Acc. Chem. Res. 1981, 14, 146-153

Gas-Phase Reactions of Organic Anions As Studied by the Flowing Afterglow Technique

CHARLES H. DEPUY* and VERONICA M. BIERBAUM*

Department of Chemistry, University of Colorado, Boulder, Colorado 80309

Received December 22, 1980

> *There is good news yet to hear and*
> *fine things to be seen*
> *Before we go to Paradise by way of*
> *Kensal Green*
>
> *G. K. Chesterton*[1]

> *It is as futile to try and understand reactions in solution by studying them in the gas phase as to try to reach Paradise by way of Kensal Green.*
>
> *W. John Albery*[2]

When ionic reactions occur in solution the solvent molecules play an important, often dominant, role. In order to investigate the reactions themselves, unobscured by the effects of solvation, an increasing number of studies of gas-phase reactions between ions and molecules are being carried out. The study of organic cations in the gas phase has a long and distinguished history dating from the earliest days of mass spectrometry.[3] Only more recently have instrumental developments made it possible to generate and examine, as to their structure and reactivity, a wide variety of organic anions in the gas phase. The newest of these techniques, at least in its applications to organic chemistry, is the flowing afterglow (FA) and its offspring, the selected ion flow tube (SIFT).

Experimental Technique

The flowing afterglow technique was developed in 1963 by Ferguson, Fehsenfeld, and Schmeltekopf[4] of the National Oceanic and Atmospheric Administration laboratories in Boulder, CO. Since that time they and their co-workers have exploited the technique to provide a wealth of data on atmospheric ion chemistry and physics while continuing to expand and refine the experimental capabilities.[5]

The heart of our instrument,[6] as shown in Figure 1, is a stainless steel flow tube (100 × 7.6 cm i.d.) in which ions are generated and allowed to react and a differentially pumped mass spectrometer system for mass analysis and detection of the ions. In addition there is a system for handling and purifying gases and measuring their flow rates, a large Roots blower/mechanical pumping unit for maintaining the helium flow, and electronics for system operation and data collection.

Table I
Gas-Phase Acidities[7]

RH	ΔH,[a] kcal/mol	RH	ΔH,[a] kcal/mol
CH_4	416	c-C_7H_8	374
NH_3	404	CH_3CN	372
C_6H_6	398	HF	371
H_2O	391	CH_3COCH_3	369
$CH_2{=}CHCH_3$	390	CF_3CH_2OH	364
CH_3OH	379	CH_3NO_2	359
$C_6H_5CH_3$	379	c-C_5H_6	356

[a] Values indicated are for the reaction $RH \rightarrow R^- + H^+$.

In a typical experiment a large flow (~200 STP $cm^3\ s^{-1}$) of purified helium buffer gas is continuously pumped through the flow tube, establishing pressures of ~0.4 torr and average flow velocities of ~10 000 cm s^{-1}. The average residence time for a helium atom as it is transported from the entrance to the exit of the flow tube is, therefore, about 10^{-2} s. For generation of ions, small flows (<1 STP $cm^3\ s^{-1}$) of other gases are added at the upstream end of the flow tube, and ionization is effected by electron impact from a thoriated iridium filament maintained at −100 V relative to a grounded accelerating grid. In unusual cases organic anions can be cleanly generated by direct interaction of electrons with neutral organic compounds; for example, alkyl nitrites react with near-thermal electrons to produce alkoxide ions:

$$\mathrm{RONO} \xrightarrow{e^-} \mathrm{RO^-} + \mathrm{NO} \tag{1}$$

In the vast majority of studies, however, we initially form highly basic precursor ions such as amide, hydroxide, or fluoride by introducing trace amounts of

Charles H. DePuy was born in Detroit, MI, in 1927. He received his B.S. degree from Berkeley and his Ph.D. degree from Yale University in 1953 where he studied with William Doering. After postdoctoral work with D. J. Cram at UCLA, he joined the faculty at Iowa State University. He moved to the University of Colorado in 1963. Before entering the field of gas-phase ion chemistry, he carried out studies in a number of areas of physical organic chemistry including cyclopropane and organometallic chemistry, the chemistry of bimolecular and pyrolytic elimination reactions, and cyclopentane chemistry.

Veronica M. Bierbaum was born in Bethlehem, PA, in 1948. She received her B.A. degree from the Catholic University of America (1970) and her Ph.D. degree in physical chemistry from the University of Pittsburgh (1974) under the direction of Frederick Kaufman. She is currently a Senior Research Associate in the Department of Chemistry at the University of Colorado. In addition to the work described in this paper, she is active in studying product state distributions of ion–molecule reactions by infrared chemiluminescence and laser induced fluorescence.

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(1) Chesterton, G. K. "The Rolling English Road". In "New Oxford Book of English Verse"; Oxford University Press: London, 1972; p 843. Kensal Green is a London cemetery in which a number of literary figures are buried.

(2) Albery, W. J. *Annu. Rev. Phys. Chem.* **1980**, *31*, 229.

(3) Franklin, J. L., Ed. "Ion-Molecule Reactions, Part I. Kinetics and Dynamics"; Benchmark Papers in Physical Chemistry and Chemical Physics Vol. 3; Dowden, Hutchinson and Ross, Inc: Stroudsburg, PA, 1979.

(4) Ferguson, E. E.; Fehsenfeld, F. C.; Schmeltekopf, A. L. *Adv. At. Mol. Phys.* **1969**, *5*, 1–56.

(5) Ferguson, E. E. *Acc. Chem. Res.* **1970**, *12*, 402–408. Ferguson, E. E.; Fehsenfeld, F. C.; Albritton, D. L. In "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 1, pp 45–82.

(6) Bierbaum, V. M.; DePuy, C. H.; Shapiro, R. H.; Stewart, J. H. *J. Am. Chem. Soc.* **1976**, *98*, 4229–4235.

