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Reactivity–Selectivity Relationships. A Quantum Mechanical Approach to Transition State Structure. Application to the S_N2 Reaction of Benzyl Derivatives

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Abstract: A model for estimating the effect of substituents on transition-state structure in S_N2 reactions is presented. The model is based on a description of the reaction complex in terms of a wave function built up from a linear combination of reactant configurations. Stabilization of a given configuration by a substituent effect is indicated to enhance its contribution to the wave function and hence to the energy and structure of the transition state. The structural effects of the substituent perturbation on the transition state are assessed by analysis of the structural requirements inherent within each of the configurations. The model is applied to the S_N2 reaction of benzyl derivatives, and the predictions are compared with experiments and the earlier models. Within a limited family, substituent effects are likely to affect the transition state in an "anti-Hammond" manner. Only for comparisons of substrates of widely differing structure and reactivity are "Hammond" effects likely to manifest themselves in addition to the "anti-Hammond" behavior.

The study of substituent effects on organic reactivity remains an important part of physical organic chemistry. Through its blending with transition-state theory significant progress has been made in developing both experimental criteria for measuring, as well as theoretical models for predicting, how substituents will affect the structure of the transition state.[1] Much of the experimental research is directed at the exploration of linear free energy relationships. Thus selectivity parameters such as ρ, m, α, and β have all been utilized as experimental parameters for estimating changes in transition-state structure.[1a–d,f–j]

The original theoretical basis for considering the transition state derives from the Bell–Evans–Polanyi[2] principle and the closely related Hammond postulate.[3] From these basic ideas have sprung all the key models which have been developed over recent years for predicting changes in transition-state structure. The most prominent models are those of Thornton,[4] More O'Ferrall,[5] Harris and Kurz,[6] and Critchlow,[7] and they have been applied successfully to a range of reactions. The important conceptual breakthrough associated with these potential energy surface models is that perturbations both parallel *and* perpendicular to the reaction profile are considered to affect the structure of the transition state.

A point of concern, however, is the fact that despite the many successes of the potential energy surface models, there are a number of cases where they appear to be inapplicable. Thus, for what is probably the most studied reaction in organic chemistry, the S_N2 substitution, certain predictions of all the models are not supported by the experimental results.[8,9] For example, a study on the nucleophilic substitution of the benzyl system by Westway and Ali[8] suggested that increasing the leaving-group ability leads to a more *advanced* transition state rather than an earlier transition state (at least for nucleophile–substrate bonding) anticipated by all the models.[10,11] Also, the reason for the similar selectivities of a series of primary alkyl derivatives toward 4-substituted pyridines, despite their widely varying reactivity, remains obscure.[12]

We believe that to obtain a more detailed understanding of a reaction family such as S_N2, one should attempt a quantum mechanical description of the way the potential energy curve is constructed. Such an approach may lead to a clearer definition as to the structure of the transition state and hopefully will enable predictions regarding the effect of substituents to be made. This is the main goal of this paper: to define the S_N2 potential curve by some quantum mechanical criterion and thereby develop a model for probing the structure of the S_N2 transition state. The model is applied in detail to the substitution reaction of substituted benzyl derivatives. The effect of substituents in the nucleophile, the aromatic ring, and the leaving group are considered, and a comparison with available experimental data is made.

Theory

How can one best approach the question of the structure of a transition state? We believe that an effective way of tackling this problem is by resolving the wave function which describes the transition state into contributions of reactant wave functions, in much the same manner as the organic chemist would express a species in terms of its resonance structures, or the qualitative theorist would discuss a delocalized orbital in terms of two or more

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(1) For recent reviews on transition-state structure see: (a) Albery, W. J.; Kreevoy, M. M. *Adv. Phys. Org. Chem.* **1978**, *16*, 87. (b) More O'Ferrall, R. A. In "The Chemistry of the Carbon Halogen Bond", Patai, S., Ed.; Wiley: New York, 1973; Vol. 2, p 609. (c) Jencks, W. P. *Chem. Rev.* **1972**, *72*, 705. (d) Kresge, A. J. *Acc. Chem. Res.* **1975**, *8*, 354. (e) Westheimer, F. H. *Chem. Rev.* **1961**, *61*, 265. (f) Albery, W. J. *Prog. React. Kinet.* **1967**, *4*, 355. (g) Bruice, T. C. *Annu. Rev. Biochem.* **1976**, *45*, 331. (h) Pross, A. *Adv. Phys. Org. Chem.* **1977**, *14*, 69. (i) McLennan, D. J. *Tetrahedron* **1975**, *31*, 2999. (j) Johnson, C. D. *Chem. Rev.* **1975**, *75*, 755.

(2) Evans, M. G.; Polanyi, M. *Trans. Faraday Soc.* **1936**, *32*, 1340. Bell, R. P. *Proc. R. Soc. London, Ser. A* **1936**, *154*, 414. For a more recent discussion see: Dewar, M. J. S. In "The Molecular Orbital Theory of Organic Chemistry"; McGraw-Hill: New York, **1969**; pp 284–288.

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

(4) Thornton, E. R. *J. Am. Chem. Soc.* **1967**, *89*, 2915.

(5) More O'Ferrall, R. A. *J. Chem. Soc. B* **1970**, 274.

(6) Harris, J. C.; Kurz, J. L. *J. Am. Chem. Soc.* **1970**, *92*, 349.

(7) Critchlow, J. E. *J. Chem. Soc., Faraday Trans.* **1972**, *68*, 1774.

(8) Westaway, K. C.; Ali, S. F. *Can. J. Chem.* **1979**, *57*, 1354.

(9) Thorstenson, T.; Eliason, R.; Songstad, J. *Acta Chem. Scand., Ser. A* **1977**, *31*, 276.

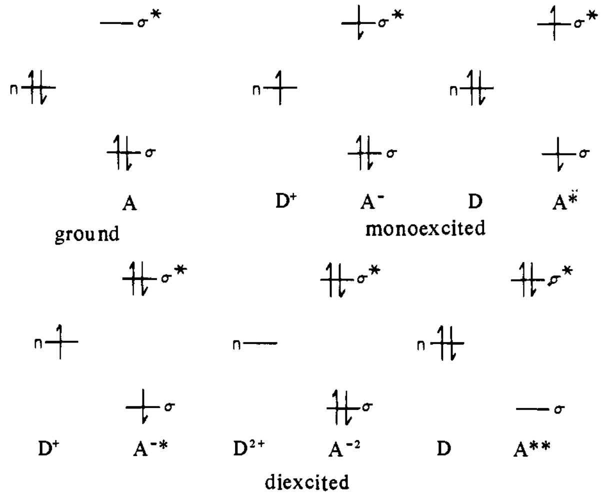
(10) For an analysis of the S_N2 reaction using the potential energy surface models see: (a) reference 8. (b) Lowry, T. H.; Richardson, K. S. "Mechanism and Theory in Organic Chemistry", Harper and Row: New York, 1976; Chapter 5. (c) Harris, J. M.; Shafer, S. G.; Moffatt, J. R.; Becker, A. R. *J. Am. Chem. Soc.* **1979**, *101*, 3295.

(11) For experimental papers on substituent effects in S_N2 transition states see: (a) Yamataka, H.; Ando, T. *Tetrahedron Lett.* **1975**, 1059. (b) Yamataka, H.; Ando, T. *J. Am. Chem. Soc.* **1979**, *101*, 266. (c) Hegazi, M. F.; Borchardt, R. T.; Schowen, R. L. *Ibid.* **1979**, *101*, 4359. (d) Buddenbaum, W. E.; Shiner, V. J. *Can. J. Chem.* **1976**, *54*, 1146. (e) Friedberger, M. P.; Thornton, E. R. *J. Am. Chem. Soc.* **1976**, *98*, 2861. (f) Frisone, G. J.; Thornton, E. R. *Ibid.* **1968**, *90*, 1211. (g) Berg, U.; Gallo, R.; Metzger, J.; Chanon, M. *Ibid.* **1976**, *98*, 1260. (h) Ko, E. C. F.; Parker, A. J. *Ibid.* **1968**, *90*, 6447. (i) Swain, C. G.; Hershey, N. D. *Ibid.* **1972**, *94*, 1901. (j) Bare, T. M.; Hershey, N. D.; House, H. O; Swain, C. G. *J. Org. Chem.* **1972**, *37*, 1972. (k) le Noble, W. J.; Miller, A. R. *Ibid.* **1979**, *44*, 889. (l) Hill, J. W.; Fry, A. *J. Am. Chem. Soc.* **1962**, *84*, 2763. (m) Ballistreri, F. P.; Maccarone, E.; Mamo, A. *J. Org. Chem.* **1976**, *41*, 3364. (n) Hudson, R. F.; Klopman, G. *J. Chem. Soc.* **1962**, 1062. (o) Haberfield, P. *J. Am. Chem. Soc.* **1971**, *93*, 2091. (p) Grimsrud, E. P.; Taylor, J. W. *Ibid.* **1970**, *92*, 739. (q) Reference 8. (r) Reference 9.

