VOLUME 40 NUMBER 1
ACCOUNTS of CHEMICAL RESEARCH®
JANUARY 2007

Dynamic Processes Leading to Covalent Bond Formation for S_N1 Reactions

KEVIN S. PETERS
Department of Chemistry and Biochemistry, University of Colorado, Boulder, Colorado 80309

Received April 19, 2006

ABSTRACT
The S_N1 reaction mechanism is one of the most fundamental processes in organic chemistry. As such, it has been the subject of study for over 70 years with the purpose of seeking to understand the fundamental parameters that control reactivity. With recent advances in both electronic structure theory and condense-phase reaction dynamics theory as well as in experimental probes of these reactions on the femtosecond and picosecond time scale, we are beginning to gain new insights into the nature of these reactions.

Introduction

The correlation of reactivity with structure has long been a fundamental goal of physical organic chemistry and no more so than in reactions that proceed by way of the S_N1 mechanism. The initial approach in these endeavors was the utilization of linear free-energy relationships to correlate reactivity with sets of molecular parameters.[1,2] Though these efforts met with some success, most notably Richie's N+ scale, a full understanding of the physical basis for the parameters controlling reactivity has not been ascertained due in part to the application of somewhat simplistic kinetic models to a complex set of molecular events. Even for this most simple of reaction mechanisms, Winstein has shown that numerous molecular species intervene along the reaction pathway, and which transformation between species controls reactivity remains an open question.[3]

Ultimately, a fundamental understanding of reactivity should probably lie within the context of transition-state theory (TST).[4] Toward this end, Marcus theory, a form of transition-state theory developed for electron transfer, has been utilized for analysis of the kinetics associated with reactions proceeding by the S_N1 mechanism.[5] Correlating the rate constant for electrophile−nucleophile combination with thermodynamic driving force, ΔG, allows for extraction of the parameter Λ, a reorganization energy. Within the Marcus framework, the free energy of activation for reaction at a zero free-energy driving force is $\Lambda/4$. Comparing reorganization energies for differing electrophile−nucleophile combinations could then, in principle, reflect underlying differences in reactivity.[6]

One of the difficulties found in kinetic studies of electrophile−nucleophile combination reactions leading to covalent bond formation is in resolving the individual molecular events. The Winstein model for the S_N1 reaction mechanism envisions the diffusional encounter of the free ions (FI) to form a solvent-separated ion pair (SSIP), which then collapses to the contact ion pair (CIP) followed by covalent bond formation (C−L).

$$\text{FI} \rightleftharpoons \text{SSIP} \rightleftharpoons \text{CIP} \rightleftharpoons \text{C}-\text{L}$$

Whether reactivity is ultimately controlled by a single molecular event, such as the actual bond formation or ion-pair interconversion, or the sum of the events is an open question. Prior experiments probing these combination reactions did not resolve the individual molecular events but subsumed these distinct molecular processes into an effective single rate constant that is then used in a free-energy relationship or a Marcus analysis for reactivity.[1,6−8] Since Marcus theory, at best, should be used for the analysis of a single molecular transformation, the validity of its application to the sum of the kinetic processes needs to be assessed.

In this Account we chronicle our experimental efforts to kinetically resolve the individual molecular events

Kevin Peters was born in Ponca City, OK, in 1949. After obtaining his B.S. degree from the University of Oklahoma in 1971, he pursed graduate studies with Professor Ken Wiberg in the Department of Chemistry, Yale University, obtaining his Ph.D. degree in 1975. After 3 years of postdoctoral studies with Professor Fred Richards at Yale University, Professor Mereithe Applebury at Princeton University, and Dr. Peter Rentzepis at Bell Laboratory, he joined the faculty of the Department of Chemistry, Harvard University, in 1978. He then moved to the Department of Chemistry and Biochemistry, University of Colorado at Boulder, in 1984. His research interests continue to be in the application of laser methodologies to study organic reaction mechanisms.

10.1021/ar0681124 CCC: $37.00
Published on Web 09/21/2006

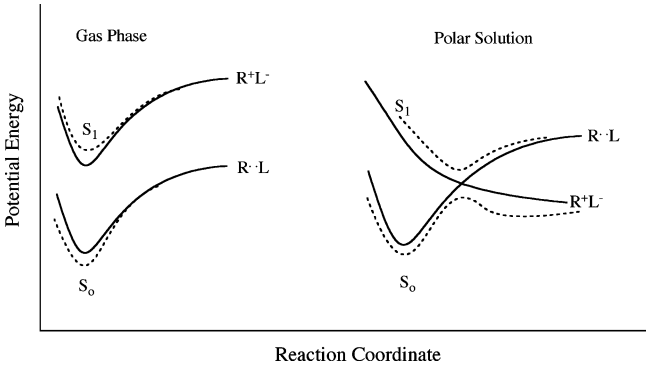

FIGURE 1. Schematic free-energy curves for covalent ($R^{\cdot}L$) and ionic (R^+L^-) states in the gas phase and polar solution: solid curve, diabatic; dashed curve, adiabatic; S_0, ground state; S_1, excited state.

