

## Perspective

### Understanding Organic Gas-Phase Anion Molecule Reactions

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Although ionic reactions in the gas phase seem on the surface to be totally different from those in solution (e.g., they typically occur about  $10^{12}$  times more rapidly than their solution analogues and go about as fast at 10 K as they do at room temperature), they can, in fact, exhibit subtle steric, electronic, and isotopic effects. In this Perspective, we show how these differences arise, explain why gas-phase ion reactions can be both fast and selective, and discuss when they can and cannot be classified as “hot” reactions. We also give examples of the use of these reactions to devise new synthetic pathways, investigate reaction mechanisms, and generate important thermochemical data such as bond dissociation energies.

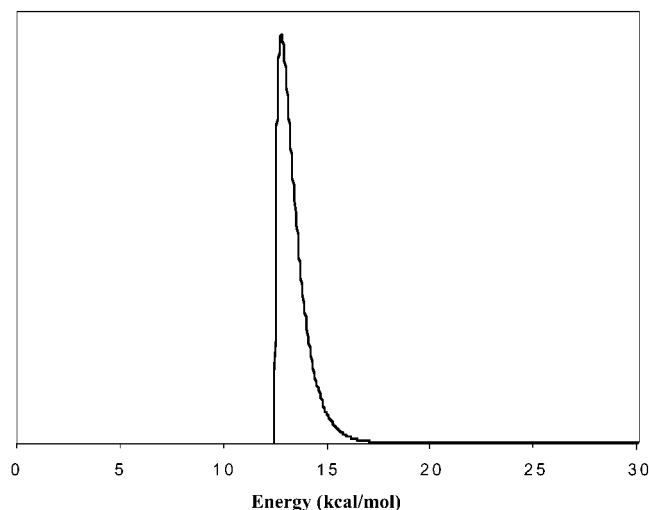
It cannot be denied that at first or even second sight, ionic organic reactions in the gas phase appear to violate the norms for what we expect from solution analogues. Consider, for example, the simple  $S_N2$  reaction of chloride ion with methyl bromide. In the gas phase, it occurs  $10^{12}$ – $10^{15}$  times more rapidly than it does in solution, goes as fast at 10 K as at room temperature, and takes place through something called an ion–dipole complex that contains so much energy that it might be considered to be at a temperature of 5000 °C! A nonexpert in the field must be forgiven for concluding that removing the solvent makes the chloride ferociously reactive and “hot”, and so cannot be compared with its solution counterpart. Yet, further investigation will disclose that this gas-phase  $S_N2$  reaction displays the same inverse hydrogen–deuterium isotope effects and the same steric and substituent effects as it does in solution, in apparent violation of the reactivity–selectivity principle so central to physical organic chemistry. It is the object of this Perspective, which is based mainly on a James Flack Norris Award address,<sup>1</sup> to illustrate how gas-phase ion chemistry relates energetically to chemistry in solution and how it can be used to shed light on reaction mechanisms, to uncover new synthetic reactions, and to measure such

important thermochemical values as bond dissociation energies. Because of its origin in an award address, this Perspective will mainly emphasize contributions from my own laboratory, but most of the points could also be illustrated by work of others.

#### 1. The Energetics of Gas-Phase Ion Reactions

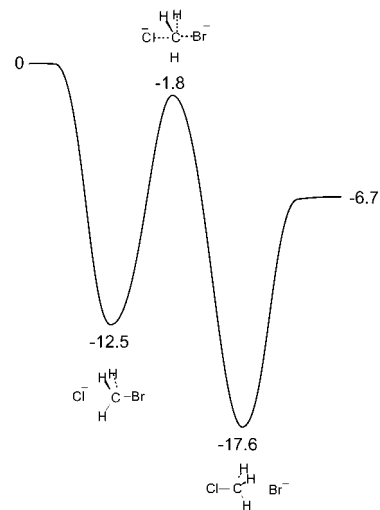
Ions and neutrals attract one another, in solution and in the gas phase. If a molecule has a dipole moment, an anion is attracted to the positive end, a cation to the negative. Even if a molecule does not have a dipole, an ion induces one and attraction occurs. In solution, an ion surrounds itself with several neutral solvent molecules, while in the gas phase the interaction is between a single ion with a neutral reactant molecule. Such an *ion–dipole complex* (sometimes called a weakly bound complex (WBC)) is held together by electrostatic forces amounting to 10–20 kcal/mol. For example, the energy required to dissociate the gas-phase complex between chloride ion and methyl, isopropyl, and *tert*-butyl bromide is 12.5, 15.2, and 17.5 kcal/mol, respectively.<sup>2</sup> If a hydrogen bond can be formed, a stronger complex results; the hydroxide–water complex is bound by about 26 kcal/mol.

Suppose we begin with ions at room temperature in the gas phase. Almost all of these ions have less than 1



**Figure 1.** Approximate energy distribution of ion dipole complexes for the reaction of chloride ions with methyl bromide. The area under the curve gives the fraction of molecules with the given energy. Each complex has just enough energy to surmount the activation barrier for an  $S_N2$  reaction.