(12) Arnett, E. M.; Reich, R. *J. Am. Chem. Soc.* **1978**, *100*, 2930.

0002-7863/81/1503-3702$01.25/0

Chart I. Ground and Excited Reactant Configurations for the Description of S_N2 Reactions



interacting fragment orbitals.[13] The appropriate starting point for our purpose is the charge-transfer model originally put forth by Mulliken.[14,15] Experience with this model shows that it readily lends itself to the construction of potential energy surfaces of organic reactions.[16] The model expresses a wave function of a donor (D)–acceptor (A) complex, as a combination of a no-bond (DA) configuration mixed in with excited ones, such as charge-transfer (e.g., D^+A^-) and locally excited (e.g., DA*) contributions. This is precisely what we seek since we wish to express the transition state in terms of *reactant configurations*. How do we locate the transition state? Recently[17] one of us has shown that, in all reactions (including S_N2) which involve bond making and bond breaking, the transition state arises from the intersection of the no-bond surface, DA, with a surface made up of a pack of excited reactant configurations (D^+A^-, DA*, etc.). Leading the pack is a configuration which is prepared for the electronic reorganization which must take place during the reaction. It must contain two odd electrons (a bond pair), per each new bond, in reactant orbitals of identical symmetry. Let us see how this operates for an S_N2 reaction.

For any S_N2 reaction

$$\mathrm{N\ (D) + RX\ (A) \rightarrow NR + X} \qquad (1)$$

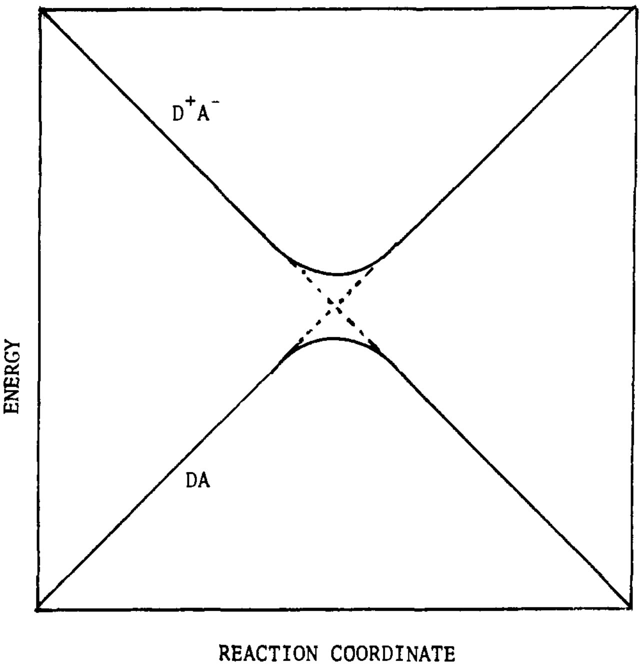


Figure 1. Avoided curve crossing of DA and D^+A^- leading to an activation barrier for the S_N2 reaction. Other contributions such as DA*, D^+A^{-*}, etc. are omitted for clarity (see text).

a nucleophile, N (D), attacks a substrate, RX (A). As a result, a new bond is formed between D and A and the bond within A is cleaved. From an orbital point of view one can say that the reaction takes place primarily through the reorganization of the principal reacting electron pairs—the nucleophile HOMO n and the substrate σ_{C-X} pair within the frontier orbitals of the reactants.[18] There are six configurations which may be obtained through the distribution of the valence electrons amongst the frontier orbitals. These are indicated in Chart I and are listed in order of excitation with respect to the reactants.

In the same manner that MO's are constructed from AO's, the set of six configurations constitutes our stock of building blocks from which the wave functions of the reaction complex may be constructed for any point along the reaction coordinate. *Thus these configurations contain the fundamental information as to what happens to the reacting molecules as they undergo chemical transformation.*

Let us examine these configurations in detail. We begin by selecting an S_N2 reaction of a nucleophile N and a substrate RX. The DA configuration is one which describes the two reactants holding on to their electrons. It is termed "no bond", and as the name implies, it does not allow any electronic delocalization.

$$\mathrm{DA = N\!:\ (R{-}X)} \qquad (2)$$

Therefore if bonding changes are to occur, the reaction complex must acquire a character which reflects the electronic reshuffle. This can be brought about by mixing in some other configuration, e.g., D^+A^-. The D^+A^- configuration describes an electron jump from the nucleophile to an empty orbital, σ*, of the substrate, and is represented by the species

$$D^+A^- = N{\cdot}^+(R\dot{-}X)^- \qquad (3)$$

Although written as a diradicaloid, eq 3 does not in any way describe a diradical; the two odd electrons are spin paired as indicated in Chart I. Mixing of this configuration into DA will express some of the effect of electronic delocalization which brings about bonding changes.

Yet another form of electronic reshuffle is the mixing of the locally excited DA* into DA. DA* describes an electronic promotion within the substrate: one σ electron is promoted into a

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[13] This method has been used for sometime by the Hoffmann group to analyze structure and reactivity problems. Some representative papers are as follows: (a) Hoffmann, R. *Acc. Chem. Res.* **1971**, *4*, 1. (b) *Pure Appl. Chem.* **1971**, *2*, 233. (c) *Ibid.* **1971**, *28*, 181. (d) Elian, M.; Hoffmann, R. *Inorg. Chem.* **1975**, *14*, 1058. (e) Libit, L.; Hoffmann, R. *J. Am. Chem. Soc.* **1974**, *97*, 1370.

[14] The donor–acceptor formalism was first introduced by Mulliken, see: (a) Mulliken, R. S. *J. Am. Chem. Soc.* **1952**, *74*, 811. (b) *J. Phys. Chem.* **1952**, *56*, 801. (c) Mulliken, R. S.; Person, W. B. "Molecular Complexes"; Wiley-Interscience: New York, 1969. See also: (d) Brown, R. D. *J. Chem. Soc.* **1959**, 2224. (e) Nagakura, S. *Tetrahedron, Suppl. 2* **1963**, *19*, 361.

[15] Much of the development, refinement and application of the approach is due to the work of Fukui's group, see: (a) Fukui, K.; Fujimoto, H. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 1989. (b) Fukui, K. *Top. Curr. Chem.* **1970**, *15*, 1. (c) Fukui, K. "Theory of Orientation and Stereoselection"; Springer-Verlag: Heidelberg, 1975. (d) Fujimoto, H.; Fukui, K. In "Chemical Reactivity and Reaction Paths"; Klopman, G., Ed.; Wiley: New York, 1974; pp 23–54.

[16] For the use of this approach to the discussion of potential energy surfaces in organic reactions, see: (a) Epiotis, N. D.; Shaik, S. In "Progress in Theoretical Organic Chemistry"; Csizmadia, I. G., Ed.; Elsevier: Amsterdam, 1977; Vol. 2. (b) Epiotis, N. D.; Shaik, S. *J. Am. Chem. Soc.* **1977**, *99*, 4936. (c) Epiotis, N. D.; Shaik, S. *J. Am. Chem. Soc.* **1978**, *100*, 1, 9, 29. (d) Shaik, S.; Epiotis, N. D. *J. Am. Chem. Soc.* **1978**, *100*, 18. (e) Epiotis, N. D.; Shaik, S.; Zander, W. In "Rearrangements in Ground and Excited States"; De Mayo, P., Ed.; Academic Press: New York, 1980. (f) Shaik, S. S. *J. Am. Chem. Soc.* **1979**, *101*, 3184. (g) Epiotis, N. D. "Theory of Organic Reactions"; Springer-Verlag: Heidelberg, 1978.