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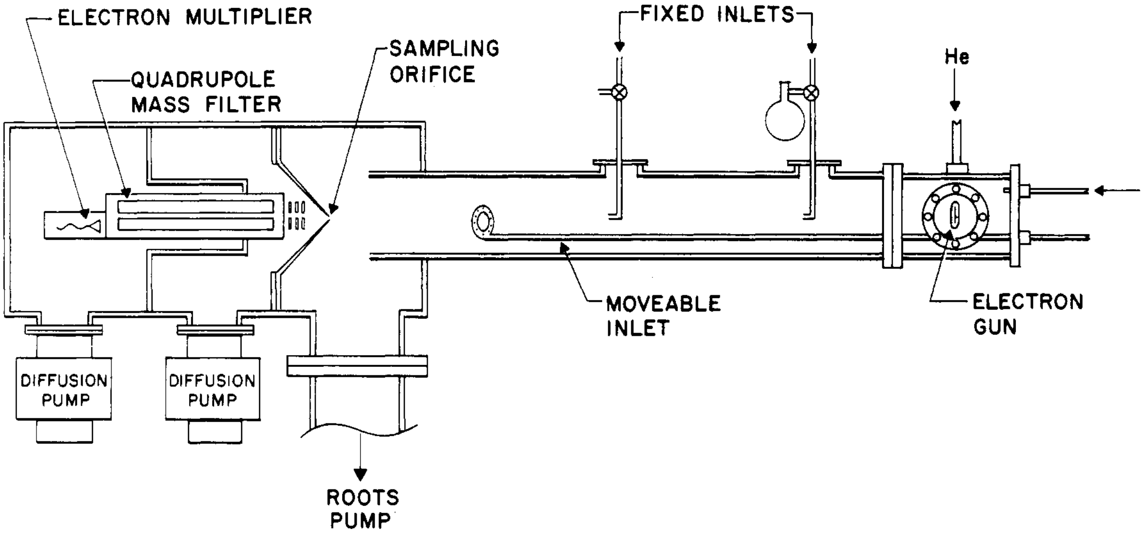

Figure 1. The Flowing Afterglow Apparatus.

ammonia, nitrous oxide and methane, or nitrogen trifluoride:

$$NH_3 \xrightarrow{e^-} NH_2^- + H \qquad (2)$$

$$N_2O \xrightarrow{e^-} O^- + N_2 \qquad (3)$$

$$O^- + CH_4 \rightarrow OH^- + CH_3 \qquad (4)$$

$$NF_3 \xrightarrow{e^-} F^- + NF_2 \qquad (5)$$

As Table I shows, NH_2^- and OH^- are two of the strongest bases available in the gas phase and are capable of abstracting a proton from most organic molecules.[7] Allylic or benzylic carbanions, or carbanions adjacent to carbonyls or other electron-withdrawing groups, are readily formed by reaction of the appropriate organic compound with hydroxide ion. Aryl and substituted-vinyl anions can be prepared by reaction with amide ion. Only the vinyl anion itself (CH_2CH^-) and unactivated aliphatic anions (CH_3^-, etc.) cannot as yet be prepared in a flowing afterglow. We thus have available nearly the full spectrum of organic anions whose reactions with nearly any organic or inorganic molecule can be investigated.

If we begin by generating hydroxide ions from N_2O and CH_4 and add acetonitrile immediately downstream of the ionization region, $^-CH_2CN$ ions are rapidly and cleanly produced by proton transfer:

$$OH^- + CH_3CN \rightarrow {}^-CH_2CN + H_2O \qquad (6)$$

After the desired reactant ion is formed in this way, the plasma of ions in helium is allowed to flow a distance of about 30 cm without further perturbations. This allows full development of a laminar velocity profile for helium, attenuation of higher diffusion modes of the ions, and collisional relaxation of excited ions and metastables. Thus the flow, diffusion, and energy characteristics become well defined. The neutral reactant of interest, for example D_2O, is now added through a fixed or movable inlet, and ion–molecule reactions commence from the point of addition of the neutral to the point of sampling of the plasma:

$$^-CH_2CN + D_2O \rightarrow {}^-CHDCN + HOD \qquad (7)$$

$$^-CHDCN + D_2O \rightarrow {}^-CD_2CN + HOD \qquad (8)$$

These hydrogen–deuterium exchange processes will be discussed in detail below.

A second neutral reagent can be added still further downstream to examine its reaction with the deuterated acetonitrile ions, and indeed multistep gas-phase ion–molecule syntheses can be carried out by adding neutrals at successive inlets along the flow tube. Most of the reaction mixture is exhausted through the Roots blower, but a small fraction is sampled through a 0.5-mm orifice in a molybdenum cone into the low-pressure differentially pumped region. The ions are focussed by a series of lenses, analyzed by a quadrupole mass filter, and detected with a continuous channel electron multiplier. By appropriate choice of the polarity of the applied voltages in the detection system, either positive or negative ions may be sampled from the plasma, mass analyzed, and detected. The pulses are counted and accumulated in a signal averager to produce mass spectra or individual ion intensities are monitored with a rate meter.

In a flow system, the interrelationship of time and distance allows straightforward measurement of kinetics. For example, the rate constant for reaction 6 can easily be determined by adding acetonitrile through the movable inlet to a plasma containing hydroxide ion and monitoring the reactant and product ion density as a function of inlet position and, therefore, of reaction time. For kinetic measurements, pressures are monitored with a capacitance manometer and flow rates are measured with mass flowmeters or by monitoring the pressure increase in a calibrated volume system. Since the concentration of helium is $\sim 10^{16}$ cm^{-3}, the concentration of the neutral reactant is $\sim 10^{12}$ cm^{-3}, and the concentration of the ionic reactant is $\sim 10^{8}$ cm^{-3}, simple pseudo-first-order kinetic expressions are applicable.

The flowing afterglow technique has been a major source of thermal energy rate constants for positive and negative ion–molecule reactions important in a variety

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(7) Bartmess, J. E.; McIver, R. T., Jr. In "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 2, pp 87–121.

of areas including atmospheric chemistry, astrophysics, lasers, combustion, discharges, and organic chemistry. The recent compilation of Albritton[8] serves as a valuable guide to the rate constants for well over a thousand ion–neutral reactions measured in flow reactors.

