Table II
Basicities of Some Annelated Pyridines (pK_a)

to indan or tetralin by claiming that out-of-plane vibrations in the less planar systems provide for poorer overlap between electronic states leading to a less likely transition.[57] Thus, the magnitude of the extinction coefficient is more strongly linked to the planarity of the ground state than to the strain inherent in the molecule. Examination of the photoelectron spectra of these molecules further suggests that changes in the hyperconjugative abilities of the fused rings may be correlated with changes in the orbital energies of the system and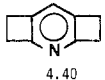 thus explain to some extent the observed variations in ionization potential as well as UV absorption energy and intensity.[58]

The basicity of the pyridine molecule provides a useful feature for studying the effect of cyclobutene ring fusion. The ability of a pyridine nitrogen to acquire a proton (pK_b, measured more conveniently as pK_a of the conjugate acid) directly reflects the availability of the nitrogen lone pair for bonding. The availability of this electron pair, existing in the plane of the σ framework, should be affected by changes in σ bonding and hybridization. Table II presents the basicities of some annelated pyridines.[59] Normally, the electron-releasing inductive effect of cycloalkyl substitution increases the basicity (raises the pK_a) of pyridine. A 2,3-fused cyclobutene ring, however, has the opposite effect and diminishes basicity by 0.45 pK_a unit, while the fusion of a second cyclobutene ring in the 5,6 position further reduces the basicity to an equivalent extent. On the other hand, 3,4-cyclobutapyridine shows almost no change when compared to its unstrained analogue.

The Streitwieser–Finnegan model for rehybridization of bridgehead carbons can again be invoked to explain this basicity behavior. The lone pair of electrons on nitrogen is held more tightly when that atom is bonded to a carbon atom by using an orbital of higher s character. A consistent variation of basicity with the size of annelated rings may be seen for the 2,3:5,6-bisannelated series shown in the bottom half of Table II. Similar observations have been made for cyclobutene-fused quinolines, quinoxalines, and naphthyridines.[60]

(57) W. R. Moore, E. Marcus, S. E. Fenton, and R. T. Arnold, *Tetrahedron*, **5**, 179 (1959).

(58) (a) C. Santiago, R. W. Gandour, K. N. Houk, W. Nutakul, W. E. Cravey, and R. P. Thummel, *J. Am. Chem. Soc.*, **100**, 3730 (1978); (b) F. Brogli, E. Giovannini, E. Heilbronner, and R. Schurter, *Chem. Ber.*, **106**, 961 (1973).

(59) (a) R. P. Thummel and D. K. Kohli, *J. Org. Chem.*, **42**, 2742 (1977); (b) R. P. Thummel and D. K. Kohli, *ibid.*, **43**, 4882 (1978); see also ref 60.

(60) (a) R. P. Thummel and D. K. Kohli, *J. Heterocycl. Chem.*, **14**, 685 (1977); (b) J. H. Markgraf and W. L. Scott, *J. Chem. Soc., Chem. Commun.*, 296 (1967); (c) J. H. Markgraf and R. J. Katt, *J. Org. Chem.*, **37**, 717 (1972).

Bimolecular Reactions of Nucleophiles in the Gas Phase

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The reactions which occur between nucleophiles and electrophiles are among the most common and important of all molecular processes. Such a reaction in solution is often dependent upon the nature of the solvent. This has been elegantly demonstrated[1] for the reaction $Cl^- + MeBr \rightarrow Br^- + MeCl$, which has rate constants, at 25 °C, of 8.2×10^{-27}, 1.1×10^{-26}, and 6.7×10^{-22} cm^3 molecule^{-1} s^{-1} for reactions in water, methanol, and dimethylformamide, respectively.