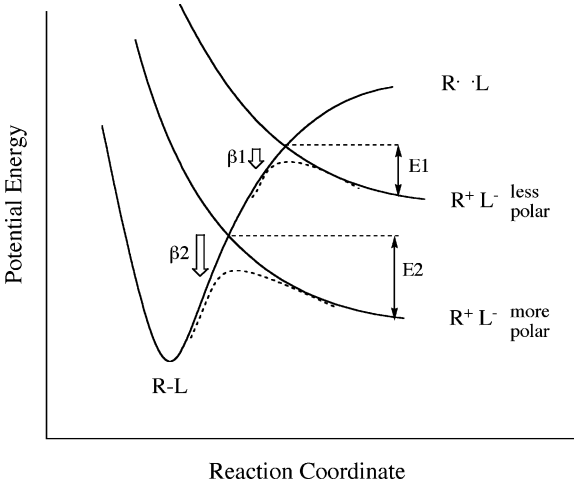

FIGURE 2. Valence-bond diagram showing the solvent dependence of the free-energy curve for the ionic state (R^+L^-) as a function of solvent polarity relative to the covalent state ($R^{\cdot}L$). The terms E_1 and E_2 are the energies of the CIP relative to the curve crossing of the two diabatic states. The terms β_1 and β_2 are the electronic coupling of the two diabatic curves at the point of their crossing.

associated with the S_N1 reaction mechanism. The results of these experiments are discussed within the framework of recent advances in electronic structure theory for the S_N1 reaction mechanism as well as a new theory for the dynamic behavior of reactive species passing through the transition state. This combination of theory and experiment points toward new directions in which to view factors that ultimately control reactivity.

Electronic Structure Theory

The initial theoretical formulation for the nature of the potential-energy surface governing bond heterolysis in the S_N1 mechanism was based on valence-bond theory and can be traced to the work of Ogg and Polanyi as well as Evans and co-workers; it has since undergone further elucidation by Pross and Shaik.[9−12] The ground-state adiabatic surface, the reaction surface, is developed by the mixing of two diabatic states: the purely covalent state, $R^{\cdot}X$, and the purely ionic state, R^+X^-, Figure 1. In the gas phase, the two diabatic states mix leading to stabilization of the ground-state surface, S_o, developing partial ionic character at bonding distances, and dissociates into a radical pair. When placed in a polar solvent, the ionic surface is stabilized relative to the covalent surface; it drops below the covalent surface for distances longer than that associated with bonding, Figure 1. At the point of crossing, there is a strong mixing between the two diabatic states that gives rise to two new adiabatic surfaces with the ground-state surface dissociating into an ion pair.

When the valence-bond model was developed for S_N1 reaction mechanism, it was tacitly assumed that the solvent maintains equilibrium solvation throughout the dissociation process. Recently, Hynes and co-workers examined the validity of this assumption within the context of a nonlinear Schrodinger equation, which incorporates the mutual influence of the solute electronic structure upon polarization of the solvent under both equilibrium and nonequilibrium conditions.[13,14] They found for *tert*-butyl chloride and *tert*-butyl bromide in a polar solvent that the position of the transition state shifts to longer distances than the distances predicted by the standard valence-bond model. Furthermore, the charge character of the wavefunction is 66% ionic for *tert*-butyl chloride and 60% ionic for *tert*-butyl bromide in acetonitrile, contrasting with the prediction of the standard valence-bond treatment of 50% ionic−50% covalent for all molecular substrates. An implication of the Hynes study is that chemical modification of the reacting system can change the electronic structure of the transition state, a view contrary to the standard model of valence-bond theory.[12]

A second line of enquiry was pursued to ascertain how the barrier associated with heterolysis varies with driving force.[13] From the vantage of the CIP collapsing to form C−L, as the stability of CIP increases relative to C−L, achieved by an increasing the solvent polarity, the crossing of the two surfaces occurs at shorter distances, leading to an increase in the barrier associated with the curve crossings, E2 > E1, Figure 2. However, the energy of the transition state is a function of not only the energy associated with curve crossing but also the electronic coupling, $\beta(r)$, between the two diabatic states which is distance dependent, Figure 2. They found that as the curve crossing moved toward the covalent state, C−L, the magnitude of the electronic coupling $\beta(r)$ increases in a highly nonlinear manner and there are regimes where it is possible that the increase in electronic coupling more than offsets the increase in the energy associated with curve crossing, Figure 2. Thus, it is possible that as the stability of the CIP increases, the barrier to covalent bond formation actually decreases, behavior contrary to the Hammond postulate.[15]

Finally, for *tert*-butyl chloride, Hynes and co-workers addressed the question of the validity of the Marcus formalism as a theoretical model for relating the free energy of activation, $\Delta G^{\ddagger}$, with driving force, ΔG, through a quadratic dependence.[13] They found that the derived intrinsic barrier, defined as the barrier for reaction at zero driving force, is in error by more than a factor of 2 and concluded that the Marcus equation for $\Delta G^{\ddagger}$ is not valid

for analysis of the reaction kinetics associated with covalent bond formation from collapse of the CIP. They speculated that the source of the error lies in the nonparabolic nature of the reaction surfaces, the highly nonlinear behavior of $\beta(r)$, and the variation of solvent stabilization with the position of the transition state.