The flowing afterglow has several features which facilitate the study of gas-phase ion–molecule reactions: (1) Both the ionic and neutral reactants possess thermal energy distributions. The presence of the helium buffer gas assures that the ions reach thermal equilibrium before reaction while the neutral reagents are added well downstream from the ionizing region so that they do not come in contact with hot filaments or high energy electrons. (2) A great variety of ionic and neutral reactants can be studied. Unusual reactant ions can be synthesized by ion–molecule processes in the flow tube, and unstable or highly reactive neutrals can be generated by, for example, pyrolysis or microwave discharge immediately before the inlet.[9] (3) Since relatively large numbers of ions are produced, it has even proven possible to isolate and analyze the neutral products of some of their reactions.[10] (4) The reaction tube can be heated or cooled to study the temperature dependence of reaction rates and branching ratios[11] or the ions can be accelerated in an electric field to study the effects of kinetic energy.[12] (5) With a suitable window in the flow tube, chemiluminescence[13] (ultraviolet, visible, or infrared) from the products of ion–molecule reactions can be detected.

The flowing afterglow is thus a powerful and versatile technique especially suitable for the study of organic anions. In addition to our laboratory, Bohme[14] and McDonald[15] have employed the flowing afterglow technique to explore the fundamental ion chemistry of organic compounds.

Three other thermal energy techniques, ion cyclotron resonance spectroscopy,[16] high-pressure mass spectrometry[17] and chemical ionization mass spectrometry,[18] have been used to study the kinetics, mechanisms, and thermodynamics of gas-phase organic ion reactions. The various techniques are complementary in their capabilities and goals and together have made major contributions to our understanding of the gas-phase ion chemistry of organic compounds.

Hydrogen-Deuterium Exchange in Carbanions

A carbanion, $C_5H_9^-$, can readily be formed by proton abstraction from 1-pentene with either amide or hydroxide ion. If D_2O is added downstream, H–D exchange in the anion occurs.[19] The extent of exchange depends upon the D_2O pressure and the reaction time, and peaks corresponding to from one to nine H–D exchanges may be observed (eq 9). Hydrogen-deuterium

$$CH_2{=}CH\bar{C}HCH_2CH_3 \xrightarrow{D_2O} C_5H_8D^-, C_5H_7D_2^- \ldots . C_5D_9^- \quad (9)$$

exchange has proven to be a general reaction of carbanions and an extremely useful tool for probing ion structure and reactivity. It is also gaining use in other areas of mass spectrometry.

In order for exchange with D_2O to be observed, the carbanion must be a weaker base than OD^-; thus allylic and benzylic anions exchange readily. Anions which are more basic than OD^-, for example $C_6H_5^-$, are neutralized by D_2O but exchange without neutralization with less acidic reagents (eq 10, 11). Weakly basic anions such

$$C_6H_5^- \xrightarrow{D_2O} C_6H_5D + OD^- \quad (10)$$

$$C_6H_5^- \xrightarrow{ND_3} C_6D_5^- \quad (11)$$

as the acetone enolate do not exhibit exchange with ND_3 or D_2O but undergo facile reaction with deuterated methanol, a more acidic deuteron source[20] (eq 12).

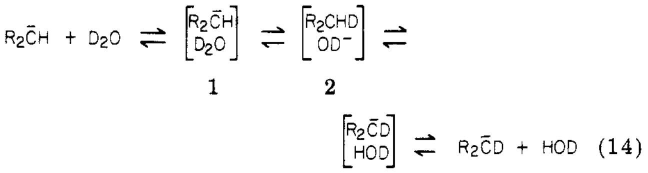
$$CH_3COCH_2^- \xrightarrow{CH_3OD} CD_3COCD_2^- \quad (12)$$

Similarly, the less basic nitromethane anion does not exchange with these reagents but does so with the more acidic reactant, deuterated trifluoroethanol (eq 13).

$$^-CH_2NO_2 \xrightarrow{CF_3CH_2OD} {}^-CD_2NO_2 \quad (13)$$

Finally, exchange in the very stable cyclopentadienyl anion is not induced by any of these deuterating agents.

As a general rule, exchange can usually be observed in the flowing afterglow between an anion and an exchange reagent which is as much as 20 kcal less acidic. We represent isotope exchange by the following mechanism:[19]



1 2

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(14)

The anion and the neutral are attracted to one another by ion–dipole and ion–induced dipole forces which can amount to 10–20 kcal/mol when the species approach typical reaction distances within an ion–dipole complex (1).[21] This same amount of energy is required to separate the ion and neutral in a nonreactive encounter. An endothermic deuteron transfer utilizing part or all of this energy can occur to form a new ion–dipole complex (2) with insufficient energy to dissociate. Reprotonation of the anion generates the original complex

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(8) Albritton, D. L. *At. Data Nucl. Data Tables* **1978**, *22*, 1–101.

(9) Schmeltekopf, A. L.; Ferguson, E. E.; Fehsenfeld, F. C. *J. Chem. Phys.* **1968**, *48*, 2966–2973. Howard, C. J.; Fehsenfeld, F. C.; McFarland, M. *J. Chem. Phys.* **1974**, *60*, 5086–5089.

(10) Smith, M. A.; Barkley, R. M.; Ellison, G. B. *J. Am. Chem. Soc.* **1980**, *102*, 6851–6852.

(11) Dunkin, D. B.; Fehsenfeld, F. C.; Schmeltekopf, A. L.; Ferguson, E. E. *J. Chem. Phys.* **1968**, *49*, 1365–1371.

(12) McFarland, M.; Albritton, D. L.; Fehsenfeld, F. C.; Ferguson, E. E.; Schmeltekopf, A. L. *J. Chem. Phys.* **1973**, *59*, 6610–6619.

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(14) Bohme, D. K.; Mackay, G. I.; Tanner, S. D. *J. Am. Chem. Soc.* **1980**, *102*, 407–409; **1979**, *101*, 3724–3730.

