

Mass Spectrometric Studies of Organic Ion/Molecule Reactions

Scott Gronert

Department of Chemistry and Biochemistry, San Francisco State University, San Francisco, California 94132

Received April 4, 2000

Contents

I. Introduction	329
II. Nucleophilic Anion Chemistry	330
1. Nucleophilic Substitution	330
A. Potential Energy Surfaces	330
B. Reactivity Trends	334
2. Elimination Reactions	339
3. Addition/Elimination Reactions	340
A. Carbonyl Systems	340
B. Aromatic Systems	342
4. Reductions	343
III. Electrophilic Cation Chemistry	344
1. Electrophilic Aromatic Substitution	344
A. Potential Energy Surfaces	345
B. Reactivity Trends	345
2. S _N 2 and Related Reactions	346
3. Cycloadditions of Cations	348
IV. Reactions of Unusual Ionic Species	350
1. Highly Strained or Reactive Carbanions	350
A. Formation	350
B. Characteristic Reactions	351
2. Distonic Radical Ions	352
A. Distonic Radical Cations	353
B. Distonic Radical Anions	354
3. Fullerene Reactions	355
V. Summary	356
VI. Acknowledgments	356
VII. References	357



Scott Gronert was born in Southern California and received his B.S. degree in Chemistry from the California State University at Long Beach in 1983. He completed his Ph.D. degree in 1987 at the University of California, Berkeley, in the lab of Andrew Streitwieser, Jr., working on the stability and ion-pairing of organolithium salts in THF. His introduction to mass spectrometry came during three years working as a postdoctoral fellow with Drs. Charles DePuy and Veronica Bierbaum at the University of Colorado, Boulder. Gronert joined the faculty at San Francisco State University in 1990. His current research focuses on using mass spectrometry and computational methods to study fundamental organic reaction mechanisms. In addition, his group is using the same techniques to investigate thermochemistry and reaction mechanisms involving peptides and metal/peptide complexes.

unambiguously characterize the intrinsic reactivity of ionic and neutral species. Moreover, comparison of gas phase and condensed phase data provides a powerful means for understanding the role that solvation and ion pairing play in determining the outcomes of ionic reactions.

Since early work with mass spectrometers, it has been recognized that reactions occur readily in these instruments. For example, the development of chemical ionization methods centers on ion/molecule reactions taking place in the source of a mass spectrometer. To study these reactions in more detail under highly controlled conditions, a number of instruments and experimental methods have been developed. These include flow instruments such as selected-ion flow tubes (SIFT) and trapping instruments such as Fourier transform mass spectrometers (FTMS) and quadrupole ion trap mass spectrometers (QITMS), as well as high-pressure mass spectrometers (HPMS). The details of the instrumentation is beyond the scope of this review, but each offers its own advantages and disadvantages in studying ion/molecule reaction chemistry.

Over the past several decades, an immense literature has evolved in the area of ion/molecule chemis-

I. Introduction

Although much of the interest in mass spectrometry is focused on its applications in analytical chemistry, mass spectrometers have proven to be powerful tools for studying the kinetics, mechanisms, and product distributions of gas phase, bimolecular organic reactions. Data from these studies have furthered our fundamental understanding of the reaction chemistry of a wide range of species from simple inorganic ions to exotic, highly reactive organic ions. In fact, mass spectrometry has allowed chemists to uncover mechanistic details that could not be probed by other means. For example, ion chemistry in the condensed phase is often dominated by ion pairing and solvation interactions which can mask the intrinsic reactivity of the reaction partners. In the absence of solvation, gas phase studies can reveal the subtle details of reaction mechanisms and

try, and it would be impractical to attempt to provide a comprehensive review of the field. Ignoring work related to chemical ionization, there still have been well over 1000 papers published in the last 10 years that directly relate to the study of ion/molecule reactions by mass spectrometry. Consequently, the present review will not try to document all the studies in the literature, but it will attempt to provide an overview of areas where mass spectrometry has made a major impact on our understanding of fundamental reactions in organic chemistry. A particular emphasis will be placed on research areas that have led to many studies by multiple research groups. The areas outlined in this review are only a few of the many in which mass spectrometry has played a significant role, and consequently, a number of important studies have not been included. The reader will notice that there is an emphasis on anion chemistry in the review. This is in part due to the fact that reactions of anions and their metal salts play a dominant role in synthetic organic chemistry mainly because carbanions do not undergo the rearrangement reactions so commonly observed in carbocations. As a result, a wider range of analogies to condensed phase reactions are found in gas phase anion chemistry. In general, this review will focus on relatively recent studies (i.e., since 1990) because much of the earlier work has been covered in other literature reviews;¹⁻¹⁷ however, key studies that provide a foundation for more recent work are included. Finally, related fields such as chemical ionization, unimolecular reactions, organometallics, atmospheric chemistry, and the reactions of biomolecules were not included for the sake of brevity. However, mass spectrometry has made important contributions in each.

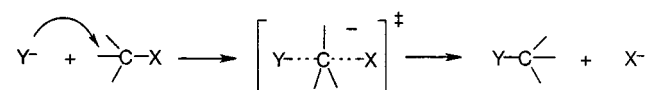
The review is organized in three parts. The first considers the reactions of nucleophilic anions and focuses on S_N2, E2, addition/elimination, and reduction reactions. The S_N2 reaction receives the most extensive treatment and is used to illustrate many of the basic principles of organic ion/molecule reactions. The second part presents studies of electrophilic cations and includes work on electrophilic aromatic substitutions, S_N2 and related reactions, and finally cycloadditions. The third part is devoted to the reactions of novel species including unusual carbanions, distonic radical ions, and fullerene cations.

II. Nucleophilic Anion Chemistry

1. Nucleophilic Substitution

Nucleophilic substitution reactions have played a central role in the development of physical organic chemistry, and it is no surprise that they have been the topic of numerous gas phase studies over the years. In fact, the S_N2 reaction is probably the most widely and thoroughly studied process in all of organic ion/molecule chemistry. From a mechanistic point of view, the S_N2 reaction is deceptively simple. A nucleophile attacks a carbon bearing a good leaving group, the bond to the leaving group breaks as a new bond to the nucleophile is formed, and the substitu-

Scheme 1



tion process is completed. Most often the reaction has been studied with an anionic nucleophile displacing an anionic leaving group, but there are numerous examples of neutral nucleophiles attacking cationic substrates and displacing a neutral leaving group (see section III.2). An example of the former is shown in Scheme 1.

Despite the superficial simplicity, it is a complex process and a number of factors must be considered in studying S_N2 reactions in the gas phase. First, what is the nature of the S_N2 potential energy surface and how do the features of the surface affect physical observables such as reaction rates? Second, how do variations in the nucleophile's and substrate's structure affect the rate of S_N2 reactions in the gas phase? Third, how well do other processes such as elimination compete with the S_N2 reaction? Each of these issues have been investigated in mass spectrometric studies of S_N2 reactions, and the results have provided new insights not only into the mechanism of substitution reactions but also into the fundamental dynamics of ion/molecule reactions. As a result, the S_N2 reaction of anionic nucleophiles is a useful starting point for this review because it illustrates many of the important features of gas phase ion/molecule reactions.

A. Potential Energy Surfaces

In a classic paper from 1977, Olmstead and Brauman¹⁸ presented the "double-well" potential energy surface model to explain the variations in S_N2 rates that they had observed for the reactions of a series of simple anionic nucleophiles with CH₃Cl, CH₃Br, CF₃CO₂CH₃, and CH₃OPh. Almost all the reactions in the study were highly exothermic, but a wide range of rate constants was observed from near the collision controlled limit to too slow to be observed. The results demanded that a barrier exist on the potential energy surface; however, the long-range interaction between an ion and a polar molecule must initially be attractive so there will be a drop in energy before the reaction barrier is reached. The "double-well" potential satisfies both of these requirements. As the reactants approach each other, the potential energy surface drops due to an ion/dipole interaction, and eventually a complex is formed. There is a barrier to the S_N2 process, and as the reaction occurs, the energy rises up to the S_N2 transition state. As the products are formed, they are initially trapped in another complex that is stabilized by an ion/dipole interaction between the substitution product and the anionic leaving group. Separation of the products leads to a final rise in energy as the ion/dipole attraction is lost. An S_N2 potential energy surface for the reaction of chloride with methyl bromide is shown in Figure 1 and is similar to the one presented in Olmstead and Brauman's¹⁸ original paper.

The height of the central barrier in this model controls the magnitude of the observed rate constant.

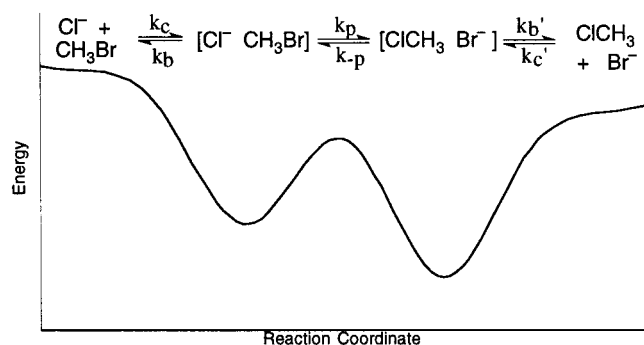
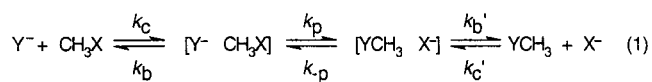


Figure 1. Double-well potential energy surface for the reaction of Cl^- with CH_3Br . Based on Figure 1 in ref 18.

If the barrier is below the energy of the separated reactants, a fast reaction is observed that may reach the collision controlled limit. An interesting aspect of such reactions is that they have negative activation barriers (the transition state is more stable than the separated reactants), and as result, they exhibit negative temperature dependencies. This is common in ion/molecule chemistry, and the rate of the $\text{S}_{\text{N}}2$ reaction of Cl^- with CH_3Br drops off as the temperature is raised in a high-pressure mass spectrometer.^{19,20} However, if the central barrier is close to or above the energy of the separated reactants, there will be competition between crossing the central barrier and simply backing out through the entrance channel (complex dissociation) to yield the reactants (i.e., nonproductive collision). In the absence of collisions with a bath gas, these are the only options for the complex because it retains all the energy from the ion/dipole attraction and therefore dissociation is always an energetically accessible possibility. If the initial complex is long-lived, there is a chance that collisions with a bath gas could remove the excess energy and lead to a stable adduct product (emission of a photon, i.e., radiative stabilization, is also a possibility in some cases). Collisional stabilization is most likely in instruments that operate with moderate background pressures such as flowing afterglows (~ 0.5 Torr), high-pressure mass spectrometers (~ 5 Torr), and quadrupole ion traps (~ 0.001 Torr), but not in ion cyclotron resonance spectrometers ($\sim 10^{-8}$ Torr). With respect to the $\text{S}_{\text{N}}2$ reaction, Brauman presented reasonable arguments that recrossing the barrier is unlikely so he could assume that k_{-p} in eq 1 is negligible. This assumption leads to a simple expression for the observed rate constant (eq 2). In this analysis, the overall rate is dependent on two important factors, the complexation rate (k_c) and the partitioning of the complex between dissociation (k_b) and central barrier crossing (k_p).



$$k' = k_c \frac{k_p}{k_b + k_p} \quad (2)$$

Brauman deftly pointed out that it is not only the height of the central barrier that matters in determining k_p but that entropic constraints at the $\text{S}_{\text{N}}2$

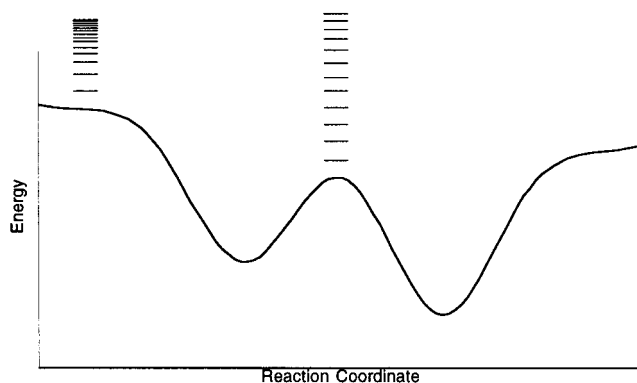


Figure 2. Graphical representation of the internal energy spacings for gas phase $\text{S}_{\text{N}}2$ reactions. Based on Figure 2 in ref 18.

transition state can play a major role. This is critical because the species involved in the competing processes are structurally very different. The $\text{S}_{\text{N}}2$ transition state is highly organized and requires a very specific orientation of the nucleophile and the leaving group, whereas the ion/molecule capture transition state is simply a loose complex of the nucleophile and the substrate with many low-energy degrees of freedom in its internal motions. The net result is that the internal energy levels are much more tightly spaced for the dissociation process than for the $\text{S}_{\text{N}}2$ process. In alternative terminology, it could be stated that there is greater phase space available on the dissociation pathway than on the $\text{S}_{\text{N}}2$ pathway. This is graphically illustrated in Figure 2. The important point is that even if the central barrier is lower in energy than the reactants, it can be more likely for the collision complex to dissociate back to the separated reactants because this process is entropically more favorable (i.e., greater number of states accessible at a given internal energy).

With the double-well potential model in hand, the next step is correlating the observed bimolecular reaction rates with the features of the surface, specifically the height of the central barrier. Olmstead and Brauman¹⁸ originally presented an analysis based on RRKM theory. Here the assumption is that when the initial ion/dipole complex is formed, the complexation energy is randomly distributed throughout the internal modes of the complex. That requires that the complex have a long enough lifetime to allow for complete energy randomization. If this is true, then the intermediate can be treated as an activated complex with two available reaction modes: dissociation back to the separated reactants or conversion to the $\text{S}_{\text{N}}2$ substitution products. The partitioning between these pathways would then be dependent on the number of accessible states available on each one at a given internal energy. Olmstead and Brauman used RRKM theory to count the number of accessible states at each transition state (dissociation and $\text{S}_{\text{N}}2$) using simple models to estimate the energetics of the internal modes (e.g., vibrational frequencies, rotational constants, etc.). With this approach, it was possible to estimate the energy of the $\text{S}_{\text{N}}2$ transition state relative to the energy of the separated reactants. Moreover, other mass spectrometry work has led to the measurement

of the complexation energies of representative nucleophiles with simple alkyl halides.^{19–23} For example, McMahon and co-workers²⁰ have determined that the initial well depth is 12.5 kcal/mol in the $\text{Cl}^-/\text{CH}_3\text{Br}$ system. In addition, Johnson has reported spectroscopic data on sample $\text{S}_{\text{N}}2$ ion/molecule complexes.²⁴ These data, combined with transition state energies determined from the RRKM analysis of kinetic data, fundamentally provide all the information needed to quantitatively derive double-well potential energy surfaces for simple $\text{S}_{\text{N}}2$ reactions. However, the assumption that energy is completely randomized in the initial ion/dipole complexes has been questioned in several recent studies, and it appears that some $\text{S}_{\text{N}}2$ reactions do not behave statistically and therefore statistical models such as RRKM cannot be applied to extract information about the potential energy surface in a quantitative manner.

During the 1990s, the question of statistical behavior in $\text{S}_{\text{N}}2$ reactions led to numerous studies employing a remarkable array of approaches across the full spectrum of mass spectrometric techniques and theoretical modeling methods. One of the first major indications that gas phase $\text{S}_{\text{N}}2$ reactions may not behave statistically came from theoretical simulations of the reactions of halides with methyl halides. Hase and co-workers^{25–31} found that energy transfer within the initial ion/dipole complex was relatively slow so that the complexation energy was mainly trapped in intermolecular modes rather than intramolecular modes. In this case, intermolecular modes are defined as those associated with motion of the halide relative to the methyl halide, whereas intramolecular modes are associated with motions within the methyl halide. For the reaction to occur, energy must be deposited in the intramolecular modes, and this process can represent a dynamic bottleneck on the reaction path. When energy remains in the intermolecular modes, the system is predisposed to dissociation back to the reactants. As a result, the ion/dipole intermediates have shorter lifetimes than predicted by statistical theories, and the rates of reaction are heavily influenced by the efficiency of energy transfer from intermolecular modes to intramolecular modes. The inefficiency of the energy transfer within the complex can be traced to a mismatch between the frequencies associated with the intermolecular modes and those associated with the intramolecular modes of the methyl halide. Another outcome of this analysis is that barrier recrossing can be a common occurrence. Once energy has been transferred into the intramolecular modes, the system can move back and forth across the barrier until sufficient energy is again transferred back into the intermolecular modes and dissociation is possible. Finally, the simulations suggest that it is possible for the system to react in a direct mechanism where the $\text{S}_{\text{N}}2$ transition state is reached without the intermediacy of an ion/dipole complex. In these cases the incoming trajectory is appropriate for the backside attack of the $\text{S}_{\text{N}}2$ mechanism, but not for the formation of a complex. As a result, reaction is possible along these trajectories, but not

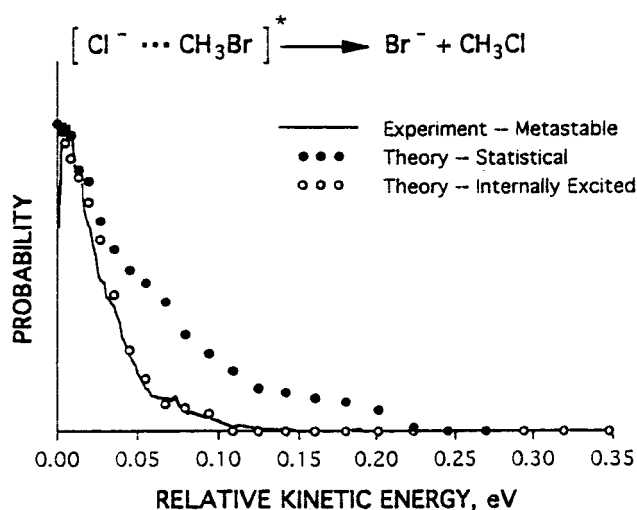


Figure 3. Kinetic energy release distributions for $\text{Cl}^- (\text{CH}_3\text{Br}) \rightarrow \text{Br}^- + \text{CH}_3\text{Cl}$ determined by Graul and Bowers.⁴³ Solid line is experimental data, and points are distributions calculated with phase space theory. Closed circles assume statistical distribution of energy, and open circles correspond to predicted distributions if vibrationally excited methyl chloride is formed as the product. Reprinted with permission from ref 43. Copyright 1994 American Chemical Society.

complex formation. Over the years, Hase and co-workers^{26–41} have developed more detailed models of halide/alkyl halide reactions and investigated other aspects of the reactions such as energy and temperature dependencies.

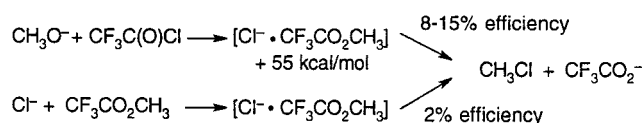
Several experimental approaches have been used to probe whether $\text{S}_{\text{N}}2$ reactions can be treated by statistical models. Graul, Bowers, and co-workers^{42–44} have investigated the relative kinetic energy release distributions (KERD) in the products of $\text{S}_{\text{N}}2$ reactions. Initially, the reaction of Cl^- with CH_3Br was studied by forming the collision complex, $[\text{Cl}^- \text{CH}_3\text{Br}]$, as a transient species and monitoring its metastable decay. The observed kinetic release distribution could not be fit by phase space theory, a statistical model. The data suggests that the reaction exothermicity is preferentially trapped in the internal modes of the product, CH_3Cl , and therefore not randomly distributed in the product complex. For example, a representation of the kinetic energy release spectrum for the reaction of chloride with methyl bromide is given in Figure 3. It can be seen that when Graul and Bowers treated the system with a statistical model, a poor fit is obtained unless a term for internal product excitation is included. Work with other systems including more complex substrates such as methyl trifluoroacetate and methyl phenyl ether indicates that this is a general phenomena in gas phase $\text{S}_{\text{N}}2$ reactions and the KERD's only fit a statistical model if one allows some of the reaction exothermicity to be trapped in the internal modes of the product and not be available for randomization into other modes.⁴⁴ The statistical modeling studies indicate that the amount of energy trapped in the internal excitation of the product correlates with the overall exothermicity of the $\text{S}_{\text{N}}2$ reaction rather than the size of the system (i.e., number of degrees of freedom in the complexes).

Graul et al.⁴⁴ also calculated the lifetime of the product complexes in S_N2 reactions using phase space theory. The lifetimes are predicted to be very short (10^{-10} to 10^{-12} s), so it is not surprising that the reaction energy cannot be completely randomized before the product complex dissociates.

Work by Viggiano and co-workers in a variable-temperature, selected-ion flow drift tube apparatus has provided a wealth of data on the temperature and kinetic energy dependencies of gas phase S_N2 reactions.^{45–48} Of course, if reactions behave statistically, the rates should depend on the total internal energy of the system, independent of whether the energy originates from thermal or translational excitation of one or both of the reactants. Conversely, if energy randomization is incomplete, different rate profiles should emerge for translational vs thermal excitations of the system. Their data for the reaction of Cl^- with CH_3Br indicate that for a given collision energy, $\langle KE_{cm} \rangle$, the rate constants do not show a temperature dependence.⁴⁶ This implies that thermal excitation of the internal modes of the methyl bromide does not affect the overall rate constant and is consistent with a nonstatistical system where energy transfer between intramolecular and intermolecular modes is inefficient. Wang and Hase³³ later applied a statistical model to this system and showed that it was unable to reproduce the experimental rate dependence on either the relative kinetic energy or the temperature of this system, providing further support for the belief that simple S_N2 reactions behave nonstatistically in the gas phase. However, Viggiano and co-workers found that when the initial ion/molecule complex in this S_N2 reaction is formed by an endothermic ligand switching reaction, $[Cl^- \cdot H_2O] + CH_3Br \Rightarrow [Cl^- \cdot CH_3Br] + H_2O$, its thermal decomposition profiles can be matched by statistical models. Complexes formed in this way will have much longer lifetimes than those formed directly in the S_N2 reaction of $Cl^- + CH_3Br$, and therefore the possibility of complete energy randomization and statistical behavior is greatly enhanced.⁴⁸ In collaboration with Brauman's group, Viggiano⁴⁷ has also studied the identity S_N2 reaction of chloride with chloroacetonitrile. In this case, an RRKM statistical model can reproduce the temperature and kinetic energy dependence of the rate. The lifetime of the complex formed in this reaction is much longer than in simple halide/methyl halide S_N2 reactions, so there is a greater opportunity for energy transfer and the establishment of a statistical energy distribution. Morris and Viggiano⁴⁹ also found that large substrates such as CF_3Br and CF_3I appear to give S_N2 reactions with F^- that behave statistically. In addition, these reactions give a large amount of association products, suggesting long-lived ion/molecule complexes.

Brauman and co-workers have continued to study the features of the S_N2 potential energy surface both experimentally and theoretically.^{47,50–56} Craig, Zhong, and Brauman⁵⁵ applied a clever approach to probe the energy dependence of the rate constant of the reaction of chloride with methyl trifluoroacetate. They used two reactions that led to the formation of

Scheme 2



the same ion/molecule complex, $[Cl^- \cdot CF_3CO_2CH_3]$, but with very different internal energies (Scheme 2). The first was the simple S_N2 reaction of Cl^- with $CF_3CO_2CH_3$ which led to this ion/molecule complex on the way to S_N2 products. The second began with the reaction of CH_3O^- with $CF_3C(O)Cl$ which leads to the same complex via a very exothermic nucleophilic acyl substitution reaction (section II.3.A). It was estimated that the latter reaction produced the ion/molecule complex with approximately 55 kcal/mol of additional internal energy. In doing this, they found that the observed reaction efficiencies are not compatible with an RRKM analysis and suggested that the lifetime of the intermediate, $[Cl^- \cdot CF_3CO_2CH_3]$, formed in the reaction with $CF_3C(O)Cl$ is too short for a statistical redistribution of the energy. Specifically, the efficiency of the reaction starting from $CF_3C(O)Cl$ is higher than expected based on the statistical model, and it was argued that this is a result of a disproportionate amount of the reaction enthalpy being trapped in the internal modes (i.e., intramolecular modes) of $CF_3CO_2CH_3$ thus activating it toward the S_N2 process. This interpretation is consistent with Graul et al.'s⁴⁴ analysis of the KERD data for the metastable decay of related complexes.

Grimsrud and co-workers^{57–60} have used high-pressure and ion mobility mass spectrometry to study S_N2 reactions over a very wide bath gas pressure range (3–1100 Torr). At high pressures, there is the possibility that the initial ion/molecule complex on the S_N2 pathway could come into thermal equilibrium with the bath gas (high-pressure limit). In other words, the collision rate with the bath gas could become larger than the rates of any of the processes leading to the destruction of the complex (i.e., dissociation or barrier crossing). In this regime, one might expect statistical behavior in the S_N2 reaction because energy could be easily exchanged and redistributed by multiple collisions with the bath gas prior to reaction. Rate increases are observed with increasing pressure in the reaction of Cl^- with CH_3Br , and it does not appear that this system has reached the high-pressure limit at bath gas pressures as high as 1100 Torr. This is consistent with calculations of the estimated lifetime of the ion/molecule complex in this reaction.³¹ However, more complex substrates such as CH_3CH_2Br and $CH_3CH_2CH_2CH_2Br$ should have longer lifetimes for their ion/molecule complexes, and they appear to have reached the high-pressure limit in their reactions with Cl^- at bath gas pressures as low as 3 Torr.

