

# Intrinsic Structure–Reactivity Relationships in Gas-Phase S<sub>N</sub>2 Reactions: Identity Exchange of Substituted Benzyl Chlorides with Chloride Ion

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**Abstract:** The potential energy surface along the gas-phase S<sub>N</sub>2 reaction coordinate for a series of substituted benzyl chlorides undergoing identity exchange with chloride ion, Cl<sup>-</sup> + X-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl, has been investigated using both experimental and theoretical methods. The rate of identity substitution and the equilibrium ion–molecule complexation energy (chloride affinity) for the series X = H, *m*-CH<sub>3</sub>, *m*-OCH<sub>3</sub>, *m*-F, *m*-Cl, and *m*-CF<sub>3</sub> have been measured using Fourier transform ion cyclotron resonance (FT-ICR) spectrometry. Application of RRKM theory to the experimental kinetics yields estimates for the activation energies. AM1 semiempirical calculations<sup>1</sup> were also used to estimate the energetics of the surface for comparison with experiment and to extend the results to other systems. We show that although the experimental observables vary over a considerable range, the intrinsic activation energy, as measured from the ion–molecule complex, remains constant for the entire series of substituted benzyl chlorides studied.

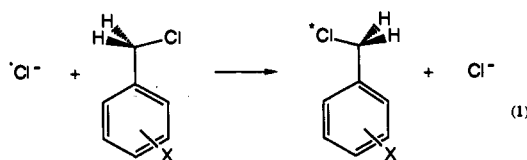
## I. Introduction

Bimolecular nucleophilic substitution (S<sub>N</sub>2) reactions have been, and still are, one of the most highly studied reactions in all of chemistry. Over the past several decades a number of aspects of S<sub>N</sub>2 reactions in solution have been thoroughly investigated including the influence of the nucleophile and leaving group on reactivity, changes in mechanism and transition state structure, effects of reaction exothermicity embodied in rate–equilibrium relationships, and the effects of substrate structure on reactivity. The complete understanding of these intrinsic issues is by no means at hand; the pursuit is partly hampered by influence of the solvent. As a result, many recent efforts in this area have focused on aspects of gas-phase reactions in order to expose more clearly the “intrinsic” properties. Both experimental and theoretical approaches have been fruitful. The basic mechanism, including the general double-minimum character of the potential energy surface, has been verified.<sup>2–4</sup> A definition of intrinsic nucleophilicity for reaction at a methyl center has been developed,<sup>5</sup> and a description of the effects of reaction exothermicity in terms of rate–equilibrium relationships has been described.<sup>6,7</sup> The effect of substrate structure on the reactivity of gas-phase S<sub>N</sub>2 systems, in particular the effect of substituents α to the reaction center, is still an area of concern.

From the early systematic work of Hine and co-workers,<sup>8–12</sup> as well as many others that followed, it became clear that the

effect of substrate structure on S<sub>N</sub>2 reactivity in solution is complex. By studying S<sub>N</sub>2 reactions in the gas phase, using both experimental and theoretical techniques, problems associated with solvation effects are removed, but complications associated with gas-phase kinetic and equilibrium measurements have hindered progress in this area. For example, as the substrate structure is altered, other reaction channels, such as proton transfer or elimination, often become important, making it difficult or impossible to probe the structural influence on the S<sub>N</sub>2 channel alone. Also, there is a limited dynamic range over which gas-phase kinetic measurements can be made in an attempt to estimate intrinsic energies of activation. Therefore, only a select set of chemical systems that contain the right energetic properties can be studied experimentally. Moreover, the gas-phase potential energy surface cannot be fully characterized from kinetic measurements alone; the relative energetics of the intermediate ion–molecule complexes must also be determined. Like the kinetic measurements, experimental determination of the intermediate ion–molecule complexation energies is also limited to a fairly narrow range. Finally, an integral part of obtaining quantitative energetic information from the experimental kinetic data has utilized statistical reaction rate theories. Over the past several years, however, the applicability of statistical theories to gas-phase S<sub>N</sub>2 systems has been questioned. Thus, given these difficulties, probing the effects of substrate structure of S<sub>N</sub>2 reactions in the gas phase remains a challenging problem.

In order to gain a better understanding of the intrinsic characteristics which govern S<sub>N</sub>2 reactions at carbon centers, and in particular the influence of substrate structure, we have studied the prototype system in eq 1 using both experimental and theoretical techniques.



The identity exchange S<sub>N</sub>2 reaction of substituted benzyl chlorides

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with chloride ion is an ideal system to investigate. The benzene ring can act as a structural probe on which substituents can be placed that will affect the electronic character of the far removed reaction center carbon. Therefore, complications associated with steric effects are eliminated. Using Hammett  $\sigma$  constants we can conveniently characterize the individual substituents relative to the unsubstituted substrate for comparison with solution-phase results. Moreover, since the reactions are thermoneutral, the potential energy surface is further simplified and complications associated with the changing thermodynamics are removed. In the absence of these factors a unique opportunity to address the "intrinsic" substituent effects is presented.

We have measured the rates of chloride substitution for eq 1 using Fourier transform ion cyclotron resonance (FT-ICR) spectrometry. The substituents investigated include  $X = m\text{-CH}_3$ ,  $\text{H}$ ,  $m\text{-OCH}_3$ ,  $m\text{-F}$ ,  $m\text{-Cl}$ , and  $m\text{-CF}_3$ . RRKM theory, within the microcanonical variational transition state ( $\mu\text{VTS}$ ) approximation, was used to interpret the kinetic results and estimate the  $\text{S}_{\text{N}}2$  barrier height relative to separated reactants. Also, the chloride affinities (CA) which correspond to the intermediate ion-molecule complexation energies were obtained from experimental equilibrium measurements. By anchoring the results to the CA of known compounds, an absolute scale for this series was obtained. The combination of these results gives a complete representation of the relative energetics for the important features of the double-minimum potential energy surfaces.

To better understand the experimental results and to obtain reasonably accurate RRKM parameters, Austin-Modeling 1 (AM1) semiempirical calculations were performed. Geometric and relative energetic information for the salient features of the surfaces, including separated reactants, ion-molecule complex, and  $\text{S}_{\text{N}}2$  transition state, were obtained for various substituents. The approach was extended to include substituents that are experimentally inaccessible in order to make predictions. The substituents studied using the AM1 method include  $X = p\text{-NH}_2$ ,  $p\text{-OCH}_3$ ,  $p\text{-CH}_3$ ,  $m\text{-CH}_3$ ,  $\text{H}$ ,  $m\text{-OCH}_3$ ,  $m\text{-F}$ ,  $m\text{-Cl}$ ,  $m\text{-CF}_3$ ,  $m\text{-CN}$ , and  $m\text{-NO}_2$ . Comparison with the experimental results is presented.

The goal of this paper is to present a generalized picture of the effects of substrate structure on the potential energy surface for gas-phase  $\text{S}_{\text{N}}2$  reactions. We first present some background information and discuss this general problem from both an experimental and a theoretical perspective. We then present experimental kinetic and thermodynamic results on our model  $\text{S}_{\text{N}}2$  systems. Using  $\mu\text{VTS}$ -RRKM theory to interpret the kinetic data and using the thermodynamic ion-molecule complexation energies we can quantify energetic features of the potential surfaces for comparison with the semiempirical AM1 results. Using both the experimental and theoretical techniques we find that the activation energies, as measured from the respective ion-molecule complexes, remain constant over the entire series of substituted benzyl chlorides investigated.

## II. Background

The correlation between structure and reactivity forms the basis for much of our understanding of basic chemical principles; its use as a tool to probe the properties of transition states and intermediates can be traced back to the beginnings of modern reaction chemistry. There have been numerous applications of these concepts to the study of  $\text{S}_{\text{N}}2$  reactions. In 1983 Shaik<sup>13</sup> wrote an excellent summary of the effects of substituents on solution-phase  $\text{S}_{\text{N}}2$  reactions.

In the early part of this century Petrenko-Kritschenko,<sup>14</sup> Backer and van Mels,<sup>15</sup> as well as Davies *et al.*<sup>16</sup> reported interesting

trends in the effects of  $\alpha$ -halogens on the  $\text{S}_{\text{N}}2$  reactivity of various alkyl halides. It was generally found that the addition of an  $\alpha$ -halogen to the reaction center had a retarding effect on the rate of substitution by orders of magnitude. In the 1950s Hine and co-workers<sup>8-11</sup> extensively explored the effects of  $\alpha$ - and  $\beta$ -halogenation. They showed the reactivity trend for the reaction:  $\text{CH}_3\text{X} > \text{CH}_2\text{X}_2 > \text{CX}_4$ . Moreover, for a given reaction, the ability of the halogen to retard the  $\text{S}_{\text{N}}2$  reaction follows the order  $\text{I} > \text{Br} > \text{Cl} > \text{F}$ . The effects of halogen substitution in the  $\beta$ -position relative to the reaction center are much less clear.  $\beta$ -Substitution does appear to reduce  $\text{S}_{\text{N}}2$  reactivity, but to a lesser extent.