[17] (a) Shaik, S. S., "What Happens to Molecules as They React? A Valence Bond Approach to Reactivity", submitted for publication in *J. Am. Chem. Soc.* (b) Shaik, S. S.; Aviram, K. "What Happens to Molecules as They React? The role of Geometric Distortions along the Reaction Coordinate", submitted for publication in *J. Am. Chem. Soc.*

[18] These are generalized orbitals which are allowed to change with the geometric distortions of the reactants, see ref 17a and b.

σ^* orbital, and thus, the substrate R–X acquires an excited $\sigma \rightarrow \sigma^*$ character (R–X)* within the complex.

$$\mathrm{DA}^* = \mathrm{N{:}\ (R\text{–}X)^*} \qquad (4)$$

These are the main three configurations. The remaining three D^+A^{-*}, $D^{2+}A^{2-}$, and DA** are subsidiary, diexcited configurations of higher energy. In principle one should include them in order to describe properly the chemical transformation. In practice, they do not appear to change the qualitative predictions reached by considering only DA, D^+A^-, and DA*. Since our goal in this paper is to develop a qualitative insight into the problem, we choose to ignore these diexcited configurations.[19]

The reaction complex may therefore be described by a combination of the main three configurations, in much the same way as the organic chemist uses resonance structures to describe a molecule or a transient. The extent of the mixing of the excited reactant configurations into DA will gradually increase along the reaction coordinate. This mixing will bring about changes in the geometry, in the charge distribution within the reactants, and in the energy of the system, to an extent which reflects both the weight and the nature of the excited configurations. The important point is that each position along the reaction profile may be defined by a wave function, ψ_i, derived from a linear combination of reactant configurations.[19] This is shown in eq 5.

$$\psi_i = C_1(\mathrm{DA}) + C_2(\mathrm{D^+A^-}) + C_3(\mathrm{DA^*}) \qquad (5)$$

The rules which govern the extent to which configurations interact[16] are similar to those which operate for MO's. The extent of interaction is proportional to the overlap and inversely proportional to the energy gap. These concepts are readily illustrated by examining the way in which a reaction profile is generated from the intersection of a DA and a D^+A^- curve for the S_N2 reaction. This is illustrated in Figure 1. D^+A^- is operationally important since this is the configuration which contains the bond pair in n and σ^* (Chart I) and will therefore lead to bonding changes. In practice, not only the D^+A^- but also other excited configurations mix into DA as well but, due to their higher energy, are less involved.

Initially the DA and D^+A^- curves are widely separated.[17] Reactants proceed along the DA curve (by approach of the nucleophile to the substrate) and increase in energy until the energy gap between the ground and excited curves is sufficiently small to allow them to interact and therefore mix. The result is an avoided crossing, and in the region of the avoided crossing, DA and D^+A^- configurations contribute roughly to a similar extent. Past the avoided crossing the reaction pathway follows the D^+A^- curve down to product.

The importance of the foregoing discussion is that *the model provides us with a unique way of characterizing the transition state.* The transition state, which is a point close to the position of the avoided crossing, is composed of a *specific combination of both ground (DA) and excited configurations.* Any substituent change, which is introduced, will have a predictable effect on the energies of the configurations. *The transition state will reflect this modification by mixing in less of any configurations destabilized by the substituent change and more of any configurations which are stabilized by the substituent change.* For example, increasing the nucleophilicity of the nucleophile (D) will lower the energy of the D^+A^- configuration since the ionization potential of the nucleophile is reduced. As a result, at the transition state, D^+A^- will mix in to a greater extent, thereby increasing the D^+A^- character of the transition state. In quantitative terms this means that C_2 of eq 5 will increase while C_1 and C_3 will decrease.

The implications of this change are clear. *If we can ascertain the bonding characteristics of each configuration which contributes to the structure of the transition state, we can make specific predictions as to how the transition state will change as a result of a given perturbation.*

Structure of the Transition State. We now proceed to examine the structural implication associated with each of the relevant configurations. This may be realized by examining both the MO and VB representations of the key configurations, and in the discussion we shall alternatively use both the MO and VB approaches. This is because for any given problem often one of the two approaches lends itself to more simple and direct application.

Let us first discuss how a bond may be viewed by using VB ideas. Consider, for example, the R–X (X = electronegative atom) bond. The VB description of this bond is

$$\psi_{\mathrm{R\text{-}X}} = (\mathrm{R\cdot\ \cdot X}) + \lambda_1(\mathrm{R^+{:}X^-}) + \lambda_2(\mathrm{R{:}^-X^+}) \quad \lambda_2 << \lambda_1 < 1 \qquad (6)$$

The principle VB form is the so-called diradicaloid form (R· ·X), while the zwitterionic forms are subsidiary forms, with the one which localizes the negative charge on X being predominant. The reader may recall that in the configurational formalism, DA (N: R–X) is the one which describes the N···R "no bond" and the R–X bond (eq 2). Therefore this configuration must contain the elements for C–X bonding which are shown in eq 6. This is indeed what one finds if one expands DA into its VB components.[20]

$$\mathrm{DA\ (N{:}\ R\text{–}X)} = (\mathrm{N{:}\ R\cdot\ \cdot X}) + \lambda_1(\mathrm{N{:}\ R^+\ {:}X^-}) + \lambda_2(\mathrm{N{:}\ R{:}^-\ X^+}) \qquad (7)$$

Thus, in order to create some N–R bonding, one must mix into DA those configurations which contribute the key diradicaloid form (N· ·R) which describes the N–R bond. Such contribution

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(19) While we have chosen to ignore the effect of diexcited configurations in our qualitative arguments, it must be realised that, strictly speaking, one must use $R{:}^-X^+$, configurations if one wants to obtain a meaningful wave function. This is because at the LCAO–MO level of theory the configurations do not excited state acquires a major $N{:}\ R^+{:}X^-$ at infinity. Thus, for example, at the reaction starting point the wave function of the nucleophile–substrate complex is not properly represented by the DA configuration alone but is mixed in with some DA** (and indirectly with some DA*). This mixing, which is a simple application of configuration interaction, improves the description of the C–X bond in the acceptor A, by emphasizing its covalent character. If we use the notation that $\sigma = (a\phi_R + b\phi_X)$ and $\sigma^* = (-b\phi_R + a\phi_X)$, where $b > a$ and ϕ_R and ϕ_X are hybrids centered on R and X, respectively, we obtain

$$\mathrm{DA} - \lambda\mathrm{DA^{**}} = \sqrt{2}ab\,(1 + \lambda)\,[\mathrm{N{:}\ R\cdot\ \cdot X}] + (a^2 - \lambda b)\,(\mathrm{N{:}\ R{:}^-X^+}) + (b^2 - \lambda a^2)\,[\mathrm{N{:}\ R^+\ {:}X^-}] \qquad \text{(i)}$$

We see that what DA** mixing does is to increase the importance of the covalent R· ·X configuration at the expense of ionic forms; $R{:}^-X^+$ and $R^+{:}\ X^-$. :X⁻. Thus we conclude that in MO terms DA (n^2 in Table I) is a good approximation for the system at the reaction starting point, while in VB terms it is best described by N: R· ·X.