Theory of Polarization Caging

The standard theoretical framework in which most studies of organic reaction kinetics have been modeled is transition-state theory.[4] One of the fundamental assumptions underlying the theory is that once the molecular system is thermally activated, it passes through the transition state with a frequency of kT/h (6.6×10^{12} s^{-1} at 298 K) and as it passes through the transition state the system maintains equilibrium solvation. The A factor for Marcus theory, as it has been applied to the S_N1 reaction mechanism, is assumed to maintain equilibrium solvation; the assumptions of transition-state theory require the solvent to adjust its structure on the time scale associated with kT/h. However, in recent years the field has come to recognize the time scales associated with solvent reorganization normally occur with longer times than that associated with kT/h.[16]

In the 1940s Kramer recognized that the solvent could in fact retard the motion of the reacting system as it passes through the transition state and introduced the concept of solvent friction often modeled as being proportional to the solvent viscosity.[4] As the solvent friction increases, the frequency for passage through the transition state decreases below the transition-state theory value of kT/h, leading to a decrease in the overall rate constant k relative to the rate constant predicted by the transition-state model, k_{TST}. The measure of the deviation is defined in terms of the parameter κ, where $\kappa = A/A_{TST}$. To determine κ, the A factor derived from experiment is compared to the A_{TST} calculated by estimating the partition functions for both the reactant and the transition state; A_{TST} is a hypothetical quantity.[17]

A significant advance in theory, relevant to the dynamics of reactions proceeding via S_N1, was achieved by Hynes in the 1980s.[16,17] The key insight underlying the new theory is that the magnitude of the solvent friction depends upon the reaction barrier frequency, ω_b, in contrast to Kramer's theory where the value of the solvent friction is independent of ω_b. The deviation in the rate constant from that predicted by transition-state theory, measured by κ, depends not only on the parabolic reaction barrier frequency at the transition state, ω_b, but also on the electrostatic solvent frequency ω_s which is a measure of the nondissipative restoring force that the charged system experiences as it attempts to move off of the transition state. The interplay between ω_b and ω_s leads to two types of kinetic behavior for the charged species in the transition state. If the electrostatic solvent frequency ω_s is less than ω_b, the reacting species feels a retarding force or a drag, which reduces the rate for the system to move off the transition state, Figure 3. This regime is identified as the

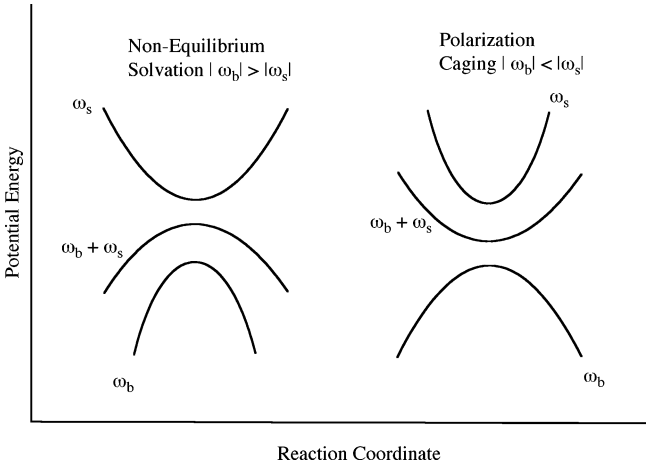

FIGURE 3. Potential curves for the reaction barrier frequency, ω_b, solvent frequency, ω_s, and result of their net interaction, $\omega_b + \omega_s$, under the conditions of nonequilibrium solvation, $|\omega_b| > |\omega_s|$, and polarization caging, $|\omega_b| < |\omega_s|$.

nonequilibrium solvation limit for as the system moves toward the product state, there is no requirement for the solvent to reorganize. From model calculations for the nonequilibrium solvation limit the deviation from transition-state theory is modest with κ approaching a limit of the order of 0.8.[17]

When the absolute value of ω_s is greater than ω_b, $|\omega_s| > |\omega_b|$, the system finds itself trapped in a "polarization cage" as it attempts to move off of the transition state and cannot evolve into the product state; only upon relaxation of the solvent cage can the charged species move toward product, Figure 3. Critical in determining the dynamics associated with relaxation of the solvent cage is the solvent longitudinal relaxation time, τ_l. In the polarization caging limit the dynamics of the passage of the charged species through the transition state is governed by solvent relaxation. Again, model calculations reveal that when $|\omega_s| > |\omega_b|$ the deviation from transition-state theory can be large with $\kappa = 0.1$ or less.[17]

Whether reaction processes leading to covalent bond formation in the S_N1 mechanism fall within either the nonadiabatic or polarization caging limit has not been determined until recently; it is only in the past few years that the actual covalent bond formation event has been kinetically resolved from all of the other molecular events associated with the S_N1 mechanism. Thus, prior to our studies it was not known if $|\omega_s|$ was indeed greater than $|\omega_b|$ and whether solvent dynamics associated with solvent relaxation play an integral role in governing reactivity.