(15) McDonald, R. N.; Chowdhury, A. K. *J. Am. Chem. Soc.* **1980**, *102*, 6146–6147. McDonald, R. N.; Chowdhury, A. K.; Setser, D. W. *Ibid.* **1980**, *102*, 6491–6498.

(16) Beauchamp, J. L. *Annu. Rev. Phys. Chem.* **1971**, *22*, 527–561.

(17) Castleman, A. W., Jr. In "Kinetics of Ion-Molecule Reactions," *NATO Adv. Study Inst. Ser., Ser. B*, **1979**, *40*, 295–321. Cunningham, A. J.; Payzant, J. D.; Kebarle, P. *J. Am. Chem. Soc.* **1972**, *94*, 7627–7632.

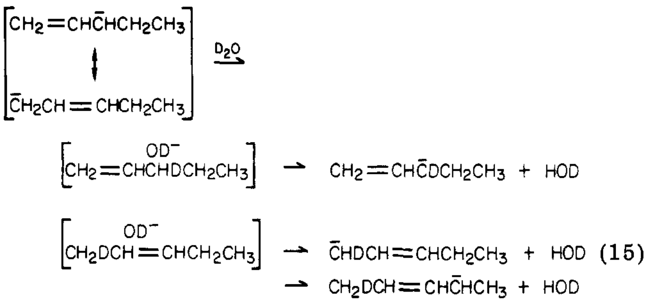
(18) Jennings, K. R. In "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 2, pp 123–151.

(19) Stewart, J. H.; Shapiro, R. H.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1977**, *99*, 7650–7653.

(20) DePuy, C. H.; Bierbaum, V. M.; King, G. K.; Shapiro, R. H. *J. Am. Chem. Soc.* **1978**, *100*, 2921–2922.

(21) Kebarle, P. *Annu. Rev. Phys. Chem.* **1977**, *28*, 445–476.

with isotope exchange (3). In delocalized anions addition and reabstraction of allylic protons and deuterons can lead to double bond isomerization (eq 15) and hence eventually to total exchange.

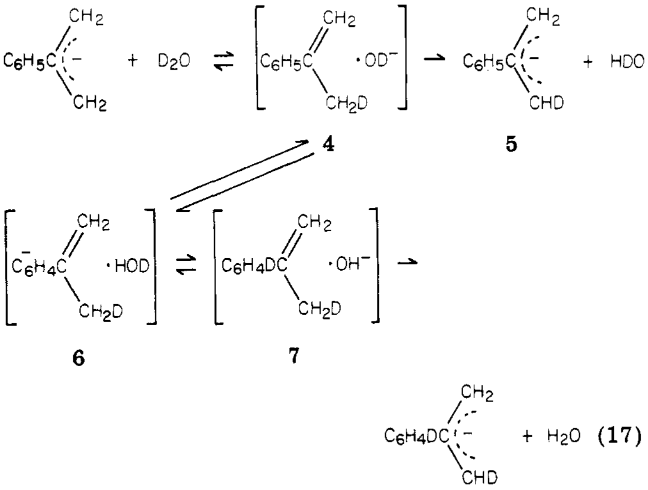

(15)

Although deuterated hydrocarbons are not good exchange agents for hydrocarbon anions, they can serve as facile exchange reagents for ions containing oxygen or nitrogen; for example, perdeuteriobenzene rapidly converts OH^- to OD^- (eq 16). This result is expected

$$OH^- \xrightarrow{C_6D_6} OD^- \qquad (16)$$

because the gas phase acidity of benzene is within 20 kcal/mol of the acidity of water.

If the system is properly chosen, H–D exchange with D_2O can be used to probe acidities of C–H bonds which are weaker acids than water.[22] A simple example is exchange in the 2-phenylpropene anion. The four propene hydrogens exchange rapidly as expected, but at high D_2O concentration it is also possible to exchange at least four aryl hydrogens. We picture this process as shown in reaction 17. The ion and D_2O come together in an ion–dipole complex in which endothermic proton transfer occurs to give **4**. This complex cannot dissociate. Proton abstraction from the allylic position generates **5** in which only allylic H–D exchange has occurred. Occasionally, however, the OD^- in **4** will induce a second endothermic proton transfer by abstracting an aryl hydrogen to produce **6**. Provided that the sum of the two endothermicities does not exceed the ion–dipole energy, these processes are possible. Deuteron transfer to give **7** and proton abstraction to give **8** are both necessary before the ion–dipole complex has sufficient energy to dissociate. We have used this technique to study vinyl and aryl H–D exchanges and hope to extend it to the study of acidities of alkyl C–H bonds.



(17)

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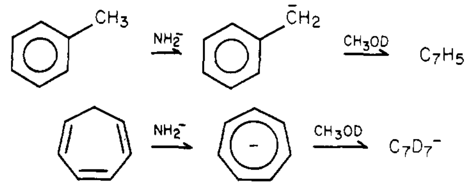
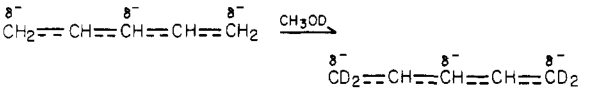
Hydrogen–deuterium exchange has enormous potential in the study of gas-phase ion structure and reactivity. Hunt and Sethi have shown its applicability in chemical ionization mass spectrometry.[23] As an example from our own work, the m/z 91 ions obtained by proton abstraction from toluene exchange two hydrogens while the ions of the same mass from cycloheptatriene exchange all seven hydrogens (eq 18, 19).


(18)
(19)

In cation chemistry the question of the structures of the $C_7H_7^+$ ions required years to unravel. H–D exchange clearly shows that the anions retain their carbon skeletons intact.