Hine and co-workers<sup>12</sup> explored the effects of many other types of substituents on the rates of  $\text{S}_{\text{N}}2$  reactions in solution. They discovered that  $\pi$ -donating substituents placed  $\alpha$  to the reaction center enhance reactivity. For example,  $\text{CH}_3\text{OCH}_2\text{Cl}$  reacts  $10^5$  times faster than simple alkyl chlorides with KI in acetone, and species of the form  $\text{RCOOCH}_2\text{X}$  also show enhanced reactivity compared to their unsubstituted analogs. Placed in the  $\beta$ -position, these same substituents appear to have a retarding effect.

Unlike the  $\sigma$ -accepting and  $\pi$ -donating substituents mentioned thus far, the effects of  $\pi$ -accepting substituents on  $\text{S}_{\text{N}}2$  reactivity in solution are much less clear. Early work by Slator and Twiss<sup>18</sup> and by Conant *et al.*<sup>19-21</sup> and later work by Bartlett and Trachtenberg<sup>22</sup> showed that substituents such as  $-\text{CN}$ ,  $-\text{COR}$ , and  $-\text{Ph}$  enhance  $\text{S}_{\text{N}}2$  reactivity relative to the unsubstituted compound when placed  $\alpha$  to the reaction center. As an example,  $\text{ClCH}_2\text{CN}$  reacts with KI in acetone  $10^5$  times faster than do simple alkyl chloride analogs. More recent work, however, suggests that these trends may be dependent on factors such as solvent and on the strength of the nucleophile.<sup>23-27</sup>

Over the years, much of the experimental effort focused on quantifying substituent effects through the use of linear-free-energy relationships. Many of the original ideas behind a quantitative approach to this concept were first developed by Hammett<sup>28-30</sup> and Burkhardt<sup>31,32</sup> in the 1930s. In this pioneering work they proposed a quantitative scale for considering substituent effects within a given class of reactions. This eventually led to the Hammett free energy relationship in which substituents are characterized by their ability to shift the equilibrium in the ionization of substituted benzoic acids in water. The Hammett free energy relationship has led to a better understanding of properties such as charge development at the reaction center and the qualitative structure of the transition state. Among these, there have been a number of studies on  $\text{S}_{\text{N}}2$  reaction in which the Hammett approach was employed through the use of benzyl derivatives.<sup>28-30,33-58</sup>

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In contrast to many other types of solution-phase reactions, nearly all S<sub>N</sub>2 reactions of substituted benzyl halides with anionic nucleophiles in solution exhibit "U-shaped" Hammett plots. Rate enhancement is observed not only with substituents that are electron withdrawing but also with substituents that are electron donating. Young and Jencks<sup>59</sup> addressed the issue of Hammett plot curvature for reactions of benzyl halides and concluded that much of the curvature in these plots is due to polar versus resonance effects of the substituents rather than a change in mechanism from S<sub>N</sub>2 to S<sub>N</sub>1 or a change in transition-state structure with substituent as many researchers have proposed.<sup>28-30,33-58</sup> The effects of differential thermodynamics and solvation may also contribute to the observed behavior.

Experimental gas-phase studies that address the issue of substituent effects in S<sub>N</sub>2 systems are much more limited. This is not surprising given the difficulties mentioned earlier regarding competitive reactions, and the quantitative interpretation of the kinetic results. Kebarle and co-workers,<sup>60,61</sup> DePuy, Bierbaum and co-workers,<sup>62-64</sup> as well as our group<sup>2,5,65-68</sup> have all made contributions to this area.

With the growing body of experimental information on structure-reactivity trends for S<sub>N</sub>2 reaction in both the solution phase and the gas phase, a number of important theoretical models have been developed to help rationalize the complex wealth of data. Among these are simple frontier molecular orbital (FMO) theory,<sup>69,70</sup> various potential energy surface/transition state models<sup>49,71-75</sup> including those of Thornton<sup>74</sup> and More-O'Farrell,<sup>71</sup>

and valence bond theory including the more sophisticated valence bond configuration mixing (VBCM) model of Pross and Shaik.<sup>13,76-82</sup>

The VBCM model of Pross and Shaik<sup>82</sup> has been extensively developed over the past decade and has been used for estimating substituent effects in S<sub>N</sub>2 reactions. The model is based on the relative importance of various configurations which contribute to the wave function at the transition state. The two factors which directly contribute to the activation energy are (a) the initial energy difference between the two configurations, which is related to the electron donor-acceptor gap of the reactants, and (b) the slope of the intersecting configuration curves, which is related to the localization ability of the reactants and the exothermicity of the reaction. Unlike the other models, the VBCM model has been successfully used to rationalize a whole range of substituent behavior including application to S<sub>N</sub>2 reactions of substituted benzyl derivatives, where structural trends and relative stabilities were postulated.<sup>83</sup> In their study, Pross and Shaik concluded that within a given family, such as substituted benzyl halides, the effects of substituents may be more complicated. Aside from any "Hammond-type" changes, the influence of the substituent is dependent on which configurations in the transition state are most stabilized. From this they were able to rationalize the many curved Hammett plots observed for these reactions in solution.

The most direct theoretical approach for elucidation of intrinsic substituent effects is through the use of rigorous quantum mechanics. Although the body of theoretical data is growing, only a limited number of studies have focused on the effects of substituent effects in S<sub>N</sub>2 reactions. Hirao and Kebarle studied alkyl substituents in the reaction of chloride ion with alkyl bromides (RCH<sub>2</sub>Br). They found that the activation energies follow the same trend as that originally found in solution by Ingold,<sup>84</sup> namely R = *i*-Pr > CH<sub>3</sub> > H. Kost and Aviram<sup>85</sup> and Pross *et al.*<sup>86</sup> studied the effects of π-acceptor and π-donor α-substituents in S<sub>N</sub>2 reactions. More recently, Wladkowski *et al.*<sup>88</sup> presented work on the α-CN substituent using *ab initio* quantum techniques.

The S<sub>N</sub>2 system in eq 1, which is the focus of this investigation, has been studied using semiempirical molecular orbital theory. In 1978 Davidson and Williams<sup>87</sup> performed a series of semiempirical CNDO/2 calculations to explore the relative energetics of the surfaces. A number of substituents were considered including X = *m*- and *p*-NH<sub>2</sub>, CH<sub>3</sub>, F, CF<sub>3</sub>, and NO<sub>2</sub>. These calculations are not sophisticated by today's standards; the geometries were not fully optimized even at the CNDO/2 level and problems associated with the assumptions made in this theory are well-known.<sup>88</sup> As one might expect, the absolute values presented by Davidson and Williams are far from the experimental values. The S<sub>N</sub>2 barriers are predicted to lie unrealistically far below the separated reactants for all substituents studied. The relative results, however, show a clear trend when plotted against Hammett σ constants. Davidson and Williams concluded that

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"what is often considered an inductive effect is in most cases not that, but rather an electrostatic field effect" as in this case.

In 1984, as part of a comprehensive study on  $S_N2$  reactions, Carrion and Dewar<sup>89</sup> presented theoretical calculations on the chemical system in eq 1 using the MNDO semiempirical method. In this study the number of substituents investigated was more limited compared to the previous study by Davidson and Williams, and the theoretical model is still affected by many of the same inadequacies as the earlier model. Once again the absolute energies determined at this level of theory are quantitatively incorrect (the absolute results are, however, substantially better compared to CNDO/2). More importantly, the results appear not to correlate with Hammett  $\sigma$  constants, at least for certain substituents with negative  $\sigma$  constants (*i.e.* *p*-OH and *p*-NH<sub>2</sub>). Although the substituents with positive  $\sigma$  constants do show a clear trend and are consistent with the earlier study, there is considerable scatter in the plot.

### III. Experimental Methods

**Materials.** All chemicals were obtained from Aldrich. Most samples were used directly and without further purification; samples that became discolored were re-distilled prior to use. Each day experimental data were taken—fresh samples were used to minimize systematic problems due to impurities. All samples were subjected to at least 3 freeze–pump–thaw cycles before introduction into the instrument.