Another tactic for measuring the activation energies for S_N2 reactions is to measure rates as a function of temperature, and Li et al.²⁰ have employed a high-pressure mass spectrometer not only to determine activation energies in S_N2 reactions but also to determine complexation energies. With this information in hand, they have been able to develop

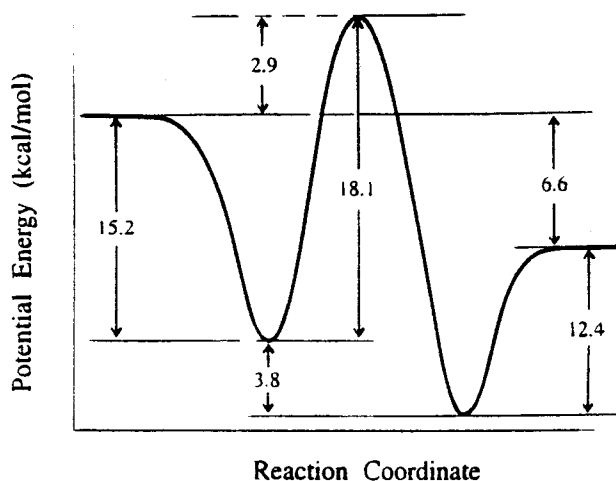


Figure 4. Potential energy diagram for the S_N2 reaction of chloride with isopropyl bromide derived from high-pressure mass spectrometry experiments by Li et al.²⁰ Reprinted with permission from ref 20. Copyright 1996 American Chemical Society.

quantitative double-well potential energy surfaces for several reactions. An example for the reaction of chloride with isopropyl bromide is presented in Figure 4. In this case, the central barrier is above the energy of the reactants, and a relatively slow reaction with a normal temperature dependence is observed. They also examined rate constants for the collisional stabilization of the initial complex in the S_N2 reaction of chloride with methyl chloride. The data suggest a very short lifetime ($\sim 10^{-11}$ s) which is in accord with theoretical work from Hase.^{27,29,30}

Overall, the "double-well" potential has proven to be a valuable and robust model for interpreting gas phase S_N2 reactions. It appears that statistical analyses of rates with this model are not valid in small systems such as the simple halide/methyl halide reactions. However, in larger systems, such as the reaction of chloride with chloroacetonitrile, the ion/dipole complexes have longer lifetimes and seem to be adequately described by statistical models.

B. Reactivity Trends

Mass spectrometry has proven to be an excellent tool for exploring intrinsic reactivity patterns in S_N2 reactions. Over the years, many studies have examined the effect of the nucleophile and the substrate structure on the rates of S_N2 reactions. In addition, competition with other processes such as elimination reactions has been examined by mass spectrometry.

i. Nucleophile. In studying the effect of the nucleophile on S_N2 rates, the best substrates usually are methyl halides because they are not capable of competing reactions such as eliminations (see below). A number of workers, including Brauman's^{18,61-66} and Bohme's^{67,68} groups, have studied rate effects with the simple halides, but the most comprehensive data set come from flowing afterglow studies in DePuy's lab.⁶⁹

In Table 1, rate constants and S_N2 efficiencies are listed for the reactions of methyl chloride with 24 nucleophiles. The reaction efficiency is defined as the ratio of the observed rate constant to the estimated

Table 1. Rate Constants and Efficiencies for Reactions with Methyl Chloride^a

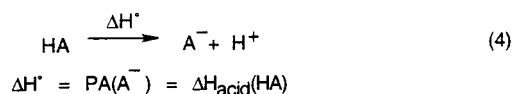
nucleophile	PA (kcal/mol) ^b	rate ^c	efficiency
NH ₂ ⁻	404	15 ^d	0.63
CH ₃ NH ⁻	403	17 ^d	0.85
Ph ⁻	402	8.7 ^g	0.54
H ⁻	400	30 ^d	0.35
HO ⁻	391	20	0.84
CH ₃ SCH ₂ ⁻	390	3.0 ^e	0.19
CH ₂ CHCH ₂ ⁻	389	2.9 ^f	0.17
O ⁻	382	17 ^g	0.71
CH ₃ O ⁻	382	13	0.65
PhCH ₂ ⁻	381	0.15 ^g	0.01
Ph ₂ C ⁻	381 ^b	0.3 ^h	0.025
HCC ⁻	378	1.3 ^d	0.062
CF ₃ ⁻	377	0.56 ⁱ	0.035
(CH ₃) ₃ CO ⁻	374	1.6 ^j	0.1
F ⁻	371	13	0.56
DO ⁻ (D ₂ O)	364	3.6	0.2
CF ₃ CH ₂ O ⁻	362	2.2	0.15
CH ₃ S ⁻	358	1.1 ^d	0.065
H ₂ NS ⁻	357	1.5	0.085
O ₂ ⁻	356	7.4 ^k	0.39
C ₂ F ₅ CH ₂ O ⁻	355	1.0	0.080
HS ⁻	351	0.12	0.006
S ⁻	351	0.3 ^l	0.016
Cl ⁻	333	0.00035 ^m	0.00002

^a Data from ref 69 unless noted otherwise. ^b Proton affinity data from ref 70. ^c Rates in units of 10^{-10} cm³/molecule/s. ^d Reference 67. ^e Reference 71. ^f Reference 73. ^g Reference 68. ^h Reference 72. ⁱ Reference 74. ^j Reference 62. ^k Reference 75. ^l Reference 76. ^m Reference 77.

collision rate constant calculated by ADO theory (eq 3).⁷⁸

$$\text{Efficiency} = \frac{k_{\text{observed}}}{k_{\text{ADO}}} \quad (3)$$

The collision rate is based on the physical properties of the reaction partners and varies considerably with changes in the dipole, polarizability, and mass of the substrate, so often it is more useful to analyze the data in terms of efficiency (i.e., fraction of collisions leading to products) rather than in terms of absolute rate constants. The data are from several labs and were obtained on flowing afterglow (FA) and ion cyclotron resonance (ICR) mass spectrometers. It has been noted that rate constants from early ICR studies were often lower than those from FA studies, probably because the ions in the ICR were not completely thermalized before the reaction.⁹ For this reason, FA values have been listed in the table when available. In analyzing the data, it is useful to have a measure of the basicity of the nucleophile, and values of proton affinities (PA) are included in the table (eq 4).



Some obvious trends are evident in the data: (1) Nucleophiles with very high proton affinities (PA) tend to have efficiencies that approach the collision controlled limit (i.e., 1.00). For example, the nucleophiles with PA's greater than 390 kcal/mol have efficiencies ranging from 0.35 to 0.85, meaning that

at least one in three collisions leads to products. DePuy⁶⁹ has argued that although the efficiencies do not reach 100% in these cases, this does not mean that the central barrier is controlling the rate. It may imply that some collisions lead to complexes whose lifetimes are too short to explore the reaction surface associated with the S_N2 process (i.e., nonstatistical behavior). This interpretation is supported by Hase's²⁷⁻²⁹ modeling of S_N2 reaction dynamics and variable energy studies by Viggiano and co-workers^{45,46,49} (see above). As a result, reactions with very high efficiencies give little information about the S_N2 potential energy surface other than that the barrier is below the energy of the reactants. (2) There is a rough correlation between the nucleophile's PA and the S_N2 efficiency (larger PA's lead to higher efficiencies); however, the correlation is far from perfect and numerous exceptions exist, many of which can easily be rationalized. For example, acetylide is less basic than the benzyl anion, but it is over 50 times more reactive with methyl chloride. Charge delocalization in the benzyl anion is a likely explanation for its lower reactivity.⁶⁸ (3) Steric hindrance plays a role in gas phase S_N2 reactions as evidenced by the fact that the bulky *tert*-butoxide anion is much less efficient in its reaction with methyl chloride than fluoride despite the fact that *tert*-butoxide is a stronger base. (4) It appears that carbon-centered nucleophiles are less reactive than nucleophiles of similar basicity that involve more electronegative reaction centers. For example, CF₃⁻ and HCC⁻ are considerably more basic than CF₃CH₂O⁻ or F⁻, but both of the carbon-centered nucleophiles give slower reactions with CH₃Cl. This is likely related to the fact that smaller, more electronegative centers have higher charge densities (i.e., more compact lone pairs). (5) Although it is widely accepted that in condensed phase S_N2 reactions third-period elements such as sulfur tend to be more reactive than analogous elements from the second period (i.e., oxygen), there is no evidence for this behavior in the gas phase. For example, CH₃S⁻, H₂NS⁻, and CF₃CF₂-CH₂O⁻ have similar gas phase PA's and roughly equivalent efficiencies in their reactions with CH₃-Cl. This is in stark contrast to data obtained in ethanol solutions where thiolates are about 500 times more reactive than alkoxides in S_N2 reactions.⁷⁹ Obviously, the enhanced nucleophilic reactivity of third-period elements is a condensed phase phenomenon probably related to the fact that they form weaker hydrogen bonds in solution, and therefore the cost of desolvation is smaller in reaching the S_N2 transition state. (6) In general, radical anions do not exhibit unusual reactivity. For example, the radical anions of S, O, and Ph₂C exhibit reactivities which seem to match their PA's. However, the radical anion of O₂ is a special case, and it is exceptionally reactive given its low PA.

In Table 1, one sees nearly the full range of rates that effectively can be determined by mass spectrometry. As noted above, the most basic nucleophiles give rates near the collision controlled limit ($\sim 2 \times 10^{-9}$ cm³/molecule/s). At the other extreme is the isotope exchange reaction of chloride with methyl chloride

which is near the limit for the slowest ion/molecule reactions that can be characterized. In 1988, Barlow, Van Doren, and Bierbaum⁷⁷ employed a flowing afterglow and obtained a rate constant of 3.5×10^{-14} cm³/molecule/s for this reaction. More recently, Ervin⁸⁰ and co-workers have also studied this reaction as a function of energy in a guided ion beam mass spectrometer. The lower limit on measurable reaction rates in ion/molecule chemistry is imposed by two important factors. First, the instruments used in these studies have practical limits on their ion residence times and reagent gas pressures that combine to set the lower limit on rate constants that can be measured accurately. Although the individual parameters (residence times and reagent pressures) vary considerably among the commonly used instruments, they balance to give fairly similar lower limits for each of the experimental approaches. For example, ion residence times are several orders of magnitude longer in an ICR (~ 10 s) than in a flowing afterglow (~ 10 ms), but flowing afterglows can employ reagent gas pressures ($\sim 10^{-2}$ Torr) that are several orders of magnitude higher than an ICR ($\sim 10^{-5}$ Torr). Second, the purity of the reagent gas becomes a problem when slow rates are measured because a small amount of a highly reactive impurity could be responsible for the observed reaction. For example, in the reaction of chloride with methyl chloride, one successful reaction occurs in about every 50 000 collisions; therefore, to be sure that at least 90% of the reactivity is from the methyl chloride, the concentration of a reactive impurity (one that reacts at every collision such as HCl) must be less than 2 ppm (1/500 000). For slower reactions, even greater demands are placed on the purity of the reagent, and therefore this can also represent a practical limit on the range of rate constants that can be measured by mass spectrometry. In the end, a dynamic range of about 10⁴ to 10⁵ is generally accessible in ion/molecule reactions. This is considerably smaller than the range available in condensed phase work, and so gas phase studies are restricted to smaller reactivity variations.

To analyze the trends in gas phase S_N2 reactivity, Brauman and co-workers^{61-64,66} have employed the Marcus equation.⁸¹ In its application to the double-well potential model, Dodd and Brauman^{63,64} redefined the terms in the Marcus equation in the following way

$$\Delta E^{\text{d}} = \Delta E_0^{\text{d}} + \frac{\Delta E^{\circ}}{2} + \frac{(\Delta E^{\circ})^2}{16(\Delta E_0^{\text{d}} - \Delta E^{\text{w}})} \quad (5)$$

where ΔE^{d} is the transition state energy (relative to the separated reactants), ΔE_0^{d} is the intrinsic activation energy (i.e., activation energy in the absence of a thermodynamic driving force), ΔE° is the overall reaction energy, and ΔE^{w} is the energy change in forming the initial ion/dipole complex. The intrinsic activation energy, ΔE_0^{d} , for nucleophile/leaving group combinations can be obtained by studying identity reactions. The well depth, ΔE^{w} , can be obtained experimentally and the transition state energy, ΔE^{d} , can be estimated from the observed rate

constant by applying statistical theories (assuming that the system behaves statistically, see above). Wladkowski and Brauman⁶⁶ have applied this approach to the reactions of benzyl and cyanomethyl halide systems. An advantage of these substrates is that the thermoneutral, identity reactions of the chlorides and bromides have rate constants in a range where reliable measurements can be obtained. They have found that the bromide/alkyl bromide reactions have lower intrinsic activation energies, ΔE_0^d , than the chloride/alkyl chloride systems. When eq 5 is applied to the cross reactions (i.e., chloride/alkyl bromide), the values for ΔE_0^d are close to the average of the ΔE_0^d values obtained for the bromide and chloride identity reactions. For example, ΔE_0^d values of +0.4 and -2.5 kcal/mol are obtained for the reactions of $^{37}\text{Cl}^-$ with $\text{C}_6\text{H}_5\text{CH}_2^{35}\text{Cl}$ and $^{81}\text{Br}^-$ with $\text{C}_6\text{H}_5\text{CH}_2^{79}\text{Br}$, respectively, whereas a value of -0.8 kcal/mol is obtained from eq 5 for Cl^- with $\text{C}_6\text{H}_5\text{CH}_2\text{-Br}$. It was also observed that the intrinsic activation energies were lower for the cyanomethyl systems than for the benzyl systems by about 5 kcal/mol. This difference is very close to the difference in the complexation energies, ΔE^w , indicating that the stabilizing effect of substituents (i.e., cyano vs phenyl) on the ion/dipole complex and the transition state are similar, probably because both are dominated by electrostatic effects. Wladkowski, Wilbur, and Brauman⁶⁵ have suggested that this could be a general result and that substituents might affect $\text{S}_{\text{N}}2$ rates by pulling down the whole surface (i.e., ion/dipole complex and transition state) rather than reducing the $\text{S}_{\text{N}}2$ barrier relative to the ion/dipole complex.

ii. Substrate. Studying the effects of substrate structure on gas phase $\text{S}_{\text{N}}2$ rates has been limited because, for many cases, there is the possibility of competition between $\text{S}_{\text{N}}2$ and E2 processes. Unfortunately, it is usually difficult to distinguish between these two types of reactions because they generally give the same ionic product. This competition is discussed in detail in the next section. To avoid this complication, one can focus on systems that are limited to $\text{S}_{\text{N}}2$ products (either for structural or thermodynamic reasons). For example, the reactions of chloride with alkyl bromides should give only $\text{S}_{\text{N}}2$ reactions because the E2 channel is endothermic. Three groups^{19,20,60} have investigated these systems at variable temperatures in high-pressure mass spectrometers. There is some variation in the data, but the general order of reactivity is the same from each group. The enthalpy and entropy of activation of some of these reactions were reported most recently by McMahan's group²⁰ and are given in Table 2. The data indicates the following order of reactivity for simple alkyl bromides with Cl^- : methyl > *n*-propyl > ethyl > isopropyl. This order of reactivity is not surprising and fits the expectation that alkyl substitution at the α -carbon reduces $\text{S}_{\text{N}}2$ rates. Ethyl halides are generally more reactive than propyl halides in solution, but there are computational data that indicate that alkyl substituents at the β -carbon can reduce $\text{S}_{\text{N}}2$ barriers in the gas phase.⁸² Moreover, DePuy and co-workers⁶⁹ found that in a flowing afterglow, *n*-propyl bromide is more reactive than

Table 2. Experimentally Measured Energetics for the Reactions of Chloride with Alkyl Bromides^a

substrate	well 1 ^b		TS ^b		well 2 ^c	
	ΔH^p	ΔS^p	$\Delta H^{p\dagger}$	$\Delta S^{p\dagger}$	ΔH^p	ΔS^p
methyl	-12.5		-1.8	-24.1	-10.9	-20.3
ethyl	-13.6	-22.4	-0.7	-22.7	-11.2	-19.6
<i>n</i> -propyl	-14.2	-20.0	-1.3	-24.0	-12.1	-20.6
isopropyl	-15.2	-22.4	2.9	-20.0	-12.4	-20.6

^a Values in kcal/mol and eu. Data from ref 20. ^b Relative to the entrance channel (i.e., reactants). ^c Relative to the exit channel (i.e., products).

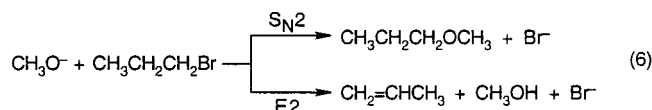
Table 3. Efficiencies Obtained for Reactions of Nucleophiles with Substituted Methyl Chlorides in a Flowing Afterglow^a

substrate	H_2NS^- efficiency	HS^- efficiency	KI/acetone relative rate ^b
CH_3Cl	0.085	0.006	1
$\text{CH}_2=\text{CHCH}_2\text{Cl}$	0.38	0.0072	0.35
$\text{CH}_3\text{OCH}_2\text{Cl}$	0.63	0.21	5
$\text{CH}_3\text{C}(\text{O})\text{CH}_2\text{Cl}$	0.88	0.6	131
NCCH_2Cl	0.96	0.6	11

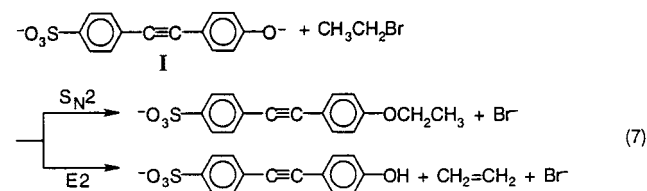
^a Data from ref 69. ^b Data derived from refs 79 and 83.

ethyl bromide in gas phase reactions with chloride ions. There are probably two factors that contribute to the differing effects of β -substituents in the gas phase and condensed phase. First, in a low dielectric medium (i.e., gas phase), polarizability is more important and the additional group at the β -carbon can stabilize the transition state in this way. Second, nucleophiles in the condensed phase are generally solvated, and as a result, they are effectively larger and more sensitive to long-range steric effects. DePuy⁶⁹ also examined the reactions of a series of substituted methyl chlorides that are structurally limited to $\text{S}_{\text{N}}2$ reactions (Table 3). The data with HS^- as the nucleophile are the most useful because the rate constants are lower, and therefore the data best reflect effects related to the $\text{S}_{\text{N}}2$ barrier. Condensed phase data for the relative reactivity of these substrates with iodide in acetone are also included in Table 3. The most important conclusion from these data is that polar substituents such as methoxy, acetyl, and cyano significantly increase the gas phase $\text{S}_{\text{N}}2$ rate probably by electrostatically stabilizing the charged species on the $\text{S}_{\text{N}}2$ potential energy surface. Predictably, the vinyl substituent has a much smaller effect in enhancing the $\text{S}_{\text{N}}2$ rate. There is only a rough correlation between the gas phase data and that from solution, but it is known that these condensed phase substituent effects are dependent on the solvent and nucleophile so variations are expected.⁷⁹ Wladkowski, Wilbur, and Brauman⁶⁵ have studied the reactions of a series of meta and para substituted benzyl chlorides with chloride ions. They found that the derived activation energies give a moderate correlation with Hammett σ values. Moreover, the study showed that there was nearly a one-to-one correspondence between the effect of the substituent on the transition state energy and the effect on the ion/dipole complexation energy. As a result, all these $\text{S}_{\text{N}}2$ reactions have nearly the same barrier height relative to the ion/dipole complex.

iii. Competition with Elimination and Other Processes. As noted above, one problem in studying gas phase S_N2 reactions is the possibility of competition with other processes such as E2 eliminations. In addition, there is the possibility that the substrate or nucleophile could have more than one site capable of an S_N2 reaction. A major difficulty in these situations is that these competing processes can lead to the same ionic product, and therefore mass spectrometry cannot distinguish between the pathways. For example, in the reaction of propyl bromide with methoxide, both the S_N2 and E2 reactions lead to the formation of bromide ions (eq 6) as the only ionic products.



To deal with this complication, several approaches have been adopted. An obvious solution to the problem would be to collect the neutral products of the reaction and identify the mechanism on the basis of their structure. Unfortunately, this is a very difficult analytical problem because these gas phase studies require a huge excess of the neutral reagent (i.e., $\text{CH}_3\text{CH}_2\text{CH}_2\text{Br}$ in eq 6) to obtain rates in a useable range. As a result, the concentration of the neutral products is very small relative to the unreacted starting material. However, Jones and Ellison⁸⁴ have successfully applied this approach to the reaction of CH_3O^- with propyl bromide by placing a coldfinger in the helium path of a flowing afterglow, and within their detection limits, they observed only elimination products. Lieder and Brauman⁸⁵ have photoionized the products of the reaction of fluoride with ethyl chloride and observed the S_N2 product, $\text{CH}_3\text{CH}_2\text{F}$. Although neutral analysis was successful in these cases, the approach has not proven to be a general method for analyzing product mixtures. Recently, Flores and Gronert⁸⁶ developed a novel approach for identifying the products of the gas phase reactions of nucleophiles with alkyl halides. They employed a doubly charged nucleophile where one anionic site is nucleophilic and the other is unreactive. This type of dianion nucleophile would be difficult to form by conventional ionization sources (i.e., electron impact) but is readily produced by electrospray ionization (ESI). With this nucleophile, reactions with alkyl halides produce two charged products: the halide ion as well as the alkylated (S_N2) or protonated (E2) nucleophile. In this way, the two mechanisms can easily be distinguished. An example involving a phenolate nucleophile is shown in eq 7.



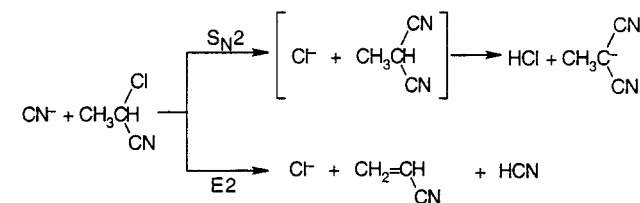
Data for the reactions of this nucleophile with a series of alkyl bromides are given in Table 4. The

Table 4. Rate Constants for the Reactions of Dianion I with Alkyl Bromides in a Quadrupole Ion Trap^a

substrate	k	k (E2) ^b	k (S_N2) ^b	E2/ S_N2
ethyl	4.0	0.4	3.6	0.1
<i>n</i> -propyl	8.2	3.3	4.8	0.7
isopropyl	3.2	2.7	0.5	5.4
<i>s</i> -butyl	13.1	11.5	1.6	7.2
<i>tert</i> -butyl	10.8	10.8	<0.05	>200

^a Data from ref 86. Rate constants are given in units of 10^{-12} $\text{cm}^3/\text{molecule}/\text{s}$. Values are corrected and slightly different than those in the reference. ^b Obtained by multiplying overall rate constant by the product fraction.

Scheme 3

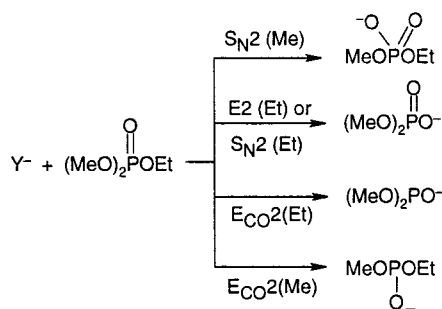


data indicate that S_N2 and E2 reactions compete with all of the substrates except *tert*-butyl bromide. As expected, the proportion of E2 products greatly increases in the progression from primary to secondary to tertiary bromides. The rate constants also confirm that β -substituents tend to increase the rate of gas phase S_N2 reactions. For example, propyl has a higher S_N2 rate constant than ethyl bromide, and *s*-butyl has a higher rate constant than isopropyl bromide. Data were also reported for the reactions of a dianion analogous to I but with a carboxylate rather than a phenolate as the nucleophile. In this case, the nucleophilic site is a weaker base and S_N2 reactions are more competitive with this dianion.

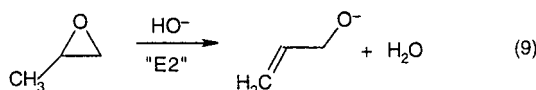
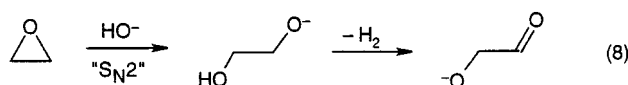
Wladkowski and Brauman⁸⁷ have taken advantage of a secondary reaction to identify the products of the reaction of cyanide with 2-chloropropionitrile. In this system, the S_N2 product is a very acidic malonitrile derivative which can react with the displaced Cl^- within the product complex to give a diagnostic ion (Scheme 3). The key assumption comes from earlier work with the reaction of CN^- with chloroacetonitrile where only S_N2 reactions are possible and deprotonated malonitrile is the major ionic product (~94%). Assuming a similar partitioning of the S_N2 products into Cl^- and deprotonated methylmalonitrile, Wladkowski and Brauman⁸⁷ determined an E2/ S_N2 ratio of 13.3 in this system. The high E2 yield is reasonable given that the S_N2 reaction involves attack at essentially a 2° carbon.