In the same manner DA* in the MO picture may be represented by

$$\mathrm{DA^*} = (a^2 - b^2)[\mathrm{N{:}\ R\cdot\ \cdot X}] - \sqrt{2}ab[(\mathrm{N{:}\ R{:}^-X^+}) - (\mathrm{N{:}\ R^+\ {:}X^-})] \qquad \text{(ii)}$$

i.e., it consists mostly of the two ionic forms $R^+\ {:}X^-$ and $R^-{:}\ X^+$, apparently of equal weight. However when we mix into DA* the DA** and DA configurations, the resulting excited acquires a major $N{:}\ R^+{:}X^-$ nature, as shown in Table II. Thus the excited state in an MO sense is best described by DA* ($n^2\ \sigma^1\ \sigma^{*1}$ of Chart I) while in VB terms it is best described by $N{:}\ R^+{:}X^-$. D^+A^- in the MO picture may be represented by

$$\mathrm{D^+A^-} = -a(\mathrm{N^{+}\cdot\ R{:}^-\cdot X}) + b(\mathrm{N\cdot^+\ \cdot R\ {:}X^-}) \quad b > a \qquad \text{(iii)}$$

Similarly

$$\mathrm{D^+A^{-*}} = -b(\mathrm{N\cdot^+R{:}^-\cdot X}) - a(\mathrm{N\cdot^+\ \cdot R\ {:}X^-}) \quad b > a \qquad \text{(iv)}$$

A proper description of the ionic (A^-) state mixes into A^- some A^{-*}. Thus

$$\mathrm{D^+A^-} - \lambda\mathrm{D^+A^{-*}} = (-a + \lambda b)[\mathrm{N\cdot^+R{:}^-\ \cdot X}) + (b + \lambda a)[\mathrm{N\cdot^+R\cdot\ {:}X^-}] \qquad \text{(v)}$$

From eq v we can see that mixing D^+A^{-*} does not really change the relative weight of the two VB structures. Therefore in MO terms D^+A^- ($n^1\ \sigma^2\ \sigma^{*1}$) is the best approximation of the charge-transfer state at the reaction starting point, while in VB terms this would be best described by a major ($N\cdot^+R\cdot{:}X^-$) form and a minor ($N\cdot^+R{:}^-\cdot X$) form. In summary, therefore, when we neglect D^+A^{-*}, DA**, and $D^{2+}A^{2-}$, our description of the transition state is only an approximate one. However, when the major MO configurations ($\sigma 2$ for A, $\sigma^1\sigma^{*1}$ for A* and $\sigma^2\sigma^{*1}$ for A^-) and the major VB contributors (Table I) are retained, most of the conclusions are not affected *qualitatively* while the analysis is greatly simplified.

(20) The states of a bond were described before. See: (a) Slater, J. C. "Quantum Theory of Molecules and Solids", McGraw-Hill, New York, 1963; Vol. 1, Chapters 3 and 4. (b) Salem, L.; Rowland, C. *Angew Chem., Int. Ed. Engl.* **1972**, *11*, 92. See also: (c) Epiotis, N. D.; Shaik, S. *J. Am. Chem. Soc.* **1977**, *99*, 4736.

can be found only in a configuration which is, a priori, open shell and which contains two odd electrons—one on one reactant ($N\cdot$) and another on the second ($R\dot{-}X$). Clearly, this fits D^+A^-. Thus, D^+A^- contains the *key element for N–R bond formation*[21] and may be described by the VB components.

$$D^+A^-\ (N\cdot^+\ R\dot{-}X^-) = (N\cdot^+\ \cdot R\ {:}X^-) + \lambda(N\cdot^+\ R^-{:}\ \cdot X) \quad (8)$$

Let us comment briefly on the effect of the relative weights of the two VB forms in eq 8. D^+A^- has a remnant of R–X bonding due to the extra bonding electron in σ (Chart I). In VB terms this bonding arises from the coupling of the two resonance structures, each having three electrons between R and X.

$$a(R{:}\ \cdot X) \leftrightarrow b(R\cdot\ {:}X) \quad (9)$$

This coupling is proportional to $ab\beta_{RX}$, where β_{RX} is the resonance integral connecting R and X. This coupling peaks when $a = b$, indicating, that when the relative contributions of the two VB structures are equal, one gets the strongest possible *three-electron bond*. This can be regulated by proper substitution on carbon (or on X). Electron-releasing substituents on R will make the VB form ($R\cdot\ {:}X$) preponderant and will describe the weakest three electron bond,[22] whereas electron-attracting substituents on carbon will increase the relative amount of $R{:}\ \cdot X$ and hence the coupling with ($R\cdot\ {:}X$), resulting in the strongest $R\dot{-}X$ three-electron bond. This electronegativity effect in radical anions has been clearly illustrated by Wang and Williams.[23] The stabilities of the $F_3C\text{–}X^{-}\cdot$ and $(CF_3)_3C\text{–}X^{-}\cdot$ radical anions, where the odd electron delocalizes itself on C and X, are substantially greater than for the $CH_3\text{–}X^{-}\cdot$ radical anion, and it was concluded that maximum stability would be observed for the homonuclear species $X_2^{-}\cdot$.[24]

Finally let us examine the VB content of the DA* configuration. The DA* configuration is really only concerned with A* since the donor (D) is unaffected. The VB description of A* is predominantly $R^+\ {:}X^-$.[20] Thus DA* becomes

$$DA^*\ \{N{:}\ (R\text{–}X)^*\} = (N{:}\ R^+\ {:}X^-) + \lambda_1(N{:}\ R\cdot\ \cdot X) + \lambda_2(N{:}\ R{:}^-X^+) \quad |\lambda_2| << |\lambda| < 1 \quad (10)$$

Having both an MO and a VB description of the key configurations[19] available, we can now examine the structural implications associated with each configuration. Specifically, the question we wish to ask is: how does each configuration contribute to the extent of N–R and R–X bonding?

We begin by considering the extent of bonding in the R–X linkage. From the orbital description of the configurations (Chart I) it is evident that the extent of R–X bonding will depend on the electron population of the σ and σ^* orbitals. The larger the number of electrons in the σ orbital the stronger the bond, the larger the number of electrons in the σ^* orbital, the weaker the bond. Thus the strongest R–X linkage will take place in the DA configuration where two electrons reside in the σ orbital and none in the σ^* orbital. The D^+A^- configuration will contain a weaker R–X linkage, and the DA* will be essentially nonbonding.

The effect of the configurations on the N–R linkage is most readily amenable from the VB analysis. Clearly DA and DA* are both nonbonding with respect to the N–R linkage since no nucleophile–substrate interaction is implied for either of these configurations. D^+A^- however does contain N–R bonding since the VB description shows that the form $N\cdot\ \cdot R$ contributes to the VB wave functions (eq 8). As we noted earlier, the diradicaloid form is the VB contributor which is primarily responsible for bond formation.[21]

Table I. Valence Bond Description[a] of Donor–Acceptor Configurations and Their Structural Effect on the Reaction Complex

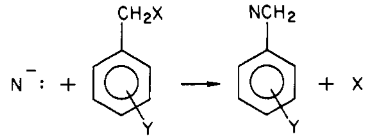
configuration	valence bond descrptn		structural effect on reaction complex	
	primary	secondary	N–R	R–X
DA	$N{:}\ R\cdot\ \cdot X$	$N{:}\ R^+\ {:}X^-$	loose	tight
D^+A^-	$N\cdot^+\ \cdot R\ {:}X^-$	$N\cdot^+\ R{:}^-\ \cdot X$	tight	loose
DA*	$N{:}\ R^+\ {:}X^-$	$N{:}\ R\cdot\ \cdot X$	loose	loose

[a] It should be noted that the diradicaloid VB forms do not actually mean that at some point along the reaction coordinate one should anticipate diradicals. It only means that the D^+A^- configuration, as written in VB or MO terms, contain two odd electrons. However, since these two electrons are spin paired, one does not expect diradicals; there are two pairs of electrons along the entire reaction coordinate.

The configurations just discussed, their primary and secondary VB contributors, and their structural effect on the reaction complex are summarized in Table I.

Application of the Model

Having established the structural effects associated with each of the important configurations, we now illustrate the model for the nucleophilic substitution reaction of benzyl derivatives (eq 11)



(11)

and compare the results with available experimental data and those predicted from the earlier models.[25] Let us begin by considering substituent effects in the leaving group.

Effect of the Leaving Group. Increasing the leaving group ability through a substituent change has the effect of lowering the energy of those configurations in which the C–X bond pair is already largely localized on the leaving group. This is true primarily for the D^+A^- and DA* configurations as may be seen from the principal VB contributors to each of the configurations (as illustrated in Table I). The effect of the substituent on the DA configuration will be, by comparison, smaller since the X^- character is less developed, as witnessed by the fact that X^- appears only within the secondary valence contributor. Thus the stabilized D^+A^- and DA* curves will lead to an increase in the amount of D^+A^- and DA* configurations in the transition state. This, in turn, is expected to have a bond-loosening effect on the C–X bond since both configurations favor a weak C–X linkage.