kcal/mol of kinetic energy, characteristic of a Boltzmann distribution at room temperature. We now add neutrals, which have a similar narrow energy distribution. The ions and neutrals attract one another, with the relative translational energy increasing to the complexation energy by the time they reach bonding distance. When they collide, some or all of the translational energy is converted to vibrational and rotational energy, but all of it must remain within the complex, since there are no solvent molecules to remove it. Thus, the energy distribution of the complexes undergoing reaction will look something like that in Figure 1, with a narrow, room-temperature spread of energies, but displaced to higher energy due to the complexation. In order for the complex to dissociate to reactants, this energy must be re-concentrated into translational energy, but this is a relatively slow process because the components are only connected by a weak electrostatic bond. If a reaction is possible with an activation energy equal to or smaller than the complexation energy, each complex will have sufficient energy to surmount the barrier. For example, the activation barrier for the gas-phase  $S_N2$  reaction between chloride ion and methyl bromide has been measured to be 10.7 kcal/mol<sup>2</sup>. Since the complexation energy is 12.5 kcal/mol, each time a chloride ion and a methyl bromide molecule come together in the gas phase they have more than enough energy to react. In contrast, in solution the chloride ions also have the same narrow, room-temperature energy distribution, but they are already complexed to (solvated by) solvent molecules. If we now add methyl bromide, little or no additional energy is generated when a methyl bromide molecule replaces a solvent molecule in the solvation shell of the chloride ion, and almost all collisions in solution are unproductive. Only if one of the very, very few extremely energetic chloride ions or methyl bromide molecules present in solution (those with enough kinetic energy to cross the activation barrier) collide can a reaction occur. This, of course, is why reactions in solution are so slow. Therefore, a very large part of the increase in rate of ionic reactions in the gas phase is due to the fact that nearly every



**Figure 2.** Potential energy profile for the  $S_N2$  reaction between chloride ion and methyl bromide in the gas phase. The energy within the complex remains constant throughout the reaction unless collisions with the bath gas occur.

encounter can lead to reaction if its activation energy is less than the complexation energy. Note that when two neutrals encounter one another in the gas phase, little complexation energy is generated, so neutral–neutral reactions are not similarly accelerated. In Figure 2, we show the energy profile for the gas-phase  $S_N2$  reaction of chloride ion with methyl bromide. Note that the total energy remains constant throughout the reaction, since at low pressure energy cannot be added or removed by collisions with a third body. If the pressure of the bath gas (usually helium) is raised sufficiently, the initial complex can be cooled by collisions and its properties studied.

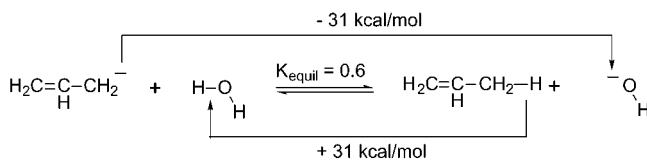
Most gas-phase ion molecule reactions proceed by way of these “double well” potentials, in which a relatively long-lived initial complex forms, which can either dissociate to reactants or cross the activation barrier to a product complex. The product complex may dissociate, re-cross the barrier to regenerate the initial complex, or undergo another reaction before dissociation. We will see examples of all of these. Note that the overall rate of reaction depends on the rate of formation of the initial complex times the fraction of these complexes that go on to products. The rate of formation of the complex depends on the mass, dipole moment, and polarizability of the neutral and can be calculated with reasonable accuracy. Since the collision rate varies somewhat from neutral to neutral, a more meaningful measure of reaction than the reaction rate coefficient is the *reaction efficiency*, the number of collisions that result in product formation. For instance, in the chloride–methyl bromide reaction about one in every 50 collisions results in the formation of bromide ion, even though every collision complex has sufficient energy to cross the reaction barrier. The lowering of reactivity is attributed to entropy; the  $S_N2$  transition state is highly structured and so disfavored entropically compared to dissociation. And since ion molecule reactions generate most of their own reaction energy, they are little affected by changes in temperature. An ion and a neutral collide at about the same rate and with the generation of about the same amount of complexation energy near absolute zero as they do at room

temperature. So ion molecule reactions rates are only slightly affected by heating or cooling.

If we lower the barrier to the  $S_N2$  reaction, for example by substituting methyl iodide for bromide, products form at every collision. If we raise the barrier somewhat by using methyl chloride as a reagent, the reaction becomes almost immeasurably slow. In general, there is only a relatively small region of energy, from at or just below the complexation energy to about 5 kcal/mol above it, where meaningful reaction rates can be measured in the gas phase. Otherwise, reactions either occur at every collision or are too slow to measure experimentally. Within this small 5 kcal/mol region of activation energy the rate changes relatively rapidly with activation energy and subtle effects of structure on reactivity can be detected. For instance, replacement of the three hydrogens in methyl bromide by deuterium results in an easily measured increase in rate for the  $S_N2$  reaction with chloride ion, just as it does in solution.<sup>3</sup> On the other hand, the effects of larger variations of structure must be measured indirectly.<sup>4</sup> To determine the relative leaving abilities of the halogens, for example, we note that methyl fluoride reacts with hydroxide ion at a slow but measurable rate, while methyl chloride and bromide react at every collision. With the weaker nucleophile  $CF_3CH_2O^-$ , methyl fluoride does not react, methyl chloride reacts measurably slowly, and methyl bromide reacts at every collision. Thus the order of leaving group abilities in  $S_N2$  reactions in the gas phase,  $Br > Cl > F$ , is the same as that in solution, but we cannot determine quantitatively the relative rates of the three leaving groups with the same nucleophile. In an analogous way it can be shown that the same order of reactivity upon alkyl substitution, methyl > ethyl > isopropyl > *tert*-butyl, applies in the gas phase and in solution.

## 2. The Determination of Bond Dissociation Energies

In contrast to the situation in aqueous solution, where water is a stronger acid than most organic molecules, in the gas phase it is extremely weak (and hydroxide ion is correspondingly a very strong base); water and propylene have the same gas-phase acidity. The weak acidity of water, despite the high electronegativity of oxygen, is due to the great strength of its H–O bond (119 kcal/mol), a bond which is lost after proton transfer and exchanged for the much weaker (89 kcal/mol) C–H bond in propylene. Indeed, water is a much weaker acid in the gas phase even than the alcohols, whose O–H bonds are only about 104 kcal/mol. It is a much stronger acid in aqueous solution because the hydroxide ion is so strongly solvated, even better solvated than are alkoxide ions.