Perhaps the most valuable application of the exchange process is as a sensitive probe of the details of ion–molecule reactions which are largely inaccessible by other means. For example, the pentadienyl anion exchanges only four hydrogens rapidly with CH_3OD, showing that reprotonation at the central diallylic position, which would lead to the intermediacy of a nonconjugated diene (and a maximum of five exchanges), does not readily occur:[20]



$$\overset{\delta^-}{C}H_2 \cdots CH \cdots \overset{\delta^-}{C}H \cdots CH \cdots \overset{\delta^-}{C}H_2 \xrightarrow{CH_3OD} \overset{\delta^-}{C}D_2 \cdots CH \cdots \overset{\delta^-}{C}H \cdots CH \cdots \overset{\delta^-}{C}D_2 \qquad (20)$$

Exchange has also been used to demonstrate that isomerization of hydrocarbons can occur during the very act of exothermic proton abstraction by OH^-, thus bringing into question the structure of the ion under investigation.[20] For example, we have shown by isotope-exchange probes that reaction of OH^- with 1,5-hexadiene generates some conjugated anion, presumably through formation of a complex in which reprotonation and reabstraction occur. Thus, hydrogen–deuterium exchange processes provide detailed information about the structure and basicity of gas-phase ions and the nature of gas-phase ion–molecule interactions.

Condensation Reactions of Gas-Phase Anions

Gas-phase organic anions undergo many reactions which have direct solution analogues. For example, enolate anions are nitrosated by alkyl nitrites[24,25] (eq 21). The initial reaction products are expected to be the nitroso ketone and methoxide ion (**9**). If separation of the complex occurred immediately, only methoxide ion would be detected and little information about the course of the reaction would be available. However, the reaction products usually remain together long enough

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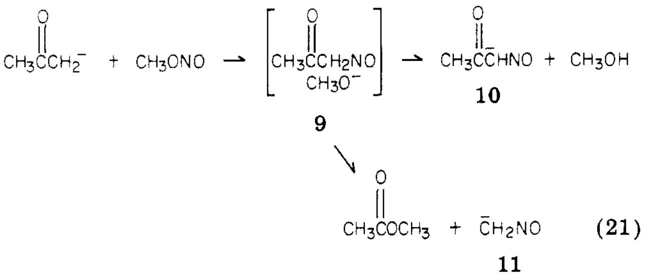
(22) Squires, R. R.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.*, submitted for publication.

(23) Hunt, D. F.; Sethi, S. K. *J. Am. Chem. Soc.* **1980**, *102*, 6953–6963.

(24) Noest, A. J.; Nibbering, N. M. M. *Adv. Mass Spectrom.* **1980**, *8*, in press.

(25) King, G. K.; Maricq, M. M.; Bierbaum, V. M.; DePuy, C. H. *J. Am. Chem. Soc.*, to be submitted for publication.

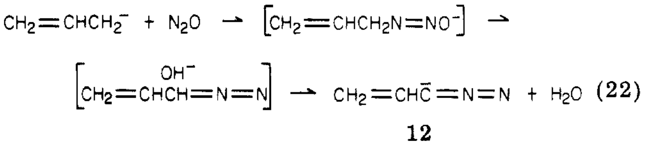


$$CH_3\overset{O}{\overset{\|}{C}}CH_2^- + CH_3ONO \rightarrow \left[\begin{matrix} CH_3\overset{O}{\overset{\|}{C}}CH_2NO \\ CH_3O^- \end{matrix}\right]_{\mathbf{9}} \rightarrow CH_3\overset{O}{\overset{\|}{C}}\bar{C}HNO + CH_3OH \ (\mathbf{10})$$

$$\mathbf{9} \rightarrow CH_3\overset{O}{\overset{\|}{C}}OCH_3 + \bar{C}H_2NO \ (\mathbf{11}) \qquad (21)$$

for secondary reactions to occur if favorable reaction channels are available. In this case no methoxide ion is formed; instead the major product is the nitroso ketone anion **10**, formed by proton transfer, together with smaller amounts of the nitrosomethane (formaldehyde oxime) anion **11** which can be formed by a reverse Claisen-type condensation.

Numerous other condensation reactions have been studied in our laboratory. A particularly interesting example is the reaction of carbanions with N_2O to form substituted diazomethane anions[26] (eq 22). Again, the



$$CH_2{=}CHCH_2^- + N_2O \rightarrow [CH_2{=}CHCH_2N{=}NO^-] \rightarrow \left[CH_2{=}CH\overset{OH^-}{CH}{=}N{=}N\right] \rightarrow CH_2{=}CH\bar{C}{=}N{=}N + H_2O \qquad (22)$$

12

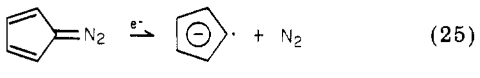
most stable product anion which is mechanistically accessible, here the vinyldiazomethane anion **12**, emerges from the ion–dipole complex. This reaction provides an in situ method for the generation of diazomethane anions whose chemistry can then be explored through further reactions. These same processes can be used for in situ syntheses of inorganic species (eq 23, 24).

$$NH_2^- + N_2O \rightarrow N_3^- + H_2O \qquad (23)$$

$$NH_2^- + RONO \rightarrow HN_2O^- + ROH \qquad (24)$$

Organic Radical Anions

McDonald and co-workers,[15] also employing a flowing afterglow, have found that direct electron impact on diazo and azido compounds readily generates interesting organic radical anions (eq 25, 26). The nitrene anion



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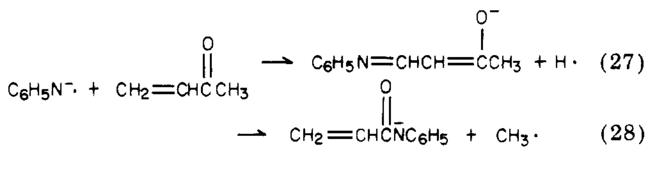
$$C_6H_5N_3 \xrightarrow{e^-} C_6H_5N^{-\cdot} + N_2 \qquad (26)$$

14

14 is especially intriguing as it reacts with a number of α,β-unsaturated carbonyl compounds by nucleophilic addition and subsequent radical fragmentation. From the product mass spectrum the relative probability of 1,4-addition (eq 27) and 1,2-addition (eq 28) can be inferred. Nitrene and carbene anions promise to add a whole new dimension to gas-phase anion studies.