The effect of the leaving group change on the N–C bond character is less clear-cut since the D^+A^- configuration favors extensive N–C bond making whereas the DA* coonfiguration favors little N–C bond making. However, as we have already noted the D^+A^- configuration mixes into the transition state to

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(21) As a reviewer has noted, in order to clarify in detail the origins of the D–A bond formation, one must also examine the cross product of DA and D^+A^-. Such analyses can be found in ref 15 and in Fujimoto, H.; Inagaki, S.; Fukui, K., *J. Am. Chem. Soc.* **1976**, *98*, 2670. However, when we say that the diradicaloid form is the key element for bonding, we only mean that it is the major VB component of most covalent bonds. We do not mean to imply that the cross product of DA with D^+A^- does not contribute to the formation of the bond.

(22) Note that if $R\cdot\ {:}X$ is the only VB form, the $R\cdots X$ interaction is a three-electron one and is destabilizing by overlap repulsion. Stabilization arises only through the delocalization $R{:}\ \cdot X \leftrightarrow R\cdot\ {:}X$. See ref 17a.

(23) Wang, J. T.; Williams, F. *J. Am. Chem. Soc.* **1980**, *102*, 2860.

(24) The three-electron resonance in O_2 is estimated by Goddard to be stabilizing by 30 kcal/mol. Goddard, W. A., III; Dunning, T. H., Jr.; Hunt, W. J.; Hay, J. P. *Acc. Chem. Res.* **1973**, *6*, 368.

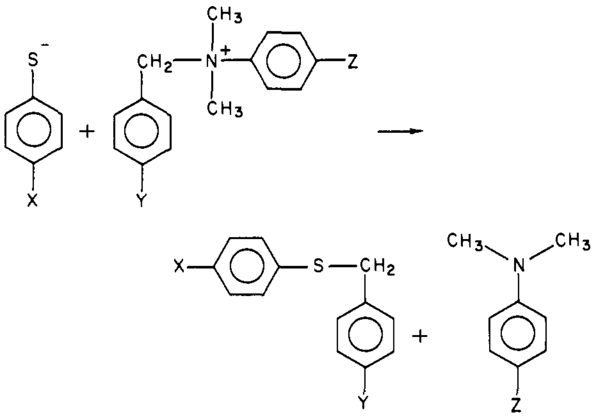
(25) Harris et al.[10c] have recently concluded that the experimental results for the changing the leaving group are actually consistent with the predictions of the More O'Ferrall approach. We question these conclusions for a number of reasons. For example, we suspect that the use of *m* values as a measure of transition-state structure is not sound.[1h] Also, it is unclear to us as to how the increase in α-D values on changing the leaving group in neophyl methanesulfonate to trifluoromethanesulfonate leads to the conclusion of less N–R bond formation and essentially unchanged R–X cleavage. Furthermore, the selectivity order of aminolysis of benzyl bromide and benzyl chloride observed by Swain and Langsdorf[26] was not clear-cut but substituent dependent. The method of Ballistreri et al.[11m] and Hudson and Klopman,[11n] on the basis of ρ values, is a more reliable method and leads to the opposite conclusion; i.e., benzyl chloride is less selective than the bromide.

(26) Swain, C. G.; Langsdorf, W. P. *J. Am. Chem. Soc.* **1951**, *73*, 2813.

a greater extent than DA* due to the greater stability of the former configuration.[27] As a consequence the effect of introducing a better leaving group is expected to lead to *greater* N–C bond making.

Let us compare the prediction of greater N–C bond making and greater C–X bond breaking with available experimental data and the predictions derived from the potential energy surface models.[4–7]

In a thorough study of the S_N2 reaction in benzyl derivatives (eq 12), Westaway and Ali[8] applied nitrogen kinetic isotope effects, secondary α-deuterium isotope effects, and Hammett ρ values[28] in order to assess the effect of leaving group changes on the structure of the transition state. In agreement with our predictions, they concluded that increasing the ability of the leaving group leads to *greater* nucleophile–substrate bond making and more extensive carbon–leaving group bond breaking. Consistent with this explanation, they noted in the transition state increased charge donation by the nucleophile as the leaving-group ability improved. This, again is consistent with an increased contribution of the D^+A^- configuration to the transition state. The results of Ballistreri et al.[11m] for the reaction of benzyl halides and substituted anilines also lend support to this interpretation. For chloride as the leaving group, a Hammett ρ value of –0.87 was observed while for the better leaving groups, bromide and iodide ions with corresponding values of –1.40 and –1.46 were observed.



(12)

Comparison of these results and predictions based on the potential energy surface models indicates substantial differences. If about equal parallel and perpendicular effects are assumed, all models predict *less* nucleophile–carbon bond making for a better leaving group in contrast to the experimental evidence and the predictions of our model. With regards to the carbon–leaving group bond, the models are all ambiguous since two opposing effects, parallel and perpendicular to the reaction coordinate, are involved so no clear prediction results.

Effect of the Nucleophile. Increasing the nucleophile strength has the effect of lowering D^+A^- since the nucleophile is now a better electron donor. As a consequence this configuration will mix increasingly into the transition state. Inspection of Table I indicates that the D^+A^- configuration encourages greater nucleophile–carbon bond formation as well as greater carbon–leaving group bond cleavage. This conclusion is again contrasted by the prediction based on the potential energy surface models.[4–7] All models predict that an increase in the nucleophilic strength will *decrease* the degree of carbon–leaving group bond cleavage and have little effect on the degree of nucleophile–carbon bond formation.

Table II. Hammett ρ Values for the Reactions of Para-Substituted Phenylbenzyldimethylammonium Nitrates with the Thiophenoxide Ion, *p*-Chloro and *p*-Methylthiophenoxide Ions at 0 °C in DMF (eq 12) (Calculated from Data of Westaway and Ali[8])

substituent on nucleophile	ρ	substituent on nucleophile	ρ
Cl	1.73	Me	2.14
H	1.91		

The experimental results obtained for the benzyl system are in support of the configuration mixing model. Utilization of the data published by Westaway et al.[8] enables us to assess the effect of nucleophile strength on the degree of carbon–leaving group bond breaking as well. The results are listed in Table II.

It can be seen that the ρ value (which can be utilized as a measure of the degree of carbon–leaving group bond breaking)[28] increases in the order X = Me > H > Cl, where X is the substituent in the thiophenoxide ring. Thus for the stronger nucleophile, *p*-methylthiophenoxide ion, greater carbon–leaving group bond breaking takes place than for a weaker nucleophile, in agreement with the present model.

Evidence that the N–C bond making is larger for strong nucleophiles than for weak nucleophiles is indicated by the work of Thorstenson et al.[9] A possible measure of the extent of electron transfer from the nucleophile to the substrate is provided by the k_{NO_2}/k_H ratio, where NO_2 and H are substituents in the benzyl ring (eq 11). Thorstenson et al.[9] observed values of $k_{NO_2}/k_H >$ 1 for powerful anionic nucleophiles but values ≤ 1 for the relatively weak neutral nucleophiles. They concluded on the basis of their results that greater N–C bond formation occurs with the anionic nucleophiles and hence the larger k_{NO_2}/k_H values in agreement with our prediction.

Effect of Ring Substituents. The effect of substituents in the ring will have a significant impact on the relative stabilities of the different configurations and hence the extent to which they contribute to the transition state. Since the intrinsic charge on the central carbon is not immediately apparent from the MO description, we switch to the VB structures (Table I) which make up each configuration. The DA configuration has a slight positive charge on carbon reflecting the polar nature of the C–X bond. The D^+A^- configuration has slight negative charge reflecting the contribution of the minor VB contributor, while the DA* configuration has a significant positive charge on carbon. Thus, an electron donor (e.g., CH_3O) will stabilize the DA* configuration at the expense of the D^+A^- and to some extent even the DA configuration.

Reference to Table I suggests that increased participation of DA* will lead to a looser transition state for both N–C and C–X bonds. This is particularly clearcut for the N–C bond which is generated from the D^+A^- surface. Since the D^+A^- surface is raised in energy by the electron-donating group, there will be a reduced N· ·R contribution, leading to a weaker (and hence looser) N–C bond. A similar argument suggests that the C–X bond will also be loosened. From the MO picure (Chart I), it is clear that the strength of the C–X bond decreases along the series DA > D^+A^- > DA*. Thus an electron-donor group in the benzene ring, which favors DA* over DA and D^+A^-, is expected to loosen the C–X bond in the transition state.