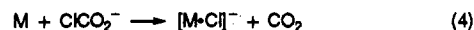
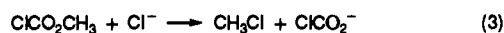
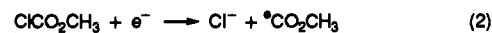
Ideally, the substituents should span a large range in expected electronic effects (some that are considered electron withdrawing and some electron donating), size, and position (meta versus para). They should also include substituents which primarily interact through the  $\sigma$ -system and ones that interact through the  $\pi$ -system. An important practical concern is volatility. Each substituted benzyl chloride must be volatile enough to be introduced into the ICR at a measurably stable pressure (this is the primary reason why certain substituents such as *m*- and *p*-NO<sub>2</sub> are not included). Also, certain substituted benzyl chlorides (*e.g.* –OH) may have multiple primary or secondary reaction channels. Ultimately, the list of compounds chosen here resulted from a combination of all of these issues.

**Instrumentation.** All experiments were performed with a Fourier transform IonSpec FTMS-2000 ion cyclotron resonance (FT-ICR) spectrometer equipped with impulse excitation. Details of the experimental apparatus can be found elsewhere.<sup>90</sup> Briefly, experiments were performed in a rectangular cell (approximately 1 × 1 × 1.5 in) in which the ions were trapped with magnetic fields in the range 0.8–1.2 T. Background pressures were in the range 0.8–2.0 × 10<sup>-8</sup> Torr. Standard notched ejection techniques were used to remove unwanted ions from the ICR cell and thereby isolate the ions of interest, which were subsequently detected via impulse excitation techniques.

During the experiments, pressures of neutral species within the ICR cell were monitored with an ion gauge (Varian 844), which was calibrated daily against a capacitance manometer (MKS 170 Baratron with a 315BH-1 head). The reaction of methane radical cation with methane (CH<sub>3</sub><sup>+</sup> + CH<sub>4</sub> → CH<sub>5</sub><sup>+</sup> + CH<sub>3</sub>), which has a rate constant of 1.1 × 10<sup>-9</sup> cm<sup>3</sup> s<sup>-1</sup>,<sup>91</sup> was used to verify that the absolute pressure readings were accurate. All experiments were carried out at an estimated temperature of 350 K.<sup>90</sup>

Impurities can affect the observed rate measurement. Most sample impurities, especially those less volatile than the substrate, pose little difficulty and can be easily removed by gas chromatography or distillation. Impurities which are more volatile than the substrate or impurities which are formed within the vacuum system and subsequently reach the ICR cell are more problematic. Nonreactive volatile impurities will affect the pressure readings during the rate measurement and ultimately produce apparent rate coefficients that are too low. This problem can be ameliorated through careful sample preparation. The presence of reactive impurities such as hydrogen chloride within the vacuum system is less amenable to such countermeasures. Because HCl reacts with most anions on nearly every collision, minute quantities can affect the observed reaction rate significantly. The problem is greatest in systems with a very slow reaction rate. Since these problems are rarely systematic, the best procedure is simply to average results over many days using many different

### Scheme 1



samples. Here, only the substrates with the slowest reaction rates (X = H and CH<sub>3</sub>) were problematic in this regard. Other substrates react more rapidly and hence are less sensitive to the presence of reactive impurities.

**Kinetic Data Collection.** The primary ion, Cl<sup>-</sup>, was generated directly from the reactive substrate by dissociative electron attachment using an electron beam pulse. Generation of the proper isotope ratio (<sup>35</sup>Cl/<sup>37</sup>Cl ≈ 3) was observed over a large time interval before each kinetic run. The data collection was initiated with primary ion formation (ca. 20–50 ms) followed by electron ejection (ca. 20 ms). After a short time delay (ca. 30–50 ms) to aid in ion thermalization, one of the chloride ion isotopes was ejected.<sup>92</sup> The ion signals for both isotopes were then monitored and signal-averaged (20–50 times) until the equilibrium chloride ion isotope ratio was reached or for as long as possible (ca. 800–4000 ms depending on the pressure of the reacting neutral in the cell). The ion signals were monitored at 7–15 different increments of time over this period. Multiple kinetic runs were performed at a variety of different pressures for each reacting system (2 × 10<sup>-7</sup> to 2 × 10<sup>-6</sup> Torr). Data were collected on multiple days, and at different total pressures.

**Thermodynamic Data Collection.** At the pressures within the ICR spectrometer, ion–molecule complex formation is difficult or impossible from direct association via three-body stabilization. The method used here for the generation of chloride ion/neutral complexes, which has found previously utility,<sup>93</sup> is shown in Scheme 1. After the conditions were optimized to make a sufficient amount of ClCO<sub>2</sub><sup>-</sup> from the reaction sequence shown in Scheme 1, the appropriate benzyl chloride was introduced into the cell along with another neutral species of comparable chloride affinity at total pressures between 0.2 and 2 × 10<sup>-6</sup> Torr. Methyl chloroformate (CH<sub>3</sub>OCOCl) was used to bracket on the low end of the chloride affinity scale and fluoroform (CF<sub>3</sub>H) was used on the high end. Ion signals over the appropriate mass range were measured and averaged (20–50 times) at each time increment until equilibrium was established between the complexes within the cell (ca. 500–3000 ms). Sums of ion intensities for all combinations of chlorine isotopes within each complex were used in the determination of equilibrium constants. Pressure measurements to determine the concentrations of neutral species were performed as described above. Equilibrium measurements were made at a variety of pressures and on different days.

### IV. Experimental Results

**Kinetic Data Analysis and Results.** The observed rates of reaction for the various benzyl chlorides in eq 1 were obtained from the ratios of ion intensities as a function of time using the method of Eyler and Richardson.<sup>94</sup> Problems arising from ion loss are eliminated with the use of this technique because the ratio of reactant and product ion intensities instead of absolute ion intensities is the measured observable. Such an analysis is valid as long as the reactant and product ion losses are nearly equivalent (which is an excellent approximation for thermoneutral reactions whose reactant and product ions differ only slightly in mass and not in structure). The rate expression as applied to the systems of interest here is given by eq 5,

(92) In this particular case, <sup>35</sup>Cl<sup>-</sup> was ejected. The rate was identical within experimental uncertainty no matter which isotope was ejected. Ejecting <sup>35</sup>Cl<sup>-</sup> is preferred, since initially the system is farther away from equilibrium. This is useful when measuring very slow identity exchange reactions.

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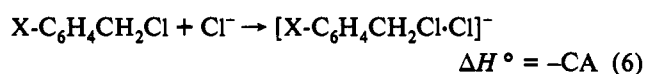
(91) Huntress, W. T.; Laudenslager, J. B.; Pinizzotto, R. F. *Int. J. Mass Spectrom. Ion Phys.* 1974, 13, 331.

$$\ln \left[ \frac{R_t - R_\infty}{R_t - 1} \right] = -k_{\text{obs}} P t \quad (5)$$

where  $P$  is the total pressure,  $R_t$  is the ratio of ion intensities ( $[^{35}\text{Cl}^-]/[^{37}\text{Cl}^-]$ ) at some time  $t$ ,  $R_\infty$  is the ratio of ion intensities at infinite time after ejection (*i.e.*, the natural abundance ratio), and  $k_{\text{obs}}$  represents the observed rate coefficient.

The observed rate coefficients for substitution reactions measured at 350 K are given in Table 1. The uncertainty represents one standard deviation of all kinetic measurements taken. We believe the absolute error to be in the range of 20–30%, and it is mainly a consequence of uncertainties in the absolute pressure measurements. Also given in Table 1 are the calculated capture rates,  $k_{\text{cap}}$ , obtained from various methods, and the corresponding efficiency ( $\Phi = k_{\text{obs}}/k_{\text{cap}}$ ) for the reaction.

**Thermodynamic Data Analysis and Results.** The complexation energies associated with formation of  $[\text{X-C}_6\text{H}_4\text{CH}_2\text{Cl}\cdot\text{Cl}]^-$ , which correspond to minus the chloride affinity (CA) of each substituted benzyl chloride, eq 6, were obtained from equilibrium measurements relative to known reference compounds.



Chloride affinities obtained by Larson and McMahon<sup>93</sup> were used to anchor the benzyl chloride results presented here.

The standard free energy changes for the equilibria were obtained from  $\Delta G^\circ_{\text{rel}} = -RT \ln K_{\text{eq}}$ , where “rel” indicates that the reaction involves a relative chloride affinity. The  $\Delta G^\circ_{\text{abs}}$  values involving the absolute chloride affinities of the reference compounds ( $\text{CH}_3\text{OCOCl}$  and  $\text{CF}_3\text{H}$ ) were taken directly from the results of Larson and McMahon. Using these data, absolute values for the chloride affinity of the various substituted benzyl chlorides were obtained. It should be noted that the results presented here were obtained from experiments carried out at approximately 350 K whereas the results of Larson and McMahon were obtained at 300 K. The resulting errors in the  $\Delta G^\circ_{\text{abs}}$  values should be on the order of 0.1 kcal mol<sup>-1</sup>.