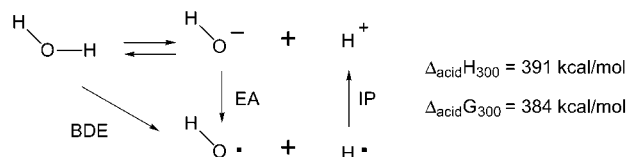
The ability of hydroxide ion to support a negative charge is measured by its electron binding energy (the energy required to detach an electron), which is the same as the electron affinity (EA) of the corresponding hydroxyl radical (42 kcal/mol). If we combine the bond dissociation energy (BDE) for water, the (EA) of the hydroxyl radical

**Table 1. Gas Phase Acidities of Some Common Molecules (kcal/mol)<sup>a</sup>**

molecule	$\Delta H_{acid}$	$\Delta G_{acid}$	molecule	$\Delta H_{acid}$	$\Delta G_{acid}$
CH <sub>4</sub>	414	409	C <sub>2</sub> H <sub>2</sub>	378	370
C <sub>2</sub> H <sub>4</sub>	409	401	CH <sub>3</sub> CON(CH <sub>3</sub> ) <sub>2</sub>	375	368
NH <sub>3</sub>	404	397	CH <sub>3</sub> COOCH <sub>3</sub>	372	365
C <sub>6</sub> H <sub>6</sub>	402	393	CH <sub>3</sub> COCH <sub>3</sub>	369	363
H <sub>2</sub>	400	394	c-C <sub>5</sub> H <sub>6</sub>	354	348
H <sub>2</sub> O	391	384	H <sub>2</sub> S	351	345
CH <sub>2</sub> CHCH <sub>3</sub>	389	383	CH <sub>3</sub> COOH	348	341
CH <sub>3</sub> OH	382	375	HCl	333	328
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	381	374			

<sup>a</sup> Data from ref 9.

and the ionization potential (IP) of the hydrogen atom (314 kcal/mol), we can determine how much energy ( $\Delta H$ ) is required to ionize water in the gas phase (391 kcal/mol). This  $\Delta H$  value is known as the proton affinity (PA) of the hydroxide ion. If we convert  $\Delta H$  to  $\Delta G$  by incorporating the entropies of the species, we obtain the gas phase acidity (GPA) of water (384 kcal/mol). However, these definitions are not always strictly followed, and GPA is sometimes used for the  $\Delta H$  rather than the  $\Delta G$  of ionization.<sup>5</sup>

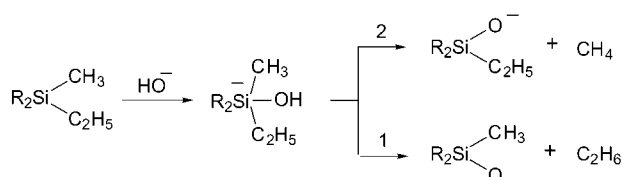


It is obvious from these equations that the PA of an anion, the EA of the neutral formed on detachment of an electron from it, and the BDE of its conjugate acid are related such that, combined with the IP of the hydrogen atom, any two determine the third. For many molecules the BDE is the most difficult value to determine experimentally, and gas-phase ion chemistry has been an important tool in determining these values. As an example, the GPA of propylene can be determined by measuring the equilibrium constant for its proton abstraction reaction with water ( $K_{equil}$ ), which is then converted to  $\Delta H$  making use of the known entropies of the particles. This value is combined with the EA of the allyl radical to give the BDE of propylene as 89 kcal/mol, in excellent agreement with other measurements.<sup>6</sup> This method is especially useful for measuring bond dissociation energies in molecules with strong C–H bonds (ethylene, benzene, acetylene) where many methods fail.<sup>7,8</sup>

## 3. Gas-Phase Acidities

With the major exception of molecules containing OH bonds, the order of acidities of organic molecules in the gas phase and in solution is essentially the same. The alkyl anions are the strongest bases, the vinyl and phenyl anions somewhat weaker, and allyl anions weaker still. Conjugation affects the gas-phase basicity in the same way it does in solution, making an anion a weaker base. The gas-phase acidities of a number of molecules are collected in Table 1.<sup>9</sup> For most molecules, these are determined by measuring equilibrium constants for acid–base reactions between pairs of molecules. Determining the gas-phase acidities of the alkanes presents a special problem. Only three alkyl anions, methyl, neopentyl, and cyclopropyl, have been detected in the gas phase, and

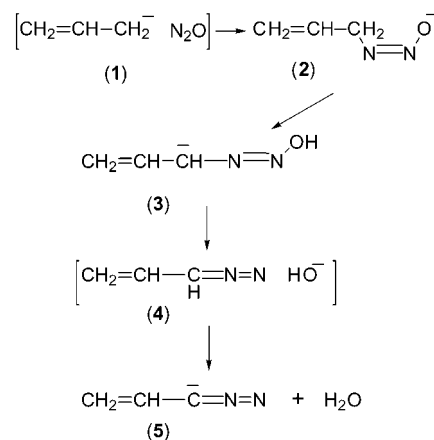
their electrons are too weakly bound for them to be used in chemical reactions. Indeed, most alkyl radicals are predicted to have negative electron affinities, so that their corresponding anions will spontaneously detach an electron. However, the relative acidities of the alkanes have been estimated by kinetic methods.<sup>10,11</sup> In one such method,<sup>10</sup> substituted silanes are allowed to react with hydroxide ion, leading to loss of an alkane molecule and the formation of a siloxide ion. Mechanistic considerations suggest that the reaction proceeds through initial addition to silicon followed by a transition state in which negative charge builds up on the leaving alkyl group, which abstracts a proton and departs as an alkane. When two different alkyl groups are allowed to compete, the relative ability of the alkyl groups to support a negative charge is indicated by the relative amounts of the two alkanes lost. For example, when dimethyl diethylsilane reacts with hydroxide ion, methane is twice as likely to be lost as ethane, suggesting that the ethyl group is less able to support a developing negative charge than the methyl group, and hence that ethane is a weaker acid than methane. This counter-intuitive result is supported by *ab initio* calculations.<sup>12</sup> By allowing various alkyl groups to compete, the acidity of other alkanes can be estimated. By combining the acidities with the well-known bond dissociation energies, the corresponding EAs can be calculated. The neopentyl and cyclopropyl anions are predicted to be bound (hence accounting for their observation), but nearly all other alkyl anions are predicted to be unbound.