For an electron-accepting group, e.g., NO_2, N–C bond tightening is predicted in the transition state. This is because it is the D^+A^- surface which is now stabilized due to the partial negative charge on the central carbon (see the secondary valence contributor of D^+A^- in Table I). Since D^+A^- is the configuration primarily responsible for N–C bond making (through the VB form N· ·R), the electron-withdrawing group is expected to tighten the N–C bond.

The effect of an electron-withdrawing group on the degree of C–X bond breaking is more complex since two opposing effects appear to be involved. On the one hand the D^+A^- surface is C–X

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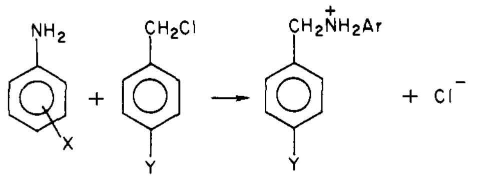
(27) This is of course true only for S_N1 reactions. For S_N1 reactions intersection of DA takes place with the DA* surface and hence the rate is nucleophile independent. Clearly also, stabilization of the carbonium ion will lead to a stabilized DA* surface which in turn leads to an enhanced rate. Thus the S_N1–S_N2 dichotomy may be viewed as a dependence on the relative energies of the DA* and D^+A^- surfaces. Intersection of DA with DA* will lead to an S_N1 reaction: intersection of DA with D^+A^- will lead to an S_N2 reaction. For cases such as benzyl derivatives, where both surfaces are likely to *mix* in the transition state, borderline character is to be expected.

(28) McLennan has recently clarified the conditions under which Hammett ρ values may serve as a measure of transition state structure. See: McLennan, D. J. *Tetrahedron* **1978**, *34*, 2331. See also ref 1h.

bond loosening. On the other hand as we have already noted, the three-electron bond, $\mathrm{R}\div\mathrm{X}$, is strongest when the VB contributors R: ·X and R· :X (eq 9) contribute equally. The effect of an electron-withdrawing group on C will lead to a larger contribution of R: ·X to the three-electron bond, and as a result a tighter bond is expected.

On the basis of our qualitative argument we cannot assess which of these two effects will be dominant. However on the basis of both theoretical and experimental work it appears that the bond-tightening effect is predominant. Thus Parker et al.[11h] concluded that the transition state for nucleophilic substitution of *p*-nitrobenzyl bromide is tighter than that of *p*-methoxybenzyl bromide on the basis of solvent activity coefficients. Ab initio calculations by Dedieu and Veillard[29] which indicate that the $[\mathrm{H{-}CH_3{-}H}]^-$ transition state is looser than the $[\mathrm{H{-}CH_2F{-}H}]^-$ transition state also lend support to the idea that electron-withdrawing substituents lead to tightening of the transition state.

The effect of substituents on the degree of N–C bond formation is also supported by the results of Ballistreri et al.[11m] for the reaction of substituted anilines and para-substituted benzyl derivatives (eq 13) and Hudson and Klopman[11n] for the corresponding reaction of thiophenoxides (eq 14). Hammett ρ values for the series of anilines varied from −0.59 for the reaction with *p*-methoxybenzyl chloride to −1.55 for *p*-nitrobenzyl chloride, indicating *greater* N–C bond making with the more electron-withdrawing ring substituents. For the thiophenoxides ρ values ranged between −0.91 for *p*-methoxybenzyl bromide to −1.60 for *p*-nitrobenzyl bromide.



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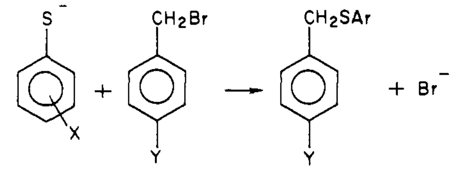

(14)

Inspection of the VB structures in Table I provides an elegant rationalization for the puzzling result[30] that *p*-nitro-substituted benzyl derivatives are more reactive than *p*-methoxy-substituted derivatives toward powerful anionic nucleophiles yet less reactive toward weaker neutral nucleophiles. Powerful nucleophiles lower the energy of the $\mathrm{D^+A^-}$ surface, thus increasing its relative contribution to the transition state. Now, from the VB description it can be seen that this configuration generates a partial negative charge on the central carbon atom. Not surprisingly, therefore, an electron-withdrawing substituent will tend to stabilize the excited $\mathrm{D^+A^-}$ configuration even further, leading to a stabilized transition state and hence a relative enhancement in the observed reactivity. The well-known curvature of Hammett plots of benzyl derivatives[31] may therefore be attributed to the fact that for the benzyl derivatives a number of excited configurations lie close together. Electron-releasing groups (e.g., $\mathrm{CH_3O}$) lower the DA* level and lead to that level contributing significantly to the transition state. Electron-withdrawing groups, on the other hand, will lower the $\mathrm{D^+A^-}$ configuration. Since stabilization of the curve which intersects the ground curve necessarily stabilizes the transition state, rate enhancement may occur for *both* electron-withdrawing and -releasing substituents. For nonborderline $\mathrm{S_N1}$ or $\mathrm{S_N2}$ reactions, only one surface is likely to be predominant in the transition state (DA* for $\mathrm{S_N1}$, $\mathrm{D^+A^-}$ for $\mathrm{S_N2}$), leading to linear Hammett plots.

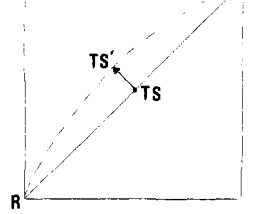

Figure 2. Potential energy surface indicating the reaction pathway and transition state for some arbitrary reacton (R → P) before stabilization of the corner, X, (firm line) and after stabilization of X (dotted line).

Relation of the Present Model to the Potential Energy Surface Models. The question arises as to the relationship between the present quantum mechanical model and its potential energy surface predecessors. Does the present model contain within it elements of the earlier models? Specifically, do "Hammond" and "anti-Hammond" effects, which are central to the earlier models, manifest themselves within the present framework? Let us first discuss the "anti-Hammond" effects.

Substituent effects perpendicular to the reaction coordinate and termed "anti-Hammond" effects lead to the transition state resembling *more closely* the species which has been stabilized. This is illustrated in Figure 2. Thus, for a reaction in which reactants, R, are transformed to products, P, stabilization of a point, *X*, on the surface, perpendicular to the reaction coordinate, will lead to a new reaction pathway in which the transition state (TS) has been shifted *toward* the point of stabilization (TS′). Thus for an $\mathrm{S_N2}$ reaction, stabilization of the potential carbenium ion intermediate which lies perpendicular to the reaction coordinate will lead to an $\mathrm{S_N2}$ transition state with *more* carbenium ion character. The predictions of our model are identical. If a substituent stabilizes the carbenium intermediate, our model suggests that the energy of the carbenium ion configuration (i.e., DA*) will be lowered and hence will mix into the transition state to a greater extent. Thus both models make the same prediction for "anti-Hammond" effects though the root causes appear to be different. The one derives from the distortion of the potential energy surface while the other derives from changes in the quantum mechanical mixing of configurations in the transition state. The difference between the two approaches is highlighted by the fact that the so-called "Hammond" effects will, within a family, manifest themselves in the present model in an "anti-Hammond" manner as well, since all perturbations will operate on the configurational mixing in such a way as to favor stabilized configurations.

The question then remains: does the present model leave a place for the parallel perturbations associated with the "Hammond" effect? The answer is yes—but not through the configurational mixing behavior. Let us develop this point.

In principle one can compare transition-state structures for a wide range of nucleophilic reactions, in which the D–A range is highly varied. The range begins for a simple $\mathrm{S_N2}$ reaction of a weak nucleophile (e.g., water), a poor electron donor, with a substrate such as $\mathrm{CH_3X}$, a relatively poor electron acceptor. At the other end of the scale lie the powerful donors such as anionic nucleophiles with strong acceptors such as the carbonyl system or free carbocations. Thus the range of the D–A relationship may be split into limited families, each of which is specified by some average magnitude *of the donor–acceptor energy gap and whose measure is* $I_\mathrm{D} - A_\mathrm{A}$, *i.e., the ionization energy of the donor less the electron affinity of the acceptor.* Within this framework one can discuss trends within a family as well as trends resulting from comparisons of reactions from different families.