Another tactic to differentiate between S_N2 and E2 reactions has been to employ substrates that contain two reactive sites. For example, Lum and Grabowski^{88,89} have used a flowing afterglow to investigate the reactions of a series of nucleophiles with ethyl dimethyl phosphate. In this system, they identified four possible reaction pathways (Scheme 4). The last two processes in Scheme 4, elimination across a C–O bond, are only observed with very basic nucleophiles. It is not possible to distinguish between S_N2 and E2 reactions at the ethyl group in this system, but it can be assumed that substitution at the ethyl group should occur less readily than at the methyl group.

Scheme 4



With this assumption, an obvious trend is apparent in the data. The localized, heteroatom-centered nucleophiles prefer elimination. For example, HO^- , CD_3O^- , $(\text{CH}_3)_3\text{CO}^-$, and F^- lead to $(\text{MeO})_2\text{PO}_2^-$ as the major product. On the other hand, carbon-centered nucleophiles of similar basicities (e.g., C_6H_5^- , $\text{CH}_2=\text{CHCH}_2^-$, PhCH_2^- , and NCCH_2^-) give mainly substitution at the methyl group. The conclusion is that the nature of the nucleophilic center rather than its basicity is most important in determining the competition between substitution and elimination. Ricci⁹⁰ has seen similar shifts in reactivity in the reactions of nucleophiles with methyl nitrate in an ICR. In early work, Bierbaum et al. examined the reactions of oxirane derivatives with strong bases such as HO^- , and found evidence for both $\text{S}_{\text{N}}2$ and E2 reactions in the observed products.^{91,92} In this case, the $\text{S}_{\text{N}}2$ reaction leads to an addition product that can be observed mass spectrometrically. They found that although oxirane itself undergoes an $\text{S}_{\text{N}}2$ reaction (followed by H_2 expulsion from the vibrationally excited addition product) at a modest rate (eq 8), methyl oxiranes react much faster and give exclusively elimination products (eq 9). This is consistent with the conclusion that strong, oxygen-centered nucleophiles prefer elimination.



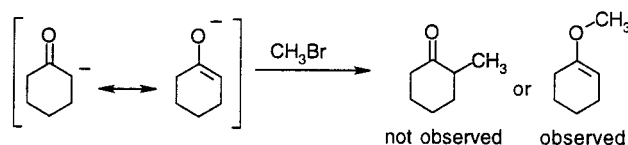
DePuy and co-workers^{69,93} have used reactivity trends to investigate the gas phase competition between substitution and elimination. In one study,⁶⁹ the reactions of a series of alkyl halides with varying substitution patterns were studied in a flowing afterglow. A wide range of nucleophiles were used, and sample data with $\text{CF}_3\text{CH}_2\text{O}^-$ and H_2NS^- as the nucleophiles are given in Table 5. This is an interesting pair of nucleophiles because they have similar proton affinities (~ 362 kcal/mol) but have nucleophilic centers from different rows of the periodic table (O vs S). Focusing on the data with H_2NS^- , there is a drop in reactivity in going from methyl to the 1° chlorides, and no reactivity is observed with the 2° or 3° chlorides. This pattern is exactly what is expected for an $\text{S}_{\text{N}}2$ reaction where α -substitution crowds the transition state and reduces the $\text{S}_{\text{N}}2$ rate.

Table 5. Efficiencies Obtained for Reactions of Nucleophiles with Alkyl Chlorides in a Flowing Afterglow^a

substrate	$\text{CF}_3\text{CH}_2\text{O}^-$ efficiency	H_2NS^- efficiency
CH_3Cl	0.15	0.085
$\text{CH}_3\text{CH}_2\text{Cl}$	0.16	0.021
$\text{CH}_3\text{CH}_2\text{CH}_2\text{Cl}$	0.19	0.043
$(\text{CH}_3)_2\text{CHCl}$	0.27	<0.0001
$(\text{CH}_3)_3\text{CCl}$	0.36	<0.0001

^a Data from ref 69.

Scheme 5



In contrast, the rate constants for the reactions of $\text{CF}_3\text{CH}_2\text{O}^-$ with these halides mildly increase in going from methyl to 1° to 2° to 3° chlorides. This is exactly the opposite of the behavior expected for $\text{S}_{\text{N}}2$ reactions. To rationalize these results, DePuy argued that, with the exception of methyl chloride, $\text{CF}_3\text{CH}_2\text{O}^-$ mainly undergoes E2 reactions with these alkyl chlorides. This explains the rate increase across the series and the fact that the substrate least capable of $\text{S}_{\text{N}}2$ reactions, $(\text{CH}_3)_3\text{CCl}$, gives the most efficient reaction. A similar effect is seen with alkyl bromides. These and other reactivity trends led DePuy to conclude that nucleophiles involving second-period centers (i.e., O or F) were capable of both substitution and elimination whereas the sulfur-centered nucleophiles are mainly limited to substitution reactions.

To provide further evidence of this effect, DePuy and co-workers⁹³ investigated deuterium isotope effects in these reactions. For the reactions of $\text{CF}_3\text{CH}_2\text{O}^-$ with $(\text{CD}_3)_2\text{CHCl}$ and $(\text{CD}_3)_3\text{CCl}$, significant deuterium isotope effects were observed ($k_{\text{H}}/k_{\text{D}} = 2.3$ and 2.1, respectively), suggesting that the rate determining step involved the loss of a β -deuterium (i.e., E2). Similar, but less dramatic effects were seen in the reactions of $\text{CF}_3\text{CH}_2\text{O}^-$ with alkyl bromides. In contrast, the reactions of H_2NS^- with $(\text{CD}_3)_2\text{CHBr}$ and $(\text{CD}_3)_3\text{CBr}$ exhibit almost no kinetic isotope effects ($k_{\text{H}}/k_{\text{D}} = 1.00$ and 1.04, respectively). The lack of a primary deuterium isotope effect in the reactions of H_2NS^- and HS^- in these systems is consistent with the idea that sulfur-centered nucleophiles are generally limited to $\text{S}_{\text{N}}2$ reactions and apparently have much larger barriers to E2 reactions than analogous second-period nucleophiles.

Some nucleophiles contain two nucleophilic sites, so multiple $\text{S}_{\text{N}}2$ pathways are possible. Enolate ions are good examples because either the oxygen or the carbon can undergo a substitution reaction with an electrophile leading to isomeric, neutral products. This presents the same problem one has in the competition between substitution and elimination reactions. Jones, Ellison, and co-workers⁹⁴ have applied their neutral trapping approach to the reaction of cyclohexanone enolate with methyl bromide (Scheme 5). In this case, only the O-alkylation product is observed.

Scheme 6

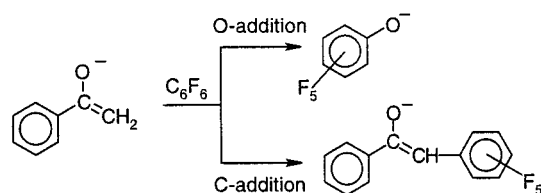


Table 6. C/O Addition Preferences in the Reactions of Enolates with Hexafluorobenzene and Hexafluoropropene^a

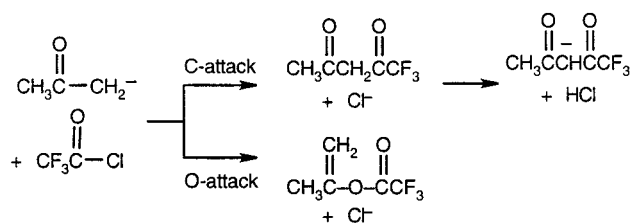
substrate	C ₆ F ₆ C/O ratio	C ₃ F ₆ C/O ratio
H ₂ C=C(O ⁻)C ₆ H ₅	94/6	94/6
H ₂ C=C(O ⁻)CH ₃	81/19	16/84
H ₂ C=C(O ⁻)CH=CH ₂	70/30	70/30
CH ₃ CH=C(O ⁻)CH ₃	74/26	18/82
C ₂ H ₅ CH=C(O ⁻)CH ₃	71/29	14/86
CH ₃ CH=C(O ⁻)H	17/83	3/97
C ₂ H ₅ CH=C(O ⁻)H	16/84	5/95

^a Data from ref 95.

Nibbering^{95–97} and Squires⁹⁸ have used secondary reactions in nucleophilic substitutions on fluorinated alkenes and arenes to analyze the competition between C- and O-alkylation of enolates. Riveros,^{99,100} Bartmess,¹⁰¹ Beauchamp,¹⁰² Squires,^{98,103} and Nibbering^{104–107} have shown that these reactions give distinctive ionic products depending on whether the reaction occurs at the carbon or the oxygen of the enolate. For example, the reaction of acetophenone enolate with hexafluorobenzene leads to two sets of products that can be associated with C- or O-addition (Scheme 6).⁹⁵ The reactions in Scheme 6 represent nucleophilic aromatic substitutions and are discussed in a later section. With acetophenone, C-addition is favored over O-addition by a factor of 94/6. The C/O addition ratio varies considerably depending on the nature of the groups attached to the carbonyl carbon and the α -carbon. A sample of Nibbering's data is given in Table 6. Hexafluoropropene has also been used as a probe reagent, and the data in Table 6 show that the nature of the probe reagent also affects the C/O selectivity.

Nibbering and co-workers found a correlation between the energy of the enolate's HOMO and the ratio of C/O addition where enolates with low energy HOMO's give more C-alkylation. This suggests that the reaction preference is controlled to some extent by frontier orbital interactions.⁹⁵ As an alternative interpretation, Brickhouse and Squires⁹⁸ have argued that C/O addition ratios can be rationalized on the basis of the keto/enol energy difference in the parent carbonyl (i.e., parent carbonyls with more stable enol forms give more O-addition). Other ambient nucleophiles, including the enolates of amides, acids, and thio-carbonyl species, have been studied by related methods.^{108–110} Finally, Brauman and co-workers¹¹¹ have investigated the reactions of ambient nucleophiles with trifluoroacetyl chloride (Scheme 7). In the reactions of enolates, the C-acetylation product is very acidic (1,3-dicarbonyl) and undergoes a proton transfer reaction with the leaving chloride ion in the product complex. The O-acetylation product is much less acidic, and with control experiments they have

Scheme 7

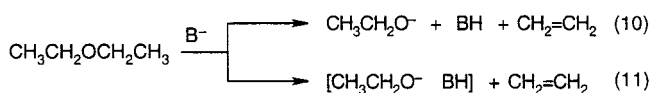


shown that proton transfer within the product complex is unlikely. For acetone enolate, this approach indicates that C-acetylation is slightly preferred over O-acetylation (60/40). A stronger preference for C-acetylation (over N-acetylation) was found for the reaction of deprotonated acetonitrile with trifluoroacetyl chloride (90/10).

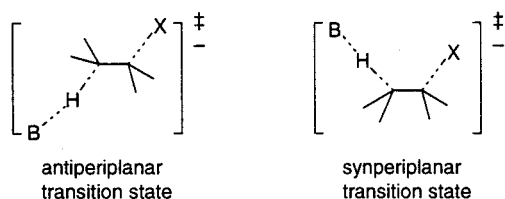
Overall, gas phase studies of S_N2 reactions have led to a striking amount of information about the process. The work has helped to clarify the factors that affect the nucleophilicity of a group and have highlighted the importance of differential solvation in controlling the relative reactivity of nucleophiles. Moreover, the gas phase studies have shown that the nature of the nucleophilic center plays a key role in determining the intrinsic preference for substitution relative to competing processes such as elimination. Finally, the S_N2 reaction has proven to be a useful system for exploring the dynamics of "double-well" potential energy surfaces and led to new insights into the limitations of using statistical models for characterizing the reactions of small molecules where relatively short-lived initial ion/molecule complexes are expected.

2. Elimination Reactions

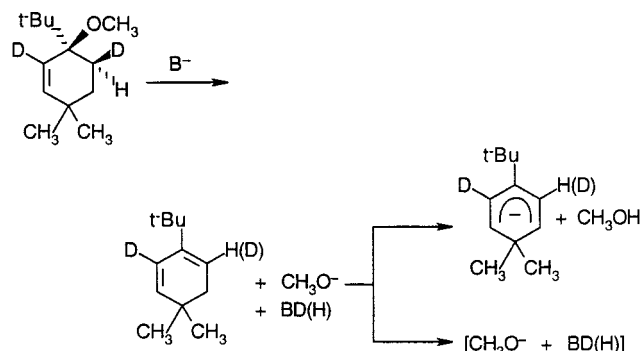
Aside from investigations of the competition between elimination and substitution reactions, a number of studies have focused on the properties of gas phase elimination reactions. The reactions of ethers with bases have been the subject of several studies dating back to early work by DePuy and Bierbaum in a flowing afterglow that indicated that there is significant selectivity in the reactions of HO⁻ and NH₂⁻ with unsymmetric dialkyl ethers.¹¹² For example, in the reaction of HO⁻ with ethyl propyl ether, elimination at the ethyl group is favored, and the observed alkoxide products (propoxide and ethoxide) are formed in a 4:1 ratio. Formation of ethene is not the thermodynamically favored pathway, so kinetic effects must be dominating (e.g., less steric crowding at the β -carbon). The reactions of HO⁻ and NH₂⁻ with diethyl ether are the most thoroughly studied of the ether eliminations, and kinetic isotope effects have been determined. Related experiments indicate that only an elimination pathway is active in these systems and two ionic products are formed, ethoxide (eq 10) and ethoxide complexed to the protonated base (eq 11).^{112–115}



Scheme 8



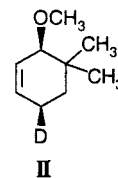
Scheme 9



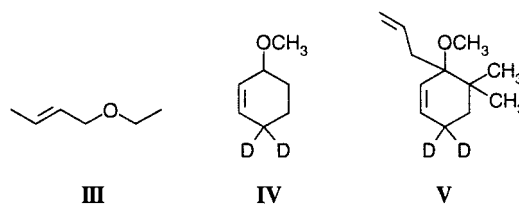
Baschky and Kass¹¹⁵ recently used their flowing afterglow to examine the temperature dependence (-35 to 200 °C) of the rate and kinetic isotope effects in these reactions. The data confirm earlier reports^{113,114} of large primary isotope effects ($k_H/k_D = 2.9$ and 7.2 for HO^- and NH_2^- , respectively, at 25 °C) in these eliminations and show that the isotope effects are maximized near 25 °C. The rates of these reactions show inverse temperature dependencies, and the efficiency for the HO^- reaction drops from 0.30 to 0.13 in going from -35 °C to 200 °C. Although previously it had been suggested that the ethoxide complex (eq 11) was formed by an elimination involving a synperiplanar transition state (Scheme 8),¹¹⁴ Rabasco et al. have used deuterium labeling to show that both anti and syn eliminations can lead to the formation of solvated base complexes (i.e., eq 11).¹¹⁶ As a result, Baschky and Kass¹¹⁵ have argued that the results can be explained by a scheme where all the products are formed by antiperiplanar eliminations and partitioning between the two pathways occurs in the product complex following the E2 transition state. Computational data also support the conclusion that the antiperiplanar path is preferred in these reactions.¹¹⁷

In a series of elegant studies, Kass and co-workers^{116,118–120} have explored the stereochemistry and regiochemistry of gas phase elimination reactions of allylic systems. Treatment of a labeled 3-methoxycyclohexene derivative with a base in the gas phase leads to two products which are indicative of the stereochemistry of the 1,2-elimination reaction (Scheme 9).¹¹⁶ After correcting for isotope effects, they found a small preference for anti elimination for a range of bases, but they noted that the lack of a strong preference for anti elimination may be a result of steric effects involving the *tert*-butyl group rather than an intrinsic preference. Using a related system that is incapable of 1,2-eliminations (II), Rabasco and Kass¹¹⁹ found that 1,4-eliminations that give cyclohexadienes as intermediate products also exhibit a

small preference for anti stereochemistry with strong bases (weaker bases prefer syn elimination).



Finally, Rabasco and Kass^{118,120} as well as Bickelhaupt et al.¹²¹ have studied the competition between the 1,2- and 1,4-elimination reactions of allylic ethers. These groups found that, for simple allylic systems (III¹²¹ and IV¹¹⁸), 1,4-elimination dominates. For example, in the reaction of III with HO^- , Bickelhaupt et al. estimated about a 5:1 preference for 1,4-elimination over 1,2-elimination. However, the preference for 1,4-elimination in these substrates may be due to the fact that it involves the loss of an usually acidic proton (allylic) compared to the 1,2 pathway. Rabasco and Kass¹¹⁸ found that the 1,4 preference was reduced when weaker bases were used, hinting that the acidity of the substrate may play an important role in the selectivity. To test this, Rabasco and Kass¹²⁰ prepared a compound where the 1,2-elimination is activated in a similar way (V) and found that 1,2-elimination dominates with strong bases such as HO^- . Overall, the results point to a very subtle balance between 1,2- and 1,4-elimination in the gas phase.



3. Addition/Elimination Reactions

The reactions of nucleophiles with carbonyl compounds and other multiply bonded systems have been the subject of numerous gas phase studies. In these reactions, the nucleophile adds to a π -bond to give an intermediate species that eventually expels a leaving group. Most work has focused on carboxylic acid derivatives and aromatic systems.

A. Carbonyl Systems

Several studies have addressed the gas phase reactions of nucleophiles with carbonyl derivatives (nucleophilic acyl substitution). The first question in these systems is whether the addition product represents a true minimum on the potential energy surface or a transition state for substitution on the carbonyl carbon. Although it is well established that tetrahedral intermediates are formed in condensed phase reactions of carbonyl species,¹²² both types of behavior have been observed in gas phase studies. The two situations are illustrated in Figure 5 where either a (a) double-well or (b) single-well potential is possible.

Work by Asubiojo and Brauman¹²³ showed that acyl transfer reactions have rates below the collision

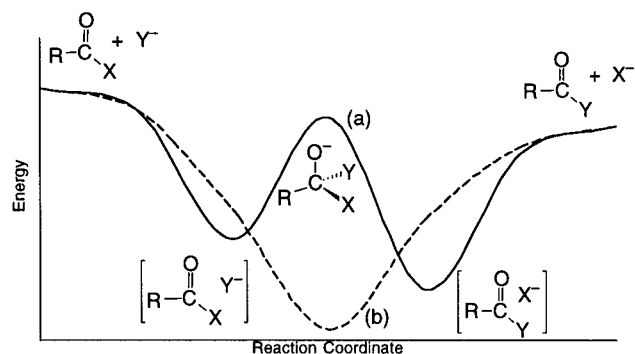
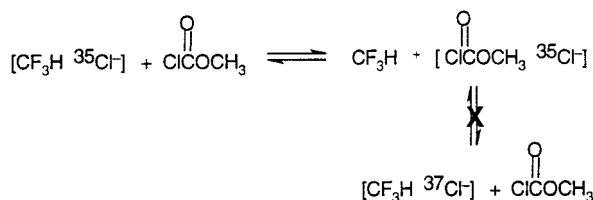


Figure 5. Double- (a) and single-well (b) potential energy surfaces for nucleophilic acyl substitution reactions.

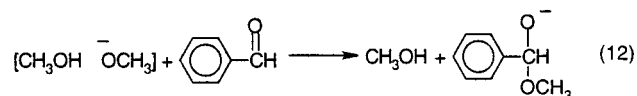
Scheme 10



controlled limit, so it is likely that a barrier exists on the surface. For example, the thermoneutral chloride isotope exchange reaction of chloride with acetyl chloride has an efficiency of only 0.05. Similar low efficiencies were seen in other reactions of nucleophiles with acetyl halides. This suggests a double-well potential with the tetrahedral species being a transition state on the surface. More recently, Wilbur and Brauman^{53,124} have studied the reactions of other acyl chlorides and isolated complexes on the reaction surface. By transferring a chloride to methyl chloroformate by a ligand swapping reaction with CF_3H , complexes were formed with relatively little excess internal energy.¹²⁴ Under the reaction conditions, an equilibrium is established between the two complexes (i.e., chloride with CF_3H and chloride with chloroformate), but in this process, only one of the chlorides is transferred back and forth to the CF_3H , the one that was initially complexed to it (Scheme 10). In other words, no chlorine exchange occurs in the complex of chloride with methyl chloroformate. Of course, this is inconsistent with a single-well potential with a symmetric tetrahedral intermediate (Figure 5b). The same authors employed a similar approach in the reactions of cyanide with substituted benzoyl chlorides and also found that distinct ion/molecule complexes exist on the surface that were separated by a significant barrier.⁵³ These results require at least a double-well potential energy surface (Figure 5a), although it is possible that the tetrahedral species could be a reactive intermediate on a triple-well surface (i.e., the tetrahedral species is stable, but separated from each of the ion/dipole complexes by significant barriers). In the reactions of Cl^- with simple acyl chlorides,¹²⁴ they were not able to isolate distinct complexes; however, they argue that this may be an artifact of the way the complexes are formed rather than an indication of a change to a single-well potential energy surface. Takashima et al.¹²⁵ have also found evidence for double-well potentials in their early work on the

reaction of labeled HO^- with methyl formate. Finally, O'Hair and co-workers have recently found evidence for barriers (i.e., tetrahedral species is a transition state) in the identity substitution reactions of N-acyl pyridinium cations with labeled pyridine.¹²⁶

The nature of the nucleophile plays an important role in the stability of the tetrahedral species formed on the reaction path, and Baer, Brinkman, and Brauman¹²⁷ have shown that the electron binding energy of the nucleophile is a key factor. In cases where the nucleophile has a high binding energy (such as Cl^- and CN^- above), the tetrahedral species is energetically disfavored relative to an ion/dipole complex and probably represents a transition state in a nucleophilic acyl substitution reaction. However, nucleophiles with low binding energies are expected to give stable tetrahedral intermediates. For example, Bohme¹²⁸ has shown that H^- gives a stable tetrahedral species with formaldehyde (i.e., methoxide), and McDonald⁷⁴ has formed stable complexes of CF_3^- with hexafluoroacetone. Some of the most compelling evidence for stable tetrahedral intermediates comes from work by Nibbering,^{129,130} Brauman,¹²⁷ and co-workers. Van der Wel and Nibbering^{129,130} found that methoxide/methanol complexes would transfer methoxide to aldehydes such as benzaldehyde (eq 12). For the process to be exothermic, the binding energy of methoxide to benzaldehyde must be greater than that between methoxide and methanol (29.3 kcal/mol¹³¹). This value is too large for a simple ion/molecule complex (10–15 kcal/mol), so a covalently bound species is implicated (i.e., tetrahedral intermediate).



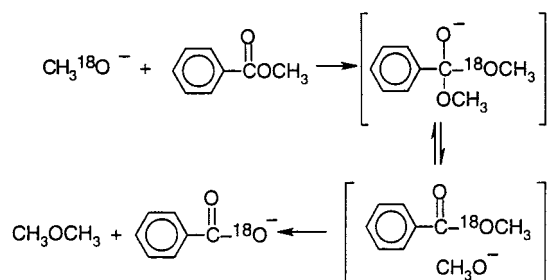
Brauman and co-workers¹²⁷ investigated the acidity of a hemiacetal ($\Delta H_{\text{acid}}^\circ = \sim 359$ kcal/mol) and found that it was a much stronger acid than typical alcohols ($\Delta H_{\text{acid}}^\circ = \sim 375$ kcal/mol). The deprotonated hemiacetal is an example of the tetrahedral species that would be formed in the addition of an alkoxide to an aldehyde, and its unusual stability suggests that the addition process (i.e., formation of the tetrahedral species) is exothermic (eq 13).



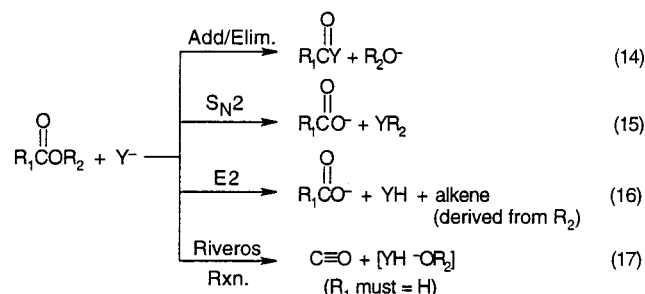
Overall, the results of these studies point to a delicate balance between the energies of ion/dipole complexes and true covalent tetrahedral intermediates in the reactions of nucleophiles with carbonyl species. The surfaces may vary from single- to double- (or higher) well potentials depending on the nature of the substrate and nucleophile.