In order to obtain an enthalpy of complexation,  $\Delta H^\circ_{\text{abs}}$ , from the free energy data, the entropy change upon complexation,  $\Delta S^\circ_{\text{abs}}$ , is needed. Larson and McMahon<sup>93</sup> used a statistical thermodynamic approximation in which a crude estimate of the geometries was used and the vibrational entropy change was neglected. Because reasonably accurate values for the appropriate parameters of the complex and separated reactants (geometry and vibrational frequencies) have been determined computationally in this study, all terms (including the vibrational entropy term) were used in the statistical thermodynamic calculation of the entropy change.

The thermodynamic results leading to the chloride affinity of the substituted benzyl chlorides are given in Table 2. The uncertainties are difficult to estimate. The accuracy in the equilibrium measurements is limited by the accuracy in the pressure measurements of the neutral species. The absolute free energy scale is based on the values of  $\text{H}_2\text{O}$  and *tert*-butyl alcohol at 300 K as presented in the Larson and McMahon paper; thus, the reference free energies contain some uncertainty. A small error is also introduced in the calculation of entropy changes. The uncertainties given in Table 2 are one standard deviation from the mean of all measurements taken, but the absolute errors may be somewhat larger.

## V. Theoretical Methods and Results

**Statistical Reaction Rate Theory.** The primary function of the RRKM analysis presented here is to estimate the activation energy for each substitution reaction from the experimental kinetic data presented in Table 1. Part of this analysis requires modeling

of an ion–molecule complex through a “loose” transition state, which is a topic of current research interest. In the analysis of such a dissociating channel, problems can arise due to the uncoupling of modes involving relative rotation of the fragments from vibrations within the system.<sup>95,96</sup> Also, ambiguity can arise in the determination of the correct reaction pathway, a variable that is important in the statistical analyses. Finally, recent experimental and theoretical work suggests that certain  $\text{S}_{\text{N}}2$  reactions may have “nonstatistical” components to their reaction dynamics.<sup>97–101</sup> With these concerns, one may question the approach used here. There is no evidence to date, however, which suggests that statistical theories, such as RRKM theory, are inappropriate or inadequate in estimating energies of activation for such systems. In fact, there are examples in the literature which suggest that, although  $\text{S}_{\text{N}}2$  reaction may behave nonstatistically, quantitative estimates for activation energies can still be made.<sup>102,103</sup> More importantly, here we are most interested in the relative energetics as opposed to the absolute values. A detailed description of the RRKM analysis used here can be found in a recent article.<sup>68</sup> A brief description of the important details relevant to the specific systems studied in this investigation is presented below.

Figure 1 shows a one-dimensional representation of the potential energy surface for the thermoneutral gas-phase  $\text{S}_{\text{N}}2$  reaction in eq 1, along with the various component steps. As seen in the figure, the reactants initially come together to form a chemically activated ion–molecule complex,  $[\text{X-C}_6\text{H}_4\text{CH}_2\text{Cl}\cdot\text{Cl}]^-$ . Once formed, this complex can either dissociate back to reactants or undergo substitution to form a post substitution complex,  $[\text{X-C}_6\text{H}_4\text{CH}_2\cdot\text{Cl}\cdot\text{Cl}]^-$ . If substitution does occur, the resultant complex can simply dissociate to give products. With this mechanism in hand, the overall rate expression for such a system can be derived using the steady-state approximation, eq 7.

$$k_{\text{obs}}(T) = \frac{k_1(T)k_2(T)}{k_{-1}(T) + 2k_2(T)} = k_1(T)\Phi(T) \quad (7)$$

In eq 7,  $\Phi(T)$  is the reaction efficiency, which is a function of only the unimolecular rate coefficients. An important assumption that must also be made is that the intermediate ion–molecule complexes have a sufficient lifetime (*i.e.* long on the time scale of reaction) to be treated as true intermediates. This concept is considered more fully in Miller’s unified statistical theory.<sup>104</sup>

The unimolecular rates, and hence the unimolecular efficiency, can then be calculated using the  $\mu\text{VTS}$ -RRKM expression, eq 8.<sup>96,105–109</sup>

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**Table 1.** Experimental Kinetic Data for the Reaction  $X-C_6H_4CH_2Cl + ^*Cl^- \rightarrow X-C_6H_4CH_2^*Cl + Cl^-$ 

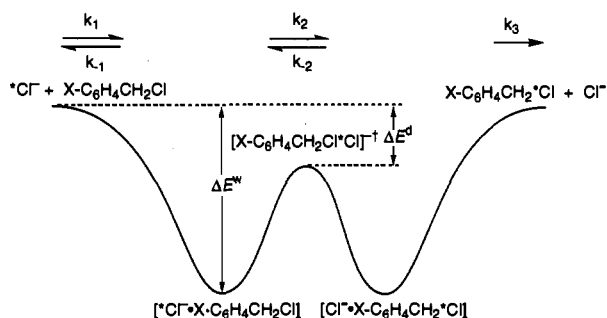
substituent	$k_{obs} \times 10^{-10}$ ( $cm^3 s^{-1}$ )	$k_{cap}(SC) \times 10^{-9}$ ( $cm^3 s^{-1}$ ) <sup>a</sup>	$k_{cap}(\mu VTS) \times 10^{-9}$ ( $cm^3 s^{-1}$ ) <sup>b</sup>	$\Phi$ (%)	$\Delta E^d$ (kcal mol <sup>-1</sup> )	$\sigma^c$
<i>m</i> -CH <sub>3</sub>	0.011 ± 0.0046	2.9	3.4	0.037	-0.2	-0.06
H	0.0065 ± 0.0026	2.3	3.3	0.029	+0.2	0.00
<i>m</i> -OCH <sub>3</sub>	0.053 ± 0.025	3.0	3.0	0.17	-1.1	0.10
<i>m</i> -F	0.18 ± 0.021	2.3	3.6	0.79	-2.6	0.34
<i>m</i> -Cl	0.62 ± 0.17	2.3	3.5	2.7	-3.6	0.37
<i>m</i> -CF <sub>3</sub>	2.5 ± 0.4	3.0	4.0	8.1	-5.0	0.46

<sup>a</sup> Data used to determine capture rate as well as the ion-molecule association potential are the following: (dipole moment (D), molecular polarizability ( $\text{\AA}^3$ )) *m*-CH<sub>3</sub> (1.84, 15.83); H (1.85, 13.98); *m*-OCH<sub>3</sub> (0.86, 16.52); *m*-F (1.97, 13.70); *m*-Cl (1.89, 15.82); *m*-CF<sub>3</sub> (3.15, 15.22). The polarizabilities were calculated using an empirical relation (Miller, K. J.; Savchik, J. A. *J. Am. Chem. Soc.* 1979, 101 (24), 7206). The dipole moments were calculated using the AM1 semiempirical method and referenced to the experimental value of benzyl chloride, 1.85 (*J. Phys. Chem.* 1975, 79, 1962; *Rev. Roum. Chim.* 1975, 20, 195). Geometries used to determine moments of inertia were obtained directly from the AM1 calculations. <sup>b</sup> Obtained directly from the RRKM calculation (see text). <sup>c</sup> Taken from ref 4.

**Table 2.** Thermodynamic Data for the Complexation Reaction  $X-C_6H_4CH_2Cl + Cl^- \rightarrow [X-C_6H_4CH_2Cl \cdots Cl^-]$  Based on Known Reference Compounds<sup>a</sup>

substituent	$\Delta G^\circ_{350,rel}$ (kcal mol <sup>-1</sup> )	$\Delta G^\circ_{350,abs}$ (kcal mol <sup>-1</sup> )	$\Delta S^\circ_{350,abs}$ (cal mol <sup>-1</sup> K <sup>-1</sup> )	$\Delta H^\circ_{350,abs} \equiv \Delta E^w$ (kcal mol <sup>-1</sup> )
<i>m</i> -CF <sub>3</sub>	-5.3 ± 0.5	-13.1	-18.2	-19.5
<i>m</i> -OCH <sub>3</sub>	-4.5 ± 0.5	-12.3	-18.1	-18.6
<i>m</i> -Cl	-4.0 ± 0.2	-11.8	-17.5	-17.9
<i>m</i> -F	-2.6 ± 0.4	-10.4	-17.4	-16.5
CF <sub>3</sub> H <sup>b</sup>	-2.0	-9.8	-22.9 <sup>c</sup>	-16.7
<i>m</i> -CH <sub>3</sub>	-0.5 ± 0.1	-8.3	-16.7	-14.1
H	-0.3 ± 0.2	-8.0	-16.7	-13.8
ClCO <sub>2</sub> CH <sub>3</sub> <sup>b</sup>	0	-7.8	-21.0 <sup>c</sup>	-14.1

<sup>a</sup> Entropy calculated from statistical thermodynamic relationships using geometries and frequencies obtained from semiempirical AM1 calculations. <sup>b</sup> Reference 93. <sup>c</sup> Entropy estimated using statistical thermodynamic approximations (refs 93 and 113).