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Solvent dependence is seldom encountered if the reaction is carried out in the gas phase at low pressure in a mass spectrometer. The rate constant for the above nucleophilic substitution reaction is 2.1×10^{-11} cm^3 molecule^{-1} s^{-1} in the gas phase, and thus more than 10^{11}-fold faster than in the most favorable of the three solvents mentioned. Moreover, the activation energy for this reaction in water as solvent is 24.7 kcal/mol, whereas in the gas phase the calculated activation energy is only 2.6 kcal/mol.[1] Indeed, it may be that the gas-phase reaction requires no activation energy. It is therefore apparent that reactivity in the gas phase is most truly representative of the intrinsic reactivity of a particular nucleophile or electrophile.

(1) K. Tanaka, G. I. Mackay, J. D. Payzant, and D. K. Bohme, *Can. J. Chem.*, **54**, 1643 (1976).

Nucleophiles in the Gas Phase
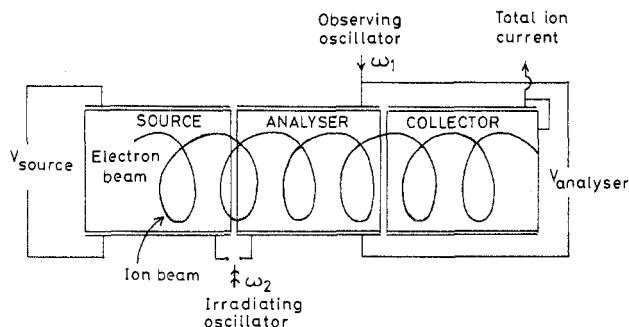
Figure 1. Three-section ion cyclotron resonance cell. The electric field is in the plane of the page, the magnetic field perpendicular to the plane of the page.

Before presenting our work on the reactivity of nucleophiles in ion–molecule reactions in the gas phase, I wish to outline the three modes of formation of negative ions in a mass spectrometer.[2] These are:

(a)   Resonance Capture

$$AB + e^- \rightarrow AB^-\cdot$$
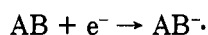
This process involves the capture of a low-energy electron (0–10 eV) by a molecule with a positive electron affinity. It increases in importance as the sample pressure is increased, or in the presence of a nonreactive gas such as nitrogen.[3]

(b)   Dissociative Resonance Capture

$$AB + e^- \rightarrow [AB^-\cdot] \rightarrow A^- + B\cdot \text{ or } B^- + A\cdot$$
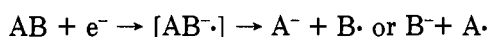
This is an important process if the electron energy is less than 15 eV, and of course providing that the molecular anion $[AB]^-\cdot$ (a radical anion) is prone to fragment.

(c)   Ion-Pair Formation

$$AB + e^- \rightarrow A^- + B^+ + e^- \text{ or } B^- + A^+ + e^-$$
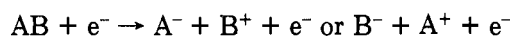
This is a nonresonance process which occurs over a range of energies above 10 eV.

In our studies, electron-energy ranges of 40–70 eV or 0–5 eV have been used to yield negative ions in electronic ground states, formed by processes a and b. The 40–70-eV range often gives the higher yield of negative ions, for in this range anions are formed by capture of secondary electrons, originating either at metal surfaces or from gas-phase positive ionization. The formation of specific molecular anions and their unimolecular decompositions to form fragment anions are interesting topics that have been reviewed elsewhere.[2]