Another facet of the reactions of nucleophiles with carbonyl species is competition between addition/elimination reactions and other processes such as $\text{S}_{\text{N}}2$ reactions. These competing processes have been the subject of many studies, and for esters,

Scheme 11



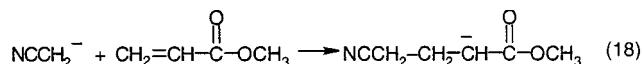
several pathways are typically observed (eqs 14–17).^{9,53,101,123–125,132–134}



Along with addition/elimination (eq 14), it is possible for the nucleophile to attack the alkoxy portion of the ester to give an S_N2 reaction (eq 15). This is very competitive when $R_2 = \text{CH}_3$. Using an ICR, Takashima and Riveros¹³⁵ found that in the reaction of labeled HO^- with HCO_2CH_3 , 27% of the HCO_2^- product resulted from an S_N2 reaction on the methyl group. In these systems, two types of eliminations are possible. An E2 reaction on the alkoxy fragment gives a carboxylate product (eq 16), and attack at the carbonyl hydrogen of formates (Riveros reaction) leads to the elimination of CO (eq 17). This last process has proven to be a very useful way of cleanly forming gas phase complexes of nucleophiles with alcohols.¹³³ Finally, nucleophiles may react at the α -carbons of esters via proton transfer to give enolates. Recently, Frink and Hadad¹³⁶ have used a flowing afterglow to study a wide range of reactions of nucleophiles with formic and acetic esters. This work illustrates the diversity of reactivity in these systems. For the acetic esters, proton transfer is very competitive with stronger bases ($\Delta H_{\text{acid}}^{\text{P}} > 380$ kcal/mol), but large yields of addition/elimination products are observed with weaker bases such as F^- and $^-\text{CH}_2\text{CN}$. Finally, Van der Wel and Nibbering¹²⁹ have shown that reversible addition of nucleophiles to carbonyls is common, and when methyl benzoate is treated with $\text{CH}_3^{18}\text{O}^-$, both CH_3O^- and $\text{C}_6\text{H}_5\text{C}^{18}\text{OO}^-$ are formed. Both result from the initial swapping of the labeled methoxy group for an unlabeled one to give methyl benzoate with an ^{18}O label that can undergo an S_N2 reaction in the reaction complex to give benzoate (Scheme 11).

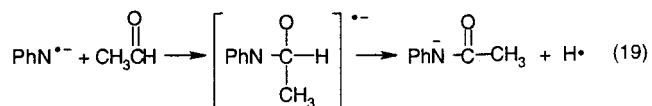
Bernasconi, DePuy, and co-workers¹³⁷ have investigated the reactions of a group of nucleophiles with methyl acrylate in a flowing afterglow. Unlike simple esters, this α,β unsaturated ester can also undergo a 1,4-addition reaction to give an enolate product. Nucleophiles ranging from very strong bases such as

hydroxide to weak, delocalized ones such as nitromethyl anion were used. Four types of reactions were observed: proton transfer, addition/elimination at the carbonyl, 1,4-addition, and S_N2 at the methyl group. One feature of the data is that for carbon-centered nucleophiles with varying levels of delocalization (benzyl, cyanomethyl, and nitromethyl), the 1,4-addition pathway dominates and enolates are formed (eq 18). The nature of the addition product was probed in part using reactions with butyl nitrite (see section II.4).



This result is consistent with preferences that have been observed in solution. When methyl acrylate is treated with stronger, more localized nucleophiles, proton transfer, addition/elimination, and S_N2 reactions dominate.

Along with closed-shell anions, there have been several reports of the addition of radical anions to carbonyl species. McDonald and co-workers^{72,74,138,139} have completed several flowing afterglow studies using carbon ($\text{Ph}_2\text{C}^{\cdot-}$, $\text{c-C}_5\text{H}_4^{\cdot-}$, and $(\text{CF}_3)_2\text{C}^{\cdot-}$) and nitrogen ($\text{PhN}^{\cdot-}$) centered nucleophiles. In general, the favored pathway is addition/elimination with the formation of a closed-shell anion and the loss of a radical. For example, phenyl nitrene radical anion reacts with acetaldehyde mainly with loss of a hydrogen atom to give a deprotonated amide product (eq 19).⁷⁴

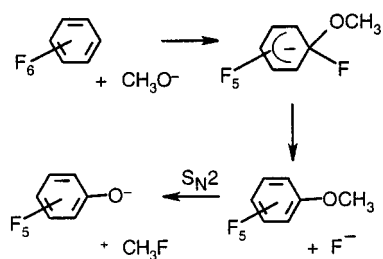


Similar addition/elimination reactions are observed with esters, and usually an alkoxy radical is lost in the process.¹⁴⁰ Nibbering and co-workers^{1,141,142} have examined the reactions of a series of stabilized carbene radical anions ($\text{ZCH}^{\cdot-}$, where $\text{Z} = \text{F}, \text{Cl}, \text{Br}, \text{NC},$ or CN) with methyl esters. Again, addition/elimination with the loss of an alkoxy radical generally is the major pathway, but competition with an S_N2 reaction at the methyl group is observed, particularly for $\text{FCH}^{\cdot-}$.¹⁴²

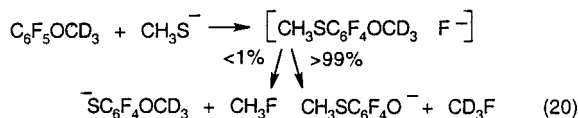
B. Aromatic Systems

As shown in a previous section involving the reactions of enolates (section II.1.B.iii), nucleophilic aromatic and vinylic substitution reactions have been observed in the gas phase, particularly with polyfluorinated species because the fluorine substituents stabilize the intermediate carb-anions.^{9,98–103,105–107,143–145} Riveros¹⁰⁰ initially showed that, in an ICR, methoxide could react with fluoro-benzene to produce anisole in a relatively efficient process. In polyfluorinated systems, a secondary reaction leads to the formation of phenoxides (Scheme 12).¹⁰⁰ After the nucleophilic aromatic substitution, the displaced fluoride attacks the alkyl portion of the resulting ether in either an S_N2 or E2 reaction to produce the fluorinated phenoxide. When methyl

Scheme 12

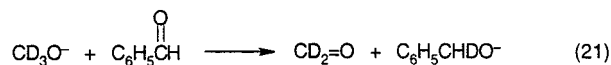


phenyl ethers are treated with nucleophiles, both S_N2 (at methyl) and S_NAr reactions are observed. Ingemann et al.¹⁰⁶ have shown that, in the reactions of series of nucleophiles with methyl pentafluorophenyl ether, nucleophilic aromatic substitution is the preferred pathway, presumably because the perfluoro-substitution stabilizes the cyclohexadienyl anion intermediate. For example, CH_3O^- gives 84% nucleophilic aromatic substitution with this substrate. However, the weakest base in the series, HS^- , predominantly gives an S_N2 product indicating that this pathway is less sensitive to the nucleophile's basicity. Substantial selectivity is observed in the secondary reactions of the product complexes of these reactions. When $\text{C}_6\text{F}_5\text{OCD}_3$ is treated with CH_3S^- , the nucleophilic aromatic substitution pathway (F^- displacement) can give two products in a secondary reaction. Virtually all of the products occur from F^- attack at the methoxy group to give a phenolate product (eq 20).



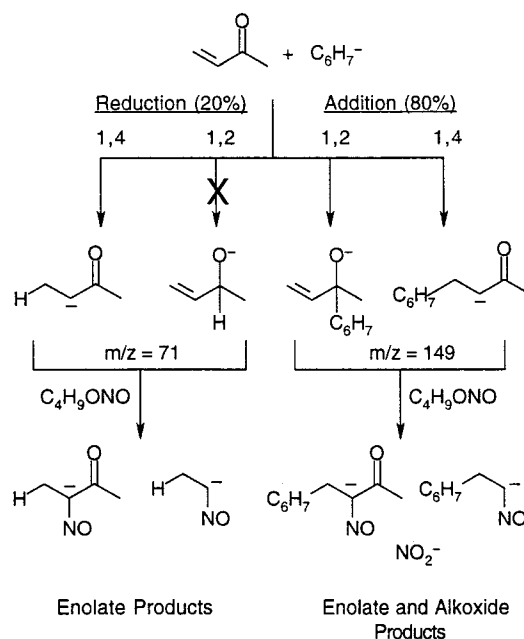
4. Reductions

Reductions of carbonyl compounds and related species have been accomplished in the gas phase by using novel hydride donors. In early work, DePuy, Bierbaum and co-workers¹⁴⁶ identified HNO^- and C_6H_7^- (cyclohexadienyl anion) as gas phase reducing agents and showed that they were capable of reducing aldehydes to alkoxides. Ingemann et al.¹⁴⁷ also have demonstrated that alkoxides could reduce aldehydes (eq 21) by a hydride transfer mechanism that is reminiscent of the well-known, condensed phase Cannizzaro reaction.

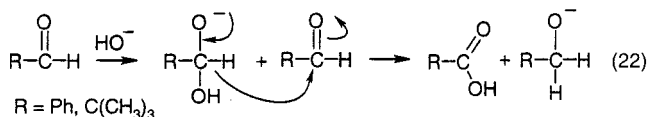


In addition, Sheldon et al.¹⁴⁸ have observed true gas phase Cannizzaro reactions in an ICR when they treat pivaldehyde or benzaldehyde with HO^- . Deprotonation of the aldehyde dominates at low substrate pressures, but at higher pressures, alkoxide products are observed. The mechanism involves attack of hydroxide on one aldehyde to give an addition

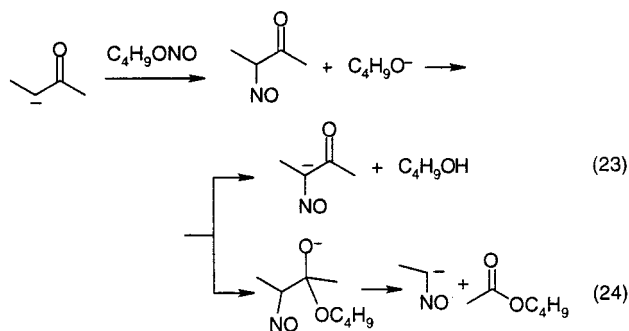
Scheme 13



complex followed by hydride transfer to a second aldehyde molecule (eq 22).

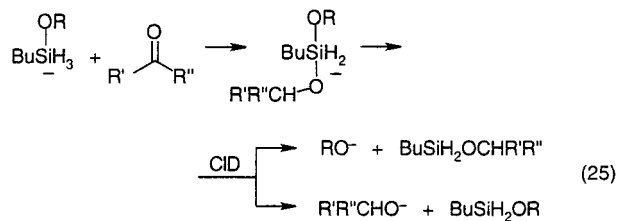


Surprisingly, no carboxylate products were detected under these conditions (one might expect that the alkoxide would deprotonate the carboxylic acid in the product complex); however, carboxylates were seen at higher pressures when the reaction was carried out in a chemical ionization source. A comprehensive study of the reductions of α,β unsaturated carbonyl derivatives by C_6H_7^- has been completed by Bernasconi, DePuy, and co-workers.¹³⁷ The cyclohexadienyl anion has two types of reactivity in these systems and can act as a nucleophile or as a reducing agent (forming benzene as a neutral product). With methyl vinyl ketone ($\text{C}_4\text{H}_6\text{O}$), nucleophilic addition dominates, but there is about a 20% yield of the reduction product, $\text{C}_4\text{H}_7\text{O}^-$. An obvious question in these systems is whether the reduction or the addition to the unsaturated system occurs in a 1,2 or 1,4 fashion to give either alkoxide or enolate products, respectively. Reactions of the products were used to answer these questions (Scheme 13). To identify the products, these workers took advantage of the fact that alkoxides and enolates both react with butyl nitrite but give different products.¹⁴⁹ Alkoxides give mainly NO_2^- (by an S_N2 or $E2$ mechanism) whereas enolates give nitrosation products (eq 23) as well as reverse Claisen reaction products (eq 24). The reduction product at $m/z = 71$ reacts with butyl nitrite to give products that are only consistent with 1,4-addition to give an enolate (Scheme 13). In contrast, the addition product at $m/z = 149$ gives products that presence of both enolates (1,4-addition) and alkoxides (1,2-addition). Similarly, acrolein and methyl acrylate give exclusively 1,4-reduction with



$C_6H_7^-$, but a mixture of 1,2- and 1,4-nucleophilic addition products (1,2-addition with methyl acrylate leads to a nucleophilic acyl substitution product). The authors suggest that the remarkable 1,4 selectivity of the reduction may be the result of a more complex pathway that involves initial nucleophilic addition of the $C_6H_7^-$ at the carbonyl carbon followed by an intramolecular hydride transfer exclusively to the 4-position, leading to the loss of C_6H_6 and the formation of the 1,4-reduction product. Overall, this study provides a good example of how chemical reactivity can be used to distinguish between isomeric (i.e., isobaric) ions.

Squires and co-workers^{150,151} have employed pentacoordinate silicon hydride ions, $Bu(RO)SiH_3^-$, to probe the diastereoselectivity of gas phase ketone reductions ($R = 3$ -pentyl) in a flowing afterglow. When treated with a ketone or aldehyde, these ions transfer a hydride to the carbonyl and produce an alkoxy siliconate product ion (eq 25).



In these systems, the addition product contains two alkoxy groups (3-pentoxide and the ketone reduction product), and during collision-induced dissociation (CID) of the product complex, either alkoxide can be expelled. The branching ratio is very sensitive to the structure of the alkoxide, and this provides an analytical tool for determining the diastereoselectivity of the reduction process. For example, in the reduction of 2-methylcyclohexanone, *cis*- and *trans*-2-methylcyclohexoxide are the expected reduction products, and they will give different branching ratios during CID. These ratios can be determined by comparison to the ratios obtained for reference siliconates prepared from the authentic alkoxides. An example involving the formation of the authentic *trans* stereoisomer is given in Scheme 14. The CID product ratio for complexes prepared from the authentic *trans* stereoisomer is 1.44 ± 0.05 and for the *cis* stereoisomer is 3.21 ± 0.02 relative to 3-pentoxide. When 2-methylcyclohexanone is reduced by $Bu(RO)SiH_3^-$ and then subjected to CID, the ratio of 2-methylcyclohexoxide to 3-pentoxide is 1.82 ± 0.03 , which translates to a 68/32 ratio of *trans* to *cis*

Scheme 14

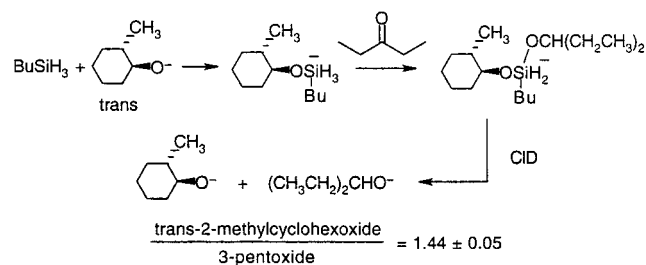


Table 7. Percentage of Axial Attack in the Reductions of Ketones by a Pentacoordinate Siliconate in a Flowing Afterglow^a

ketone	gas phase	condensed phase ^b
4- <i>tert</i> -butylcyclohexanone	99	92
2-methylcyclohexanone	68	76
3,3,5-trimethylcyclohexanone	9	21
norcamphor ^c	93	91
2- <i>tert</i> -butyl-1,3-dioxan-5-one	46	93

^a Data from ref 150. See text for details. ^b Data for lithium aluminum hydride reduction in THF. See ref 150 for appropriate literature citations. ^c Exo attack.

products. This approach has been applied to several ketones, and the results are shown in Table 7 along with data from solution. In the table, axial attack refers to the approach pathway of the hydride. Overall, one sees a very good correlation between the gas phase siliconate reductions and those done in solution under typical conditions (i.e., $LiAlH_4$ in THF). This again points out that, in general, the major factors that control organic reactivity are equally evident in gas phase studies as in solution, and as a result, gas phase studies are very useful in probing the fundamental features of organic reactions. Of the five ketones in Table 7, there is only one example where different products are favored in the gas phase and in solution, 2-*tert*-butyl-1,3-dioxan-5-one; however, Wu and Houk¹⁵² had predicted this would be true on the basis of ab initio calculations that showed that this substrate would be especially sensitive to repulsive electrostatic effects in the axial addition. In solution, this is mediated by solvation effects, but in the gas phase, it plays a more important role and equatorial attack is preferred.

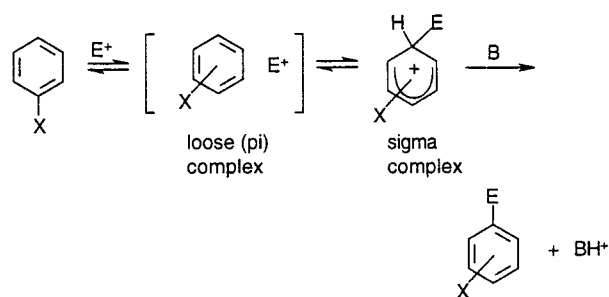
Overall, these studies show that with the appropriate hydride donor reagents, reductions can easily be accomplished in the gas phase. The limited stereochemical data that are available suggest that the gas phase reductions are governed by the same factors that drive the stereoselectivity of condensed phase reductions.

III. Electrophilic Cation Chemistry

1. Electrophilic Aromatic Substitution

Electrophilic aromatic substitution is a classic reaction in organic chemistry, and numerous studies have focused on this reaction in the gas phase. In particular, it was the topic of many early studies of organic ion/molecule reactions. In electrophilic aromatic substitution, an electrophile reacts with the π -system of the aromatic ring to produce a cyclohexa-

Scheme 15



dienyl cation intermediate which eventually expels a cationic leaving group to give the substitution product (Scheme 15). It appears that any of these steps may be rate-determining depending on the reaction conditions. Often only the first step, addition to give stabilized complexes (π or σ), has been probed in mass spectrometry work. Many of the studies of gas phase electrophilic aromatic substitution have employed the radiolytic technique in which reactant ions are formed by radiolysis at relatively high pressures (~ 760 Torr) in a bulk reactor.⁴ The reactant ion may be used for chemical ionization of a substrate, and the resulting ions participate in the reaction of interest with other gases in the reactor. The products of these reactions then can be collected and analyzed by conventional methods. Although the method does not involve mass spectrometry, studies using it have been included because they have had a large impact on our understanding of gas phase electrophilic aromatic substitution reactions.

The mechanism of gas phase aromatic substitution reactions has been reviewed by Fornarini¹⁵³ and Aschi et al.¹⁵⁴ in 1996, and a review of arenium ions was presented by Fornarini and Crestoni⁶ in 1998. Consequently, only a brief discussion of the general features of the reaction will be provided. First, the nature of the potential energy surface corresponding to Scheme 15 will be considered.

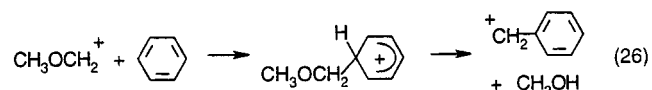
A. Potential Energy Surfaces

In the initial reaction step, the electrophile interacts with the aromatic system to give an ion/molecule complex.^{155,156} This may dissociate back to reactants or proceed to a covalently bound σ complex. The lifetime of the initial, loose complex, particularly under the high-pressure conditions used in radiolytic studies, is believed to play an important role in determining the rate of the substitution process. For example, Crestoni, Fornarini, and co-workers^{157,158} have completed radiolytic studies with $1,\omega$ -diphenylalkanes. In these systems, the ability of the electrophile to interact with two aromatic rings provides extra stabilization and enhances the lifetime of the loose complex relative to dissociation. This allows more time for collisional stabilization of the activated ion/molecule complex by the buffer gas in the system and therefore enhances the rate of substitution pathway relative to a simple aromatic compound like toluene. In a series of studies, Aschi and co-workers^{159–162} have investigated the lifetimes of ion/molecule complexes between cationic electrophiles and aromatics. In one study,¹⁵⁹ the ion/molecule

complex was formed by treating the protonated arene with a deuterated ethene. Proton transfer generates a new complex consisting of a deuterated ethyl cation and the neutral arene, the same complex that would be formed in the direct electrophilic aromatic substitution reaction of the ethyl cation with the arene. Isotopic scrambling in the ethyl cation can only occur before it forms the σ complex. By evaluating the product distributions and estimating the rate constant for isotope scrambling in the ethyl cation, they derived lifetimes on the order of 10–100 ps for the loose complex. Under their reaction conditions, σ complex formation is effectively irreversible. Competition can occur in the loose complex between transfer of the electrophile or a proton to the aromatic ring. For example, Cerichelli et al.¹⁶³ and Angelini et al.¹⁶⁴ have used the radiolytic technique to study the products of the reactions of alkyl cations with aromatics such as toluene, *N*-methylpyrrole, and thiophene. For ethyl cations, proton transfer to the arene dominates in all cases, but the isopropyl cation predominately adds to the arene to give an alkylation product. This is most likely due to the much greater acidity of the ethyl cation than the isopropyl cation. In addition, the cation can react with substituents on the arene. For example, Harrison has shown that the ethyl cation predominately reacts with the carboxyl group of ethyl benzoate rather than the ring.¹⁶⁵ Gross and co-workers^{166,167} have used mass spectrometry to study the coexistence of σ (covalent) and π (loose) complexes in the reactions of carbocations with aromatic rings. They have found that electron-rich aromatic systems such as thiophene and pyrrole are less likely to exist as π complexes than electron deficient aromatics such as fluorobenzene.

B. Reactivity Trends

Numerous studies have addressed the rates and regioselectivity of the reactions of electrophiles with arenes,^{163,164,168–183} and the radiolytic studies have been reviewed by Cacace.⁵ In general, the gas phase systems give trends that are very similar to those found in solution (although exceptions are well-known^{182,184}). For example, Dunbar et al.¹⁸³ found that in the methenylation of benzene by the methoxymethyl cation (eq 26), alkyl substituents increase the rate by a factor of 2–5 and that fluorine or trifluoromethyl groups decrease the rate by factors of 10 or greater. Other reactions of the methoxymethyl cation are presented in the next section.



Attina and Cacace^{5,179} have found that in radiolytic studies, protonated methyl nitrate gives nitration rates that vary as expected for a series of electron-donating and electron-withdrawing groups (Table 8). In addition, ortho and para products predominate with $-\text{OCH}_3$, $-\text{CH}_3$, $-\text{F}$, and $-\text{Cl}$ substituents whereas the strongly deactivating $-\text{CF}_3$ substituent leads exclusively to meta products. Attina et al.¹⁸⁵ have found that in the partitioning between ortho

Table 8. Relative Rates and Positional Selectivities of Radiolytic Reactions of Substituted Benzenes (Ph-X) with Protonated Methyl Nitrate^a

X	relative rate	orientation		
		ortho	meta	para
OCH ₃	7.6	41	0	59
CH ₃	5.1	59	7	34
H	1			
F	0.15	14	13	73
Cl	0.19	36	10	54
CF ₃	0.0037	0	100	0

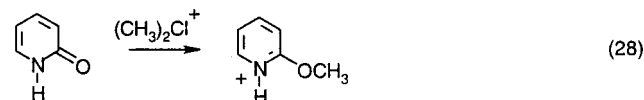
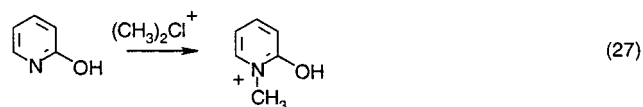
^a Data from ref 5.

and para products in reactions with protonated methyl nitrate, typical steric effects are observed and the ortho/para ratio monotonically drops across the series X = CH₃ (1.7), CH₃CH₂ (1.0), (CH₃)₂CH (0.5), (CH₃)₃C (0.2). The rates of these nitration reactions correlate very well on a Hammett plot using substituent parameters derived from condensed phase studies, indicating that the gas phase system is a good model for probing the mechanisms of electrophilic aromatic substitutions.⁵

2. S_N2 and Related Reactions

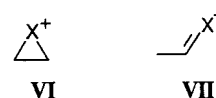
Although not as commonly used in organic synthesis, there have been several reports of gas phase S_N2 reactions between neutral nucleophiles and cationic substrates. One simple system that has received considerable study is the reaction of dialkylhalonium ions, R₂X⁺ (X = F, Cl, Br, I) with neutral nucleophiles leading to S_N2 reactions with alkyl halides being the leaving group (e.g., eqs 27 and 28). Kebarle and co-workers¹⁸⁶ have studied the reactions of dialkylchloronium ions with a range of nucleophiles of varying basicity. For oxygen and nitrogen centered nucleophiles, there is only a weak correlation between S_N2 rates and the basicity of the nucleophile; however, most of these reactions have rate constants that approach the collision-controlled limit, and therefore the S_N2 barrier may be having a limited effect on the observed rate. For example, the reactions with dimethyl and diethyl ether exhibit negative temperature dependencies (i.e., faster at lower temperatures). This is consistent with an S_N2 transition state that is below the energy of the separated reaction partners, leading to a negative activation barrier. Regioselectivity was examined by studying the reactions of an unsymmetric dialkylchloronium ion, CH₃Cl⁺CH₂CH₃. An interesting outcome is that the ethyl group is preferentially transferred to ethers (CH₃Cl is the leaving group) whereas a methyl group is preferentially transferred to stronger bases such as ammonia and trimethylamine. Of course, the S_N2 reaction is expected to prefer the least hindered site (i.e., CH₃) in CH₃Cl⁺CH₂CH₃. It is possible that the preferential transfer of the ethyl group with the ethers is related to thermochemistry and that some type of equilibration occurs in the product complex to yield the most stable oxonium ion (ethylated). O'Hair and co-workers¹⁸⁷ have studied the selectivity of the reactions of (CH₃)₂Cl⁺ with pyridine derivatives. They find that the chloronium ion selectively methylates at the site

with the greatest methyl cation affinity (i.e., most exothermic pathway). For example 2-hydroxypyridine methylates at nitrogen (eq 27) and 2-pyridone methylates at oxygen (eq 28) to give related pyridinium ion products.