#### 4. Gas-Phase Chemical Reactions

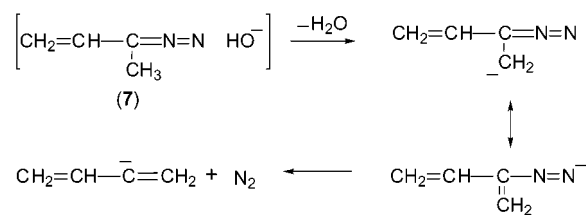
Nearly all reactions that have been observed in solution can be duplicated in the gas phase, and they appear to take place by the same mechanisms, and with the same general stereoelectronic effects, as they do in solution. The  $S_N2$  and E2 reactions have been the most extensively investigated mechanistically, and excellent reviews are available.<sup>13</sup> As for other gas-phase reactions, esters can be hydrolyzed, aldehydes and ketones reduced or oxidized, Claisen condensations carried out. Even subtle stereochemical effects have been determined.<sup>14</sup> In every case, it appears that an initial ion-dipole complex between the reactants forms first, followed by reaction within the complex. After reaction, a complex between the products is formed, and frequently further reactions occur within this product complex. Eventually a product complex dissociates. Reactions between organic anions and nitrous oxide are particularly illustrative of how some complex reactions occur in the gas phase, and they have also proven to be useful in helping to determine ion structure.<sup>15</sup> Consider the reaction between the allyl anion and  $N_2O$  (Scheme 1). The energy gained in forming the initial complex (1) (designated by brackets) is used to overcome a reaction barrier to form an adduct (2) in which the components are joined by a covalent bond, as compared to the electrostatic bond in the complex. In the adduct, the entire exothermicity of the reaction is depos-

#### Scheme 1. Reaction of a Primary Carbanion with $N_2O$



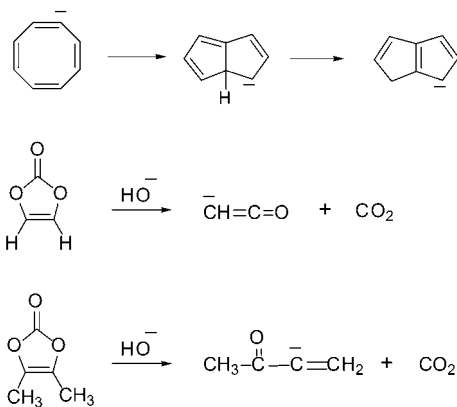
ited in the resulting ion and, depending upon its magnitude, adducts can be exceedingly "hot". But since the same amount of energy is deposited into each ion, the collection of ions still maintains its overall narrow, room-temperature energy distribution, in contrast to the broad energy distribution it would have if formed thermally. In this sense, gas-phase ion addition reactions can be thought of as ground-state analogues of photochemical reactions, where a fixed amount of energy is deposited by irradiation. In both cases, very specific, high-yield reactions can occur at high energy.

Within the adduct, an intramolecular proton-transfer reaction occurs to form 3. Loss of hydroxide ion generates a new ion dipole complex (4), which has sufficient energy to dissociate, but does not do so immediately. Instead, the complex lives long enough for the hydroxide ion to search for a reaction it can undergo and, finding an acidic proton, abstracts it. Thus the ionic product after dissociation of the final complex is vinyl diazomethyl anion (5), whose chemistry can be explored by subsequent reactions. If the acidic proton is replaced by a methyl group, the hydroxide ion induces the gas-phase analogue of the Shapiro reaction by abstracting a proton from the methyl group, eliminating nitrogen and forming a vinyl anion. Since vinyl anions are exceedingly basic in the gas phase, and hence difficult to form, this can be a useful synthetic procedure. And because the reaction leads to ions of different masses depending upon whether it is primary or secondary, it is useful in determining ion structure. Nitrous oxide also undergoes unique reactions with ions of other types.

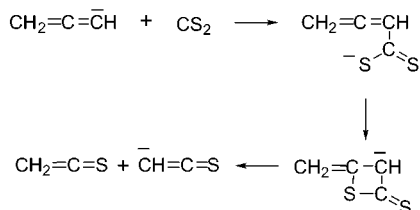


Carbon disulfide and carbon oxysulfide are also useful reagents for the synthesis of new types of ions or for gaining clues as to ion structure. COS is a sulfur transfer agent, generating sulfide ions from strongly basic anions by attack on the sulfur and loss of CO. A particularly useful reaction of  $CS_2$ , and one not yet seen in solution, is characteristic of allenyl and related (e.g., ketenyl and

## Scheme 2. Three Gas-Phase Synthetic Reactions



diazomethyl) ions. The reaction is initiated by an exothermic addition which generates a "hot" adduct. The exothermicity in the addition fuels a cyclization reaction, which is followed by cleavage. Reactions such as this, which fragment ions almost like ozone does in solution, are especially useful in the gas phase, as they give important clues to the ion's structure.



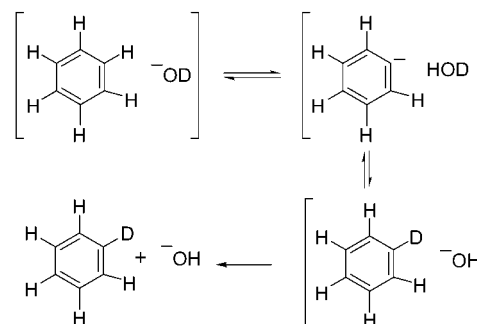
If one is willing to accept the idea that gas-phase anion reactions mimic those in solution, then the gas phase can be a good environment for discovering new reactions that might be useful synthetically. For example (Scheme 2), we found that upon abstraction of a proton from cyclooctatetraene, a facile rearrangement occurs, forming the bicyclic anion shown.<sup>16</sup> Since this reaction does not occur by way of an adduct, but rather is initiated by proton transfer, its activation energy must be low and might well occur in solution. If so, it will provide access to a bicyclic system difficult to obtain synthetically. As other examples, reaction of vinylidene carbonate is a convenient precursor of the ketyl anion while dimethyl vinylidene carbonate generates the vinyl anion shown when allowed to react with base.<sup>17</sup> It is tempting to think that these reactions could be duplicated in solution if a halogen or trimethylsilyl group were substituted for the proton whose removal initiates the gas-phase reaction.