Nucleophilic Substitution—Application of Ion Cyclotron Resonance Spectrometry

Ion cyclotron resonance spectrometry (ICR) is a powerful technique for investigation of gas-phase ion–molecule reactions. It has been described in a number of recent reviews,[4] and so only a brief introduction is now presented. Figure 1 shows a diagram of a simple ICR cell. Ions, produced by electron impact, take up a cyclotron motion in the crossed magnetic/electric field and under the influence of small voltages applied to the cell plates drift down the cell as shown in Figure 1. The ion path length is long (typically 15–30 m); hence the probability of a collision with a neutral molecule is high even at modest cell pressures (e.g., 10^{-6} torr). The mass resolution $(M/\Delta M_{1/2})$ obtained with such a cell is normally 300, and ion transit times of 10^{-2} to 10^{-3} s are usual, but mass resolutions of up to 5000^5 and transit times of several seconds[6] have been achieved under special conditions. An ion absorbs energy from the rf field ω_1 at its cyclotron frequency ω (ω = magnetic field $\times$ mass of ion/charge of ion). An ICR spectrum, linear in mass, is obtained by keeping the electric field ω_1 constant and scanning the magnetic field. The Adelaide instrument, a Dynaspec I.C.R. 9 spectrometer, has a three-section cell (see Figure 1) and operates typically with an ion transit time of 10^{-3} s, a mass resolution of 300, and magnetic fields of up to 15 000 G.

Perhaps the most characteristic feature of ICR spectrometry is that the precursor ion(s) in an ion-molecule reaction may be uniquely defined. In a reaction $A^- + B \rightarrow C^- + D$, if the magnetic field and ω_1 are set to observe C^-, and A^- is then irradiated at its cyclotron frequency with a second oscillator (ω_2; see Figure 1), the signal due to C^- will change in intensity. This is the basis of the ion cyclotron double resonance and cyclotron ejection techniques.[4] Finally, expressions which allow the calculation of both relative and absolute rate constants are available for reactions occurring in ICR cells.[4]

Until the early 1970s, the ICR technique had been little explored for the detection of possible intermediates in organic chemical reactions. Such reactions frequently proceed through transient intermediates whose existence can often be shown only by indirect evidence. Peaks corresponding to charged intermediates should be detected by ICR spectroscopy if the lifetime of the intermediate is longer than, e.g., 10^{-6} s.

Nucleophilic Substitution at Saturated Carbon. Our first and perhaps most ambitious effort was to attempt to observe the activated complex in an S_N2 reaction (eq 1) in which Nu = MeO, MeS, Cl, F, or Br,

$$Nu^- \cdot \,{>}C{-}Y \rightleftarrows \left[Nu{\cdots}\overset{|}{\underset{/}{C}}{\cdots}Y \right]^- \rightleftarrows Nu{-}C{<} \cdot \, Y^- \quad (1)$$

$$COCl^- + M \rightarrow Cl^-(M) + CO \quad (1a)$$

and Y = F, Cl, or Br. However, neither we nor others[7] were able to detect such transient species in an ICR cell under these conditions.

Halide cluster ions $[RX_2]^-$ (and $[RXY]^-$), stabilized by collisional deactivation, have been noted by Kebarle[8,9] and Dougherty,[10,11] using high-pressure mass

(2) M. von Ardenne, K. Steinfelder, and R. Tümmler, "Electronenanlagerungs Massenspectrographie Organischen Substanen", Springer-Verlag, Berlin, 1971; J. G. Dillard, *Chem. Rev.*, 73, 589 (1973); J. H. Bowie and B. D. Williams, *MTP Int. Rev. Sci.: Phys. Chem.*, Ser. Two, 5, 89 (1975); J. H. Bowie, *Mass Spectrom., Spec. Rep., Chem. Soc.*, 3, 287 (1975); 4, 237 (1977); 5, 279 (1979).

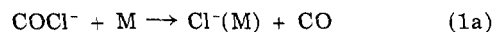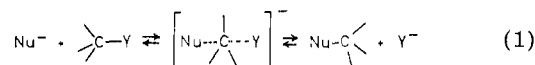(3) R. C. Dougherty and C. R. Weisenberger, *J. Am. Chem. Soc.*, 90, 6570 (1968).