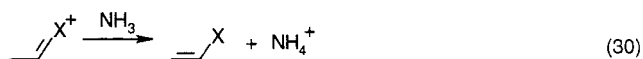
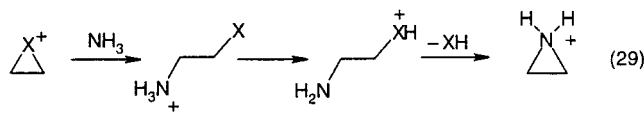


O'Hair and co-workers have also studied the reactions of (CH₃)₂Cl⁺ with glycine and cysteine and found limited regioselectivity in the competition between addition at the oxygens and nitrogen atoms.^{188,189}

Cyclic halonium ions are well-known intermediates in the reactions of alkenes with halogens. These species have been generated in the gas phase, and several groups have studied their reactions. In early work, Berman, Anicich, and Beauchamp¹⁹⁰ used an ICR to investigate the reactions of C₂H₄X⁺ (X = Cl, Br) ions with a range of simple nucleophiles such as H₂O, NH₃, H₂S, and PH₃. These workers generated two forms of these ions (cyclic, **VI**, from 1,2 dihaloalkanes and acyclic, **VII**, from 1,1-dihaloalkanes) which did not interconvert under their reaction conditions.

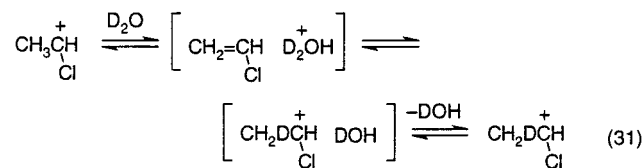


In reactions with ammonia, they found that the cyclic ions, **VI**, underwent substitution reactions presumably by an addition/elimination pathway (eq 29) whereas **VII** mainly underwent proton transfer reactions presumably leading to vinyl halides (eq 30).

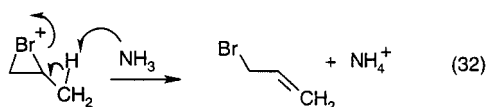


More recently, Heck, de Koning, and Nibbering^{191,192} have looked at hydrogen/deuterium exchange in the reactions of **VI** and **VII** with D₂O. They found that **VII** (X = Cl, Br) undergoes up to three exchanges to give C₂HD₃X⁺ ions whereas **VI** does not undergo exchange reactions. As noted above, deprotonation of **VII** leads to a stable neutral (vinyl halide) so there is not a large barrier to the exchange process. The process follows the standard mechanism of gas phase H/D exchange and involves first a transfer of a proton to the D₂O in the collision complex to give a complex of the vinyl halide and D₂OH⁺. Dissociation of this complex would be endothermic (the vinyl halide is a stronger base than D₂O), so a deuterium (or proton) must be transferred back to the vinyl halide before dissociation occurs. The exchange of one deuterium

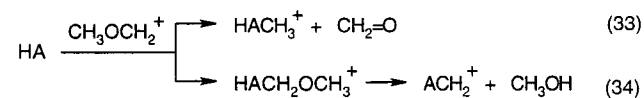
is shown in eq 31, and repetition of this process leads to the three exchanges on the methyl group.



Interestingly, when the isomeric $\text{C}_2\text{H}_4\text{Br}^+$ ions are allowed to react with simple alkenes, bromine cation transfer is observed with **VI** to presumably produce new, cyclic bromonium ions. This pathway is absent with **VII**, and addition followed by the loss of HX is the major pathway with these ions, presumably to form allylic cations through rearrangements (this pathway was also observed with **VI**). This is indicated by proton scrambling when deuterated alkenes are used. Heck and Nibbering¹⁹¹ recently studied the reactions of isomeric $\text{C}_3\text{H}_6\text{Br}^+$ ions. Again, they were able to identify both cyclic and acyclic isomers, in part, by studying their proton transfer behavior with NH_3 . The ions derived from electron impact on 1,2-dibromopropane are expected to have a cyclic structure analogous to **VI**. These ions give a relatively slow proton transfer reaction with NH_3 (compared to acyclic forms), but they react considerably faster than the cyclic $\text{C}_2\text{H}_4\text{Br}^+$ ions with NH_3 . The authors suggest that the additional methyl group may increase the rate of isomerization (within collision complexes) of the cyclic to the acyclic form, but it also may be an example of an E2-like reaction at the methyl group (eq 32). This would be analogous to DePuy and Bierbaum's observation that methylation opens a new pathway (E2) in the reactions of oxiranes with anionic bases (see above).^{91,92}



The methoxymethyl cation, $\text{CH}_3\text{OCH}_2^+$, is an interesting species because it is capable of transferring a CH_3^+ group in a simple $\text{S}_{\text{N}}2$ reaction (eq 33) or effectively a CH^+ group in an addition/elimination pathway (eq 34). This ion has been the subject of many studies,^{188,189,193–204} including important early work by Caserio.^{205–207}



In a recent paper, Freitas and O'Hair¹⁹⁹ have summarized much of the early work with this cation and provided new experimental and computational data related to its reactivity. The $\text{S}_{\text{N}}2$ behavior (eq 33) is observed with ethers,^{196,199,206} carbonyl compounds (ketones, aldehydes, acids),^{195,197–199} tertiary amines,¹⁹⁹ and disulfides^{199,206} as the dominant process (aside from simple adduct formation). Mixtures of products are observed with addition/elimination and other processes dominating when the nucleophilic atom of

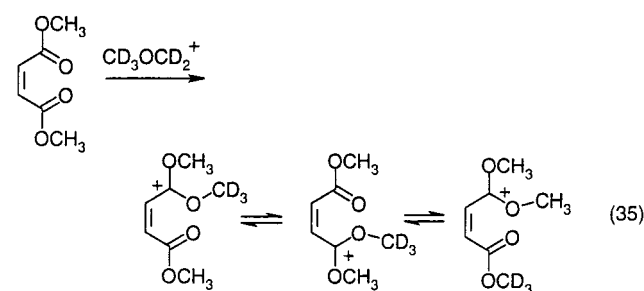
Table 9. Products in the Reactions of the Methoxymethyl Cation with Neutral Nucleophiles in a Flowing Afterglow^a

nucleophile	efficiency	product branching ratios		
		$[\text{M} + \text{CH}]^+$	$[\text{M} + \text{CH}_3]^+$	adduct
$\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$	0.88	0.20	0.15	0.65
$(\text{CH}_3\text{CH}_2)_2\text{O}$	1.00	0.00	0.10	0.90
$\text{CH}_3\text{CO}_2\text{H}$	0.80	0.00	0.70	0.30
$\text{CH}_3\text{CO}_2\text{CH}_2\text{CH}_3$	1.00	0.00	0.15	0.85
$(\text{CH}_3)_2\text{NH}$	0.63	0.65	0.05	0.30
$(\text{CH}_3)_3\text{N}$	1.00	0.00	0.05	0.95
$\text{CH}_3\text{CH}_2\text{SH}$	0.60	0.30	0.25	0.45
$(\text{CH}_3)_2\text{S}$	1.00	0.00	0.50	0.95
C_6H_6	1.00	0.85	0.15	0.00

^a Data from ref 199.

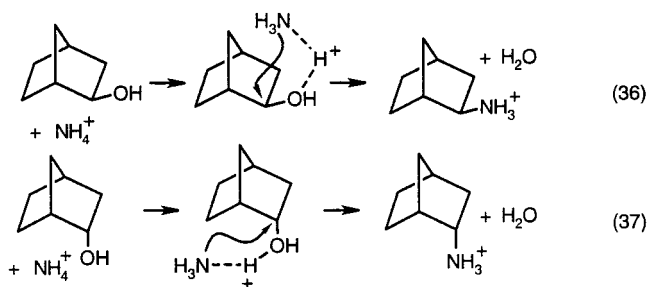
the reagent bears a hydrogen such as in alcohols,^{194,199,205,207} amines (primary and secondary),^{193,199,205} and thiols.^{199,205} Of course, the presence of an acidic hydrogen after addition at the CH_2 group of the methoxymethyl cation facilitates the elimination of CH_3OH (eq 34). A summary of work in a flowing afterglow is given in Table 9. In their examination of the potential energy surfaces for the reactions of the methoxymethyl cation, Freitas and O'Hair¹⁹⁹ concluded that the $\text{S}_{\text{N}}2$ pathway is generally more exothermic than addition/elimination but suffers from a significant barrier that limits the efficiency of the process, and therefore $\text{S}_{\text{N}}2$ is most important when other pathways are suppressed. This situation is not unlike reactivity patterns that have been observed in the gas phase $\text{S}_{\text{N}}2$ reactions of anionic nucleophiles (see above). The methoxymethyl cation shows a different type of reactivity with amides, and in the reaction with formamide, it cleaves the peptide bond to give protonated methyl formate, $\text{HC}(\text{OH})\text{OCH}_3^+$, and an imine, $\text{CH}_2=\text{NH}$, as the major products.¹⁹⁹

Brodbelt and co-workers^{200–203} have completed several studies with the methoxymethyl cation and have investigated the effects of multiple functional groups in the substrate. For example, they have examined the reactions of the methoxymethyl cation with the dimethyl esters of diacids and observed scrambling of the methyl groups in the methylated products.²⁰² This was confirmed by CID of products from the reaction with deuterated methoxymethyl cations. The results suggest that once the carbonyl is methylated, a methyl group (labeled or unlabeled) can be transferred between the two ester groups in an intramolecular $\text{S}_{\text{N}}2$ reaction leading to a random distribution of the labeled and unlabeled methyl groups (eq 35).



Finally, Bache-Andreassen and Uggerud²⁰⁴ have studied the reactions of ammonia with a series of alkoxymethyl cations (ROCH_2^+ , $\text{R} = \text{CH}_3, \text{CH}_3\text{CH}_2, \text{CH}_3\text{CH}_2\text{CH}_2,$ and $(\text{CH}_3)_2\text{CH}$). The predominant pathway is addition/elimination (eq 34), but some $\text{S}_{\text{N}}2$ products are observed (eq 33). The yield of $\text{S}_{\text{N}}2$ products is significant for $\text{R} = \text{CH}_3$, but drops off dramatically for the other alkyl groups. This is perfectly consistent with the methyl group being the best substrate for $\text{S}_{\text{N}}2$ reactions.

There have been several mechanistic studies of the acid-induced substitution reactions of alcohols and alkyl halides. Protonation of a hydroxyl or a halide converts it into a good leaving group (i.e., H_2O or HX) and allows for the substitution reaction. In early radiolytic work, Speranza and co-workers^{208–210} examined key features of the mechanism and found many parallels with condensed phase chemistry. One advantage of the radiolytic approach is that it allows for the isolation and characterization of the neutral products. As expected for an $\text{S}_{\text{N}}2$ process, the majority of the products in the reactions of protonated alkyl halides with H_2O are consistent with an inversion of stereochemistry at the reacting carbon.²⁰⁹ More recently, Uggerud and Bache-Andreassen²¹¹ have used an ICR to study the reactions of protonated alcohols with H_2^{18}O . A very interesting result is that the rate of the substitution reaction increases across the series $\text{CH}_3\text{CH}_2\text{OH}_2^+ < (\text{CH}_3)_2\text{CHOH}_2^+ < (\text{CH}_3)_3\text{COH}_2^+$. This is exactly the opposite reactivity pattern expected for $\text{S}_{\text{N}}2$ reactions where steric bulk at the reaction center is expected to crowd the transition state and reduce the rate. The observed reactivity pattern is more consistent with an $\text{S}_{\text{N}}1$ reaction. It appears that reactions with very weak nucleophiles (i.e., H_2O) are displaying some of the characteristics of both types of mechanisms. Computational studies as well as the earlier experimental work point to inversion at the reaction center in the reactions of protonated alcohols, an indication of an $\text{S}_{\text{N}}2$ process.^{11,209,212–215} On the other hand, the transition states that Uggerud and Bache-Andreassen have found in their computational work indicate very long C–O distances (1.9–2.7 Å), and they look very much like a carbocation is being transferred between the two water molecules. With so much carbocation character at the transition state, it is no surprise that the stability of the transition state is mainly dictated by carbocation stability. Their calculations also show that for the more highly substituted systems, the barrier to a frontside substitution reaction (i.e., retention of stereochemistry at the reaction center) is only slightly higher (~ 3 kcal/mol) than the one for the backside attack pathway. Tabet and co-workers²¹⁶ have reported interesting results on the stereochemistry of substitution reactions between ammonium cations and the endo and exo stereoisomers of norborneol (eqs 36 and 37). In this case, there is nearly perfect retention of configuration (i.e., exo alcohol \Rightarrow exo ammonium and endo alcohol \Rightarrow endo ammonium). Apparently the need to maintain a hydrogen bond between the nucleophile and leaving group forces retention of configuration in this system.

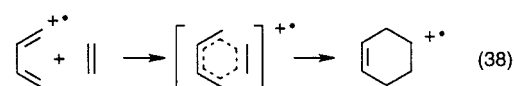


The competition between substitution and elimination has been evaluated in an ICR and by radiolytic methods for the reactions of related species, trialkyloxonium ions.²¹⁷ Amines were used as the nucleophiles, and not surprisingly, the amount of elimination increases as more basic amines are used. Finally, Speranza and co-workers^{218–221} have recently used their radiolytic method to study the competition between $\text{S}_{\text{N}}2$ and $\text{S}_{\text{N}}2'$ reactions in the acid-induced substitutions of allylic alcohols. The results show that $\text{S}_{\text{N}}2'$ reactions can compete successfully with $\text{S}_{\text{N}}2$ reactions in these systems. The $\text{S}_{\text{N}}2'$ reaction prefers an anti orientation of the entering and leaving groups, but the $\text{S}_{\text{N}}2$ reaction proceeds with retention of configuration at the reaction center via what is best described as a ligand switching reaction. This reaction may be explained by the high stability of allylic cations that allows for swapping the waters on the same face of the carbon in essentially an $\text{S}_{\text{N}}1$ process.

Overall, the studies of the gas phase $\text{S}_{\text{N}}2$ reactions of positive ions have many similarities with those described previously for negative ions. Moreover, the differences parallel those found in solution. Finally, although true $\text{S}_{\text{N}}1$ reactions (complete ionic dissociation) are not energetically viable in the gas phase, many of the characteristics of $\text{S}_{\text{N}}1$ reactions appear when weak nucleophiles such as H_2O are used with substrates that can potentially form unusually stable cations (e.g., $(\text{CH}_3)_3\text{COH}_2^+$).

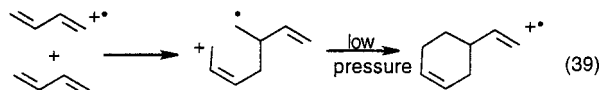
3. Cycloadditions of Cations

Cycloadditions play an important role in condensed phase chemistry and are very useful in the synthesis of complex substrates. Moreover, cycloadditions are of theoretical interest and have been a testing ground for the Woodward–Hoffmann rules²²² and frontier molecular orbital theory.²²³ Mass spectrometric studies of the reactions of the radical cations of alkenes have shown that [4+2] cycloaddition products can be formed in the gas phase, but there is evidence that the mechanisms may be more complicated than concerted, pericyclic additions (i.e., eq 38) and probably involve two or more steps.

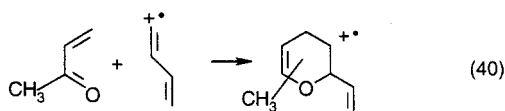


In early work, Groenewold and Gross²²⁴ examined the reactions of 1,3-butadiene radical cation with 1,3-butadiene. At different source pressures in their sector instrument, they were able to generate adducts that gave different products during collision-induced dissociation. At low source pressures, they formed

$C_8H_8^+$ ions that gave a fragmentation pattern that was consistent with ionized 4-vinylcyclohexene, the expected [4+2] cycloaddition (Diels–Alder) product. At high pressures, the $C_8H_8^+$ ions gave a fragmentation pattern that was consistent with an acyclic adduct resulting from the addition of the butadiene radical cation at carbon-2 of neutral butadiene to give a distonic radical cation (eq 39).

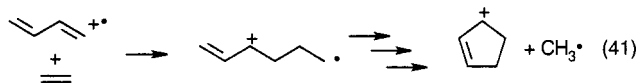


They reasoned that at high pressures, the initial, acyclic addition product could be collisionally stabilized whereas at low pressure, it would retain the internal energy from the addition process for a longer time and could cyclize in a second step to give the Diels–Alder product. Therefore, the addition process is not a true pericyclic reaction (i.e., governed by Woodward–Hoffmann rules), but a stepwise ionic/radical process. Groenewold and Gross²²⁵ also reexamined the reactions of vinyl methyl ether radical cation with butadiene.²²⁶ Again by varying source pressures, they were able to isolate an acyclic intermediate that suggested a stepwise mechanism for the formation of the Diels–Alder product. When methyl vinyl ketone reacts with ionized butadiene, Castle and Gross²²⁷ found evidence in the CID spectra of the collisionally stabilized adducts for the formation of dihydropyrans. In other words, the unsaturated ketone is acting as the “diene” and the butadiene as the “ene” in the formation of the Diels–Alder cycloadduct (eq 40).



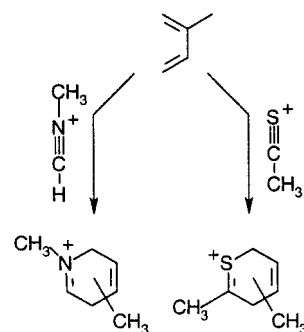
This is a notable result because Diels–Alder reactions of neutral dienes with vinyl ketones usually lead to the opposite regiochemistry with the vinyl ketone acting as the “ene” and the products are cyclohexenyl substituted ketones.

Bouchoux and Salpin²²⁸ have investigated the prototypical, cationic Diels–Alder reaction, butadiene radical cation plus ethene, in an ICR. In this case, the low background pressure in the ICR does not allow for the collisional stabilization of adducts, and only fragmentation products are observed (eq 41). However, experiments with deuterium labels are consistent with the initial formation of an acyclic, distonic radical cation that eventually cyclizes to give what appears to be a cyclopentenyl cation as the final product (the gas phase acidity of the product is consistent with this assignment).



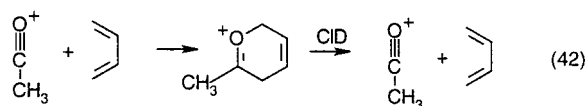
Experiments with deuterium labels indicate that when the acyclic adduct is formed, it can dissociate back to reactants after having undergone hydrogen/deuterium scrambling. Hofmann and Schaefer^{229,230}

Scheme 16



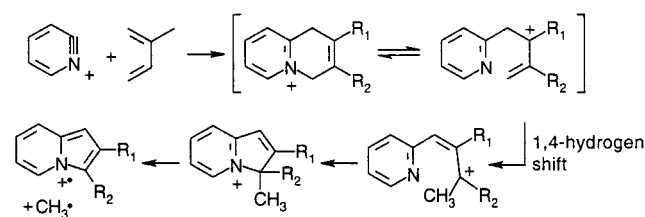
have studied the potential energy surface of this reaction in great detail using computational methods. Their work reveals a very complex network of competing reaction processes within the adduct that can account for the scrambling observed in Bouchoux and Salpin's reaction. Clearly the cycloaddition process in radical cations is more complex than the pericyclic process outlined in eq 38.

Eberlin, Cooks, and co-workers^{231–238} have completed a number of studies in a pentaquadrupole instrument involving the cycloadditions of closed-shell cations with dienes to give Diels–Alder products. This has proven to be a good gas phase synthesis of heterocycles. For example, when the acetyl cation is allowed to react with butadiene, an addition product is formed in high yield that when subjected to CID cleanly dissociates back to the acetyl cation.^{231,232} These workers formulate the product as a cycloaddition species (eq 42).



Preparation of a related cyclic cation by an independent route (electron impact on a dihydropyran precursor) led to an ion that gave CID fragments that were consistent with a retro-Diels–Alder process (i.e., acyl cations). In addition, the experiments show that the adduct is much more strongly bound than a hydrogen-bonded complex. The pathway is general, and the acetyl cation gives addition products with other dienes such as isoprene and cyclopentadiene. Moreover, a range of cations can be used so a wide variety of cycloaddition products can be formed. For example, nitrilium²³⁷ and thioacetyl²³¹ cations have been used to form nitrogen- and sulfur-containing heterocycles (Scheme 16). The mechanism of the reaction is not known and could be either stepwise or concerted; however, analogies to the radical cation systems might suggest that a multistep path is more likely. In addition, a recent study with 2-pyridyl and 2-pyrimidyl cations shows that rearrangements involving open-chain forms are possible in the adducts.²³³ When the 2-pyridyl cation reacts with isoprene, an indolizine product is formed. The proposed mechanism involves a 1,4-hydrogen shift followed by cyclization to a five-membered ring with loss of a methyl radical (Scheme 17).

Scheme 17



Calculations indicate that although the cyclic form of the initial addition product is more stable, formation of the open form is still exothermic by over 60 kcal/mol, so it is not surprising that rearrangements are possible and that a fragmentation is needed to release the excess energy in the adduct.

Overall, these studies show that a range of ionic cycloadditions can be performed in the gas phase. In some cases, the cycloadduct cannot be observed because the reaction exothermicity leads to subsequent fragmentation reactions. Although some of the cycloadducts appear to be Diels–Alder products, there is no evidence at this point for concerted cycloadditions (i.e., eq 38), and with radical cations, there are data that indicate that the additions are stepwise. Nonetheless, this approach is a promising method for producing unusual, cyclic cations.

IV. Reactions of Unusual Ionic Species

1. Highly Strained or Reactive Carbanions

Carbanions and their metal salts play a pivotal role in organic synthesis and have been explored in detail in gas phase studies. In this work, it has been possible to generate and characterize highly reactive and highly strained species. As Squires⁷ pointed out in a review from 1992, carbanions in solution are generally tightly ion-paired and often form aggregates; therefore, the gas phase provides a unique opportunity to study their intrinsic reactivity. A major challenge in this work has been the selective formation of the carbanion and the verification of its structure. A range of chemical approaches have been developed to address these issues.

A. Formation

Deprotonation is one route to the formation of carbanions, but it suffers from two critical limitations. First, the precursor must be sufficiently acidic so that it can be deprotonated by an easily formed, gas phase base. Because NH₂⁻ is the strongest, commonly used base, deprotonation is limited to ions with proton affinities (PA) less than 404 kcal/mol. This is sufficient for carbanions stabilized by resonance or electron-withdrawing groups, but generally not for localized hydrocarbons. Second, deprotonation is not selective so the site of interest must be significantly more acidic than others in the precursor. To avoid these problems, two approaches have been widely used. Taking advantage of analogies to condensed phase chemistry, DePuy and co-workers^{239–242} developed fluorodesilylation reactions for the formation of carbanions. Kass and co-workers have exploited this method for the selective formation

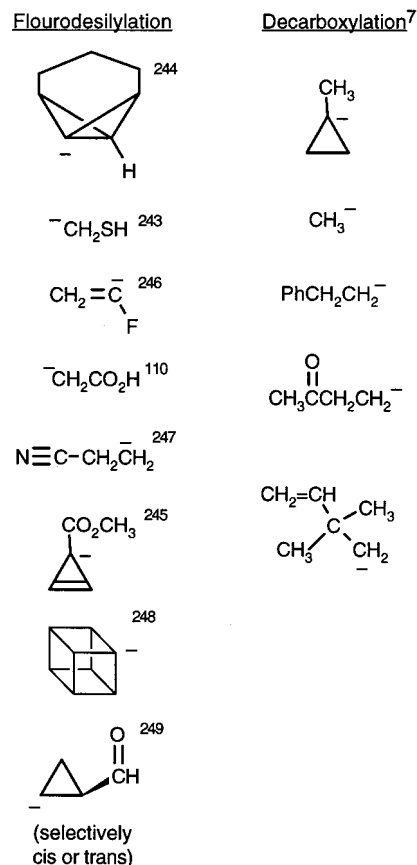
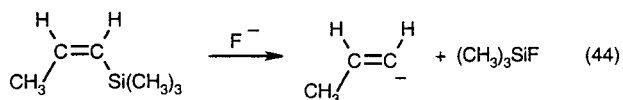
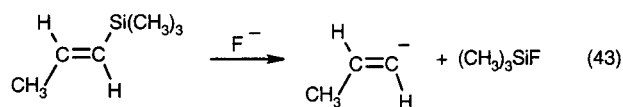


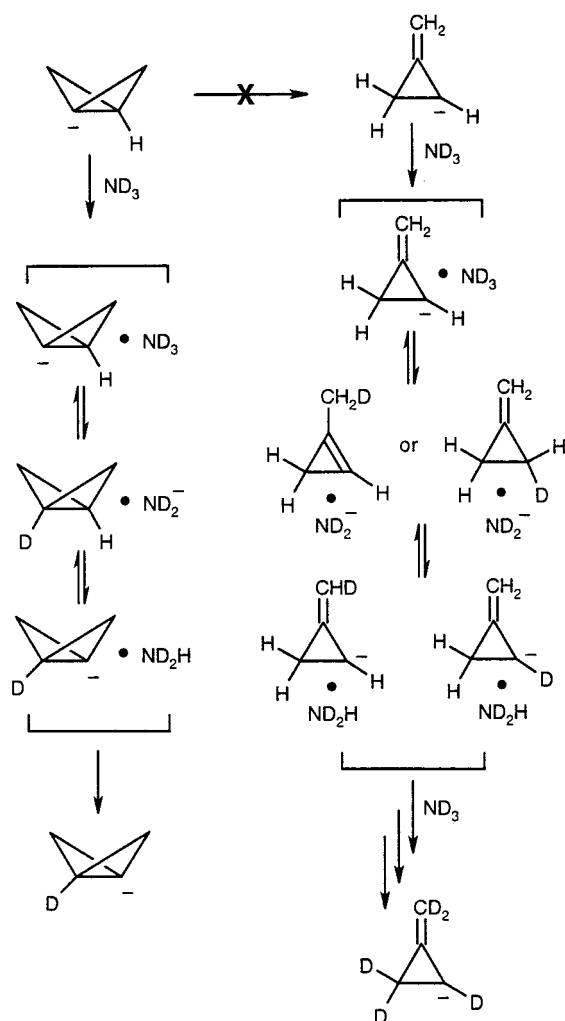
Figure 6. Novel carbanions formed in the gas phase by fluorodesilylation and decarboxylation. Appropriate references are shown. Decarboxylations are all documented in ref 7.

of many unusual hydrocarbon and related carbanions.^{243–249} For example, at elevated temperatures (200 °C) in their flowing afterglow, Chou and Kass²⁴⁴ were able to stereoselectively form vinyl anions by treatment of the appropriate trimethylsilyl precursor with fluoride (eqs 43 and 44).