**Figure 1.** Generalized potential energy surface for gas-phase  $S_N2$  reactions involving substituted benzyl chlorides.

$$k(E, J) = \sigma \frac{\int_0^{\epsilon(J; R^*)} \rho_{\mu VTS}^{\dagger}(\epsilon') d\epsilon'}{h\rho[\epsilon(J; R_e)]} = \sigma \frac{W_{\mu VTS}^{\dagger}[\epsilon(J; R^*)]}{h\rho[\epsilon(J; R_e)]} \quad (8)$$

In eq 8,  $\sigma$  is the reaction path degeneracy,  $R$  denotes the reaction coordinate,  $\epsilon(J; R) = E - V(R) - E_r(J; R)$ ,  $W_{\mu VTS}^{\dagger}[\epsilon(J; R^*)]$  is the number of accessible states at the transition state (located at  $R = R^*$ ) for each  $(E, J)$  channel, and  $\rho[\epsilon(J; R_e)]$  is the corresponding density of states for the appropriate ion-molecule complex (for which  $R = R_e$ ).  $V(R)$  and  $E_r(J; R)$  represent the approximate potential energy and orbital rotational energy, respectively, along the reaction coordinate.  $V(R)$  can be modeled using simple electrostatics incorporating experimental molecular parameters, polarizability, and dipole moment for each neutral. Once averaged over the appropriate chemically activated energy and angular momentum distribution, the macroscopic efficiency is obtained for a given temperature. To obtain an estimate of  $\Delta E^d$  which reproduces the experimental kinetics, we must first determine the experimental efficiency using a calculated capture rate,  $k_1$ . In this study we calculated the capture rate a number of different ways; for simplicity we have chosen the parameterized trajectory

model of Su and Chesnavich,<sup>110</sup> which has been shown to give accurate results. Details regarding the specific choice of the reaction pathway including the potential used, the assumption regarding conservation of angular momentum, and the specifics of the program are given elsewhere.<sup>68</sup>

Data for the unsubstituted benzyl chloride system obtained from semiempirical AM1 calculations discussed below are given in Table 3 as a representative example. These data include the vibrational frequencies and rotational constants for the three important parts of the surface including separated reactants, intermediate ion-molecule complex, and  $S_N2$  transition state. Similar data were computed for each of the substituted benzyl chlorides studied in this investigation. Using these sets of data in a  $\mu VTS$ -RRKM analysis, we can determine for which value of  $\Delta E^d$  the calculated reaction efficiency matches the experimental efficiency at a given temperature. This procedure gives an estimate of the value of  $\Delta E^d$  based on our statistical model for each substituted benzyl chloride system. As can be seen in Table 3 there are differences between the experimental frequencies and those calculated using the AM1 Hamiltonian. For the purposes of consistency, however, the calculated spectroscopic values were used without modification since it is the relative activation energies we are most interested in. The details associated with the  $\mu VTS$ -RRKM analysis including modeling of the "loose" association channel and "tight"  $S_N2$  transition state can be found in a recent publication.<sup>68</sup>

Shown in Figure 2 is the calculated reaction efficiency as a function of temperature for the prototype reaction,  $C_6H_5CH_2Cl + Cl^-$ , at several different assumed values of  $\Delta E^d$  and using the data given in Table 3. On the basis of this figure, a value of  $\Delta E^d = +0.2$  is found to best reproduce the experimental efficiency,  $2.9 \times 10^{-4}$ , at 350 K. Figure 2 also provides useful information regarding the expected temperature dependence for this reaction. As Kebarle and co-workers<sup>61</sup> pointed out several years ago, the temperature dependence of the overall reaction rates for simple gas-phase  $S_N2$  reactions is a strong function of the observed  $S_N2$  barrier height relative to separated reactants; the temperature dependence was found to change sign from negative to positive for systems where the activation barrier extends above separated reactants. Consistent with this picture, the reaction in Figure 2 shows the expected behavior; as the assumed activation energy,  $\Delta E^d$ , is varied from -2.0 to +1.0, the calculated temperature dependence of the reaction efficiency changes from negative to positive. In fact, on the basis of the predicted activation energy for this particular reaction, the reaction efficiency is expected to show little or no temperature dependence over a range of 200–600 K. This might be a useful test of the statistical model used here.

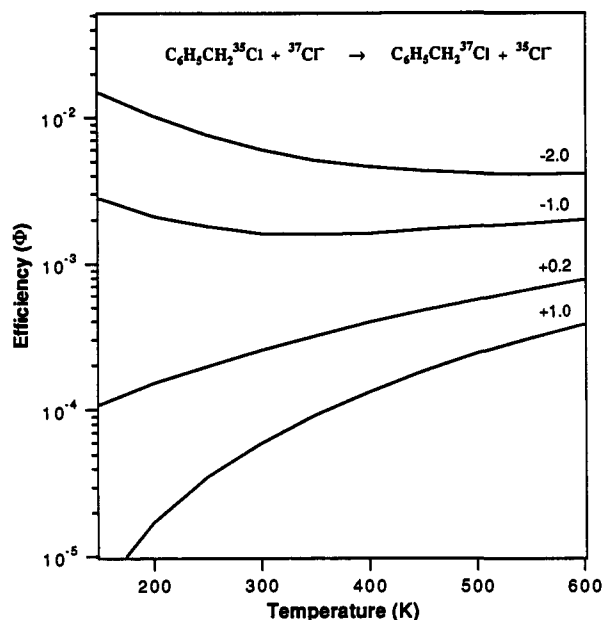
**Semiempirical Molecular Orbital Calculations.** The salient features along the reaction coordinate for the reactions in eq 1 have been investigated using AM1 semiempirical molecular orbital theory.<sup>1</sup> The important areas of each surface studied include the

**Table 3.** Parameters Used in the RRKM Analysis of the Reaction Cl<sup>-</sup> + C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>Cl, as a Representative Example

	dissociation transition state Cl <sup>-</sup> ...ClCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub>			complex [Cl <sup>-</sup> ClCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> ]			S <sub>N</sub> 2 transition state [Cl <sub>2</sub> CH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> ] <sup>†</sup>		
$\nu_i^a$	3421.2 (3107)	1275.2 (1242)	662.0 (678)	3419.6	1275.5	655.2	3419.3	1273.0	624.9
	3413.4 (3088)	1271.8 (1209)	622.8 (623)	3411.9	1272.7	622.4	3410.7	1267.3	548.7
	3400.7 (3033)	1185.3 (1157)	479.1 (467)	3398.4	1183.2	478.6	3400.7	1177.3	407.8
	3400.5 (3006)	1171.0 (1073)	366.4 (462)	3392.2	1173.0	365.2	3398.9	1174.0	369.0
	3309.8 (2959)	1101.4 (1028)	361.7 (330)	3307.6	1094.5	359.8	3356.4	1138.1	237.2
	3262.0 (2868)	1069.7 (1002)	258.2 (269)	3266.0	1065.1	253.8	3340.9	1060.0	233.6
	1729.4 (1604)	1057.8 (986)	111.0 (130)	1730.9	1055.0	116.6	1729.2	1051.4	172.9
	1707.0 (1585)	1038.6 (965)	43.8 <sup>b</sup>	1706.5	1036.3	60.0	1706.1	1034.5	135.0
	1596.1 (1497)	1001.4 (922)		1596.9	999.9	49.9 <sup>b</sup>	1599.5	993.6	83.7
	1535.8 (1456)	945.7 (842)		1534.1	933.1	31.4	1534.8	981.3	57.9 <sup>b</sup>
	1465.3 (1445)	914.8 (815)		1450.3	912.2	19.4	1437.8	909.9	439.6 <sup>i</sup>
	1381.9 (1333)	905.2 (803)		1379.1	886.7		1372.9	871.1	
	1372.5 (1323)	857.8 (766)		1372.8	842.7		1364.6	827.9	
	1325.3 (1264)	810.6 (697)		1310.9	793.4		1277.0	668.4	
$B_{\text{int}}(\text{tors}), \sigma_i^c$	799, 1 (1)			7.99, 1 (1)			648, 1 (1)		
$B_{\text{int}}(\text{hind}), \sigma_i^c$	0.0659, 1 (2)								
$B_{\text{ext}}(\text{act}), \sigma_i^c$	0.0288, 1 (1)			0.0288, 1 (1)			0.0204, 1 (1)		
$B_{\text{ext}}(\text{inact}), \sigma_i^c$	$d$			0.0291, 1 (1)			0.0337, 1 (2)		

<sup>a</sup> Values in parentheses are the experimental frequencies (Bellanato, J.; Schmid, E. D. *Anales de la Real Sociedad Espanola de Fisica y Quimica* 1960 56B (12), 949; Chattopadhyay, S. *Indian J. Phys.* 1967, 41 (10), 759; Verdonck, L.; van der Kelen, G. P. *Spectrochim. Acta* 1972, 28A, 51).