$$C_6H_5N^{-\cdot} + CH_2{=}CH\overset{O}{\overset{\|}{C}}CH_3 \rightarrow C_6H_5N{=}CHCH{=}\overset{O^-}{\overset{|}{C}}CH_3 + H\cdot \qquad (27)$$

$$\rightarrow CH_2{=}CH\overset{O}{\overset{\|}{C}}\bar{N}C_6H_5 + CH_3\cdot \qquad (28)$$

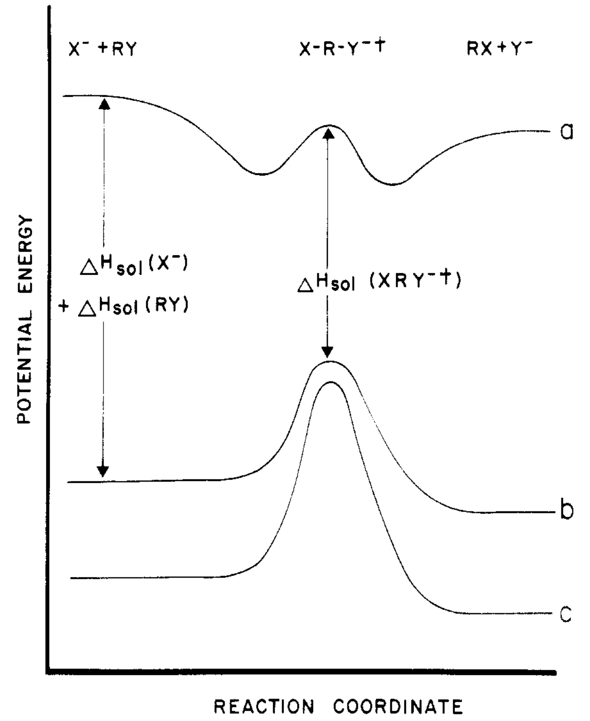


Figure 2. Representative reaction coordinate diagrams for a nucleophilic displacement reaction in the gas phase (a) and in dipolar aprotic (b) and protic (c) solvents (from ref 27).

Reaction Mechanisms

One of the fascinating areas of comparison between gas-phase and solution chemistry is in the detailed mechanisms by which ion–molecule processes occur. Rate constant measurements, which serve as valuable tools in the arsenal of solution chemistry techniques, tend to be less useful in gas-phase studies since most exothermic gas-phase ion–molecule reactions proceed rapidly. For example, both methyl chloride and neopentyl chloride undergo rapid S_N2 reactions with F^- in the gas phase (greater than 1:10 collisions result in reaction); the large rate depression (10^6) seen for the neopentyl group in S_N2 processes in solution is diminished to a factor of 2 in the gas phase.[27] This occurs because the ion–dipole attraction endows the reactants with sufficient energy to surmount many barriers on the reaction surface.

These types of processes have been schematically represented as shown in Figure 2.[27,28] The ion and neutral are attracted by ion–dipole forces into a complex ($X^-\cdots RY$) which has sufficient energy to overcome the barrier to Walden inversion. A product complex ($XR\cdots Y^-$) is formed which then dissociates. Even in such reactions, Brauman has described how variations in barrier height can affect the overall reaction rates. The existence of a barrier was conclusively demonstrated by Olmstead and Brauman[27] and by Riveros et al.;[29] using gentle halide transfer processes they generated complexes with inadequate energy for intercon-

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version as confirmed by subsequent halide transfer reactions.

Figure 2 also illustrates the relationship between the reaction coordinate diagram for a nucleophilic substitution reaction in the gas phase (2a) and those for reactions in dipolar aprotic (2b) or protic (2c) solvents. In S_N2 processes in solution there is greater solvation of the reactants, where the charge is localized, than of the transition state; thus the energy of the reactants lies below that of the central barrier, and these solution reactions are slow. The greater the differential solvation, the slower the reactions become.

It might be expected that gas-phase reactions, which occur so rapidly and with energy in excess of reaction barriers, would be nonselective and relatively random and thus of little mechanistic interest. On the contrary, there is considerable evidence that within an ion–dipole complex steric, electronic, and even isotopic effects can dramatically manifest themselves. For example, methyl and neopentyl nitrite react with fluoride at essentially every collision.[25] In contrast to the corresponding halides, however, two reaction channels are available in the nitrites, S_N2 to form NO_2^- and the alkyl fluoride (eq 29) and elimination ($E_{CO}2$) to form NO^-, an aldehyde, and HF (eq 30). Neopentyl nitrite reacts exclusively by the latter process (no detectable NO_2^- is formed), while methyl nitrite reacts primarily (80%) by the former. Thus, when measured by an intramolecular competition, the steric retardation of the neopentyl group manifests itself much more strikingly than it does on the basis of rate data.

$$F^- + CH_3ONO \rightarrow CH_3F + NO_2^- \qquad (29)$$

$$F^- + (CH_3)_3CCH_2ONO \rightarrow (CH_3)_3CCHO + HF + NO^- \qquad (30)$$

We have observed[30] similar effects in the E2 reactions of mixed alkyl ethers with strong gas-phase bases. Dialkyl ethers react rapidly with both amide and hydroxide ion to form alkoxide ions and alkoxide–ammonia or alkoxide–water clusters. Labeling studies in cyclic systems together with the observation of the comparative unreactivity of ethers lacking β hydrogens demonstrate that the reactions proceed by elimination rather than substitution. Despite their rapidity, these processes can be highly selective (eq 31).