Kinetic Studies of S_N1 Reaction Mechanism for Benzhydryl Derivatives

In 1994 we began a series of investigations into the reaction dynamics associated with the photochemically induced bond homolysis and heterolysis of a variety of benzhydryl derivatives, $(C_6H_5)_2CH-L$ (L = chloride, bromide, or acetate).[18−25] From our femtosecond and picosecond studies we developed the reaction scheme shown in Figure 4. The 266-nm irradiation places the system in

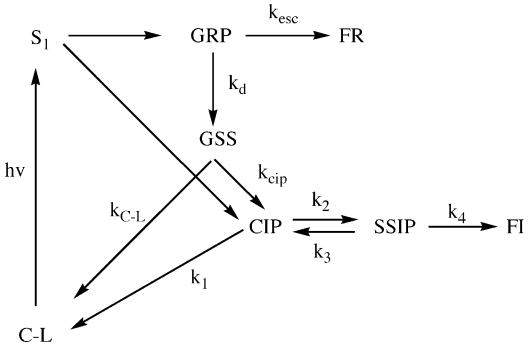

FIGURE 4. Reaction diagram the for photochemically induced bond homolysis and bond heterolysis for benzhydryl derivatives and their subsequent reactions in a polar solvent: C-L, ground state; S_1, first excited singlet state; GRP, geminate radical pair; FR, free radicals; GSS, ground-state surface; CIP, contact ion pair; SSIP, solvent-separated ion pair; FI, free ion. *k*'s are the rate constants for the depicted processes.

the first excited state, S_1, which decays on the 100-fs time scale through bond homolysis forming the geminate radical pair, GRP, or through bond heterolysis forming the contact ion pair (CIP). In polar solvents the GRP is higher in energy compared to the CIP, and thus, the GRP is an excited state of the system. The GRP decays by two pathways on the 10−100-ps time scale: diffusional separation to form free radicals, FR, or internal conversion onto the ground-state surface, GSS, partitioning between the CIP and the initial reactant, C−L. In turn, the CIP decays through formation of a covalent bond, k_1, or diffusional separation to the solvent-separated ion pair (SSIP), k_2. The SSIP may then revert back to the CIP, k_3, or undergo further separation to FI, k_4. On the time scale of our experiments (10 ns) the collapse of the FI to form SSIP is not observed. A discussion of the method for distinguishing the kinetic behavior for the various ion species can be found in ref 18.

The concept of nucleophilicity, as defined within the context of the S_N1 reaction mechanism, was developed from kinetic studies for the rates of reaction of resonance-stabilized carbocations with various nucleophiles where the reaction starts with the ions in the form of free ions.[1] Given the nature of these experiments, the rate of reaction reflects all of the interconversions of various ion pairs as well as the rate for formation of the covalent bond. As defined, nucleophilicity represents a complex combination of molecular events and cannot be identified with one molecular event. However, with our ability to kinetically resolve each of the molecular transformations associated with the S_N1 mechanism, one can now discuss the nature of the processes leading to bond formation, k_1, as well as the dynamics of conversion between ion pairs, k_2, k_3, and k_4; unfortunately the only molecular event that has not been resolved is the formation of SSIP from FI.

Given the ability to resolve these molecular events, the individual processes can then be examined as a function of temperature to obtain the energies of activation, E_a, and the frequency factors, A, to see if there is any deviation from the predictions of transition-state theory. The results of such a study for 3-methoxy- benzhydryl acetate (D+),

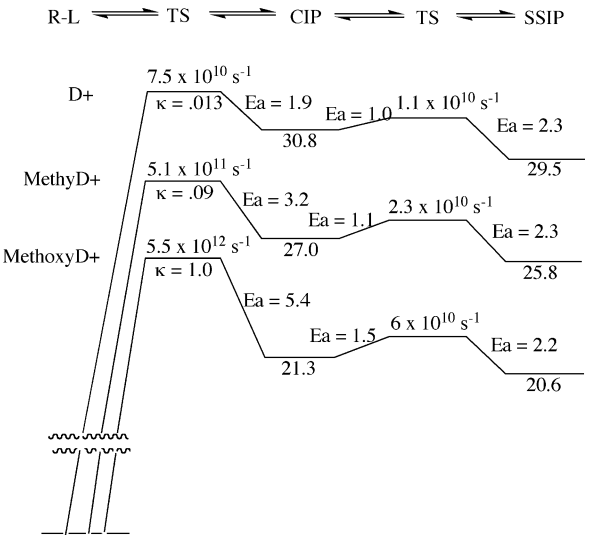

FIGURE 5. Reaction profile for 3-methoxy-benzhydryl acetate (D+), 3-methoxy-4′-methyl-benzhydryl acetate (MethylD+), and 3,4′-dimethoxy-benzhydryl acetate (MethoxyD+) in acetonitrile. Energies of each species and the energy of activation, E_a, are in kcal/mol. κ is defined in the text. Standard deviations for E_a and A can be found in ref 24.