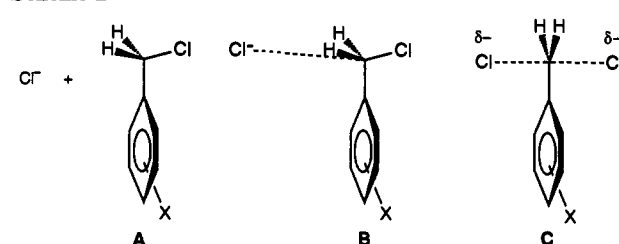
<sup>b</sup> Treated as torsional rotations. <sup>c</sup> Rotational constants (cm<sup>-1</sup>) obtained from AM1 theoretical structures, dimensionality given in parentheses. <sup>d</sup> The value of the moment of inertia and hence rotational constant of the 2-dimensional external inactive rotor for the loose transition state is a function of the separation of center of mass of the two species and is listed as follows: ( $r(\text{C}-\text{Cl})$  in Å,  $2D - B_{\text{ext}}(\text{inact})$  in cm<sup>-1</sup>) 6.0, 0.00983; 7.0, 0.00790; 8.0, 0.00646; 10.0, 0.00452; 12.0, 0.00332; 14.0, 0.00253; 20.0, 0.00132; 25.0, 0.000868; 35.0, 0.000468; 45.0, 0.000288.



**Figure 2.** Calculated RRKM reaction efficiency as a function of temperature for the parent identity system. The numbers associated with each curve represent the value of  $\Delta E^d$  used in the calculation.

separated reactants, intermediate backside ion-molecule complex, and S<sub>N</sub>2 transition state. Complete optimized geometries, heats of formation, and quadratic force fields were determined for each structure using the MOPAC<sup>111</sup> molecular orbital package running on a DEC 3100.

With such large molecular systems there are a number of local minima that represent valid conformations that differ slightly in energy. Since we are most interested in the S<sub>N</sub>2 reaction, we focused only on those structures pertinent to the S<sub>N</sub>2 reaction coordinate. As shown in Scheme 2, the reactants, complex, and transition state represented as A, B, and C, respectively, were maintained in an orientation with the C-Cl bond vector perpendicular to the benzene ring. Such an orientation in the transition state presumably allows for overlap of the chlorine

**Scheme 2**

p-orbitals with the  $\pi$ -system in the benzene ring to lower the energy of the system. This orientation was found to be lowest in energy.

The primary purpose for these semiempirical calculations was to determine reasonably accurate structural and spectroscopic data to be used in the RRKM analysis to estimate the energies of activation from the experimental kinetic data. As seen in Table 3 the agreement between the experimental and theoretical frequencies is reasonably good for benzyl chloride, although the high-frequency modes are calculated to be 5–10% too high. It is also useful to determine the surface energetics directly from the calculated AM1 heats of formation. These calculations give a method of comparison for the experiment and give further insight into the details of the energetics. Table 4 shows heats of formation and the corresponding energetics obtained using the AM1 method.

## VI. Discussion

In order to gain an understanding of the intrinsic structure-reactivity relationships in these reactions, we focus on the individual energetic features of the potential surface.

**Effective Activation Energy,  $\Delta E^d$ .** The energy difference between separated reactants and the S<sub>N</sub>2 transition state is the effective activation energy that directly influences the observed kinetics. As seen in Table 1, the rate of identity substitution varies over nearly 3 orders of magnitude for the series of substituted benzyl chlorides studied in this investigation. The corresponding reaction efficiencies range from 0.03% to 8% for X = H and CF<sub>3</sub>, respectively. All of the exchange rates are considerably less than 50% of the collision rate. Since these reactions are all thermo-neutral, efficiencies of 50% would be expected for barrierless potential energy surfaces, assuming the reactions behave statis-

Table 4. Energetics for the Reactions  $\text{Cl}^- + \text{X-C}_6\text{H}_4\text{CH}_2\text{Cl} \rightarrow \text{Cl}^- + \text{X-C}_6\text{H}_4\text{CH}_2^*\text{Cl}$  from AM1 Semiempirical Calculations<sup>a,b</sup>

substituent (X)	$\sigma^c$	$\Delta H^\circ_f$ (kcal mol <sup>-1</sup> )			$\Delta E^w$ (kcal mol <sup>-1</sup> )	$\Delta E^d$ (kcal mol <sup>-1</sup> )
		reactants	ion-molecule complex	S <sub>N</sub> 2 transition state		
<i>p</i> -NH <sub>2</sub>	-0.57	-49.94	-56.17	-42.22	-6.23	+7.72
<i>p</i> -OCH <sub>3</sub>	-0.28	-89.63	-95.69	-82.22	-6.06	+7.41
<i>p</i> -CH <sub>3</sub>	-0.14	-58.11	-64.12	-50.67	-6.00	+7.45
<i>m</i> -CH <sub>3</sub>	-0.06	-57.97	-64.15	-50.42	-6.18	+7.56
H	0	-50.34	-56.22	-42.61	-5.89	+7.72
<i>m</i> -OCH <sub>3</sub>	+0.10	-89.21	-96.10	-82.83	-6.89	+6.38
<i>m</i> -F	+0.34	-96.04	-104.75	-91.39	-8.71	+4.65
<i>m</i> -Cl	+0.37	-57.51	-66.44	-52.92	-8.93	+4.59
<i>m</i> -CF <sub>3</sub>	+0.46	-198.17	-209.93	-196.62	-11.76	+1.56
<i>m</i> -CN	+0.62	-18.93	-28.67	-16.12	-9.74	+2.81
<i>m</i> -NO <sub>2</sub>	+0.71	-34.41	-47.40	-34.56	-12.99	-0.15

<sup>a</sup> Reference 1. <sup>b</sup> All calculations refer to the S<sub>N</sub>2 "backside" complex and a C-Cl bond vector perpendicular to the benzene ring to maximize overlap. <sup>c</sup> Obtained directly from ref 4.

tically. Qualitatively, this implies that there is a substantial energetic barrier that separates reactants from products. Because the identity exchange rates for eq 1 are measurable, however, the energetic barrier cannot extend much above the reaction threshold. Estimates for the activation energies, as measured by  $\Delta E^d$  (the energy difference between the S<sub>N</sub>2 barrier and separated reactants) and obtained from the RRKM analysis described above, are given in Table 1. As expected, the values for  $\Delta E^d$  vary consistently with the observed rate coefficients, spanning a range of just over 5 kcal mol<sup>-1</sup>. Benzyl chloride identity substitution has a barrier that extends just above separated reactants (+0.2 kcal mol<sup>-1</sup>), while the barrier for identity substitution of *m*-(trifluoromethyl)benzyl chloride lies well below separated reactants (-5 kcal mol<sup>-1</sup>). All other substituted benzyl chlorides fall in between.

The identity exchange rates of a few substituted benzyl chlorides have been measured previously. In 1986 as part of a larger study, Dodd and Brauman<sup>112</sup> estimated values for  $\Delta E^d$  based on previous kinetic results. Although the trend in their results is qualitatively correct, the kinetic and energetic results are quantitatively incorrect. Since the significance of the relative results was not addressed in this earlier paper, the conclusions are unaffected. Impurities and a general lack of sensitivity with the earlier experimental setup were likely contributing factors to the lack of agreement with our present results.

Effective activation energies for an extended series of substituents (X), determined by the semiempirical AM1 method, are given in Table 4. As seen in the table, the calculated S<sub>N</sub>2 barrier heights relative to separated reactants ( $\Delta E^d$ ) are approximately 7–8 kcal mol<sup>-1</sup> higher than those predicted from the experimental kinetics, although they vary over a similar range. Given the inadequacies inherent in any semiempirical approach these results are not surprising. The results are, however, consistent relatively when comparing the AM1 calculations with the experimental results. It is with the relative comparisons that the most predictive power lies. For example, based on the available data, we predict that identity substitution rates for substituted benzyl chlorides X = *m*-NO<sub>2</sub> or *m*-CN should be relatively facile, while X = *m*- and *p*-NH<sub>2</sub> should be slow.