In our discussion of the benzyl system we confined ourselves to a limited family of reactions and interpreted the results in terms of the configuration mixing model. If, however, the donor-acceptor energy gap is modified drastically an additional effect is likely to manifest itself. This may be understood by reference to Figure 3. If the donor–acceptor energy gap is reduced significantly, then the original $\mathrm{D^+A^-}$ curve is replaced by a lower $(\mathrm{D^+A^-})'$ curve. As a consequence, intersection of the curves occurs

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(29) Dedieu, A.; Veillard, A. *J. Am. Chem. Soc.* **1972**, *94*, 6730.

(30) Young, P. R.; Jencks, W. P. *J. Am. Chem. Soc.* **1979**, *101*, 3288.

(31) For a recent discussion on the reason for curved Hammett plots in benzyl derivatives, see ref 30.

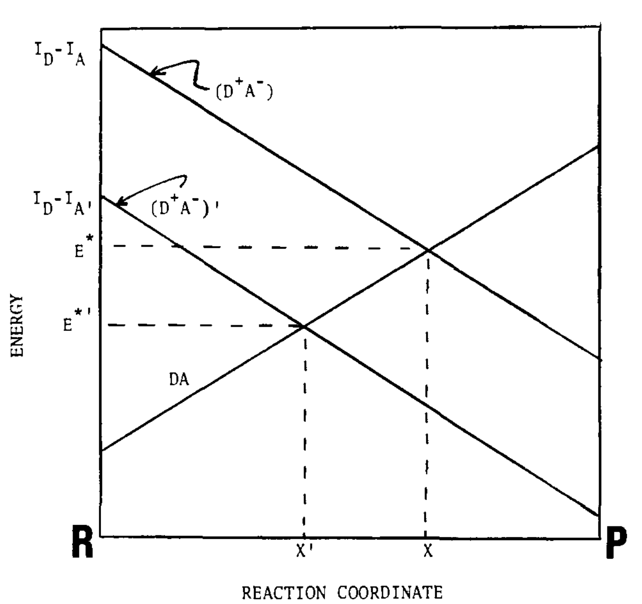

Figure 3. Curve crossing diagram for DA and D^+A^- surfaces. R and P are reactants and products, respectively, X and X′ are the positions of the transition states along the reaction coordinate, A′ is a better acceptor than A, the diagram is schematic and neglects all other configurations which mix into D^+A^-, and E^* and $E^{*\prime}$ are barriers and usually $E^{*\prime} < E^{*\circ}$, i.e., the better acceptor reacts faster and will have an earlier (X′) transition state. (For clarifications on the position of the transition state, see ref 32.) The avoided crossing is omitted (review Figure 1).

earlier along the reaction coordinate (from X to X′).[32] This implies *less* nucleophile–substrate bond formation as well as *less* substrate dissociation and is a direct manifestation of the "Hammond" effect. If we compare the reaction of a substrate with two nucleophiles, then for the case of the more powerful nucleophile, reactants need move up the DA curve to a *lesser* extent before becoming isoenergetic with the $(D^+A^-)'$ surface, thereby enabling electron transfer to occur. Consequently less nucleophile–substrate approach is necessary. Similarly, we could compare nucleophilic attack of the same nucleophile on a weak acceptor such as CH_3X and on a good acceptor such as the carbonyl group. Reasoning this way, we again reach the conclusion that the CX bond in the good acceptor will have to stretch *less* than in the weak acceptor in order to effect DA–D^+A^- crossing.[32,33] Again, the electron jump (D → A) will occur at a larger nucleophile–substrate distance. This behavior is exemplified by the fact that the electron jump from Na to Cl takes place at the large bond distance of ~10 Å compared to the corresponding reaction for H and Cl (a worse D–A pair) which takes place at ~1.5 Å.[34,35]

It is possible, therefore, that within a family of closely related reactions (such as the benzyl system), where reactivity changes are slight, that quantum mechanical effects on transition-state structure will be dominant over changes in the intrinsic "earliness" or "lateness" of the curve intersection. However for large perturbations or for comparisons within different families, where large reactivity differences are likely, "Hammond effects" may become evident. Therefore, in making predictions, one should recognize the inherent complexity of the problem and make some simplifying assumptions. This is something we are compelled to do if we wish to gain an overview. Our assumption would be that the extent of quantum mechanical mixing of the various configurations will dominate the trends within a family, whereas both the quantum mechanical mixing of configurations *as well as* the position of avoided curve crossing will determine behavior patterns for representatives of different families. One further point which requires clarification is the relationship between charge transfer (between D and A) and the tightness of the N–C bond. It is widely believed that the extent of charge transfer in the transition state is an indication of bond tightness. Considerable charge transfer is often equated with a tight bond. However, it appears that for widely varying structures no such relationship necessarily holds. Thus the large β values commonly observed for cation–anion combination reactions and nucleophile addition to carbonyls compared to nucleophilic substitution reactions only indicates extensive charge transfer rather than tight bonding in the former two.[36] As we have already noted, for a favorable donor–acceptor pair, extensive charge transfer may actually take place at large intermolecular separation.

Conclusion

The key point expressed in this paper is that the nature of the transition state of an ionic reaction may be analyzed by the method of reactant configurations. This method suggests that changes in transition-state structure as a result of a substituent perturbation will, in part, be due to changes in the proportion of the various configurations from which the entire reaction coordinate may be defined. Stabilization of a given configuration by a substituent will lead to an enhanced contribution of that configuration along the entire length of the reaction coordinate, including the point at which the transition state is located. This quantum mechanical effect on the structure of the transition state takes place *in addition to* any "Hammond-type" changes suggested by the potential energy surface models.[4-7]

Since two discrete kinds of effects appear to be responsible for defining the reaction profile, the prediction of changes in transition-state structure may be considerably more complex than previously thought. In this context, a growing body of data which was inexplicable in terms of existing ideas now may be rationalized and organized in terms of the reactant configuration model. Thus the invariant selectivity (and hence invariant transition-state structure) observed recently for methyl derivatives[12] resulting in the failure of the reactivity–selectivity principle[1h] may be more readily understood with the present model. For example, increasing the leaving-group ability in methyl derivatives may lead to small changes in N–C bonding in the transition state due to the opposing influence of more D^+A^- mixing (leading to more N–C bonding) and an "earlier" transition state (leading to less N–C bonding). Be this as it may, it is apparent that at this point, application of the present model does not always necessarily lead to clear-cut predictions and that further work will be necessary

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[32] We have shown in ref 17b that stretching of the C–X bond in CH_3X and flattening of the CH_3 moiety lead to 4–10-eV (depending on the method of computation) stabilization of σ^*_{CX}. Thus, these distortions which *lie on the reaction coordinate* make the substrate a much better acceptor and therefore stabilize the D^+A^- surface. These geometric distortions are necessary to effect DA–D^+A^- avoided crossing; i.e., it is only when $E(D^+A^-) = E(DA)$ that avoided crossing can occur and this occurs when molecules distort in a specific manner dictated by D^+A^-. Consequently, when the substrate is not a good electron acceptor, more C–X stretching is needed in order to lower D^+A^- and hence cross DA, whereas, when the substrate is a good acceptor, less C–X stretching is needed to fulfill the condition $E(DA) = E(D^+A^-)$.