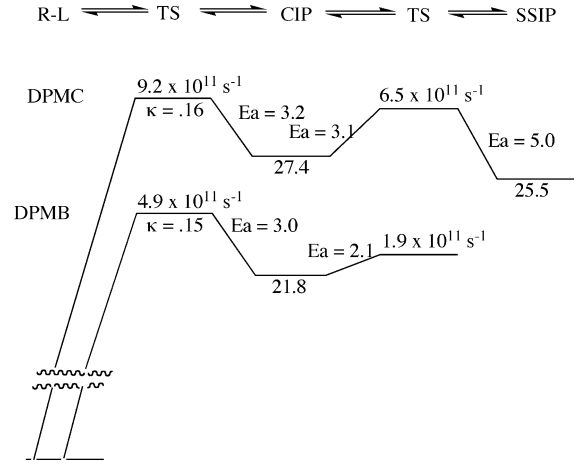

FIGURE 6. Reaction profile for benzhydryl chloride (DPMC) and benzhydryl bromide (DPMB) in acetonitrile. Energies of each species and the energy of activation, E_a, are in kcal/mol. κ is defined in the text. Standard deviations for E_a and A can be found in refs 19 and 20.

3-methoxy-4′-methyl-benzhydryl acetate (MethylD+), and 3,4′-dimethoxy-benzhydryl acetate (MethoxyD+) are shown in Figure 5.[24] For comparison of nucleophiles, the results for benzhydryl chloride and benzhydryl bromide are shown in Figure 6.[24] The energies displayed for the CIP are obtained from thermochemical and electrochemical experiments as well as calculations.[24] The energies for the SSIP are relative to the CIP derived from the equilibrium constant for these two species, $K = k_2/k_3$.

Nonequilibrium Solvation vs Polarization Caging in Bond Heterolysis

To understand the nature of the dynamic processes leading to covalent bond formation through collapse of the CIP, it is necessary to ascertain the role that the solvent

plays in governing those dynamics. At one extreme, the nonequilibrium solvation limit, the solvent does not maintain equilibrium solvation as the reacting species passes through the transition state; in this regime the limiting value of κ approaches 0.8, leading only to a small deviation from the prediction of transition-state theory. At the other extreme, the polarization caging limit, the forces associated with interaction of the solvent with the reacting charged species are greater than the force associated with the reaction barrier so that the dynamics of the solvent govern the passage through the transition state, leading to significant deviations from the predictions of transition-state theory; in this regime the limiting value of κ approaches values of 0.1 or less.[17]

The derived value of κ is predicated upon determination of A_{TST} obtained through analysis of the estimated partition functions for the reactant and transition states; for the benzhydryl systems the value is on the order of 5.5×10^{12} s^{-1}.[19] For the benzhydryl acetates shown in Figure 5, as the energies of the CIP increase as a result of effect of substituents, the energy of activation for the collapse of the CIP giving rise to covalent bond formation decreases from a value of 5.4 to 1.9 kcal/mol. Accompanying the decrease in E_a is a decrease in the A factor changing from 5.5×10^{12} to 7.5×10^{10} s^{-1}, leading to a decrease in κ from a value of 1.0 to 0.013. For the benzhydryl chloride and bromide the values for κ are 0.16 and 0.15, respectively, Figure 6. These observations for κ strongly suggest that the transition state for covalent bond formation in a polar solvent, such as acetonitrile, falls within the limit of polarization caging; it is the motion of the solvent that controls passage through the transition state.

If solvent motion is integral to formation of a covalent bond, then the dynamics of the solvent should manifest itself in the A factors and κ should vary as $1/\tau_l$, where τ_l is the solvent longitudinal relaxation time.[17] Examination of the A factors for the collapse of the benzhydryl chloride CIP in the solvents acetonitrile and propionitrile yielded values of 9.2×10^{11} and 5.1×10^{12} s^{-1}, a ratio of 1.8.[19] The corresponding ratio of the longitudinal relaxation time for acetonitrile ($\tau_l = 0.2$ ps) and propionitrile (($\tau_l = 0.3$ ps) is 1.5, which again supports the conclusion that solvent motion is fundamental in controlling the dynamics of covalent bond formation.

It is evident in the set of activation parameters associated with the acetates, Figure 5, that as the energy of activation for collapse of the CIP decreases the corresponding A factors also decrease. Presumably as the energy of activation decreases the curvature of the reaction barrier, ω_b, also decreases, that is the barrier curvature becomes less sharp; this proposed relationship between E_a and ω_b has been observed for the potential-energy surface associated with the excited-state isomerization of *trans*-stilbene.[26] For this series of benzhydryl species interaction of the ions in the transition state with the solvent should, to a first approximation, remain constant, and thus, the value of ω_s should not vary. Within the polarization caging limit the theoretical model predicts that as ω_b decreases while ω_s and τ_l remain constant, the A factor will decrease. What is perhaps the most surprising finding is the magnitude of the decrease as reflected in the value of κ of 0.013 for 3-methoxy-benzhydryl acetate contact ion pair. The deviation from the predicted value of transition-state theory is a factor of 77, the largest deviation found to date for S_N1.