Hammett  $\sigma$  constants listed in Tables 1 and 4 can be used to characterize the various substituents and may provide further insights into the intrinsic substituent effects. Because the  $\sigma$  values are determined from the ionization of benzoic acids in water, such a correlation is only applicable to the extent that the effects important in stabilizing the free energy of benzoate ions in solution are similar to those important in influencing the potential energy surfaces of gas-phase S<sub>N</sub>2 reactions. Given in Figure 3 are both the experimental and theoretical effective activation energies plotted against the solution-phase  $\sigma$  constants. As seen in the figure, there is only a general trend;  $\Delta E^d$  decreases as the electron-withdrawing character of the substituent increases. Placing an

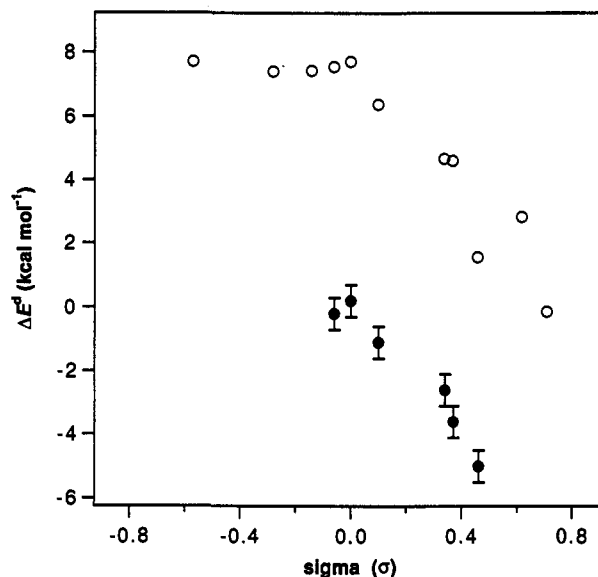


Figure 3. Activation energies relative to separated reactants,  $\Delta E^d$ , for the various substituted benzyl chloride systems as a function of the solution-phase Hammett  $\sigma$  constants. Values were obtained from the application of RRKM to the experimental kinetics (solid circles) and computationally using the AM1 semiempirical method (open circles).

electron-donating substituent on the benzene ring, however, appears to have little or no effect on  $\Delta E^d$ .

**Complexation Energy,  $\Delta E^w$ .** Given in Table 2 are the experimental thermodynamic quantities for formation of the intermediate ion-molecule complexes,  $\text{Cl}^- + \text{X-C}_6\text{H}_4\text{CH}_2\text{Cl} \rightarrow [\text{X-C}_6\text{H}_4\text{CH}_2\text{Cl}\cdot\text{Cl}]^-$ , at 350 K, also defined as the chloride affinity in eq 6. Consistent with the kinetic results, the experimental complexation energies,  $\Delta E^w$ , vary over a considerable range for the set of substituted benzyl chlorides studied here. Benzyl chloride has the smallest well depth ( $\Delta E^w = -13.8$  kcal mol<sup>-1</sup>), while *m*-(trifluoromethyl)benzyl chloride has the largest ( $\Delta E^w = -19.5$  kcal mol<sup>-1</sup>). Such large variation in the observed well depths seems surprising given the similarities of the species involved, but the results clearly show that the substituents have a dramatic effect on the stabilities of the chloride complexes. Because the focus of this investigation is the potential energy surface along the S<sub>N</sub>2 reaction coordinate, the ion-molecule structure of interest is the S<sub>N</sub>2 "backside" structure, where Cl<sup>-</sup> sits opposite the C-Cl bond vector in the substrate. It is possible, however, that other ion-molecule structures of comparable or lower energy exist on the complex hypersurface. Consequently, the experimental equilibrium measurement will reflect the stability of the most stable species,<sup>113</sup> not necessarily the S<sub>N</sub>2 "backside"

(112) Dodd, J. A.; Brauman, J. I. *J. Phys. Chem.* 1986, 90, 3559.

(113) There may be some kinetic barrier to complete equilibration within the ion-molecule complex itself.



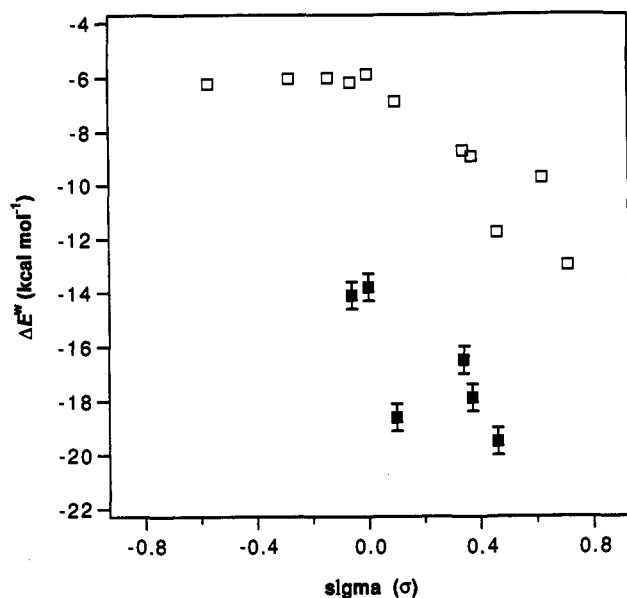


Figure 4. Complexation energies relative to separated reactants,  $\Delta E^w$ , for the various substituted benzyl chloride systems as a function of the solution-phase Hammett  $\sigma$  constants. Values were obtained from direct thermodynamic measurement (solid squares) and computationally using the AM1 semiempirical method (open squares).

structure. This may have consequences for the interpretation of the results and is discussed further below.

The complexation energies ( $\Delta E^w$ ) were also computed directly from the semiempirical AM1 heats of formation data given in Table 4. Similar to the effective activation energies, if we compare the calculated results for the ion-molecule complexation energies ( $\Delta E^w$ ) with those obtained experimentally, the theoretical values are also approximately 7–8 kcal mol<sup>-1</sup> too high (*i.e.* shallow). Once again, however, the relative results appear to be reasonably consistent.

A plot of the experimental and theoretical complexation energies versus the solution-phase Hammett  $\sigma$  constants is given in Figure 4. Analogous to the data presented in Figure 3, there is a general trend in  $\Delta E^w$  for electron-withdrawing substituents. Placing an electron-donating substituent on the benzene ring appears to have little or no effect. These results are surprisingly similar to those found for the effective activation energy discussed above; changing the ring substituent does effect the stability of the ion-molecule complex and S<sub>N</sub>2 transition state in a similar manner.

**Intrinsic Activation Energy,  $\Delta E^*$ .** Although the two experimental observables, rate of substitution which is used to determine  $\Delta E^d$  and thermodynamics of complexation used to determine  $\Delta E^w$ , fully characterize the potential energy surface, the important energetic quantity which describes the reaction is arguably  $\Delta E^*$ , the activation energy as measured from the equilibrium ion-molecule complex ( $\Delta E^* = \Delta E^d - \Delta E^w$ ). Recent experimental and theoretical work on the nature of ion-molecule complexes and the factors influencing their stabilities also suggests this is true. Larson and McMahon<sup>93,114</sup> have carried out extensive experimental studies on complexes involving F<sup>-</sup> and Cl<sup>-</sup>. In comparing the results they concluded that chloride binds with more electrostatic character than does fluoride ion. They also found a strong correlation between the chloride ion binding energy and the gas-phase acidity of the neutral. This suggests that the stability of these complexes is related in some way to the stability of the conjugate base of the neutral. In recent theoretical work Wladkowski *et al.*<sup>68</sup> and Allen and co-workers<sup>115</sup> studied the nature of chloride ion complexes in more detail. Stabilities of complexes

Table 5. Intrinsic Activation Energies,  $\Delta E^*$ , for the Reactions X-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl + Cl<sup>-</sup>

substituents (X)	$\Delta E^* = \Delta E^d - \Delta E^w$	
	AM1	expt
<i>p</i> -NH <sub>2</sub>	13.95	
<i>p</i> -OCH <sub>3</sub>	13.47	
<i>p</i> -CH <sub>3</sub>	13.45	
<i>m</i> -CH <sub>3</sub>	13.74	13.9
H	13.61	14.0
<i>m</i> -OCH <sub>3</sub>	13.27	17.5
<i>m</i> -F	13.36	13.9
<i>m</i> -Cl	13.52	14.3
<i>m</i> -CF <sub>3</sub>	13.32	14.5
<i>m</i> -CN	12.55	
<i>m</i> -NO <sub>2</sub>	12.84	