## 5. Hydrogen/Deuterium Exchange Reactions

In Figure 1, we can delineate three distinct energy regions. The first extends from near the complexation energy to about five kcal/mol above this energy. In this region, where the chloride–methyl bromide reaction takes place, the cluster energy and the activation energy are approximately equal, and the rate of reaction changes rapidly with small changes in the activation energy. As a consequence, very subtle structural changes (e.g., kinetic isotope effects) can be detected. A second region lies to the right in Figure 1, where the activation energy greatly exceeds the complexation energy. Here, there is insufficient energy in the cluster to cross the barrier. Reactions in this region can, however, be induced by the

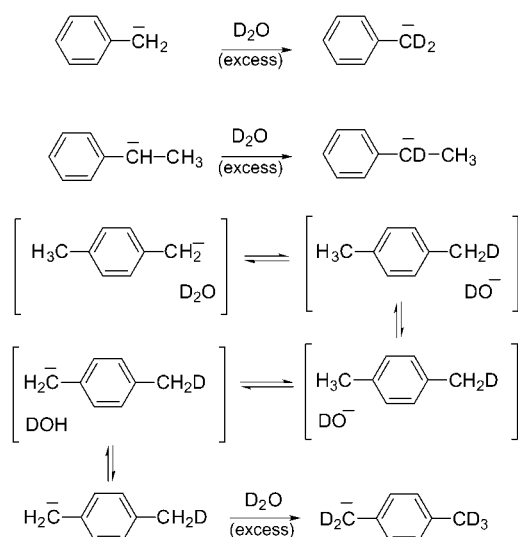
exothermic formation of adducts, as in the CS<sub>2</sub> addition reaction. As an addition reaction becomes more and more exothermic, more and more energy is deposited in the ion formed. For example, addition of CS<sub>2</sub> to an anion is more exothermic than addition of COS, which in turn is more exothermic than addition of CO<sub>2</sub>. So CS<sub>2</sub> is best, and CO<sub>2</sub> worst, at inducing reactions. A third region lies to the left end in Figure 1, where activation energies lie significantly below the complexation energy. In this region reactions occur at every collision. While such reactions are useful if our only goal is to demonstrate whether a reaction occurs, we would like to enter this region experimentally, to explore "cool" complexes in some detail. For example, most esters undergo ester interchange reaction with an alkoxide ion at every collision. How can we get information about the relative rates of such reactions?

One way to enter this "cool" region is by way of an endothermic proton transfer reaction within an ion dipole complex. A simple example is shown by the reaction of deuterioxide ion with benzene; a rapid hydrogen/deuterium exchange reaction occurs to form hydroxide ion. The first step is formation of a benzene deuterioxide ion dipole complex, containing approximately 15 kcal/mol energy. This is not enough energy to form an adduct, e.g., by addition to the benzene ring; however, as one can see from Table 1, the proton affinity of the phenyl anion is only 11 kcal/mol greater than that of hydroxide ion. Consequently, there is more than enough energy within the complex to carry out an endothermic proton transfer and, in the process, cool the resulting phenide–HOD complex, which will now contain only about 4 kcal/mol complexation energy. The cooled complexes will be unable to dissociate, since the overall reaction would be endothermic. However, they can regain their lost energy by abstraction of a proton, to form complexes that can dissociate with overall H/D exchange. A key constraint is that the endothermicity of the proton-transfer step must not exceed the complexation energy. For example, deuterioxide ion will not exchange with ethylene, because the difference in PA between it and the vinyl anion, at 18 kcal/mol, is larger than the available complexation energy.



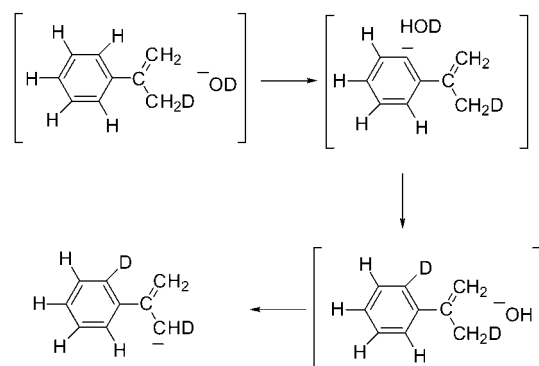
The observation of exchange between DO<sup>−</sup> and an organic molecule is not particularly revealing because we can detect only ionic species in our experiments. Exchange becomes extremely useful, on the other hand, if we begin with a carbanion more weakly basic than hydroxide ion and examine exchange between it and D<sub>2</sub>O.<sup>18,19</sup> In an experiment of this type we can watch the incorporation of deuterium into the organic anions, and from the number of protons exchanged for deuterium we gain valuable information about the structure of the ions.

For example, abstraction of a proton from toluene results in a benzyl ion that exchanges two protons for deuterium when allowed to react with  $D_2O$ . This is the result expected, since the benzyl anion is 10 kcal/mol less basic than hydroxide, so that the initial deuterium transfer can occur, and there are two benzylic protons to exchange. The anion from ethyl benzene exchanges only one proton, as one would expect. We learn more about ion dipole complexes when we examine H/D exchange in the anion from *p*-xylene. In this molecule, all five benzylic protons exchange for deuterium. After the initial endothermic deuterium transfer, the deuterioxide ion is free to move to the para position and abstract a proton from that methyl group, demonstrating the weak interaction between the ionic and neutral components of the complex, and its relatively long lifetime. The extent of exchange (5 vs 1 protons) serves to distinguish the xylyl anions from the isomeric ions from ethylbenzene.