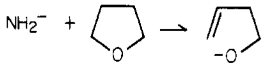
$$OH^- + C_2H_5OC(CH_3)_3 \begin{array}{l} \xrightarrow{99\%} \left\{ \begin{array}{l} C_2H_5O^- + H_2O + CH_2{=}C(CH_3)_2 \\ C_2H_5O^-(H_2O) + CH_2{=}C(CH_3)_2 \end{array} \right. \\ \xrightarrow{1\%} \left\{ \begin{array}{l} (CH_3)_3CO^- + H_2O + CH_2{=}CH_2 \\ (CH_3)_3CO^-(H_2O) + CH_2{=}CH_2 \end{array} \right. \end{array} \qquad (31)$$

Although the reactants possess sufficient energy to traverse either reaction barrier, high product specificity may result if this energy is not readily available *along the reaction coordinate*. In other words, in these large organic systems the reactants enter a potential well in which the energy can be distributed among many vibrational and rotational modes. If only one pathway is exothermic, for example the S_N2 reaction for neopentyl chloride, eventually this process will occur. Alternatively, if several exothermic paths are accessible, then subtle differences in relative energy barriers can play a decisive role.

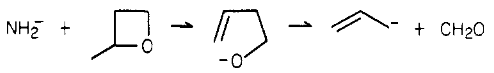
There is increasing evidence that these ion–dipole complexes can be sufficiently long-lived to allow extensive excursions on the reaction surface and a sampling of other energy minima. For example, the reaction of OH^- with $CH_3OCH_2CH_2OCH_2CH_3$ generates the three alkoxide ions expected from direct β elimination as well as the CH_2CHO^- anion; we formulate this latter species as arising from a double elimination process[31] (eq 32). This mechanism demonstrates that the reaction intermediate **15**, although formed in an exothermic process, possesses a considerable lifetime in which secondary reactions can occur to form thermodynamically more stable products. The exact magnitude of these lifetimes remains an interesting and as yet unanswered question. However the observation of ion–molecule association processes in the low pressures of ion cyclotron resonance experiments implies that some complexes must have lifetimes of milliseconds.[32]

$$OH^- + CH_3OCH_2CH_2OCH_2CH_3 \rightarrow \underset{\textbf{15}}{\begin{bmatrix} CH_2CHOCH_2CH_3 \\ CH_3O^- \;\; H_2O \end{bmatrix}} \rightarrow CH_2CHO^- + CH_2CH_2 + CH_3OH + H_2O \qquad (32)$$

By appropriate choice of the organic substrate it is sometimes possible to explore higher energy regions of the reaction surface. For example, reaction of NH_2^- with the unstrained cyclic ether tetrahydrofuran produces only the β-elimination product; in contrast, reaction of NH_2^- with the strained isomer methyloxetane proceeds both by simple elimination and by elimination with subsequent fragmentation[30,33] (eq 33, 34). Release of the strain energy in methyloxetane allows traversal of barriers and sampling of product channels which were inaccessible to reactants possessing only the ion–dipole attraction energy. The directing of strain energy and reaction exothermicity into fragmentation seems to be a common gas-phase phenomenon in comparison to solution studies where extensive third-body stabilization can occur.



(33)



(34)

Oxidation and Reduction Reactions

Although proton transfer reactions have been extensively examined in the gas phase, there have been few studies of hydride transfer processes. We found[34] that the cyclohexadienyl anion, $C_6H_7^-$, produced by proton abstraction from 1,4-cyclohexadiene, readily transfers hydride ion to a variety of organic and inorganic substrates. In particular hydride transfer to nitric oxide generates a versatile reducing agent, HNO^-, while transfer to oxygen produces a powerful oxidant, HO_2^- (eq 35, 36). These oxidation and reduction reagents

$$C_6H_7^- \xrightarrow{NO} HNO^- \xrightarrow{C_6H_5CHO} C_6H_5CH_2O^- \qquad (35)$$

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(30) DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1981**, in press.

(31) Bierbaum, V. M.; DePuy, C. H.; Shapiro, R. H., Twenty-Fifth Annual Conference on Mass Spectrometry and Allied Topics, Washington, DC, May 29–June 3, 1977.

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(34) DePuy, C. H.; Bierbaum, V. M.; Schmitt, R. J.; Shapiro, R. H. *J. Am. Chem. Soc.* **1978**, *100*, 2920–2921.

$$C_6H_7^- \xrightarrow{O_2} HO_2^- \xrightarrow{C_6H_5CHO} C_6H_5CO_2^- \quad (36)$$

can be used, in turn, to generate many other ions of interest[34] (eq 37, 38). The mechanisms by which most

$$HNO^- + N_2O \rightarrow HN_2O^- + NO \quad (37)$$

$$HO_2^- + CO_2 \rightarrow CO_3^- + OH \quad (38)$$

of these interesting ions will react with organic molecules remain to be explored.

Organosilicon Chemistry

We initially used substituted silanes as alternative substrates for the formation of carbanions.[35] Although proton abstraction is a simple and efficient process for the generation of carbanions, in many cases it may result in a mixture of anionic species (eq 39). This ex-

$$\begin{aligned} OH^- + CH_3C{\equiv}CH &\xrightarrow{>60\%} \bar{C}H_2C{\equiv}CH + H_2O \\ &\xrightarrow{<40\%} CH_3C{\equiv}C^- + H_2O \end{aligned} \quad (39)$$

ample is an interesting contrast to solution results where only the acetylenic anion is formed. In order to circumvent this and other problems related to proton abstraction, we have shown that the reaction of fluoride with certain trimethylsilyl derivatives cleanly produces single isomeric species (eq 40, 41). The method is

$$F^- + (CH_3)_3SiCH_2C{\equiv}CH \rightarrow {}^-CH_2C{\equiv}CH + (CH_3)_3SiF \quad (40)$$

$$F^- + (CH_3)_3SiC{\equiv}CCH_3 \rightarrow {}^-C{\equiv}CCH_3 + (CH_3)_3SiF \quad (41)$$

applicable to the generation of a wide variety of carbanions in the gas phase, including isomeric enolates, the diazomethane anion, and alkenyl, alkynyl and benzyl anions. Trimethylsilyl compounds are usually easy to synthesize, stable, and relatively volatile. The allyl anion is, however, the most basic anion we have prepared efficiently by this method.