(4) C. J. Drewery, G. C. Goode, and K. R. Jennings, *MTP Int. Rev. Sci.: Phys. Chem., Ser. One*, 5, 183 (1972); J. M. S. Henis in "Ion Molecule Reactions", Vol. 2, J. L. Franklin Ed., Butterworths, London, 1972, Chapter 9; T. A. Lehman and M. M. Bursey, "Ion Cyclotron Resonance Spectrometry", Wiley-Interscience, New York, 1976.

(5) R. T. McIver and A. D. Baranyi, *Int. J. Mass Spectrom. Ion Phys.*, 14, 449 (1974).

(6) R. T. McIver, E. B. Ledford, and J. S. Miller, *Anal. Chem.*, 47, 692 (1975).

(7) J. I. Brauman, W. N. Olmstead, and C. A. Lieder, *J. Am. Chem. Soc.*, 96, 4030 (1974); C. A. Lieder and J. I. Brauman, *Int. J. Mass Spectrom. Ion Phys.*, 16, 307 (1975); O. I. Asubiojo, L. K. Blair, and J. I. Brauman, *J. Am. Chem. Soc.*, 97, 6685 (1975).
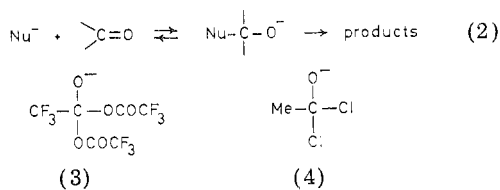
(8) R. Yamdagni and P. Kebarle, *J. Am. Chem. Soc.*, 93, 7139 (1971).

(9) R. Yamdagni and P. Kebarle, *J. Am. Chem. Soc.*, 94, 2940 (1972), and references cited therein.

(10) R. C. Dougherty, J. Dalton, and J. D. Roberts, *Org. Mass Spectrom.*, 8, 77 (1974).

spectrometry. Kebarle suggested that the species Cl⁻(MeCl) is stabilized by H bonding,[8] whereas Dougherty, from a consideration of the heats and entropies of association in the Cl⁻/chloromethane series, suggested the possibility of S_N2 intermediates[10] (see eq 1). In an elegant ICR experiment, Riveros[12] showed that reaction 1a (M = R–halogen, ROH, and RNO₂) will produce a detectable intermediate with CO acting as the "energy sink" for the reaction. Evidence was provided that the two chlorines in Cl⁻(MeCl) are nonequivalent.[12] It seems probable that there are at least two intermediates in reaction 1a, one stabilized by H bonding [e.g., Cl⁻(CHF₃), which appears as an intense adduct[12]], the other an S_N2 intermediate (perhaps from Cl⁻ and CF₄, which form a very weak adduct[12]).

Nucleophilic Addition to Carbonyl Systems. The intermediacy of a tetrahedral complex[13] (of the sort shown in eq 2) in solution reactions has been substantiated by the observation of salts of such intermediates from fluoro esters[14] and by much indirect evidence[15] in other systems. We expected that reactive intermediates of this type, perhaps of lower energies than reactants, might be detected by ICR spectrometry. We found reactions between the perfluoroacetate anion (CF₃CO₂⁻) and a variety of carbonyl-containing compounds to produce detectable 1:1 adducts.[15,16] For example, the perfluoroacetate anion reacts with perfluoroacetic anhydride to form an adduct, the decomposing form of which undergoes a number of rearrangement reactions, including loss of CF₂CO.

$$Nu^- \ + \ \rangle C=O \ \rightleftharpoons \ Nu-\overset{|}{\underset{|}{C}}-O^- \ \rightarrow \ products \qquad (2)$$

$$
\begin{array}{cc}
CF_3-\overset{O^-}{\underset{OCOCF_3}{\overset{|}{\underset{|}{C}}}}-OCOCF_3 & Me-\overset{O^-}{\underset{C:}{\overset{|}{\underset{|}{C}}}}-Cl \\
(3) & (4)
\end{array}
$$