Transition States for Ion-Pair Interconversion

No explicit theoretical formulation exists for describing the dynamic processes associated with transformation between ion pairs. Our current understanding of these processes comes from molecular dynamic simulations and a limited number of experimental studies.[27−32] Perhaps the most in-depth experimental study to date is our experiments probing the CIP diffusional separation for *trans*-stilbene/fumaronitrile contact radical ion pair in a series of four alkyl nitrile solvents where the rate processes were examined as a function of temperature.[29] The experimental findings were examined within the context of Kramer's model for solution-phase reaction. By assuming that the friction felt by the ion pairs in the transition state for separation could be modeled by the viscosity of the medium, Kramer's model gave an excellent account for the observed kinetic behavior and its temperature dependence. The values for the A factor for CIP/SSIP interconversion were on the order of 10^{11} s^{-1}, deviating by more than an order of magnitude from predictions of the standard transition-state formalism.

From the studies of the various nucleophiles shown in Figures 5 and 6 there is again a strong dependence of the A factor for ion-pair interconversion with E_a. For the largest barrier from the perspective of the CIP, the benzhydryl chloride CIP has an energy of activation of 3.1 kcal/mol and associated A factor of 6.5×10^{11} s^{-1} while the 3-methoxy-benzhydryl acetate CIP has an energy of activation of 1.0 kcal/mol and an A factor of 1.1×10^{10} s^{-1}. Even in this limited series of ion pairs the A factors differ by more than a factor of 60. There appears to be no basis for assuming that A factors for ion-pair interconversions are constant. Also, a model for ion-pair interconversion based upon standard transition-state theory is inadequate. A more fruitful approach for interpreting ion-pair dynamics is within the context of Kramer's theory. These molecular events clearly require more study.

Comparisons of Nucleophilicity

In light of the above observations, discussion of the nature of the parameters controlling nucleophilicity in S_N1 reaction processes has become significantly more complicated. Historically, nucleophilicity is often defined in terms of the relative rates of reaction for a series of nucleophiles with a common cation.[1] This method, developed by Ritchie, has been further advanced by Richards to include a measure of the nucleophilicity parameter, N_+, for bromide, chloride, and acetate with respective values of 2.2, 1.2, and 0.60, where the bromide is the better nucleophile.[7] Now with the current experimental meth-

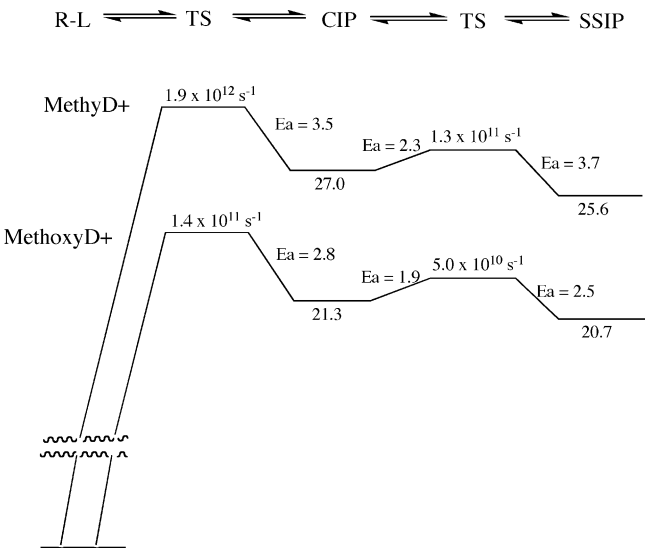

FIGURE 7. Reaction profile for 3-methoxy-4′-methyl-benzhydryl acetate (MethylD+) and 3,4′-dimethoxy-benzhydryl acetate (MethoxyD+) in DMSO. Energies of each species and the energy of activation, E_a, are in kcal/mol. κ is defined in the text. Standard deviations for E_a and A can be found in ref 24.

odologies, the concept of nucleophilicity can be parsed into processes associated with bond formation as well as ion-pair interconversion. However, probing for a deeper understanding leads to confusing correlations. For example, comparing chloride and bromide one finds that the rate of covalent bond formation with the benzhydryl cation is larger for chloride (3.8×10^9 s^{-1}) than for bromide (3.2×10^9 s^{-1}).[20] Although the E_a is less for bromide, the source of the increase in rate for chloride lies in chloride having a larger A factor. Thus, the enhanced overall nucleophilicity of bromide relative to chloride must reside in the ion-pair interconversion processes. Unfortunately, we have yet to be able to determine the rate of the collapse of the bromide SSIP to the CIP in order to address this issue.