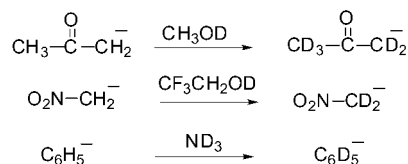


We can see from the results reported so far that  $D_2O$  can engage in two types of exchange. The neutral can exchange with carbanions (e.g., the benzyl anion) while its anion,  $DO^-$ , can exchange with a neutral (e.g., benzene). In some cases, both types of exchange can occur in a single encounter. For example, when the 2-phenylallyl anions is allowed to react with  $D_2O$ , both allylic and aromatic hydrogens exchange.<sup>20</sup> The mechanism for this type of exchange is shown below. In the initial complex a very slightly endothermic deuterium transfer leads to the formation of  $DO^-$  and a deuterated neutral. There is still sufficient energy within the complex for  $DO^-$  to abstract a proton from the benzene ring and exchange it for a deuterium, in analogy to the exchange of hydroxide ion with  $C_6D_6$  shown above. In order for this type of double exchange to occur, two conditions are necessary. Obviously the exchange reagent must bring two or more deuterium atoms into the complex. In addition, there must be sufficient energy left after the first endothermic deuterium transfer to carry out the second. For example the aromatic protons in the benzyl anion do not exchange because the initial deuterium transfer, which is endothermic by 10 kcal/mol, leaves only about 5 kcal/mol in the resulting complex, too little to allow exchange of aromatic hydrogens.

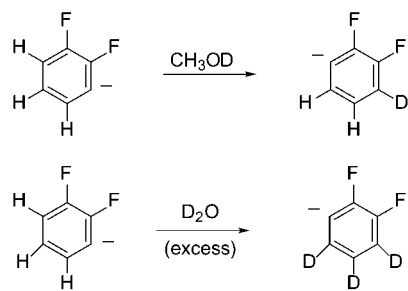
If a carbanion is too weakly basic, it will not exchange at all with  $D_2O$  because the initially formed complex does



not contain enough energy to bring about the initial deuterium transfer. The acetone enolate ion has a proton affinity of 369 kcal/mol, 22 kcal/mol less than that of hydroxide ion, and so no exchange is observed. However, the enolate is only 13 kcal/mol less basic than methoxide ion (PA 382), and so it will exchange all five of its hydrogens for deuterium with  $CH_3OD$ . Similarly, the nitromethyl anion (PA 358) will not exchange with  $CH_3OD$ , but will do so with  $CF_3CH_2OD$ , whose anion has a PA of 362. At the other end of the acidity scale, the phenide ion, which is neutralized by  $D_2O$ , exchanges all of its protons with  $ND_3$ . As one can see from these results, the number of hydrogens that exchange for deuterium and the nature of the reagent required to induce the exchanges give a great deal of information about the ion structure.

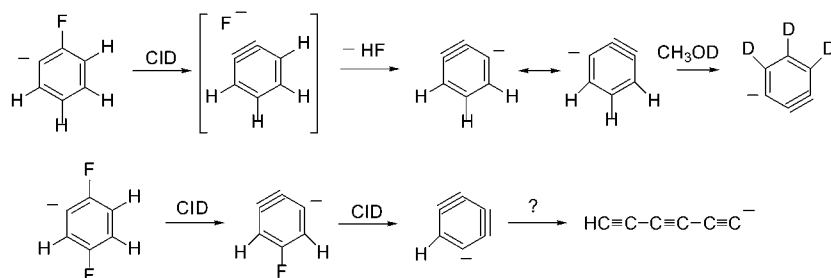


The extent of H/D exchange sometimes gives us information about the dynamics of the complexes themselves. Exchange within the anions derived from the isomeric difluorobenzenes is particularly interesting.<sup>21</sup> All three have PAs between 380 and 376 kcal/mol, values that are within 15 kcal/mol of those for both water and methanol, so that they undergo exchange with either reagent. First, consider the anion from the ortho isomer;  $CH_3OD$  can exchange only the ortho hydrogen, giving an anion of the same PA as that of the starting anion, while  $D_2O$ , because it brings two deuterium atoms into the complex, can exchange the meta hydrogens as well. In

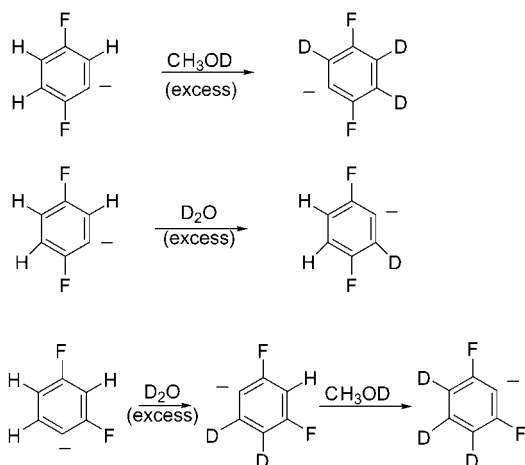


*p*-difluorobenzene, all hydrogens are equally acidic, and in the anion all three remaining hydrogens are exchanged by  $CH_3OD$ , as expected. Unexpectedly, only one is exchanged by  $D_2O$ . The following explanation has been proposed for these results.<sup>22</sup> After an initial deuterium