The appearance of a peak corresponding to a 1:1 adduct does not by itself constitute proof of the intermediacy of the tetrahedral species (3), since the formation of a loose association complex is a distinct possibility. However, the decomposition reactions of the adduct suggest the intermediacy of a species which has a fully developed C–O bond as shown in structure 3. During parallel ICR studies[17,18] of nucleophilic substitution in acid chlorides, it was shown[18] that tetrahedral intermediate 4 is formed by the reaction between COCl⁻ and acetyl chloride, with the elimination of CO carrying off the excess energy of the adduct. A recent extension of this work, based on rate studies, suggests the possibility of three intermediates being involved in such a reaction, viz., the tetrahedral species and two

association complexes, one that looks like reactants, the other like products.[19]

Acetate[20] and benzoate anions[21] also react with anhydrides to give collision-stabilized adducts. For example, the gas-phase reaction between the acetate anion and acetic anhydride occurs as shown in eq 5. The

$$MeCO_2^- \ + \ (MeCO)_2O \ \rightleftharpoons \ \cdots \ \rightarrow \ \cdots \ + \ CH_2CO \qquad (5)$$
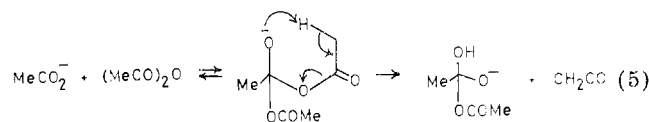
adduct can be detected at cell pressures greater than 1×10^{-5} torr, and its decomposing form eliminates ketene by a negative ion McLafferty rearrangement. The primary deuterium isotope effect (k_H/k_D) for the proton transfer reaction is 2.4 (for an acetic anhydride pressure of 6×10^{-5} torr and an acetate anion transit time of 1×10^{-3} s); thus proton transfer is involved in the rate-determining step of the reaction. It is not known whether the elimination of ketene is concerted (as shown in eq 5) or stepwise. When the cell pressure and the ion transit time are reduced to 1×10^{-5} torr and 5×10^{-4} s, respectively, the isotope effect falls to 1.2. Under these conditions, the adduct from acetic anhydride and $CD_3CO_2^-$ approaches a situation where CH_2CO and CD_2CO are lost equally (apart from the small isotope effect). This suggests the intermediacy of a tetrahedral species, of structure MeC(OCOMe)-(OCOCD₃)O⁻.

The two oxygens of the acetate anion are of course equivalent, and hence react identically in sequence 5. What course would the reaction take if one of the oxygens were replaced by sulfur? The thioacetate anion (MeCOS⁻) is an ambident species in that it may react through either oxygen or sulfur. Which of these will react at a carbonyl center in the gas phase? Reaction through oxygen should occur as shown in sequence 6

$$Me-\overset{O^-}{\underset{S}{\overset{|}{\underset{||}{C}}}} \ + \ (MeCO)_2S \ \rightleftharpoons \ \cdots \ \rightarrow \ \cdots \ + \ CH_2CS \qquad (6)$$
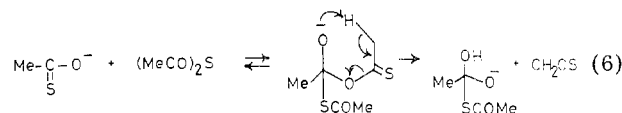
and is expected since formation of a C–O bond in the intermediate should be more favored thermodynamically than formation of the alternative C–S bond. However, sulfanions (e.g., RS⁻) are better nucleophiles than corresponding oxyanions (e.g., RO⁻) in solution, particularly in polar solvents which preferentially solvate oxygen. In solution the thioacetate anion and thioacetic acid normally react through sulfur irrespective of the nature of the electrophile.[22] There are rare exceptions; e.g., thiolacetic acid may react with silyl compounds to form O–Si bonds.[23]

To test the reactivity of MeCOS⁻ in the gas phase, we chose to study the MeCOS⁻/thioacetic anhydride

(11) R. C. Dougherty and J. D. Roberts, *Org. Mass Spectrom.*, **8**, 81 (1974); R. C. Dougherty, *Org. Mass Spectrom.*, **8**, 85 (1974).