This complexity is even more evident if one exams the relative reactivity where the overall energies are similar. For example, the energies for collapse of the CIP for benzhydryl chloride and 3-methoxy-4′methyl-benzhydryl acetate are very similar, and yet the rate of reaction for chloride, 3.8×10^9 s^{-1}, is almost a factor of 2 larger than for acetate, 2.2×10^9 s^{-1}.[24] Surprisingly, the E_a's are the same, but it is the A factor that is governing the relative dynamics with the A factor for acetate almost a factor of 2 smaller. In contrast, for the collapse of the CIP for benzhydryl bromide and 3,4′-dimethoxy-benzhydryl acetate, again of similar energy, the slowness of the acetate, 0.6×10^9 s^{-1}, relative to the bromide, 3.2×10^9 s^{-1}, is due to the larger E_a and not in the A factor, which is an order of magnitude larger than that for bromide.

Finally, the question arises as to whether a regime is ever achieved in which stabilization of the CIP actually leads to a reduction in the energy of activation for bond formation, behavior in direct opposition to the Hammond postulate.[15] From the electronic structure theory based on the work of Hynes, it is possible that as the CIP is stabilized the increase in the electronic coupling β_1 to β_2 increases to a greater extent than the increase in E_1 to E_2, leading to a reduction in the energy of activation E_a, Figure 2.[13] We actually observed this phenomenon for the collapse of 3-methoxy-4′-methyl-benzhydryl acetate CIP and 3,4-dimethoxy-benzhydryl acetate CIP in DMSO, Figure 7.[24] The more stable of the two ion pairs actually has a lower energy of activation for bond formation, which is contrary to the behavior found in acetonitrile, Figure 5. The source of the effect can be traced to DMSO having a larger dielectric constant ($\epsilon = 47$) than acetonitrile ($\epsilon = 37$), leading to a more stabilized CIP. As the position of the curve crossing of the two diabatic surfaces decreases there is an almost exponential increase in β.[13] Thus, very small changes in the distance of the separation of the ion pair can have a profound effect upon electronic coupling.

Conclusion

Understanding the parameters controlling reactivity for S_N1 processes clearly involves assessing the contributions of E_a and A for each of the molecular events. For E_a the key parameter is the electronic coupling integral $\beta(r)$ that mixes the two valence-bond states. For A the key parameters are ω_b, ω_s, and τ_l. At present we are only beginning to get a glimpse into how these parameters depend upon molecular structure.

This work was supported by a grant from the National Science Foundation, CHE-0408265.

References

(1) Ritchie, C. D. Nucleophilic Reactivities towards Cations. *Acc. Chem. Res.* **1972**, *5*, 348−354.
(2) Minegishi, S.; Loos, R.; Kobayashi, S.; Mayr, H. Kinetics of the Reaction of Halide Anions with Carbocations: Quantitative Energy Profiles for SN1 Reactions. *J. Am. Chem. Soc.* **2005**, *127*, 2641−2649.
(3) Winstein, S.; Clippinger, E.; Fainberg, A. H.; Robinson, G. C. Salt Effects and Ion-Pairs in Solvolysis. *J. Am. Chem. Soc.* **1954**, *76*, 2597−2598.
(4) Steinfeld, J. I.; Francisco, J. S.; Hase, W. L., *Chemical Kinetics and Dynamics;* Prentice Hall: Englewood Cliffs, 1989; p 548.
(5) Albery, W. J. The Application of the Marcus Relation to Reactions in Solution. *Ann. Rev. Phys. Chem.* **1980**, *31*, 227−263.
(6) Richard, J. P.; Williams, K. B.; Amyes, T. L. Intrinsic Barriers for the Reactions of an Oxocarbenium Ion in Water. *J. Am. Chem. Soc.* **1999**, *121*, 8403−8404.
(7) Richard, J. P.; Toteva, M. M.; Crugeiras, J. Structure−Reactivity Relationships and Intrinsic Barriers for Nucleophile Additions to a Quinone Methide: A Strongly Resonance-Stabilized Carbocation. *J. Am. Chem. Soc.* **2000**, *122*, 1664−1674.
(8) Richard, J. P.; Amyes, T. L.; Toteva, M. M. Formation and Stability of Carbocations and Carbanions in Water and Intrinsic Barriers to Their Reactions. *Acc. Chem. Res.* **2001**, *34*, 981−988.
(9) Ogg, R. A.; Polanyi, M. Mechanism of Ionic Reactions. *Trans. Faraday Soc.* **1935**, *31*, 604−620.
(10) Evans, A. G. The Reactions of Organic Halides in Solution. *Trans. Faraday Soc.* **1946**, *42*, 719−742.
(11) Pross, A.; Shaik, S. S. A Qualitative Valence-Bond Approach to Organic Reactivity. *Acc. Chem. Res.* **1983**, *16*, 363−370.
(12) Shaik, S.; Shurki, A.; Valence Bond. Diagrams and Chemical Reactivity. *Angew. Chem., Int. Ed.* **1999**, *38*, 586−625.
(13) Kim, H. J.; Hynes, J. T. A Theoretical Model for SN1 Ionic Dissociation in Solution. 1. Activation Free Energetics and Transition-State Structure. *J. Am. Chem. Soc.* **1992**, *114*.
(14) Mathis, J. R.; Kim, H. J.; Hynes, J. T. A Theoretical Model for SN1 Ionic Dissociations in Solution. 3. Analysis of *tert*-Butyl Halides. *J. Am. Chem. Soc.* **1993**, *115*, 8248−8262.