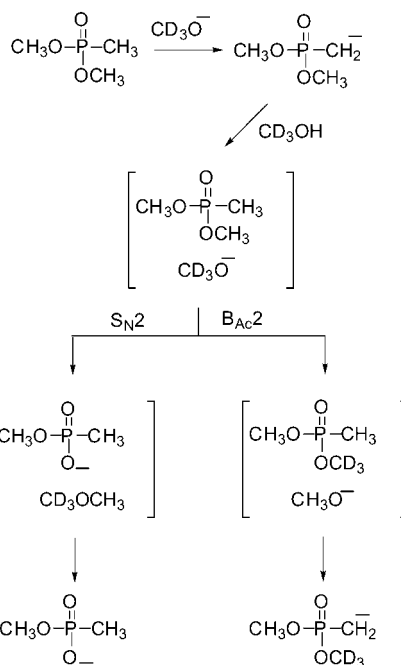
## Scheme 3. Collision-Induced Dissociation of Anions from Fluorobenzenes Produce Benzynes



transfer, either base can abstract the adjacent proton, leading to one exchange. However, to exchange the other two hydrogens the base must move to the other side of the benzene ring. Movement in the plane of the ring is blocked totally by repulsions between the electrons on the fluorine atoms and the negative charge on the base. Movement over (or under) the ring is difficult because of repulsions between the anion and the pi electrons, but can proceed with an activation energy of about 13 kcal/mol. Methoxide ion has sufficient energy to accomplish this because the initial deuterium transfer is only slightly endothermic, leaving the required 13 kcal/mol still within the complex. Deuterioxide ion cannot; its complex is too cold because of the highly endothermic deuterium transfer step. This explanation is supported by the results for exchange in the anion from *m*-difluorobenzene. Reaction with  $D_2O$  results in exchange of only two hydrogens for deuterium because hydroxide ion is unable to reach the most acidic hydrogen between the fluorines. Subsequent addition of  $CH_3OD$  results in an additional exchange, as predicted by the mechanism.

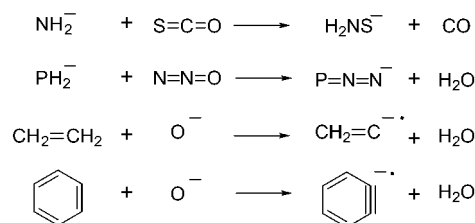


The cooling effect of an endothermic proton transfer reaction also provides a method to slow gas-phase ion reactions that ordinarily occur at the collision rate or that are obscured by fast, competing proton transfers. Dimethyl methylphosphonate reacts with base almost exclusively by proton abstraction to form the enolate (PA 373) with only a small amount of  $S_N2$  product observed and no ester interchange.<sup>23</sup> However, when this enolate is allowed to react with  $CD_3OH$ , the major product (90%) is ester interchange, with a smaller amount of  $S_N2$  product. Endothermic proton transfer cools the complex and allows the  $S_N2$  and  $B_{Ac}2$  reactions to compete. When ethanol is used as the neutral reagent, ester interchange and  $S_N2$  reactions occur in equal amounts.

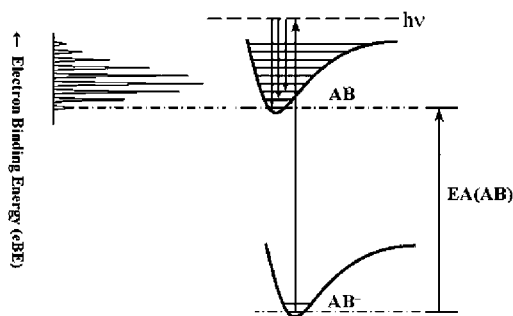


## 6. Highly Reactive Gas-Phase Anions

Many unusual and previously unknown ions can be prepared in the gas phase, ions that are too reactive to be prepared in solution. We can then study their chemistry with the reasonable assurance that it will parallel that which would occur in solution. For example, a number of exotic inorganic anions have been generated,<sup>24</sup> including  $H_2NS^-$ ,  $PN_2^-$ ,  $NSO^-$ , and their basicity, nucleophilicity, and other chemical properties determined. These and other studies have shown that sulfur anions have no special reactivity in  $S_N2$  reactions when compared to oxygen anions of the same basicity, one of the few cases where there is a drastic difference from results in solution.<sup>25</sup> Stable organic radical anions can often be formed by abstraction of  $H_2^+$  by  $O^-$  from simple organic neutrals.<sup>26</sup>



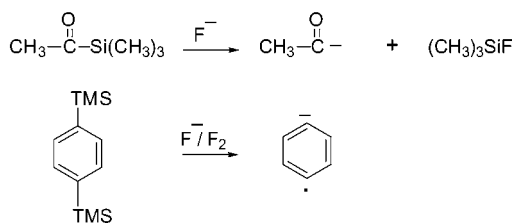
Others arise when ions are subjected to collision-induced dissociation (CID) upon collisions with rare gas atoms. One striking example<sup>27</sup> is shown in Scheme 3 where the anion derived by proton abstraction from



**Figure 3.** In negative-ion photoelectron spectroscopy, a beam of ions is crossed with a fixed frequency laser and the energies of the detached electrons are recorded. The result is the vibrational spectrum of the neutral.

fluorobenzene loses a molecule of HF upon CID to generate  $C_6H_3^-$ . The structure of this ion is strongly supported by the observation that all three hydrogens can be exchanged for deuterium upon treatment with  $CH_3OD$ . The ion, which has two identical resonance structures, is that which would be generated by proton abstraction from benzyne, and has an intact benzene pi electron system with an allylic anion in the plane of the ring. CID of the anions from difluorobenzenes gives rise to the  $C_6H^-$  anion by loss of two molecules of HF. It is not yet known whether it remains cyclic or undergoes ring-opening to the linear acetylide.