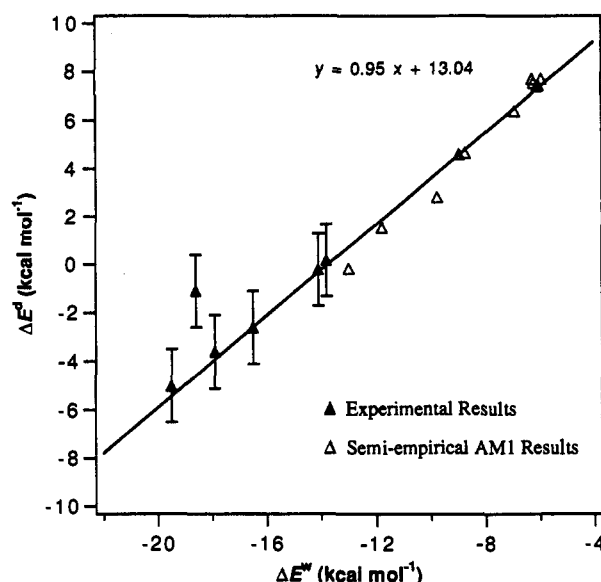


Figure 5. Activation energies relative to separated reactants,  $\Delta E^d$ , as a function of the complexation energies relative to separated reactants,  $\Delta E^w$ , for the various substituted benzyl chloride systems. Values were obtained using experimental data (solid triangles) and computationally using the AM1 semiempirical method (open triangles).

such as [CH<sub>3</sub>Cl·Cl]<sup>-</sup>, [ClCH<sub>2</sub>CN·Cl]<sup>-</sup>, and [FH·Cl]<sup>-</sup> relative to separated reactants could be completely accounted for by electrostatics. In other words, the difference in chloride affinities of the various neutrals is a direct result of the difference in the preexisting electrostatic field of each neutral.

Viewed in this way, the ion-molecule complexes which exist before and after the substitution event can be thought of as non-chemically interacting since little or no electron rearrangement occurs upon their formation. As a result, the important energetic quantity which characterizes the intrinsic substitution process should be the activation energy associated with conversion of one ion-molecule complex to another, at least for chloride substitution reactions. Shown in Table 5 are the intrinsic activation energies for eq 1 obtained from the experimental and theoretical data. With the exception of *m*-OCH<sub>3</sub> the activation energy  $\Delta E^*$  remains constant (13–14 kcal mol<sup>-1</sup>) for all substituents. We can graphically represent both the experimental and theoretical  $\Delta E^*$  data for the system studied here by plotting  $\Delta E^d$  versus  $\Delta E^w$ , since  $\Delta E^d - \Delta E^w = \Delta E^*$ . As can be seen in Figure 5, nearly all of the data fall on a single straight line with slope  $\approx 1$  and intercept +13 kcal mol<sup>-1</sup>. That the experimental and theoretical results produce the same activation energy is certainly encouraging.

Both the transition-state energy and the complexation energy are influenced primarily by the electrostatic stabilization of the substituent. The entire potential energy surface shifts up or down uniformly with no differential effects. Thus, it appears there are

(114) Larson, J. W.; McMahon, T. B. *J. Am. Chem. Soc.* **1985**, *107*, 766.

(115) Klepeis, N. E.; East, A. L.; Caszar, A. G.; Allen, W. D.; Lee, T. J.; Schwenke, D. W. *J. Chem. Phys.* **1993**, *99*, 3865–3897.

no special interactions present in the transition state that can be associated with resonance or other similar electronic effects.

**The  $\alpha$ -Effect.** The data presented here can also tell us something about  $\alpha$ -substituent effects and steric effects in gas-phase  $S_N2$  reactions. We can compare the behavior of the various substituted benzyl chlorides to the extensively studied prototype system, eq 9,<sup>63,68,93,97-100,103,116-123</sup>



This prototype system was also found to have an intrinsic activation energy,  $\Delta E^* \approx 12-14$  kcal mol<sup>-1</sup>. That  $\Delta E^*$  remains constant for the various systems studied here and is the same as the prototype reaction, eq 9, indicates that the magnitude of the  $\alpha$ -effect is modest at best. Interestingly, the  $\alpha$ -cyano-substituted system ( $Cl^- + ClCH_2CN$ ), which was the focus of a recent investigation,<sup>68</sup> was also found to have a comparable intrinsic activation energy,  $\Delta E^* \approx 13$  kcal mol<sup>-1</sup>. In each of these cases, the  $\alpha$ -substituent accelerates the reaction by increasing the complexation energy, reducing the effective barrier to reaction. Because these substituents are electron withdrawing, it is not surprising that the general electrostatic picture would predict an enhanced stabilization. Importantly, both the complex and the transition state are stabilized by these substituents to the same extent.

Shaik has argued that the invariance in the intrinsic activation energy for such  $\alpha$ -substituted alkyl chlorides toward nucleophilic substitution is a result of the balancing of the two opposing factors which contribute to the activation energy. These two factors, which form the basis of the VBCM model, are the initial donor-acceptor gap for the reactants and the localization ability of the reactants. As an electron-withdrawing substituent is placed  $\alpha$  to the reaction center, the initial donor-acceptor gap will be reduced due to a reduction in the electron affinity of the substrate which will tend to lower the activation energy. On the other hand, the slope of the intersecting configuration curves is also expected to be reduced, effectively increasing the activation energy for the reaction. These two factors nearly offset one another exactly in the VBCM model such that the relative activation energies reported by Shaik<sup>13,80</sup> for the identity substitution of  $CH_3Cl$ ,  $ClCH_2CN$ , and  $ClCH_2C_6H_5$  are all within 2 kcal mol<sup>-1</sup> in excellent agreement with the results reported here. Whether or not the VBCM model can account for the observed behavior for other types of  $\alpha$ -substituents, including those characterized as electron donating, remains to be seen. These results, however, are encouraging.

Steric interactions may contribute to the observed behavior. Steric destabilization must occur in the complex as well as in the transition state and thus may not contribute to the gas-phase

activation energy,  $\Delta E^*$ , to the extent that it does in the solution phase. The extent to which steric effects are offsetting electronic effects cannot be fully evaluated without a much wider range of systems. At the moment, the effects do not appear to be major. In short, our current evidence suggests that the  $\alpha$ -effect as generally described<sup>85</sup> is not a significant factor for these reactions.

***m*-OCH<sub>3</sub> Substituent.** *m*-Methoxybenzyl chloride clearly behaves differently from the rest of the compounds studied experimentally. The energy of the transition state is about what might be expected based on the plot in Figure 3, but the complexation energy is unusually large, as indicated in Figure 4. Consequently, the intrinsic activation energy,  $\Delta E^*$ , appears anomalously large as indicated in Table 5 and illustrated in Figure 5. In contrast with the experimental data, the AM1 energetic results for this substituent do not appear anomalous, predicting an intrinsic activation energy very close to the those of the other compounds. The most obvious source of the discrepancy lies in the structure of the complex. If some structure on the global surface for the complex is more stable than the backside complex, the experimental complexation energy will be larger than expected, and the activation energy will not be meaningful in comparison with those of the other substituents. This is the case since the intrinsic activation energy,  $\Delta E^*$ , is referenced only to the  $S_N2$  backside complex. Since the AM1 calculations were restricted to aspects of the  $S_N2$  reaction coordinate, this was not a problem. Using the AM1 method we explored the potential surface of the chloride complex of *m*-methoxybenzyl chloride in search of alternative structures which could account for the experimentally observed behavior. Indeed, we found a number of such structures that were of comparable energy which had the  $Cl^-$  bound to different parts of the neutral, in particular the methoxy group. None of these structures, however, was sufficiently stable to account for the experimental result. As a result we cannot confirm the proposed hypothesis, so we reserve judgment as to the origin of this effect.

## VII. Summary

We find that for the various substituted benzyl chlorides studied in this investigation, the intrinsic activation energy toward identity substitution remains constant despite large variations in the experimental observables. Thus the substituent's ability to stabilize the intermediate ion-molecule complex and the  $S_N2$  transition state is similar and resonance stabilization in the transition state appears to be unimportant. Moreover, given the similarities to other  $\alpha$ -substituted methyl chlorides, this phenomenon may be general. Given these results and what we know to be true about the corresponding substituents effects for  $S_N2$  reaction in solution, it becomes clear that much of the observed behavior for these systems in solution is a direct result of the differential interactions of the solvent molecules. This has been postulated for many years, although it has not been directly quantified. The substituents studied here are not completely representative of all substituents; the generality remains to be demonstrated.

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