k$ in solvents where a high ρ value was obtained. Since $^{13}\text{C}_\beta$ chemical shift is a ground-state property, it is reasonable to assume that correlation with $\log k$ should prevail mainly for early TSs which resemble the reactants.

(21) The case where the substituent bearing aryl group is geminal to the activating group is much more complicated. Semiquantitative analysis of the interaction of the LUMO of the phenyl ring with a benzylic carbanion on the one hand and a radical anion on the other suggests that the relative sensitivity to substituent variation depends on the geometry and the other substituents.

(22) Gross, Z.; Hoz, S. Unpublished results.

(23) Gross, Z.; Hoz, S. *J. Am. Chem. Soc.* 1988, 110, 7489.

(24) Hammond, G. S. *J. Am. Chem. Soc.* 1955, 77, 334.

(25) The increase in the ρ value cannot be attributed to simple solvent effects on substituent selectivity. This is usually smaller than a factor of 3 for a whole unit of charge; see ref 24.

(26) Gross, Z.; Hoz, S. *Tetrahedron Lett.* 1991, 32 (38), 5163; *Can. J. Chem.* 1992, 70, 1022.

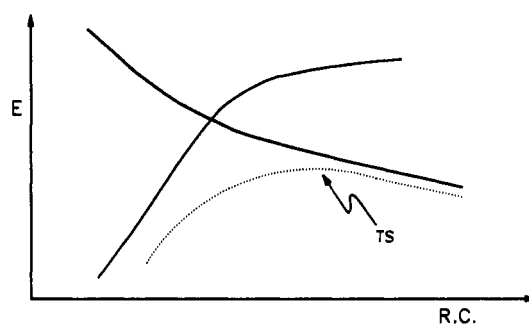


Figure 5. A sidewise shift in transition-state position due to a large dissimilarity in the curvature of the two configurations.

These three examples are highly consistent with the proposed model, according to which high ρ values are associated with an early TS, while small ρ values correlate with a late one. It should be emphasized, however, that consistency with the proposed model does not necessarily deny the possibility of finding a more traditional explanation of these observations.

We turn now to a case which, at least with regard to charge vs TS location, should behave according to traditional expectations. This case can be encountered if, for example, the curvature of the two configurations in this region is highly asymmetric. As a result, the TS will suffer a sidewise shift from the avoided crossing region. In general, a TS is achieved at a point where the trend to go up in energy, following the ascent of the lower configuration, is equalized by energy lowering due to resonance between the two configurations. This point will be an energy maximum and, therefore, a TS. For the schematic case depicted in Figure 5, the tendency of the system to go down in energy (due to the increase in overlap and decrease in the energy gap between the two configurations) while moving toward the crossing point is not effectively counterbalanced by the mildly ascending slope. As a result, the TS will be achieved before the crossing point is reached. In this case, there will be a direct correlation between the position of the TS and the amount of charge transferred from the nucleophile to the substrate. It should be noted, however, that, in such a case, TS location is highly sensitive to small variations in the configuration energy, i.e., to substituent effects. Therefore, in a series of reactions, each member of the series may have a TS of a different structure. Nevertheless, as Williams has already shown, the FER may still be linear in spite of structural variations in the TS.²⁷

Epilogue

The development of the proposed model (which is still in its initial stages) was not initiated as a result of an experimental observation which was not amenable to interpretation in the traditional way. Rather it resulted from an intellectual interest in the curve-crossing model and its application to Michael addition reactions. The three aforementioned examples are, therefore, cited as part of an attempt to find possible manifestations or "questions" for which the model may serve as a solution.

When this model was presented in part at the ESOR III,²⁸ it attracted two kinds of responses. The first

(27) Williams, I. H.; Hammond, R. B. *J. Chem. Soc., Perkin Trans.* 2 1989, 59.

(28) Third European Symposium of Organic Reactivity in Goteborg, Sweden, July 7-12, 1991.

claimed that the model attacks a "nonproblem", whereas the second took the diametrically opposite approach referring to the model as approaching sacrilege and blasphemy. These two approaches reflect well the conflict within the scientific community. The literature clearly shows that there is a rapidly growing school of chemists who believe that the TS may not necessarily possess an intermediate structure between reactants and products. On the other hand, it is clear that it is extremely difficult to part from the beautiful and highly appealing traditional logic which underlies the use of LFERs as TS structure probes. This conflict or confusion stems mainly from one pivotal problem, namely, our inability to directly observe the structure of a TS. As a result, the search for its structure has been considered by some as lying on the border between science and fiction. Arnett has made probably the most provocative statement in this regard by suggesting that "... speculation about an inherently elusive entity (the transition state)... has scarcely had a parallel since the close of medieval scholasticism."²⁹ This vilification assumes that TS structures are not directly observable. However, two methodologies are now racing in this very

(29) Arnett, E. M.; Reich, R. *J. Am. Chem. Soc.* **1980**, *102*, 5892.

direction. The first is femtosecond laser spectroscopy, while the second is quantum mechanics via ab-initio or similar calculations. Theoretical chemistry, in particular, is moving rapidly to this goal in both efficiency and reliability. Unfortunately, when it succeeds, much of the intellectual fun (along with many job opportunities) of our business will vanish; for it may be easier, faster, and cheaper to get the answer from the computer than from the chemist at the bench.

Shaik has recently noted that classical physical organic chemistry and the corresponding theoretical discipline often progress in non-interactive parallel lines. Thus, for example, it is not apparent where "the origins [are] of rate-equilibrium relationships or the Hammond Lefler postulate in MO theory; nor can the principle of orbital symmetry be traced to anywhere in the underlying conceptual frame of classical physical organic chemistry".³⁰ We hope that until computational chemistry will be suitably advanced, further development of models such as the one presented in this Account will be used to make the two parallel lines meet.

(30) Shaik, S. S. *Pure Appl. Chem.* **1991**, *63*, 195.