[33] Compare for example the structure of the S_N2 transition state in $H^- + CH_4$ with that in $H^- + H_2C{=}CH_2$. $CH_2{=}CH_2$ is a better acceptor than CH_4, and the transition state is indeed earlier. See: (a) Reference 29. (b) Dedieu, A.; Veillard, A. *Chem. Phys. Lett.* **1970**, *5*, 328. (c) Duke, A. J.; Bader, R. F. W. *Ibid.* **1971**, *10*, 631. (d) Bader, R. F. W.; Duke, A. J.; Messer, R. R. *J. Am. Chem. Soc.* **1973**, *95*, 7715. (e) Ishida, K.; Morokuma, K.; Komornicki, A. *J. Chem. Phys.* **1977**, *66*, 2153. (f) Keil, F.; Ahlrichs, R. *J. Am. Chem. Soc.* **1976**, *98*, 4787. (g) Baybutt, P. *Mol. Phys.* **1975**, *29*, 389. (h) Dyczmons, V.; Kutzelnigg, W. *Theor. Chim. Acta* **1974**, *33*, 239. (i) Van der Lugt, W. Th. A. M.; Ros, P. *Chem. Phys. Lett.* **1969**, *4*, 389. (j) Ritchie, C. D.; Chappell, G. A. *J. Am. Chem. Soc.* **1979**, *92*, 1819. (k) Mulder, J. J. C.; Wright, J. S. *Chem. Phys. Lett.* **1970**, *5*, 445. (l) Berthier, G.; David, D.-J.; Veillard, A. *Theor. Chim. Acta* **1969** *14*, 329. The reaction of $H^- + H_2C{=}CH_2$ is described in: Strowzier, R. W.; Caramella, P.; Houk, K. N. *J. Am. Chem. Soc.* **1979**, *101*, 1340. Although the basis sets are different, the trend is clear cut.

[34] One can calculate the distance of the electron jump by setting $I_D - A_A = e^2/r$. Thus in Na + Cl where $I_D - A_A$ is small (~1.4–1.5 eV), r is large, whereas in H + Cl where $I_D - A_A$ is large (~10 eV), r is small.

[35] It is appropriate to note that an S_N2 reaction, strictly speaking, should be viewed as a *single* electron jump rather than attack of an electron pair as is commonly thought. Thus the actual S_N2 process may be represented as

$$N\!:\ C\cdot\ \cdot X \rightarrow N\cdot\ C\cdot\ :X$$

i.e., an electron jump from the nucleophile N to the leaving group X. The remaining two odd electrons are spin paired and represent the new bond.

[36] Jencks, D. A.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 7948.

in order to generate a greater appreciation of the relative importance of the possible effects.

One final point that emerges from this work is that the present model suggests that within a family of reactions (say the benzyl system) there are two parameters which govern reactivity. These are $(I_D - A_A)$, the ionization potential of the donor less the electron affinity of the acceptor, and $E_{\sigma\sigma^*}$, the excitation energy of the C-X bond to be cleaved. Thus, substituents may be classified in terms of their effects on these two parameters and rates may be correlated with them. This approach may lead to a direct check on the structure of the transition state and may provide necessary information about the degree of charge transfer from the nucleophile to the substrate, $[\mathrm{N}\cdot^{+}(\mathrm{R}\dot{-}\mathrm{X})^{-}]$ and/or on the extent of its carbenium ion character ($\mathrm{N}\colon \mathrm{R}^{+} \colon\!\mathrm{X}^{-}$).

Acknowledgment. We thank Professors R. A. More O'Ferrall and D. J. McLennan and a reviewer for helpful suggestions. S.S.S. thanks the Ministry of Absorption for financial support.

The pH Jump: A Rapid Modulation of pH of Aqueous Solutions by a Laser Pulse

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Abstract: The first electronically excited state of compounds like 8-hydroxypyrene-1,3,6-trisulfonate or 2-naphthol-3,6-disulfonate is characterized by an acid dissociation constant ($pK^* = 0.5$) much lower than that of the ground state ($pK^0 = 7$). Thus excitation of such compounds is equivalent to introduction of a strong acid to the solution. In this study we utilized high-intensity (~50 mJ) short laser pulse (50 ns full width at half-maximum) to acidify aqueous solutions by exciting the above proton emitters. The discharged protons were detected both by their reaction with various pH indicators or by following the reprotonation of the proton emitter after its decay to the ground state. The maximal proton concentrations determined by either method are comparable and in typical experiments amount to 10^{-5}–5×10^{-5} M. The maximal proton concentration is built up during the laser pulse and decays to the initial level within a few microseconds. The protonation of pH indicators is a second-order diffusion-controlled reaction; the measured rate constants are compatible with the values calculated according to Debye's equation for diffusion-controlled reactions. Though the proton pulse is short, groups which have been protonated during the pulse remain in their protonated state for much longer periods, which are proportional to their intrinsic acid dissociation constant. The applicability of this method as a perturbing system for fast kinetics is discussed.

Introduction

The rapid diffusion of a proton in aqueous solution hampers kinetic studies of protonation. Thus in most cases only equilibrium studies can reveal the mechanism by which the proton participates in the chemical reaction. Though the electric field jump[2] is suitable for measuring rates of protonation, it is limited to pure water and cannot be applied to complex biochemical reactions.

In a recent publication[3] we described a new method which can generate within 50 ns some 10^{-4} M of protons. This proton pulse, called the pH jump, is achieved by irradiation of aqueous solutions of certain naphthol derivatives with an intense laser pulse. As a consequence, these compounds are pumped to their first excited singlet state which is characterized by a pK^* value much lower than that of the ground state (pK^0). Thus the laser pulse converts the proton emitter from a weak acid to a strong acid and within 100 ps[4] it dissociates releasing the protons to the water. Of the many compounds which on excitation exhibit a pK shift,[5,6] we selected two for our studies: 8-hydroxypyrene-1,3,6-trisulfonate and the 2-naphthol-3,6-disulfonate which, because of their negative charges, cannot permeate phospholipid bilayers.[3]

While the previous reports[3,7] were more descriptive in nature, the present one analyzes the postpulse events and quantitates the concentration of the ejected protons, the kinetics of protonation of the various protonatable groups present in the solution, and the final relaxation of the system to its equilibrium, prepulse state.

As will be demonstrated, the proton pulse can lower the pH by 3–5 pH units, it can be carried out in the presence of electrolytes, and the monitoring of the reaction is rather simple. These properties render the laser-induced pH jump as a convenient method for perturbing chemical and biochemical reactions by a brief intense proton pulse.

Materials and Methods

The optical arrangements for excitation and monitoring of the sample were described before.[3] A passively *Q*-switched ruby laser generated a giant pulse at 694.3 nm of about 1 J, with 30 ns full width at half-maximum. The pulse was passed through a KDP crystal generating the second harmonic frequency at 347.2 nm. The red light was filtered so that only the UV frequency irradiated the sample cell.

Absorbance changes of the sample were monitored either at 632.8 nm (using the line of a continuous He-Ne laser (Spectra-physics 2 mW)) or at 442 nm (using the He-Cd laser). The interrogating beam was passed either perpendicular or nearly colinear with the excitation pulse, collimated, and directed into the entrance slit of a Jarral-Ash 250-mm monochromator. The changes in the sample absorbance were detected by a Philips TVP 56 or an RCA 1P-28 photomultiplier, with rise time of 1–2 ns, traced on an oscilloscope (Tektronix 454 or a 7623A) and photographed. The changes in transmittance were converted to absorbance units.

Energy-dependence studies were carried out using a Molectron UV14 nitrogen laser (8 mJ/pulse, 10-ns pulse width), and the transient absorbancy changes of the monitoring beam (632.8 nm) were recorded by a Biomation 8100 transient recorder coupled to a Nicolet 1170 signal averager. The energy of the excitation pulse was measured by a Molectron energy meter placed at the place of the observation cell.

8-Hydroxypyrene-1,3,6-trisulfonate was Eastman Kodak laser grade. 2-Naphthol-3,6 disulfonate was Merck, Sharp and Dohme preparation, recrystallized before use.

Results

Energy Dependence of the Light-Driven Proton Pulse. In order to evaluate the nature of the photochemical reaction involved in

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[1] (a) Department of Biochemistry. (b) Department of Chemistry.

[2] Eigen, M.; DeMayer, L. *Z. Electrochem.* **1955**, *59*, 986–993.

[3] Gutman, M.; Huppert, D. *J. Biochem. Biophys. Methods* **1979**, *1*, 9–19.

[4] Smith, K. K.; Huppert, D.; Gutman, M.; Kaufman, K. J. *Chem. Phys. Lett.* **1979**, *64*, 522–525.

[5] Schulman, S. G. "Fluorescence and Phosphorescence Spectroscopy"; Pergamon Press: New York, 1977.

[6] Weller, A. *Prog. React. Kinet.* **1961**, *1*, 189–214.

[7] Campillo, A. J.; Clark, J. H.; Shapiro, L. S.; Winn, K. R. In "Picosecond Phenomena"; Shank, C. V., et al., Ed., Springer-Verlag: Berlin, 1978; pp 319–326.