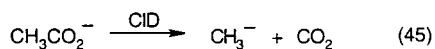


These ions are derivatives of propene, but of course deprotonation of propene would lead to the much more stable allyl anion. This demonstrates the power of the approach in that it was possible to form a carbanion at one of the least acidic sites in the parent hydrocarbon and select between two sites of relatively equal acidity (vinylic). A sample of carbanions formed by this method is shown in Figure 6. Squires has found that carbanions can be selectively formed in the collision-induced decarboxylation (CID) of carboxylates.^{7,250–253} This has proven to be a particularly useful way of forming very basic carbanions, and complements the fluorodesilylation method which at ambient temperatures is generally limited to the formation of carbanions with proton affinities below

Scheme 18



400 kcal/mol. Graul and Squires^{251,252} were able to produce the most basic of all known carbanions, CH_3^- (PA = 418 kcal/mol), by the decarboxylation of acetate (eq 45). Other species synthesized in this way are shown in Figure 6.



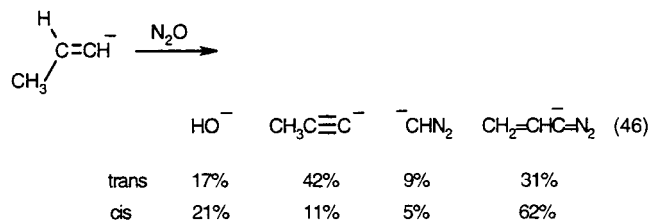
B. Characteristic Reactions

To verify the structures of carbanions, a number of simple reagents have been used, and a rich chemistry has been discovered with them. In this section, the carbanion reaction chemistry of several of these reagents will be presented and their utility in identifying structures will be illustrated.

Hydrogen/deuterium exchange has proven to be a useful tool for identifying the structures of gas phase ions.^{10,254–258} For example, when Kass and Chou²⁵⁹ treated the anion derived from bicyclobutane with ND_3 , one exchange was observed. If this ion had undergone a ring-opening reaction in the flowing afterglow to give the deprotonation product of methylenecyclopropane, five exchanges would be expected. This is outlined in Scheme 18. The process is analogous to the one described briefly earlier for the reactions of halonium ions with D_2O (section III.2). The bicyclobutyl anion forms a complex with ND_3 in

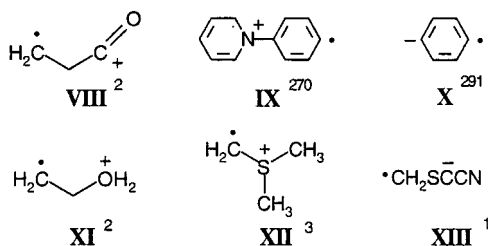
an exothermic process. Deuteron transfer is endothermic (bicyclobutane is more acidic than ND_3), but it is possible because the system is activated by the initial complexation energy (10–15 kcal/mol). However, dissociation of the new bicyclobutane/ ND_2^- complex would be endothermic (the complexation energy is lost during dissociation), and therefore a proton (or deuteron) must be transferred back to the ND_2^- before dissociation. If a proton is transferred, the monodeuterated bicyclobutane anion is formed. Since the methylene positions in bicyclobutane are much less acidic than the bridgehead position, there is only one proton that can be exchanged in the complex. For the possible rearrangement product, deprotonated methylenecyclopropane, the situation is more complicated. When the ND_3 complexes with this anion, a deuteron can be transferred to either the exocyclic carbon (to give 1-methylcyclopropene) or the ring (to give methylenecyclopropane). These two pathways do not have the same energetics, but both are accessible because the system is activated by the complexation energy. These pathways allow a mechanism for exchanging protons both on the ring carbons and on the exocyclic carbon. Again, a proton or deuteron must be transferred back to the ND_2^- before dissociation. However, the complex may undergo another exchange process before dissociation because the neutral reagent (ND_2H) still has deuteriums that can be transferred to the carbanion within the reaction complex. In addition, the partially deuterated methylenecyclopropane anion that is formed can react with additional ND_3 in the flow tube, and eventually all five protons can be exchanged. By comparison to authentic samples, Kass and Chou confirmed the expected exchange patterns and were able to show that the bicyclobutyl anion had not rearranged under their conditions.

A collection of simple inorganic triatomics (CO_2 , COS , CS_2 , N_2O)^{8,242,254,260–262} has proven to be invaluable in the characterization of carbanions by mass spectrometry. Of these, N_2O ^{260,262} has proven to be the most versatile, and its subtle reactivity patterns are well suited for distinguishing among isomeric ions. Chou and Kass's²⁴⁴ study of the 1-vinyl anions from propene provides an excellent example of isomeric ions giving different product distributions in their reactions with N_2O . Each ion gives four significant products with N_2O (eq 46). The formation of this set of diverse products hints at the wide range of pathways that are available with this simple reagent.



Likely mechanisms for the formation of the three most characteristic products are outlined in Scheme 19.²⁶³ In the cis ion, the major product is a diazo anion, a type of product that is commonly formed in the reactions of carbanions with N_2O . Initial attack

Scheme 21

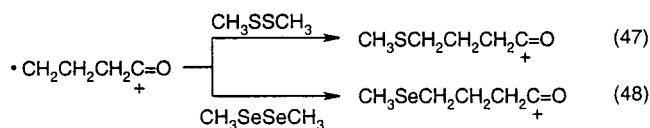


rearrangement products, but collision-induced dissociation as well as chemical ionization has been used in some cases. In these ions, the radical is generally localized at an alkyl or a vinyl site, but a wide variety of ionic sites have been observed including stabilized carbocations, ammonium ions, oxonium ions, and carbanions. A few examples are shown in Scheme 21.

The reactions of distonic radical cations and anions have been reviewed recently by Kenttämaa^{2,3} and Nibbering,¹ respectively, so this section of the present review will focus on more recent work.

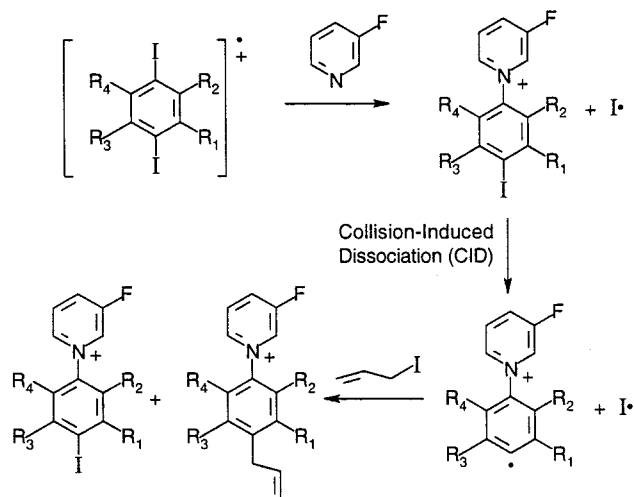
A. Distonic Radical Cations

Much of the effort with these ions has been directed toward developing reactions that can verify that the radical cation does have a distonic structure. This is particularly important because the distonic radical ions usually are formed from substrates that could potentially produce conventional radical cations. To address this issue, several reagents have been developed which can distinguish between conventional and distonic structures. Most of these methods rely on reagents that are highly reactive toward radical centers and produce diagnostic ions usually by transferring a neutral group from the test reagent. Kenttämaa and co-workers^{265–268} have been very active in this field in recent years, and based on their work in an ICR, they have identified several useful reagents including dimethyl disulfide,²⁶⁵ dimethyl diselenide,²⁶⁶ *tert*-butyl isocyanide,²⁶⁷ and triethylamine.²⁶⁸ With distonic radical cations, dimethyl disulfide and dimethyl diselenide generally act as radical traps and transfer $\text{CH}_3\text{S}^\bullet$ and $\text{CH}_3\text{Se}^\bullet$, respectively, to the distonic ion. For example, the distonic ion $\bullet\text{CH}_2\text{CH}_2\text{-CH}_2\text{C}=\text{O}^+$ reacts with both of these reagents to give group transfer reactions (eqs 47–48).



In contrast, conventional radical cations such as the molecular ions of ketones and ethers react exclusively by electron transfer with these reagents to produce the reagent's molecular ion. This difference in reactivity therefore provides a convenient way to distinguish between distonic and conventional radical cations. A more subtle measure of reactivity in distonic ions is found with *tert*-butyl isocyanide.²⁶³ This reagent readily transfers cyanide to localized cations (in conventional or distonic ions), resulting

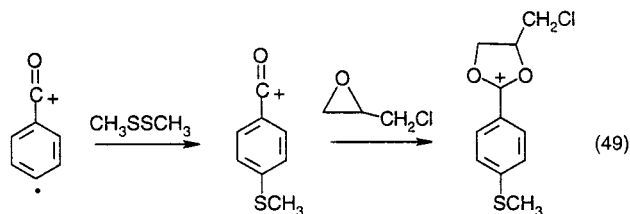
Scheme 22



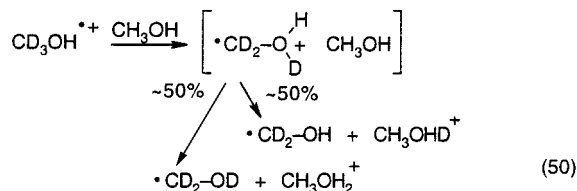
in the appearance of *tert*-butyl cations in the spectrum. If the ionic site of the distonic radical cation is unreactive (e.g., **IX** and **XII**), then radical behavior is observed and the isocyanide transfers a cyano radical to give a closed-shell cation. Finally, reagents such as triethylamine rely on the fact that many distonic radical cations are more acidic (e.g., **XI**) than their conventional analogues and give proton transfer reactions whereas the conventional radical cations have higher recombination energies and give electron transfer reactions.

A considerable amount of work has been completed for distonic ions that incorporate a phenyl radical. In these systems, interaction between the radical and charge sites is often prevented by geometric constraints. Kenttämaa and co-workers have investigated several aryl distonic radical cations where the charge carrier is designed to be inert.^{266,267,269–271} In this way, the charge is simply an ionic handle for mass spectrometric analysis of the reaction products, and the systems can provide a novel approach for studying radical reactions. Much of the work has involved pyridinium ions, and Heidbrink et al.²⁷⁰ have investigated the effects of substituents on the reactions of these ions with allyl iodide (Scheme 22). The distonic ions are synthesized in two steps beginning with the addition of a pyridine derivative to an ionized diiodobenzene followed by collision-induced dissociation (CID) to produce the distonic radical ion by cleavage of a C–I bond. In the reactions with allyl iodide, iodine transfer dominates over allyl transfer for all the substrates, and they find that there is no correlation between the computed reaction exothermicities and the reaction rates. However, it is clear from the data that electron-withdrawing groups such as CF_3 , F, and CN increase the rate of iodine transfer. In addition, halogenation of the radical (i.e., $\text{R}_1, \text{R}_2, \text{R}_3, \text{R}_4 = \text{F}$) greatly enhances the yield of allyl transfer products. Overall, this is an excellent example of using distonic ions to probe the subtle details of the intrinsic reactivity of organic radicals. Moraes and Eberlin²⁷² have studied the reactions dehydrobenzoyl cations with several reagents and have observed reactions characteristic of both radicals and acylium ions. In fact, they have demonstrated that sequential

reactions are possible with both the radical and charge site being modified (eq 49).

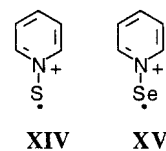


Kenttämäa and co-workers have studied a series of simple α distonic radical cations of the general structure $\cdot\text{CH}_2\text{XH}^+$ where $\text{X} = \text{SH}^{273}$ and PH_2^{274} (α indicates a 1,2 relationship between the radical and charge site). In both cases, the distonic ion is less stable than the conventional radical cation CH_3X^+ ; however, the two distonic radical cations display markedly different behavior in their reactions. The phosphorus-containing species ($\cdot\text{CH}_2\text{PH}_3^+$) reacts like a typical distonic ion and gives a $\text{CH}_3\text{S}\cdot$ transfer reaction with CH_3SSCH_3 . In contrast, $\cdot\text{CH}_2\text{SH}_2^+$ reacts with CH_3SSCH_3 via electron transfer, the pathway expected for the conventional radical cation, CH_3SH^+ . Apparently isomerization to the conventional structure can occur within the ion/molecule complex for the sulfur system by a proton transfer from the sulfur to the carbon assisted by the neutral reagent. This type of behavior had been seen in earlier studies^{275,276} with $\cdot\text{CH}_2\text{OH}_2^+$. In this case, the distonic radical cation is more stable than the conventional one (CH_3OH^+). The conventional cation undergoes reactions that are different than those of the distonic ion for reagents with proton affinities less than that of $\cdot\text{CH}_2\text{OH}$. For the more basic reagents, the distonic and conventional radical cations give virtually the same products. Audier and co-workers^{275,276} explained this shift in reactivity on the basis of a proton transfer catalyzed by the neutral reagent in the reaction complex. This can be shown via deuterium labeling where deprotonation of CD_3OH^+ by CH_3OH leads to nearly an equal mixture of $\text{CH}_3\text{-OH}_2^+$ and CH_3OHD^+ , suggesting the formation of a distonic ion, $\cdot\text{CD}_2\text{OHD}^+$, as an intermediate (eq 50).

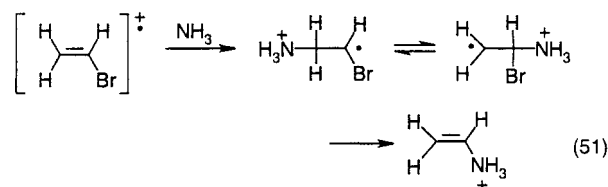


Isomerization does not occur in the reactions of the phosphorus-containing distonic radical cation ($\cdot\text{CH}_2\text{-PH}_3^+$), possibly because it is less acidic, and therefore the assisted, intramolecular proton transfer is less likely. Schwarz and co-workers²⁷⁷ have prepared related species, $\cdot\text{CH}_2\text{XCH}_3^+$ ($\text{X} = \text{Cl}, \text{Br}$), and they exhibit both cation (CH_3^+ transfer to CH_3CN) and radical ($\cdot\text{CH}_2$ transfer to NO) reactivity. Gerbaux, van Haverbeke, and Flammang^{278,279} have also prepared α distonic radical cations based on pyridine *N*-thioxide (**XIV**) and *N*-selenoxide (**XV**) frameworks. These ions give typical group transfer reactions with

dimethyl disulfide and dimethyl diselenide as evidence of their distonic radical ion character.



Audier and co-workers^{280–282} have studied several β distonic radical cations. Here, the radical site has a 1,3 relationship with the charge site. A common pathway with such ions is the transfer of the radical cation of ethene to the neutral reagent. For example, the reaction of $\cdot\text{CH}_2\text{CH}_2\text{OH}_2^+$ with $\text{CH}_2=\text{O}$ leads to the formation of $\cdot\text{CH}_2\text{CH}_2\text{OCH}_2^+$ with the loss of water.²⁸⁰ Audier²⁸³ has also studied the effect of solvation by H_2O on the reactivity of β distonic radical cations and found that the solvates undergo some (e.g., iodine transfer with allyl iodide), but not all, of the reactions of typical β distonic ions (ethene radical cation transfer with $\text{CH}_2=\text{O}$). They also find that the solvated distonic radical cations undergo ligand exchange reactions with alcohols and other groups to give new solvates. Nixdorf, Grutzmacher, and co-workers^{284–286} have identified β distonic ions as intermediates in the reaction of ammonia with ionized vinyl halides. Addition to the alkene to give the distonic ion is followed by carbon–halogen bond cleavage to give a vinylammonium ion. For example, addition of ammonia to ionized vinyl bromide gives an equilibrating mixture of addition products, only one of which can lead to the expulsion of the bromine atom to give a vinylammonium (eq 51).²⁸⁵

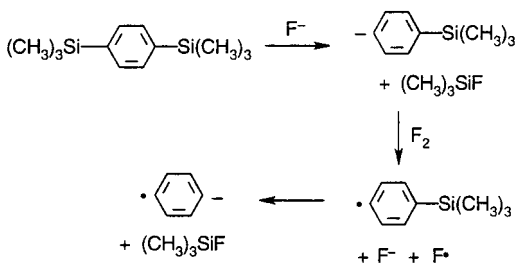


B. Distonic Radical Anions

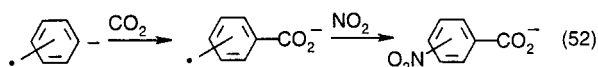
Less work has been reported on the reactions of distonic radical anions, but some fascinating species have been identified. Squires and co-workers^{287–292} have completed a series of flowing afterglow studies on the properties and reactivities of distonic ions that incorporate a phenyl radical. In the *o*-, *m*-, and *p*-benzyl radical anions, there is an electronic interaction between the radical and charge sites (particularly in the *o*-benzyl radical anion), but much of their reactivity is characteristic of distonic ions.^{290–292} Easy access to these ions was made possible by the development of an unusual desilylation procedure involving molecular fluorine.^{290,292} The application of this method to the formation of the *p*-benzyl radical anion is shown in Scheme 23.

Attack of fluoride ion causes the first desilylation to give a phenide anion. Electron transfer to F_2 gives a phenyl radical, a fluorine radical, and fluoride. Within the product complex of this reaction, the fluoride attacks the second trimethylsilyl group, producing the distonic radical anion product. The

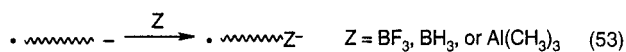
Scheme 23



method is general, and distonic biradical anions have also been synthesized in this way.²⁹⁰ The structures of the *o*-, *m*-, and *p*-benzyne radical anions were confirmed by converting them to nitrobenzoates in a two-step process by initially adding CO_2 to give a distonic benzoate species (i.e., reaction at the anionic site) followed by addition of NO_2 to the radical site (eq 52). Interestingly, the reagents cannot be added in the reverse order because the anionic site undergoes a charge transfer reaction with NO_2 faster than the radical site can add NO_2 . Conversion of the phenyl anion to the carboxylate eliminates the electron transfer pathway because the carboxylate has a higher electron binding energy. This behavior again points to the dual reactivity of distonic species. Comparison of the gas phase basicities of the synthesized nitrobenzoates to those of authentic samples confirmed the structural assignments of the *o*-, *m*-, and *p*-benzyne radical anions.²⁹¹



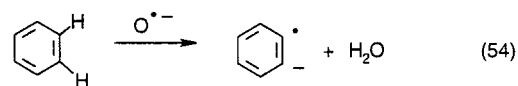
Species incorporating alkyl radicals have been reported by Squires,^{290,292–294} Nibbering,^{295,296} and their co-workers. For example, Wenthold and Squires²⁹³ have generated the $\cdot\text{CH}_2\text{CO}_2^-$ radical anion by their fluorine-induced desilylation method. This ion reacts with NO , NO_2 , and SO_2 by effectively transferring a CH_2^- group and expelling CO_2 . In the case of SO_2 , this produces a new distonic ion, $\cdot\text{CH}_2\text{SO}_2^-$. With CH_3SSCH_3 , the $\cdot\text{CH}_2\text{CO}_2^-$ radical anion abstracts a $\text{CH}_3\text{S}^\bullet$ group in a reaction analogous to those seen for distonic radical cations. Recently, Squires and co-workers²⁹⁴ studied the gas phase reactions of a group of distonic radical anions that they have referred to as “ate” complexes. These ions are formed in the reaction of a radical anion (distonic or conventional) with a Lewis acid (BH_3 , BF_3 , or $\text{Al}(\text{CH}_3)_3$) leading to a product where the charge is localized on a borate or aluminate group (eq 53 where the wavy line is used to represent the organic group linking the anionic and radical sites).



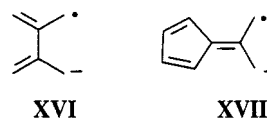
In this way, the charge carrier is relatively inert and these species are expected to display mainly radical behavior (much like Kenttämäa's pyridiniums). An interesting result from this study is that although several distonic radical anions abstract a $\text{CH}_3\text{S}^\bullet$ group from CH_3SSCH_3 (a reaction routinely used to identify radical reactivity),^{293,295,297} most of the “ate” distonic

radical anions do not. This suggests that the anionic site may play a role in the $\text{CH}_3\text{S}^\bullet$ transfer process of distonic radical anions. Finally, Zhong, Chabinyk, and Brauman²⁹⁸ have formed distonic radical enolate anions with the general structure $\text{RCH}=\text{C}(\text{O}^-)\text{CF}_2^\bullet$ by electron impact in an ICR. These distonic radical anions do not react with CH_3SSCH_3 by $\text{CH}_3\text{S}^\bullet$ group transfer and give only a small yield of Br atom abstraction from Br_2 . However, these distonic anions do undergo radical mediated addition/elimination reactions with both aryl and carbonyl groups (section II.3.A).

It is difficult to discuss the chemistry of distonic radical anions without some mention of the reactions of oxygen atom radical anions with organic substrates. The reactivity of O^\bullet has been reviewed comprehensively by Lee and Grabowski¹³ in 1992 and more recent studies appear in a review by Born, Ingemann, and Nibbering.¹ With respect to radical anions, the most interesting reaction of O^\bullet is the formal abstraction of H_2^+ to give a radical anion and H_2O as products. For example, O^\bullet reacts with benzene to give the *o*-benzyne radical anion (eq 54).²⁹⁹



Grabowski and co-workers have used this reagent to generate π -conjugated distonic radical anions of tetramethyleneethane (**XVI**)³⁰⁰ and cyclopentadienylidene-trimethylenemethane (**XVII**).³⁰¹

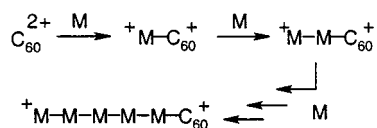


The latter distonic anion abstracts a $\text{CH}_3\text{S}^\bullet$ group from dimethyl disulfide, but the former does not. This result combined with work by Squires²⁹⁴ and Brauman²⁹⁸ suggests that dimethyl disulfide may not be as useful for identifying distonic radical anions as it is for identifying distonic radical cations.