Tetramethylsilane reacts readily with fluoride in the flowing afterglow to form the fluorotetramethylsilyl anion[36] (eq 42). Association reactions are usually slow

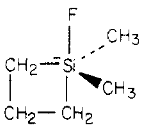
$$F^- + (CH_3)_4Si \rightarrow (CH_3)_4SiF^- \quad (42)$$

in the gas phase because they require collisions to remove excess energy from the complex. In contrast, reaction 42 is exceedingly fast in a flowing afterglow. We formulate the product ion as a pentacovalent silyl anion of the type postulated as intermediates in reactions of silicon compounds.

This ion serves as a gentle fluoride ion transfer agent; it reacts with allyltrimethylsilane to add fluoride without rupture of the silicon–allyl bond[37] (eq 43). This

$$(CH_3)_4SiF^- + (CH_3)_3SiCH_2CH{=}CH_2 \rightarrow (CH_3)_3(CH_2{=}CHCH_2)SiF^- + (CH_3)_4Si \quad (43)$$

product ion can, in turn, transfer F^- to other silanes, and by a succession of such reactions we can generate a scale of gas-phase fluoride affinities of organosilicon compounds. Silacyclobutanes have fluoride affinities of about 30 kcal/mol greater than those of other tetraalkylsilanes. This is understandable in terms of a trigonal-bipyramidal structure for the anion (**16**) in which the ring strain in the silacyclobutane is relieved in the anion. Indeed dimethylsilacyclobutane reacts with allyl anion to form a pentaalkylsilyl anion (**17**). Organosilanes exhibit an interesting and varied anion chemistry[37] which we are continuing to explore.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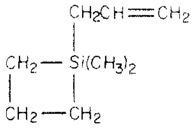
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Product Isolation from Anion–Molecule Reactions

Since high densities of ions can be produced in a flowing afterglow, this technique offers especially good prospects for the isolation and identification of the neutral products of ion–molecule reactions. Ellison and co-workers[10] have recently isolated and characterized neopentyl fluoride as a product of the reaction of neopentyl chloride with F^- in our flowing afterglow system. Their technique seems widely applicable and should greatly expand the scope of studies which can be undertaken. In particular, stereochemical aspects of ion–molecule reaction mechanisms appear to be more accessible through neutral isolation techniques than by the more usual detection of only ionic products.

The SIFT Technique

Although a flowing afterglow offers great versatility for ion production and reaction, it does have limitations. For example, the neutral precursors of the ions are present throughout the flow tube. These species can undergo secondary reactions with the product ions or even destroy the reactant ions of interest. Direct ionization of organic molecules may lead to a mixture of ions, making it difficult to study the reactions of any one ionic species. To overcome these and other problems, Smith and Adams[38] of the University of Birmingham have developed the selected ion flow tube (SIFT).

In a SIFT, ions are generated in a region external to the flow tube by a variety of methods, the neutral precursors are removed by pumping, and ions of the desired mass to charge ratio are selected by a quadrupole mass filter and injected through a Venturi inlet into the flow tube. We have recently constructed a SIFT apparatus and shown that it can be used to generate and inject carbanions to study their ion–molecule chemistry. Smith and Adams have already demonstrated that such highly reactive positive ions as CH_n^+ (n = 0–4) can be examined.[39] Thus the SIFT will serve as a valuable complement to the FA for the study of gas-phase organic ion chemistry.

Concluding Remarks

In a comparison of gas-phase and solution chemistry of organic anions, one might expect that there would

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(35) 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.

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be few similarities. Solvation of ions causes delocalization of charge, lowering of intrinsic reactivity, and possible steric hindrance to reaction. Moreover, the abundant solvent molecules may serve as an efficient energy reservoir, rapidly removing any reaction exothermicity.

On the contrary, solution chemistry seems to serve as an excellent guide to the exploration of gas-phase phenomena. The whole realm of traditional organic chemistry is manifested in the gas phase: proton transfer reactions, oxidations and reductions, substitutions, eliminations, condensations, and adduct formation. However, more fundamentally, the underlying principles and conceptual framework of organic chemistry, formulated from more than a century of research, are dramatically reinforced by gas-phase studies; reactions sensitively respond to structural modifications and energy variations in the reactants in ways that are familiar to us from solution studies.

The differences which arise are usually explicable in simple terms. In the gas phase, reaction exothermicity and strain energy are often revealed as fragmentation of the products due to the absence of solvent stabilization. Acidity differences can often be understood by the necessity of effecting charge dispersal by resonance or by polarization rather than by solvation. The higher intrinsic reactivity which ions exhibit in the gas phase arises from ion–permanent dipole and ion–induced dipole forces; the ionic and neutral reactants approach along an attractive surface which provides sufficient energy to surmount many traditional reaction barriers. Nevertheless these processes often demonstrate striking selectivity; for organic systems the ion–dipole complexes appear to have moderately long lifetimes which allow extensive exploration of the reaction surface and selection from among a manifold of product channels.

The study of the gas-phase chemistry of organic anions, although still in its infancy, has revealed a fascinating world that is both familiar and new. It remains to be seen how much these studies will in the end contribute to our understanding of reactions in solution,[2] but there is certainly a great deal of "good news yet to hear and fine things to be seen" before the burial of the field in Kensal Green and the undoubted arrival of its practitioners in Paradise.

We thank our co-workers whose contributions far exceeded the merely experimental. Without their willingness to venture into a new area with inexperienced guides this work would never have been accomplished. We wish especially to thank the National Science Foundation for seed money to help us get started and for further financial support. The Army Research Office and the donors of the Petroleum Research Fund, administered by the American Chemical Society, have also supported our research, for which we are extremely grateful. None of this work would have been possible without the invaluable advice and encouragement of Eldon Ferguson, Fred Fehsenfeld, Art Schmeltekopf, Dan Albritton, and Carl Howard of NOAA. David Smith and Nigel Adams generously shared their knowledge of the SIFT technique with us. Above all, we thank Bob Shapiro without whose collaboration this work would never have been initiated. Many others in the field of gas-phase ion chemistry have been extremely helpful with advice and patient with our overenthusiasms.