(15) Hammond, G. S. A Correlation of Reaction Rates. *J. Am. Chem. Soc.* **1955**, *77*, 334−338.
(16) Zichi, D. A.; Hynes, J. T. A Dynamical Theory for Unimolecular Ionic Dissociation Reactions in Polar Solvents. *J. Chem. Phys.* **1988**, *88*, 2513−2525.
(17) Zwan, G. v. d.; Hynes, J. T. Dynamical Polar Solvent Effects on Solution Reactions: A Simple Continuum Model. *J. Chem. Phys.* **1983**, *76*, 2993−3001.
(18) Peters, K. S.; Li, B. Picosecond Dynamics of Contact Ion Pairs and Solvent-Separated Ion Pairs in the Photolysis of Diphenylmethyl Chloride. *J. Phys. Chem.* **1994**, *98*, 401−403.
(19) Deniz, A. A.; Li, B.; Peters, K. S. Role of Polarization Caging in the SN1 Reaction of Diphenylmethyl Chloride: A Picosecond Kinetic Study. *J. Phys. Chem.* **1995**, *99*, 12209−12213.
(20) Dreyer, J.; Lipson, M.; Peters, K. S. Picosecond Kinetic. Study of the Photoinduced Homolysis and Heterolysis of Diphenylmethyl Bromide. 2. Role of Polarization Caging in Contact Ion Pair Recombination. *J. Phys. Chem.* **1996**, *100*, 15162−15164.
(21) Dreyer, J.; Peters, K. S. Picosecond Kinetic Study of the Photoinduced Homolysis and Heterolysis of Diphenylmethyl Bromide. 1. The Nature of the Conversion from Radical Pairs to Ion Pairs. *J. Phys. Chem.* **1996**, *100*, 15156−15161.
(22) Lipson, M.; Deniz, A. A.; Peters, K. S. Picosecond Kinetic Study of the Dynamics for Photoinduced Homolysis and Heterolysis in Diphenylmethyl Chloride. *J. Phys. Chem.* **1996**, *100*, 3580−3586.
(23) Lipson, M.; Deniz, A. A.; Peters, K. S. Nature of the Potential Energy Surfaces for the SN1 Reaction: A Picosecond Kinetic Study of Homolysis and Heterolysis for Diphenylmethyl Chlorides. *J. Am. Chem. Soc.* **1996**, *118*, 2992−2997.
(24) Peters, K. S.; Gasparrini, S.; Heeb, L. R. Dynamic Nature of the Transition State for the SN1 Reaction Mechanism of Diphenylmethyl Acetates. *J. Am. Chem. Soc.* **2005**, *127*, 13039−13047.
(25) Lipson, M.; Deniz, A. A.; Peters, K. S. The Sub-Picosecond Dynamics of Diphenylmethyl chloride Ion Pairs and Radical Pairs. *Chem. Phys. Letts.* **1998**, *288*, 781−784.
(26) Waldeck, D. H. Photoisomerization Dynamics of Stilbenes. *Chem. Rev.* **1991**, *91*, 415−436.
(27) Ciccotti, G.; Ferrario, M.; Hynes, J. T.; Kapral, R. Constrained Molecular Dynamics and the Mean Potential For an Ion Pair in A Polar Solvent. *Chem. Phys.* **1989**, *129*, 241−251.
(28) Ciccotti, G.; Ferrario, M.; Hynes, J. T.; Kapral, R. Dynamics of Ion Pair Interconversion in a Polar Solvent. *J. Chem. Phys.* **1990**, *93*, 7137−7147.
(29) Li, B.; Peters, K. S. Application of Kramers Theory to the Diffusional Separation of the trans-Stilbene/Fumaronitrile Contact Radical Ion Pair in Alkyl Nitrile Solvents. *J. Phys. Chem.* **1993**, *97*, 7648−7651.
(30) Vauthey, E.; Parker, A. W.; Nohova, B.; Phillips, D. Time-Resolved Resonance Raman Study of the Rate of Separation of a Geminate Ion Pair into Free Ions in a Medium Polarity Solvent. *J. Am. Chem. Soc.* **1994**, *116*, 9182−9186.
(31) Zhong, C.; Zhou, J.; Braun, C. L. Solvent-Separated Radical Ion Pairs and Free Ion Yields. 1. Effect of Temperature on Free Ion Formation in Solution. *J. Phys. Chem. A* **2004**, *108*, 6842−6849.
(32) Arnold, B. R.; Noukakis, D.; Farid, S.; Goodman, J. L.; Gould, I. R. Dynamics of Interconversion of Contact and Solvent-Separated Radical-Ion Pairs. *J. Am. Chem. Soc.* **1995**, *117*, 4399−4400.

AR0681124