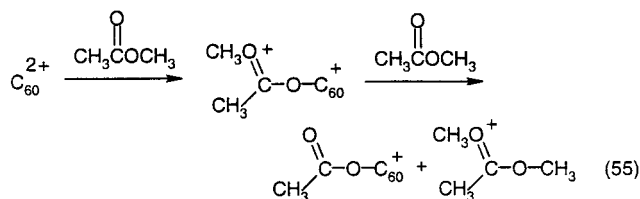
3. Fullerene Reactions

Since it was recognized that C_{60} cations in the mass spectrum of ionized graphite have a fullerene cage structure,³⁰² there have been many studies of the bimolecular reactivity of fullerene cations. A large amount of work has been completed by Bohme and co-workers using a selected-ion flow tube (SIFT).^{303–323} In these systems, ionization energies play an important role in determining the reactivity. The singly charged fullerene, C_{60}^+ , has the lowest recombination energy (7.6 eV³²⁴) and gives the least varied reactivity. The great majority of the reactions with C_{60}^+ are simple additions to give adduct ions.³¹⁵ For example, cyclopentadiene adds to give an ion with the formula $\text{C}_{65}\text{H}_6^+$ which may be assumed to be a Diels–Alder addition product.³²² Cooks and co-workers have also observed what appears to be a Diels–Alder product in the reactions of C_{60}^+ with 2,3-dimethoxy-1,3-butadiene.³²⁵ As expected for adduct forming reactions, more complex reagents give faster reaction

Scheme 24



rates presumably because the initial ion/molecule complexes have longer lifetimes and are more likely to be stabilized by collisions with the helium buffer gas in the flow tube. With amines, the rate climbs from 1.5×10^{-11} to 1.0×10^{-9} $\text{cm}^3/\text{molecule/s}$ in going from methylamine to trimethylamine.³⁰⁶ Although C_{60}^{2+} does not react with simple alkenes,^{322,326} the dication, with a recombination energy of over 11 eV,³⁰⁷ undergoes charge transfer as well as addition reactions with a variety of alkenes and polyenes.^{310,311,326} Multiple additions are possible, and Bohme and co-workers³¹¹ have observed over 10 additions of allene to C_{60}^{2+} . Bohme has presented data that indicate that these systems are undergoing "ball-and-chain" polymerizations where, after the first monomer is attached, a chain grows beginning with the first monomer unit.³¹⁰ This is outlined in Scheme 24. One outcome is that the distance between the two charges is increased, and therefore internal electrostatic repulsion is reduced in the chain growth process. Alternatively, the sequential additions may occur at different carbons on the fullerene cage, and Bohme has characterized this behavior as "surface derivatization". For example, up to 15 methoxy groups have been added to the surface of C_{60}^{2+} in reactions with CH_3ONO .³¹² It has also been observed that the initial adducts of addition reactions may react with a second molecule of the reagent by a proton or methyl cation transfer. For example, esters of C_{60}^{2+} can be made in this way by the reaction of C_{60}^{2+} with methyl acetate (eq 55).³¹⁷



When alcohols react with C_{60}^{2+} , alkyl cations can be formed by the abstraction of HO^- from the alcohol.³⁰⁴ This process competes with adduct formation, and the yield of the hydroxide abstraction product correlates with the stability of the resulting carbocation: methanol gives only an adduct, ethanol and *n*-propanol give a mixture of adduct formation and hydroxide transfer, and 2-propanol gives exclusively hydroxide transfer to form C_{60}OH^+ . Finally, Stry and Garvey³²⁷ have also studied the reactions of C_{60}^{2+} with a range of simple molecules and mainly observed addition processes, although an unusual reaction with dimethyl ether was detected that led to a product with the formula $\text{C}_{60}\text{C}_2\text{H}_2\text{O}^+$. The trication, C_{60}^{3+} , does many of the same reactions as the dication³¹⁵ but is more reactive. In fact, it will abstract Cl^- from HCl to give $\text{C}_{60}\text{Cl}^{2+}$ and a bare proton.³¹⁴

Even though fullerenes were discovered only recently, there is already a relatively large literature concerning the gas phase reactivity of their cations. It seems likely that the results from gas phase studies will point to useful methods for derivatizing fullerenes that eventually could be applied in condensed phase syntheses.

V. Summary

In the past 25 years, a tremendous amount of work has been published on the ion/molecule reactions of organic species. This review provides an overview of the areas where gas phase ion chemistry has made a contribution to our understanding of fundamental organic reaction processes. It is clear that the gas phase work can provide insights into subtle features of reaction mechanisms that could not be addressed by conventional condensed phase methods. The study of ion/molecule reactions has already had a major impact on the way that organic chemists think about reaction mechanisms and interpret substituent effects. Moreover, it has heightened our awareness of the importance of solvation effects and how they can alter not only absolute rates but also relative rates, leading in some cases to complete reversals in reactivity patterns.

A large body of work could not be included in this review due to space limitations. For example, the study of thermochemistry in the gas phase (i.e., acidities, basicities, bond strengths, binding energies, etc.) has provided a wealth of data that has been exceptionally useful in interpreting organic reaction mechanisms. This has spilled over into the study of organometallic systems, and several groups are making major headway in using mass spectrometry to probe the stability and reactivity of transition metal species. Finally, work involving chemical ionization has provided abundant information on gas phase reaction mechanisms.

The future appears to be very promising for the study of gas phase organic reaction mechanisms. In particular, the emergence of new ionization techniques and more powerful mass analyzers will allow chemists to explore a wider range of species. Although still at an early stage, the gas phase study of biochemical transformations offers great promise and has been facilitated by electrospray and matrix-assisted laser desorption ionization methods. In addition, these techniques provide a means for introducing important, metal-centered catalytic species into the gas phase and exploring the details of their reactivity. Finally, mass spectrometry continues to play a major role in the study of atmospheric ion chemistry and is providing important kinetic as well as mechanistic data.

VI. Acknowledgments

The author thanks the NSF for continuing support of his research program in gas phase ion chemistry. In addition, the author thanks the referees for reading this lengthy manuscript and providing numerous helpful suggestions. Finally, the author thanks Drs. Charles DePuy and Veronica Bierbaum for

introducing him to the wonderful world of gas phase organic reactions.

VII. References

- Radical anions: Born, M.; Ingemann, S.; Nibbering, N. M. M. *Mass Spectrom. Rev.* **1997**, *16*, 181.
- Distonic radical cations: Stirk, K. M.; Kiminkinen, L. K. M.; Kenttämää, H. I. *Chem. Rev.* **1992**, *92*, 1649.
- Distonic radical cations: Kenttämää, H. I. *Org. Mass Spectrom.* **1994**, *29*, 1.
- Radiolytic work: Speranza, M. *Mass Spectrom. Rev.* **1992**, *11*, 73.
- Radiolytic work: Cacace, F. *Acc. Chem. Res.* **1988**, *21*, 215.
- Electrophilic aromatic substitution: Fornarini, S.; Crestoni, M. E. *Acc. Chem. Res.* **1998**, *31*, 827.
- Carbanion reactions: Squires, R. R. *Acc. Chem. Res.* **1992**, *25*, 461.
- Carbanion reactions: DePuy, C. H.; Bierbaum, V. M. *Acc. Chem. Res.* **1981**, *14*, 146.
- Nucleophilic substitution: Riveros, J. M.; Jose, S. M.; Takashima, K. *Adv. Phys. Org. Chem.* **1985**, *21*, 197.
- Reactions of organic anions: Nibbering, N. M. M. *Adv. Phys. Org. Chem.* **1988**, *24*, 1.
- Gas phase solvolysis-like reactions: Morton, T. H. *Tetrahedron* **1982**, *38*, 3195.
- Organophosphorous and sulfur anion reactions: O'Hair, R. A. *J. Mass Spectrom. Rev.* **1991**, *10*, 133.
- Reactions of oxygen atom radical anions: Lee, J.; Grabowski, J. *J. Chem. Rev.* **1992**, *92*, 1611.
- Organosilicon anions: Damrauer, R.; Hankin, J. A. *Chem. Rev.* **1995**, *95*, 1137.
- Mass spectrometry and reactions: Bowers, M. T.; Marshall, A. G.; McLafferty, F. W. *J. Phys. Chem.* **1996**, *100*, 12897.
- Analytical applications of ion/molecule reactions: Brodbelt, J. S. *Mass Spectrom. Rev.* **1997**, *16*, 91.
- Enantioselectivity: Filippi, A.; Giardini, A.; Piccirillo, S.; Speranza, M. *Int. J. Mass Spectrom.* **2000**, *198*, 137.
- Olmstead, W. N.; Brauman, J. I. *J. Am. Chem. Soc.* **1977**, *99*, 4219.
- Caldwell, G.; Magnera, T. F.; Kebarle, P. *J. Am. Chem. Soc.* **1984**, *106*, 959.
- Li, C.; Ross, P.; Szulejko, J. E.; McMahon, T. B. *J. Am. Chem. Soc.* **1996**, *118*, 9360.
- Dougherty, R. C.; Dalton, J.; Roberts, J. D. *Org. Mass Spectrom.* **1974**, *8*, 77.
- Dougherty, R. C. *Org. Mass Spectrom.* **1974**, *8*, 85.
- Dougherty, R. C.; Roberts, J. D. *Org. Mass Spectrom.* **1974**, *8*, 81.
- Ayotte, P.; Kim, J.; Kelley, J. A.; Nielsen, S. B.; Johnson, M. A. *J. Am. Chem. Soc.* **1999**, *121*, 6950.
- Hase, W. L. *Science* **1994**, *266*, 998.
- Vande Linde, S. R.; Hase, W. L. *J. Am. Chem. Soc.* **1989**, *111*, 2349.
- Vande Linde, S. R.; Hase, W. L. *J. Chem. Phys.* **1990**, *93*, 7962.
- Vande Linde, S. R.; Hase, W. L. *J. Phys. Chem.* **1990**, *94*, 6148.
- Cho, Y. J.; Vande Linde, S. R.; Zhu, L.; Hase, W. L. *J. Chem. Phys.* **1992**, *96*, 8275.
- Hase, W. L.; Cho, Y. J. *J. Chem. Phys.* **1993**, *98*, 8626.
- Wang, H.; Perlhörbe, G. H.; Hase, W. L. *J. Am. Chem. Soc.* **1994**, *116*, 9644.
- Wang, H.; Zhu, L.; Hase, W. L. *J. Phys. Chem.* **1994**, *98*, 1608.
- Wang, H.; Hase, W. L. *J. Am. Chem. Soc.* **1995**, *117*, 9347.
- Wang, H.; Hase, W. L. *Chem. Phys.* **1996**, *212*, 247.
- Peslherbe, G. H.; Wang, H.; Hase, W. L. *J. Am. Chem. Soc.* **1996**, *118*, 2257.
- Wang, H.; Hase, W. L. *J. Am. Chem. Soc.* **1997**, *119*, 3093.
- Wang, H.; Goldfield, E. M.; Hase, W. L. *J. Chem. Soc., Faraday Trans.* **1997**, *93*, 737.
- Hase, W. L.; Wang, H.; Peslherbe, G. H. *Adv. Gas Phase Ion Chem.* **1998**, *3*, 125.
- Su, T.; Wang, H.; Hase, W. L. *J. Phys. Chem. A* **1998**, *102*, 9819.
- Mann, D. J.; Hase, W. L. *J. Phys. Chem. A* **1998**, *102*, 6208.
- Li, G.; Hase, W. L. *J. Am. Chem. Soc.* **1999**, *121*, 7124.
- Graul, S. T.; Bowers, M. T. *J. Am. Chem. Soc.* **1991**, *113*, 9696.
- Graul, S. T.; Bowers, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 3875.
- Graul, S. T.; Carpenter, C. J.; Bushnell, J. E.; van Koppen, P. A. M.; Bowers, M. T. *J. Am. Chem. Soc.* **1998**, *120*, 6785.
- Su, T.; Morris, R. A.; Viggiano, A. A.; Paulson, J. F. *J. Phys. Chem.* **1990**, *94*, 8426.
- Viggiano, A. A.; Morris, R. A.; Paschkewitz, J. S.; Paulson, J. F. *J. Am. Chem. Soc.* **1992**, *114*, 10477.
- Viggiano, A. A.; Morris, R. A.; Su, T.; Wladkowski, B. D.; Craig, S. L.; Zhong, M.; Brauman, J. I. *J. Am. Chem. Soc.* **1994**, *116*, 2213.
- Seeley, J. V.; Morris, R. A.; Viggiano, A. A. *J. Phys. Chem. A* **1997**, *101*, 4598.
- Morris, R. A.; Viggiano, A. A. *J. Phys. Chem.* **1994**, *98*, 3740.
- Wladkowski, B. D.; Wilbur, J. L.; Brauman, J. I. *J. Am. Chem. Soc.* **1992**, *114*, 9706.
- Wilbur, J. L.; Wladkowski, B. D.; Brauman, J. I. *J. Am. Chem. Soc.* **1993**, *115*, 10823.
- Wilbur, J. L.; Brauman, J. I. *J. Am. Chem. Soc.* **1991**, *113*, 9699.
- Wilbur, J. L.; Brauman, J. I. *J. Am. Chem. Soc.* **1994**, *116*, 9216.
- Craig, S. L.; Brauman, J. I. *Science* **1997**, *276*, 1536.
- Craig, S. L.; Zhong, M.; Brauman, J. I. *J. Am. Chem. Soc.* **1998**, *120*, 12125.
- Chabinc, M. L.; Craig, S. L.; Regan, C. K.; Brauman, J. I. *Science* **1998**, *279*, 1882.
- Sahlstrom, K. E.; Knighton, W. B.; Grimsrud, E. P. *J. Phys. Chem. A* **1997**, *101*, 1501.
- Sahlstrom, K. E.; Knighton, W. B.; Grimsrud, E. P. *J. Phys. Chem. A* **1997**, *101*, 5543.
- Strode, K. S.; Grimsrud, E. P. *Int. J. Mass Spectrom. Ion Proc.* **1994**, *130*, 227.
- Knighton, W. B.; Bogner, J. A.; O'Connor, P. M.; Grimsrud, E. P. *J. Am. Chem. Soc.* **1993**, *115*, 12079.
- Pellerite, M. J.; Brauman, J. I. *J. Am. Chem. Soc.* **1980**, *102*, 5993.
- Pellerite, M. J.; Brauman, J. I. *J. Am. Chem. Soc.* **1983**, *105*, 2672.
- Dodd, J. A.; Brauman, J. I. *J. Am. Chem. Soc.* **1984**, *106*, 5356.
- Dodd, J. A.; Brauman, J. I. *J. Phys. Chem.* **1986**, *90*, 3559.
- Wladkowski, B. D.; Wilbur, J. L.; Brauman, J. I. *J. Am. Chem. Soc.* **1994**, *116*, 2471.
- Wladkowski, B. D.; Brauman, J. I. *J. Phys. Chem.* **1993**, *97*, 13158.
- Tanaka, K.; Mackay, G. I.; Payzant, J. D.; Bohme, D. K. *Can. J. Chem.* **1976**, *54*, 1643.
- Bohme, D. K.; Young, L. B. *J. Am. Chem. Soc.* **1970**, *92*, 7354.
- DePuy, C. H.; Gronert, S.; Mullin, A.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1990**, *112*, 8650.
- Bartmess, J. E. In *NIST Standard Reference Database Number 69*; Mallard, W. G., Linstrom, P. J., Eds.; National Institute of Standards and Technology (<http://webbook.nist.gov>): Gaithersburg, MD, 1999.
- Ingemann, S.; Nibbering, N. M. M. *Can. J. Chem.* **1984**, *62*, 2273.
- McDonald, R. N.; Gung, W. Y. *J. Am. Chem. Soc.* **1987**, *109*, 7328.
- McDonald, R. N.; Chowdhury, A. K. *J. Am. Chem. Soc.* **1983**, *105*, 2194.
- McDonald, R. N.; Chowdhury, A. K. *J. Am. Chem. Soc.* **1983**, *105*, 7267.
- McDonald, R. N.; Chowdhury, A. K. *J. Am. Chem. Soc.* **1985**, *107*, 4123.
- McDonald, R. N.; Chowdhury, A. K. *J. Am. Chem. Soc.* **1983**, *105*, 198.
- Barlow, S. E.; Van Doren, J. M.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1988**, *110*, 7240.
- Su, T.; Bowers, M. T. In *Gas Phase Ion Chemistry*; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 1, p 83.
- Streitwieser, A., Jr. *Solvolytic Displacement Reactions*; McGraw-Hill: New York, 1962.
- DeTuri, V. F.; Hintz, P. A.; Ervin, K. M. *J. Phys. Chem.* **1997**, *101*, 5969.
- Marcus, R. A. *Annu. Rev. Phys. Chem.* **1964**, *15*, 155.
- Gronert, S. *J. Am. Chem. Soc.* **1993**, *115*, 652.
- Bordwell, F. G.; Branner, W. T., Jr. *J. Am. Chem. Soc.* **1964**, *86*, 4545.
- Jones, M. E.; Ellison, G. B. *J. Am. Chem. Soc.* **1989**, *111*, 1645.
- Lieder, C. A.; Brauman, J. I. *Int. J. Mass Spectrom. Ion Phys.* **1975**, *16*, 307.
- Flores, A. E.; Gronert, S. *J. Am. Chem. Soc.* **1999**, *121*, 2627.
- Wladkowski, B. D.; Brauman, J. I. *J. Am. Chem. Soc.* **1992**, *114*, 10643.
- Lum, R. C.; Grabowski, J. J. *J. Am. Chem. Soc.* **1992**, *114*, 9663.
- Lum, R. C.; Grabowski, J. J. *J. Am. Chem. Soc.* **1988**, *110*, 8568.
- Ricci, A. *Int. J. Mass Spectrom. Ion Proc.* **1997**, *164*, 121.
- Bierbaum, V. M.; DePuy, C. H.; Shapiro, R. H.; Stewart, J. H. *J. Am. Chem. Soc.* **1976**, *98*, 4229.
- DePuy, C. H.; Beedle, E. C.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1982**, *104*, 6483.
- Gronert, S.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1991**, *113*, 4009.
- Jones, M. E.; Kass, S. R.; Filley, J.; Barkley, R. M.; Ellison, G. B. *J. Am. Chem. Soc.* **1985**, *107*, 109.
- Freriks, I. L.; De Koning, L. J.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1991**, *113*, 9119.
- Freriks, I. L.; De Koning, L. J.; Nibbering, N. M. M. *J. Phys. Org. Chem.* **1992**, *5*, 776.
- Freriks, I. L.; De Koning, L. J.; Nibbering, N. M. M. *J. Org. Chem.* **1992**, *57*, 5976.
- Brickhouse, M. D.; Squires, R. R. *J. Phys. Org. Chem.* **1989**, *2*, 389.
- Riveros, J. M.; Takashima, K. *Can. J. Chem.* **1976**, *54*, 1839.
- Briscese, S. M.; Riveros, J. M. *J. Am. Chem. Soc.* **1975**, *97*, 230.

- (101) Bartmess, J. E.; Hays, R. L.; Cardwell, G. *J. Am. Chem. Soc.* **1981**, *103*, 1338.
- (102) Sullivan, S. A.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1977**, *99*, 5017.
- (103) Brickhouse, M. D.; Squires, R. R. *J. Am. Chem. Soc.* **1988**, *110*, 2706.
- (104) Maas, W. P. M.; van Veelen, P. A.; Nibbering, N. M. M. *Org. Mass Spectrom.* **1989**, *24*, 546.
- (105) Ingemann, S.; Nibbering, N. M. M. *Nouv. J. Chim.* **1984**, *8*, 299.
- (106) Ingemann, S.; Nibbering, N. M. M.; Sullivan, S. A.; DePuy, C. H. *J. Am. Chem. Soc.* **1982**, *104*, 6520.
- (107) Dawson, J. H. J.; Nibbering, N. M. M. *Int. J. Mass Spectrom. Ion Phys.* **1980**, *33*, 3.
- (108) Freriks, I. L.; De Koning, L. J.; Nibbering, N. M. M. *Int. J. Mass Spectrom. Ion Proc.* **1992**, *117*, 345.
- (109) Freriks, I. L.; de Koning, L. J.; Nibbering, N. M. M. *Rapid Commun. Mass Spectrom.* **1993**, *7*, 757.
- (110) O'Hair, R. A. J.; Gronert, S.; DePuy, C. H.; Bowie, J. H. *J. Am. Chem. Soc.* **1989**, *111*, 3105.
- (111) Wladkowski, B. D.; Wilbur, J. L.; Zhong, M.; Brauman, J. I. *J. Am. Chem. Soc.* **1993**, *115*, 8833.
- (112) DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1981**, *103*, 5034.
- (113) Bierbaum, V. M.; Filley, J.; DePuy, C. H.; Jarrold, M. F.; Bowers, M. T. *J. Am. Chem. Soc.* **1985**, *107*, 2818.
- (114) de Koning, L. J.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1987**, *109*, 1715.
- (115) Baschky, M. C.; Kass, S. R. *Int. J. Mass Spectrom.* **2000**, *195/196*, 411.
- (116) Rabasco, J. J.; Gronert, S.; Kass, S. R. *J. Am. Chem. Soc.* **1994**, *116*, 3133.
- (117) Gronert, S. *J. Am. Chem. Soc.* **1992**, *114*, 2349.
- (118) Rabasco, J. J.; Kass, S. R. *Tetrahedron Lett.* **1991**, *32*, 4077.
- (119) Rabasco, J. J.; Kass, S. R. *J. Org. Chem.* **1993**, *58*, 2633.
- (120) Rabasco, J. J.; Kass, S. R. *Tetrahedron Lett.* **1993**, *34*, 765.
- (121) Bickelhaupt, F. M.; Buisman, G. J. H.; de Koning, L. J.; Nibbering, N. M. M.; Baerends, E. J. *J. Am. Chem. Soc.* **1995**, *117*, 9889.
- (122) Bender, M. L. *Chem. Rev.* **1960**, *60*, 53.
- (123) Asubiojo, O. I.; Brauman, J. I. *J. Am. Chem. Soc.* **1979**, *101*, 3715.
- (124) Wilbur, J. L.; Brauman, J. I. *J. Am. Chem. Soc.* **1994**, *116*, 5839.
- (125) Takashima, K.; Jose, S. M.; do Amaral, A. T.; Riveros, J. M. *J. Chem. Soc., Chem. Commun.* **1983**, 1255.
- (126) O'Hair, R. A. J.; Androutsopoulos, N. K. *Org. Lett.* **2000**, *2*, 2567.
- (127) Baer, S.; Brinkman, E. B.; Brauman, J. I. *J. Am. Chem. Soc.* **1991**, *113*, 805.
- (128) Bohme, D. K.; MacKay, G. I.; Tanner, S. D. *J. Am. Chem. Soc.* **1980**, *102*, 407.
- (129) Van der Wel, H.; Nibbering, N. M. M. *Recl. Trav. Chim. Pays-Bas* **1988**, *107*, 479.
- (130) Van der Wel, H.; Nibbering, N. M. M. *Recl. Trav. Chim. Pays-Bas* **1988**, *107*, 491.
- (131) Paul, G. J. C.; Kebarle, P. *J. Phys. Chem.* **1990**, *94*, 5184.
- (132) Riveros, J. M. *J. Chem. Soc., Chem. Commun.* **1990**, 773.
- (133) Faigle, J. F. G.; Isolani, P. C.; Riveros, J. M. *J. Am. Chem. Soc.* **1976**, *98*, 2049.
- (134) DePuy, C. H.; Grabowski, J. J.; Bierbaum, V. M.; Ingemann, S.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1985**, *107*, 1093.
- (135) Takashima, K.; Riveros, J. M. *J. Am. Chem. Soc.* **1978**, *100*, 6128.
- (136) Frink, B. T.; Hadad, C. M. *J. Chem. Soc., Perkin Trans. 2* **1999**, 2397.
- (137) Bernasconi, C. F.; Stronach, M. W.; DePuy, C. H.; Gronert, S. *J. Am. Chem. Soc.* **1990**, *112*, 9044.
- (138) McDonald, R. N.; Chowdhury, A. K.; Setser, D. W. *J. Am. Chem. Soc.* **1980**, *102*, 6491.
- (139) McDonald, R. N.; Chowdhury, A. K.; McGhee, W. D. *J. Am. Chem. Soc.* **1984**, *106*, 4112.
- (140) McDonald, R. N. *Tetrahedron* **1989**, *45*, 3993.
- (141) Matimba, H. E. K.; Crabbendam, A. M.; Ingemann, S.; Nibbering, N. M. M. *Int. J. Mass Spectrom. Ion Proc.* **1992**, *114*, 85.
- (142) Born, M.; Ingemann, S.; Nibbering, N. M. M. *J. Chem. Soc., Perkin Trans. 2* **1996**, 2537.
- (143) Kleingeld, J. C.; Nibbering, N. M. M. *Tetrahedron Lett.* **1980**, *21*, 1687.
- (144) Ingemann, S.; Nibbering, N. M. M. *J. Org. Chem.* **1983**, *48*, 183.
- (145) Bowie, J. H.; Stapleton, B. J. *Aust. J. Chem.* **1977**, *30*, 795.
- (146) DePuy, C. H.; Bierbaum, V. M.; Schmitt, R. J.; Shapiro, R. H. *J. Am. Chem. Soc.* **1978**, *100*, 2920.
- (147) Ingemann, S.; Kleingeld, J. C.; Nibbering, N. M. M. *J. Chem. Soc., Chem. Commun.* **1982**, 1009.
- (148) Sheldon, J. C.; Bowie, J. H.; Dua, S.; Smith, J. D.; O'Hair, R. A. J. *J. Org. Chem.* **1997**, *62*, 3931.
- (149) King, G. K.; Maricq, M. M.; Bierbaum, V. M.; DePuy, C. H. *J. Am. Chem. Soc.* **1981**, *103*, 7133.
- (150) Artau, A.; Ho, Y.; Kenttämaa, H.; Squires, R. R. *J. Am. Chem. Soc.* **1999**, *121*, 7130.
- (151) Ho, Y.; Squires, R. R. *J. Am. Chem. Soc.* **1992**, *114*, 10961.
- (152) Wu, Y.; Houk, K. N. *J. Am. Chem. Soc.* **1993**, *115*, 10993.
- (153) Fornarini, S. *Mass Spectrom. Rev.* **1997**, *15*, 365.
- (154) Aschi, M.; Attina, M.; Cacace, F. *Res. Chem. Intermed.* **1996**, *22*, 645.
- (155) Berthomieu, D.; Brenner, V.; Ohanessian, G.; Denhez, J. P.; Millie, P.; Audier, H. E. *J. Phys. Chem.* **1995**, *99*.
- (156) Berthomieu, D.; Audier, H. E.; Denhez, J. P.; Monteiro, C.; Mourgues, P. *Org. Mass Spectrom.* **1991**, *26*, 271.
- (157) Crestoni, M. E. *J. Phys. Chem.* **1993**, *97*, 6197.
- (158) Crestoni, M. E.; Fornarini, S.; Kuck, D. *J. Phys. Chem.* **1995**, *99*, 3144.
- (159) Aschi, M.; Attina, M.; Cacace, F. *Chem. - Eur. J.* **1998**, *4*, 1535.
- (160) Aschi, M.; Attina, M.; D'Arcangelo, G. *Chem. Phys. Lett.* **1998**, *283*, 307.
- (161) Aschi, M.; Attina, M.; Cacace, F.; D'Arcangelo, G. *J. Am. Chem. Soc.* **1998**, *120*, 3982.
- (162) Aschi, M.; Attina, M.; Cacace, F. *J. Am. Chem. Soc.* **1995**, *117*, 12832.
- (163) Cerichelli, G.; Crestoni, M. E.; Fornarini, S. *J. Am. Chem. Soc.* **1992**, *114*, 2002.
- (164) Angelini, G.; Bucci, R.; Laguzzi, G.; Siciliano, C.; Segre, A. L. *J. Phys. Chem. A* **1998**, *102*, 6464.
- (165) Harrison, A. G. *Can. J. Chem.* **1986**, *64*, 1051.
- (166) Holman, R. W.; Eary, T.; Whittle, E.; Gross, M. L. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2187.
- (167) Holman, R. W.; Gross, M. L. *J. Am. Chem. Soc.* **1989**, *111*, 3560.
- (168) Crestoni, M. E.; Fornarini, S.; Speranza, M. *J. Am. Chem. Soc.* **1990**, *112*, 6929.
- (169) Laguzzi, G.; Bucci, R.; Grandinetti, F.; Speranza, M. *J. Am. Chem. Soc.* **1990**, *112*, 3064.
- (170) Angelini, G.; Sparapani, C.; Speranza, M. *J. Am. Chem. Soc.* **1990**, *112*, 3060.
- (171) Speranza, M. *Pure Appl. Chem.* **1991**, *63*, 243.
- (172) Bucci, R.; Grandinetti, F.; Filippi, A.; Laguzzi, G.; Occhiucci, G.; Speranza, M. *J. Am. Chem. Soc.* **1991**, *113*, 4550.
- (173) Filippi, A.; Occhiucci, G.; Speranza, M. *Can. J. Chem.* **1991**, *69*, 732.
- (174) Cecchi, P.; Pizzabiocca, A.; Renzi, G.; Sparapani, C.; Speranza, M. *Can. J. Chem.* **1991**, *69*, 2094.
- (175) Filippi, A.; Occhiucci, G.; Sparapani, C.; Speranza, M. *Can. J. Chem.* **1991**, *69*, 740.
- (176) Bortolini, O.; Yang, S. S.; Cooks, R. G. *Org. Mass Spectrom.* **1993**, *28*, 1313.
- (177) Giacomello, P.; Pepi, F. *J. Phys. Chem.* **1993**, *97*, 4421.
- (178) Attina, M.; Cacace, F.; Ricci, A. *J. Phys. Chem.* **1996**, *100*, 4424.
- (179) Attina, M.; Cacace, F. *J. Am. Chem. Soc.* **1986**, *108*, 318.
- (180) Sharma, D. K. S.; Kebarle, P. *J. Am. Chem. Soc.* **1982**, *104*, 19.
- (181) Chatfield, D. A.; Bursey, A. M. *J. Am. Chem. Soc.* **1976**, *98*, 6492.
- (182) Dunbar, R. C.; Shen, J.; Olah, G. A. *J. Am. Chem. Soc.* **1972**, *94*, 6863.
- (183) Dunbar, R. C.; Shen, J.; Melby, E.; Olah, G. A. *J. Am. Chem. Soc.* **1973**, *95*, 7200.
- (184) Benezra, S. A.; Hoffman, M. K.; Bursey, M. M. *J. Am. Chem. Soc.* **1970**, *92*, 7501.
- (185) Attina, M.; Cacace, F.; Yanez, M. *J. Am. Chem. Soc.* **1987**, *109*, 5092.
- (186) Sen Sharma, D. K.; Kebarle, P. *J. Am. Chem. Soc.* **1982**, *104*, 19.
- (187) O'Hair, R. A. J.; Freitas, M. A.; Schmidt, J. A. R.; Hatley, M. E.; Williams, T. D. *Eur. Mass Spectrom.* **1995**, *1*, 457.
- (188) Freitas, M. A.; O'Hair, R. A. J.; Williams, T. D. *J. Org. Chem.* **1997**, *62*, 6112.
- (189) O'Hair, R. A. J.; Freitas, M. A.; Gronert, S.; Schmidt, J. A. R.; Williams, T. D. *J. Org. Chem.* **1995**, *60*, 1990.
- (190) Berman, D. W.; Anicich, V.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1979**, *101*, 1239.
- (191) Heck, A. J. R.; de Koning, L. J.; Nibbering, N. M. M. *Org. Mass Spectrom.* **1993**, *28*, 235.
- (192) Heck, A. J. R.; de Koning, L. J.; Nibbering, N. M. M. *Org. Mass Spectrom.* **1993**, *28*, 245.
- (193) Wilson, P. F.; McEwan, M. J.; Meot-Ner, M. *Int. J. Mass Spectrom. Ion Proc.* **1994**, *132*, 149.
- (194) Audier, H. E.; McMahon, T. B. *J. Mass Spectrom.* **1997**, *32*, 201.
- (195) Van Doorn, R.; Nibbering, N. M. M. *Org. Mass Spectrom.* **1978**, *13*, 527.
- (196) Karpas, Z.; Meot-Ner, M. *J. Phys. Chem.* **1989**, *93*, 1859.
- (197) Audier, H. E.; Bouchoux, G.; McMahon, T. B.; Milliet, A.; Vulpius, T. *Org. Mass Spectrom.* **1994**, *29*, 176.
- (198) Van der Rest, G.; Bouchoux, G.; Audier, H. E.; McMahon, T. B. *Eur. Mass Spectrom.* **1998**, *4*, 339.
- (199) Freitas, M. A.; O'Hair, R. A. J. *Int. J. Mass Spectrom. Ion Proc.* **1998**, *175*, 107.
- (200) Bauerle, G. F.; Brodbelt, J. S. *J. Am. Soc. Mass Spectrom.* **1995**, *6*, 627.
- (201) Eichmann, E. S.; Brodbelt, J. S. *Org. Mass Spectrom.* **1993**, *28*, 737.
- (202) Isbell, J. J.; Brodbelt, J. S. *J. Am. Soc. Mass Spectrom.* **1996**, *7*, 565.
- (203) Alvarez, E. J.; Brodbelt, J. S. *J. Mass Spectrom.* **1996**, *31*, 901.