A particularly useful method of generating anions in solution is to react a trimethylsilyl (TMS) derivative with fluoride ion. This method works extremely well in the gas phase; reaction of acetyl TMS produces the acetyl anion.<sup>28</sup> If a substrate contains two TMS groups, reaction with fluoride ion plus fluorine generates an anion radical. Anion diradicals and anion carbenes have also been formed by analogous reactions of compounds that contain three TMS groups.<sup>29</sup>

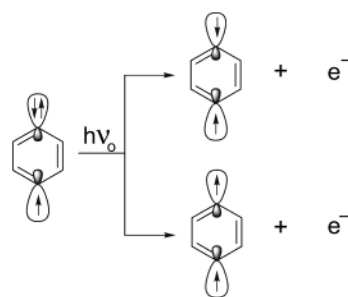


### 7. Negative-Ion Photoelectron Spectroscopy

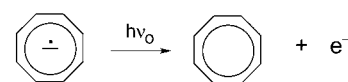
The combination of gas-phase ion chemistry and negative-ion photoelectron spectroscopy is an amazingly powerful method for gaining information about the structures of reactive intermediates and transition states.<sup>30</sup> The role of anion chemistry in this partnership is to develop methods for generating a specific ion in high yields, and to verify the structure of the ion by chemical reactions. In the photoelectron spectrometer a cold beam of these negative ions is crossed with a fixed frequency laser whose photons (typically,  $h\nu_0 = 351$  nm) have more than enough energy to detach an electron. Neutrals result from the detachment and these neutrals may be formed in nearly any vibrational state; the higher the vibrational energy left behind in the neutral, the lower the kinetic energy of the departing electron, as shown in Figure 3. Therefore, if one measures the kinetic energy (KE) of the electrons and subtracts their energy from the energy of the incident photons, one obtains the vibrational spec-

trum of the neutral. The energy required to detach an electron from the ground state of the anion to produce the ground state of the neutral gives the electron affinity of the neutral. The nature of the vibrations giving rise to each peak can often be inferred by the effect of isotopic labeling in the anion on the spectrum. The relative intensities of the peaks in the spectrum reflect the probability of the neutral being produced in a particular vibrational state, and this in turn depends on the relative geometry of the anion and the neutral. If these have the same or nearly the same structure, the two Morse curves will lie directly above each other and there will be a high probability of detachment into the low vibrational states of the neutral. If they have quite different structures then detachment will lead mainly to higher vibrational states, and the peak that reflects the EA will be small.

Photoelectron spectra of radical anions are especially interesting, because they give information about both singlet and triplet states. For example, depending upon the spin of the electron that is detached from the *p*-benzyne radical anion, either the singlet or triplet *p*-benzyne neutral is produced.<sup>29</sup> In addition to information about the vibrational states of each species, the singlet–triplet splitting is also given by the spectrum (see the cover of this issue for a diagram).



Finally, a particularly exciting area of research is to use photoelectron spectroscopy to investigate the structures of transition states. One approach is to study a unimolecular reaction, like the inversion of cyclooctatetraene, which proceeds through an extremely short-lived planar transition state.<sup>31</sup> Cyclooctatetraene itself, with eight  $\pi$  electrons, is tub-shaped, but addition of an electron produces its planar, semiaromatic radical anion. Detachment of an electron from this anion occurs very much faster than any nuclear motion, so that the resulting spectrum is that of planar cyclooctatetraene, the transition state for the ring-inversion reaction.



To obtain the spectrum of the transition state of a bimolecular reaction, it is sometimes possible to begin with a cooled cluster ion, one in which the neutral has a structure similar to the transition state for the corresponding neutral–neutral reaction of interest. For example, to obtain the spectrum of the transition state for the hydrogen atom abstraction reaction from HI by a bromine atom, one begins with a bromide ion–HI complex, in which the bromide ion will certainly be complexed to the proton of HI. Detachment of an electron will result in a neutral BrHI species that is close to the transition state for the hydrogen atom transfer, and the vibrational



levels revealed in the spectrum will be those in which the hydrogen atom moves between the halogen atoms<sup>32</sup>

### 8. Instrumentation

The instruments commonly used to study gas-phase ion molecule reactions fall into three distinct pressure regimes. Fourier transform mass spectrometers (FT-MS), in which ions are trapped in a crossed electric and magnetic field, operate at very low pressures ( $10^{-5}$ – $10^{-9}$  Torr).<sup>33</sup> At these pressures, ions can be held for relatively long periods of time, although reactions are slowed by the low concentrations of neutrals which can be present for reaction. In this method, all the powerful techniques of ion cyclotron resonance spectrometry can be brought to bear. In our work, we use a meter-long flow tube known as a flowing afterglow (FA), in which ions are entrained in a rapidly flowing helium buffer gas at approximately 0.5 Torr. Neutral reagents are added downstream and the ionic products are sampled into a quadrupole mass filter and detected by a multiplier. Although the ions are present in the flow tube for only a short time (0.01 s), the neutral concentration can be quite high, so that the range of rates which can be determined in the FA and the FT-MS is approximately the same. This method is especially useful for determining rate coefficients, since in a flow tube the time available for reaction is proportional to the distance along the flow tube the neutral reagent is added.<sup>34</sup> Conventional mass spectrometers equipped with a high-pressure pulsed ion source are well suited to the study of ionic equilibria. In these experiments an equilibrium is established between an ion and an excess of two neutrals. At the high pressure, complexes between the ion and the two neutrals are cooled by collisions with the bath gas and equilibrate. Then the source is sampled and the ratio of the two complexes is measured to determine the relative complexation energies.<sup>2</sup>

### 9. Conclusions

While it would certainly not be true to say that gas-phase anionic reactions are “just like those in solution”, the similarities are sufficient to make comparisons useful and informative. In reactions such as the  $S_N2$  and  $E2$ , which occur exclusively through a cluster and do not involve adducts, the energy required to traverse a reaction barrier comes almost exclusively from clustering, and such reactions can be slow and highly dependent upon the structure of both reactants. Even if a particular group of reactions occur at every collision, the complexes are not necessarily very “hot”, and techniques are available (e.g., endothermic proton transfers) to reduce the initial collision energy once they are formed. However, if a covalent bond is formed exothermically within the complex, the resulting adduct will usually be hot, since it will contain this exothermicity. However, it will be “hot” in a way quite different than if heated thermally, because the ions will have a very narrow, room temperature distribution of energies rather than the broad distribution characteristic of high temperature reactions. As a consequence, it is much more likely that they will produce only a single product ion rather than the large mixture of products that usually result from high-temperature reactions.

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