- (204) Bache-Andreassen, L.; Uggerud, E. *Int. J. Mass Spectrom.* **2000**, *195/196*, 171.
- (205) Pau, J. K.; Kim, J. K.; Caserio, M. C. *J. Am. Chem. Soc.* **1978**, *100*, 3838.
- (206) Kim, J. K.; Bonicamp, J.; Caserio, M. C. *J. Org. Chem.* **1981**, *46*, 4236.
- (207) Caserio, M. C.; Kim, J. K. *J. Org. Chem.* **1982**, *47*, 2940.
- (208) Attina, M.; Angelini, G.; Speranza, M. *Tetrahedron* **1981**, *37*, 1221.
- (209) Speranza, M.; Angelini, G. *J. Am. Chem. Soc.* **1980**, *102*, 3115.
- (210) Angelini, G.; Speranza, M. *J. Chem. Soc., Chem Commun.* **1978**, 213.
- (211) Uggerud, E.; Bacher-Anfreassen, L. *Chem. Eur. J.* **1999**, *5*, 1917.
- (212) Hall, D. G.; Gupta, C.; Morton, T. H. *J. Am. Chem. Soc.* **1981**, *103*, 2416.
- (213) Sheldon, J. C.; Currie, G. J.; Bowie, J. H. *J. Chem. Soc., Perkin Trans. 2* **1986**, 941.
- (214) Kleingeld, J. C.; Nibbering, N. M. M. *Org. Mass Spectrom.* **1982**, *17*, 136.
- (215) Bass, L. M.; Cates, R. D.; Jarrold, M. F.; Kirchner, N. J.; Bowers, M. T. *J. Am. Chem. Soc.* **1983**, *105*, 7024.
- (216) Despeyroux, D.; Cole, R. B.; Tabet, J.-C. *Org. Mass Spectrom.* **1992**, *27*, 300.
- (217) Occhiucci, G.; Speranza, M.; De Koning, L. J.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1989**, *111*, 7387.
- (218) Dezi, E.; Lombardozi, A.; Pizzabiocca, A.; Renzi, G.; Speranza, M. *J. Chem. Soc., Chem. Commun.* **1995**, 547.
- (219) Dezi, E.; Lombardozi, A.; Renzi, G.; Pizzabiocca, A.; Speranza, M. *Chem. - Eur. J.* **1996**, *2*, 323.
- (220) Renzi, G.; Lombardozi, A.; Dezi, E.; Pizzabiocca, A.; Speranza, M. *Chem. - Eur. J.* **1996**, *2*, 316.
- (221) Speranza, M.; Troiani, A. *J. Org. Chem.* **1998**, *63*, 1020.
- (222) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781.
- (223) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley-Interscience: London, 1976.
- (224) Groenewold, G. S.; Gross, M. L. *J. Am. Chem. Soc.* **1984**, *106*, 6569.
- (225) Groenewold, G. S.; Gross, M. L. *J. Am. Chem. Soc.* **1984**, *106*, 6575.
- (226) Van Doorn, R.; Nibbering, N. M. M.; Ferrer-Correia, A. J. V.; Jennings, K. R. *Org. Mass Spectrom.* **1978**, *13*, 729.
- (227) Castle, L. W.; Gross, M. L. *Org. Mass Spectrom.* **1989**, *24*, 637.
- (228) Bouchoux, G.; Salpin, J. Y. *Rapid Commun. Mass Spectrom.* **1994**, *8*, 325.
- (229) Hofmann, M.; Schaefer, H. F. *J. Phys. Chem.* **1999**, *103*, 8895.
- (230) Hofmann, M.; Schaefer, H. F. *J. Am. Chem. Soc.* **1999**, *121*, 6719.
- (231) Eberlin, M. N.; Majumdar, T. K.; Cooks, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 2884.
- (232) Eberlin, M. N.; Cooks, R. G. *J. Am. Chem. Soc.* **1993**, *115*, 9226.
- (233) Gozzo, F. C.; Eberlin, M. N. *J. Org. Chem.* **1999**, *64*, 2188.
- (234) Augusti, R.; Gozzo, F. C.; Moraes, L. A. B.; Sparrapan, R.; Eberlin, M. N. *J. Org. Chem.* **1998**, *63*, 4889.
- (235) Eberlin, M. N. *Mass Spectrom. Rev.* **1997**, *16*, 113.
- (236) Lu, L.; Yang, S. S.; Wang, Z.; Cooks, R. G.; Eberlin, M. N. *J. Mass Spectrom.* **1995**, *30*, 581.
- (237) Eberlin, M. N.; Morgon, N. H.; Yang, S. S.; Shay, B. J.; Cooks, R. G. *J. Am. Soc. Mass Spectrom.* **1995**, *6*, 1.
- (238) Sparrapan, R.; Mendes, M. A.; Carvalho, M.; Eberlin, M. N. *Chem. - Eur. J.* **2000**, *6*, 321.
- (239) DePuy, C. H.; Bierbaum, V. M.; Flippin, L. A.; J., G. J.; King, G. K.; Schmitt, R. J.; Sullivan, S. A. *J. Am. Chem. Soc.* **1980**, *102*, 5012.
- (240) Squires, R. R.; DePuy, C. H. *Org. Mass Spectrom.* **1982**, *17*, 187.
- (241) DePuy, C. H.; Bierbaum, V. M.; Damrauer, R.; Soderquist, J. A. *J. Am. Chem. Soc.* **1985**, *107*, 3385.
- (242) DePuy, C. H.; Bierbaum, V. M.; Flippin, L. A.; Grabowski, J. J.; King, G. K.; Schmitt, R. J. *J. Am. Chem. Soc.* **1979**, *101*, 6443.
- (243) Kass, S. R.; Guo, H.; Dahlke, G. D. *J. Am. Soc. Mass Spectrom.* **1990**, *1*, 366.
- (244) Chou, P. K.; Kass, S. R. *J. Am. Chem. Soc.* **1991**, *113*, 4357.
- (245) Sachs, R. K.; Kass, S. R. *J. Am. Chem. Soc.* **1994**, *116*, 783.
- (246) Rabasco, J. J.; Kass, S. R. *J. Am. Soc. Mass Spectrom.* **1992**, *3*, 91.
- (247) Merrill, G. N.; Dahlke, G. D.; Kass, S. R. *J. Am. Chem. Soc.* **1996**, *118*, 4462.
- (248) Hare, M.; Emrick, T.; Eaton, P. E.; Kass, S. R. *J. Am. Chem. Soc.* **1997**, *119*, 237.
- (249) Baschky, M. C.; Peterson, K. C.; Kass, S. R. *J. Am. Chem. Soc.* **1994**, *116*, 7218.
- (250) Graul, S. T.; Squires, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 2517.
- (251) Graul, S. T.; Squires, R. R. *J. Am. Chem. Soc.* **1988**, *110*, 607.
- (252) Graul, S. T.; Squires, R. R. *J. Am. Chem. Soc.* **1989**, *111*, 892.
- (253) Graul, S. T.; Squires, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 2506.
- (254) Nibbering, N. M. M. *Recl. Trav. Chim. Pays-Bas* **1981**, *100*, 297.
- (255) Grabowski, J. J.; DePuy, C. H.; Van Doren, J. V.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1985**, *107*, 7384.
- (256) Stewart, J. H.; Shapiro, R. H.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1977**, *99*, 7650.
- (257) Squires, R. R.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1981**, *103*, 4256.
- (258) Squires, R. R.; Bierbaum, V. M.; Grabowski, J. J.; DePuy, C. H. *J. Am. Chem. Soc.* **1983**, *105*, 5185.
- (259) Kass, S. R.; Chou, P. K. *J. Am. Chem. Soc.* **1988**, *110*, 7899.
- (260) Kass, S. R.; Filley, J.; Van Doren, J. M.; DePuy, C. H. *J. Am. Chem. Soc.* **1986**, *108*, 2849.
- (261) Schmitt, R. J.; Bierbaum, V. M.; DePuy, C. H. *J. Am. Chem. Soc.* **1979**, *101*, 6443.
- (262) O'Hair, R. A. J.; Gronert, S.; DePuy, C. H. *Eur. Mass Spectrom.* **1995**, *1*, 429.
- (263) Kass, S. R., Personal communication.
- (264) Lee, H. S.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1996**, *118*, 5068.
- (265) Stirk, K. M.; Orłowski, J. C.; Leeck, D. T.; Kenttämä, H. I. *J. Am. Chem. Soc.* **1992**, *114*, 8604.
- (266) Thoen, K. K.; Beasley, B. J.; Smith, R. L.; Kenttämä, H. I. *J. Am. Soc. Mass Spectrom.* **1996**, *7*, 1245.
- (267) Nelson, E. D.; Li, R.; Kenttämä, H. I. *Int. J. Mass Spectrom.* **1999**, *185/186/187*, 91.
- (268) Leeck, D. T.; Stirk, K. M.; Zeller, L. C.; Kiminkinen, L. K. M.; Castro, L. M.; Vainiotalo, P.; Kenttämä, H. I. *J. Am. Chem. Soc.* **1994**, *116*, 3028.
- (269) Smith, R. L.; Kenttämä, H. I. *J. Am. Chem. Soc.* **1995**, *117*, 1393.
- (270) Heidbrink, J. L.; Thoen, K. K.; Kenttämä, H. I. *J. Org. Chem.* **2000**, *65*, 645.
- (271) Chyall, L. J.; Kenttämä, H. I. *J. Mass Spectrom.* **1995**, *30*, 81.
- (272) Moraes, L. A. B.; Eberlin, M. N. *J. Am. Chem. Soc.* **1998**, *120*, 11136.
- (273) Chou, P. K.; Smith, R. L.; Chyall, L. J.; Kenttämä, H. I. *J. Am. Chem. Soc.* **1995**, *117*, 4374.
- (274) Schweighfor, A.; Chou, P. K.; Thoen, K. K.; Nanayakkara, V. K.; Keck, H.; W., K.; Kenttämä, H. I. *J. Am. Chem. Soc.* **1996**, *118*, 11893.
- (275) Mourgues, P.; Audier, H. E.; Leblanc, D.; Hammerun, S. *Org. Mass Spectrom.* **1993**, *28*, 1098.
- (276) Audier, H. E.; Leblanc, D.; Mourgues, P.; McMahon, T. B.; Hammerun, S. *J. Chem. Soc., Chem Commun.* **1994**, 2329.
- (277) Weiske, T.; Van der Wel, H.; Nibbering, N. M. M.; Schwarz, H. *Angew. Chem.* **1984**, *96*, 694.
- (278) Gerbaux, P.; Van Haverbeke, Y.; Flammang, R. *Int. J. of Mass Spectrom.* **1999**, *184*, 39.
- (279) Gerbaux, P.; Van Haverbeke, Y.; Flammang, R. *J. Mass Spectrom.* **1997**, *32*, 1170.
- (280) Mourgues, P.; Audier, H. E.; Hammerun, S. *Rapid Commun. Mass Spectrom.* **1994**, *8*, 53.
- (281) Audier, H. E.; Fossey, J.; Leblanc, D.; Mourgues, P. *Bull. Soc. Chim. France* **1996**, *133*, 59.
- (282) Brenner, V.; Milliet, A.; Mourgues, P.; Ohanessian, G.; Audier, H. E. *J. Phys. Chem.* **1995**, *99*, 10837.
- (283) Troude, V.; Vanderrest, G.; Mourgues, P.; Audier, H. E. *J. Am. Chem. Soc.* **1997**, *119*, 9287.
- (284) Nixdorf, A.; Grutzmacher, H. F. *Eur. Mass Spectrom.* **1999**, *5*, 93.
- (285) Nixdorf, A.; Grutzmacher, H. F. *J. Am. Chem. Soc.* **1997**, *119*, 6544.
- (286) Buchner, M.; Nixdorf, A.; Grutzmacher, H. F. *Chem. - Euro. J.* **1998**, *4*, 1799.
- (287) Wenthold, P. G.; Squires, R. R. *J. Am. Chem. Soc.* **1994**, *116*, 6401.
- (288) Wenthold, P. G.; Squires, R. R.; Lineberger, W. C. *J. Am. Chem. Soc.* **1998**, *120*, 5279.
- (289) Wenthold, P. G.; Squires, R. R. *Int. J. Mass Spectrom. Ion Proc.* **1998**, *175*, 215.
- (290) Wenthold, P. G.; Hu, J.; Hill, B. T.; Squires, R. R. *Int. J. Mass Spectrom.* **1998**, *180*, 173.
- (291) Wenthold, P. G.; Hu, J.; Squires, R. R. *J. Am. Chem. Soc.* **1996**, *118*, 11865.
- (292) Wenthold, P. G.; Hu, J.; Squires, R. R. *J. Am. Chem. Soc.* **1994**, *116*, 6961.
- (293) Wenthold, P. G.; Squires, R. R. *J. Am. Chem. Soc.* **1994**, *116*, 11890.
- (294) Hill, B. T.; Poutsma, J. C.; Chyall, L. J.; Hu, J.; Squires, R. R. *J. Am. Soc. Mass Spectrom.* **1999**, *10*, 896.
- (295) Born, M.; Ingemann, S.; Nibbering, N. M. M. *J. Am. Soc. Mass Spectrom.* **1995**, *6*, 71.
- (296) Kawu, J.; Born, M.; Ingemann, S.; Nibbering *Rapid Commun. Mass Spectrom.* **1996**, *10*, 1400.
- (297) Hill, B. T.; Squires, R. R. *J. Chem. Soc., Perkin Trans. 2* **1998**, 1027.
- (298) Zhong, M.; Chabinc, M. L.; Brauman, J. I. *J. Am. Chem. Soc.* **1996**, *118*, 12432.
- (299) Bruins, A. P.; Ferrer-Correia, A. J.; Harrison, A. G.; Jennings, K. R.; Mitchum, R. K. *Adv. Mass Spectrom.* **1978**, *7*, 355.
- (300) Lee, J. H.; Chou, P. K.; Dowd, P.; Grabowski, J. J. *J. Am. Chem. Soc.* **1993**, *115*, 7902.
- (301) Zhao, J.; Dowd, P.; Grabowski, J. J. *J. Am. Chem. Soc.* **1996**, *118*, 8871.

- (302) Kroto, H. W.; Heath, J. R.; O'Brien, S. C.; Curl, R. F.; Smalley, R. E. *Nature* **1985**, *318*, 162.
- (303) Petrie, S.; Bohme, D. K. *Nature* **1993**, *365*, 426.
- (304) Javahery, G.; Petrie, S.; Wincel, H.; Wang, J.; Bohme, D. K. *J. Am. Chem. Soc.* **1993**, *115*, 6295.
- (305) Javahery, G.; Petrie, S.; Wang, J. R.; Wincel, H.; Bohme, D. K. *J. Am. Chem. Soc.* **1993**, *115*, 9701.
- (306) Javahery, G.; Petrie, S.; Wincel, H.; Wang, J. R.; Bohme, D. K. *J. Am. Chem. Soc.* **1993**, *115*, 5716.
- (307) Bohme, D. K. *Int. Rev. Phys. Chem.* **1994**, *13*, 163.
- (308) Petrie, S.; Bohme, D. K. *Can. J. Chem.* **1994**, *72*, 577.
- (309) Wang, J.; Javahery, G.; Petrie, S.; Hopkinson, A. C.; Bohme, D. K. *Angew. Chem., Int. Ed. Eng.* **1994**, *33*, 206.
- (310) Wang, J.; Javahery, G.; Baranov, V.; Bohme, D. K. *Tetrahedron* **1996**, *52*, 5191.
- (311) Baranov, V.; Wang, J. R.; Javahery, G.; Petrie, S.; Hopkinson, A. C. *J. Am. Chem. Soc.* **1997**, *119*, 2040.
- (312) Baranov, V.; Hopkinson, A. C.; Bohme, D. K. *J. Am. Chem. Soc.* **1997**, *119*, 7055.
- (313) Sun, J.; Bohme, D. K. *Int. J. of Mass Spectrom.* **1998**, *196*, 401.
- (314) Ling, Y.; Koyanagi, G. K.; Caraiman, D.; Baranov, V.; Bohme, D. K. *Int. J. Mass Spectrom.* **1999**, *183*, 349.
- (315) Bohme, D. K. *Can. J. Chem.* **1999**, *77*, 1453.
- (316) Baranov, V.; Bohme, D. K. *Int. J. Mass Spectrom. Ion Proc.* **1997**, *165*, 249.
- (317) Petrie, S.; Javahery, G.; Wincel, H.; Wang, J. R.; Bohme, D. K. *Int. J. of Mass Spectrom. Ion Proc.* **1994**, *138*, 187.
- (318) Sun, J.; Bohme, D. K. *Int. J. Mass Spectrom.* **1998**, *180*, 267.
- (319) Becker, H.; Scott, L. T.; Bohme, D. K. *Int. J. Mass Spectrom. Ion Proc.* **1997**, *167*, 519.
- (320) Petrie, S.; Becker, H.; Baranov, V. I.; Bohme, D. K. *Int. J. Mass Spectrom. Ion Proc.* **1995**, *145*, 79.
- (321) Ling, Y.; Koyanagi, G. K.; Caraiman, D.; Hopkinson, A. C.; Bohme, D. K. *Int. J. Mass Spectrom.* **1999**, *192*, 215.
- (322) Becker, H.; Javahery, G.; Petrie, S.; Bohme, D. K. *J. Phys. Chem.* **1994**, *98*, 5591.
- (323) Sun, J.; Bohme, D. K. *Int. J. Mass Spectrom.* **2000**, *195/196*, 401.
- (324) Lichtenburger, D. L.; Rempe, M. E.; Gogosha, S. B. *Chem. Phys. Lett.* **1992**, *198*, 454.
- (325) Hoke, S. H.; Molstad, J.; Kahr, B.; Cooks, R. G. *Int. J. Mass Spectrom. Ion Proc.* **1994**, *138*, 209.
- (326) Stry, J. J.; Garvey, J. F. *J. Phys. Chem.* **1994**, *98*, 8289.
- (327) Stry, J. J.; Garvey, J. F. *Int. J. Mass Spectrom. Ion Proc.* **1994**, *138*, 241.

CR9900836