(12) J. M. Riveros, A. Celso Breda, and L. Blair, *J. Am. Chem. Soc.*, **95**, 4066 (1973).

(13) E. S. Gould, "Mechanism and Structure in Organic Chemistry", Holt, Rinehart and Wilson, New York, 1959, pp 316, 317.

(14) F. Swarts, *Bull. Soc. Chim. Belges*, **35**, 414 (1926); F. Adickes, *Chem. Ber.*, **58B**, 1992 (1925).

(15) J. H. Bowie and B. D. Williams, *Aust. J. Chem.*, **27**, 1923 (1974), and references cited therein.

(16) J. H. Bowie and B. D. Williams, *Int. J. Mass Spectrom. Ion Phys.*, **17**, 395 (1975); *Org. Mass Spectrom.*, **10**, 141 (1975).

(17) L. K. Blair, P. C. Isolani, and J. M. Riveros, *J. Am. Chem. Soc.*, **95**, 1057 (1973).

(18) O. I. Asubiojo, L. K. Blair, and J. I. Brauman, *J. Am. Chem. Soc.*, **97**, 6685 (1975).

(19) O. I. Asubiojo and J. I. Brauman, *J. Am. Chem. Soc.*, **101**, 2715 (1979).

(20) J. H. Bowie, *Aust. J. Chem.*, **28**, 559 (1975); J. H. Bowie and J. C. Wilson, *ibid.*, **28**, 1993 (1975).

(21) J. H. Bowie and P. Y. White, *Aust. J. Chem.*, **31**, 1511 (1978).

(22) E. E. Reid, "Organic Chemistry of Bivalent Sulphur", Vol. 4, Chemical Publishing Co., New York, 1965, p 19; L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. 1, Wiley, New York, 1967, p 1154.

(23) G. A. Gornowicz and J. W. Ryan, *J. Org. Chem.*, **31**, 3439 (1966); S. Cradock, E. A. V. Ebsworth, and H. F. Jessep, *J. Chem. Soc., Dalton Trans.*, 359 (1972); J. E. Drake, R. T. Hemmings, and H. E. Henderson, *Inorg. Nucl. Chem. Lett.*, **12**, 563 (1976).

system. If the thioacetate anion reacts through oxygen, reaction sequence 6 will occur (i.e., thioketene will be lost from the adduct). If thioacetate reacts through sulfur, only ketene will be eliminated from the intermediate. At a pressure of 1×10^{-5} torr in the ICR cell, the adduct eliminates CH_2CS and CH_2CO in the ratio 10:1.[24] Deuterium labeling studies demonstrate that the CH_2CS is lost from that part of the adduct contributed by the original $MeCOS^-$, whereas CH_2CO comes from the thioacetic anhydride portion. The ambident thioacetate anion therefore reacts as shown in 6, in agreement with prediction and in contrast to its reactivity in solution.

Reaction of Nucleophiles with α,β-Unsaturated Systems. We chose particularly to study nucleophilic (Michael) addition to α,β-unsaturated ketones (eq 7) and to acrylonitrile (cyanoethylation reaction 8).

$$Nu^- + \overset{}{\underset{}{}} \rightleftharpoons Nu\overset{}{\underset{Me}{}}O^- \rightarrow products \quad (7)$$

$$Nu^- + \overset{}{\underset{}{}} \rightleftharpoons Nu\overset{}{\underset{N}{}}^- \rightarrow products \quad (8)$$

$$Nu^- + \overset{NC}{\underset{NC}{}}\overset{CN}{\underset{CN}{}} \rightarrow \overset{NC}{\underset{Nu}{}}C\overset{CN}{\underset{CN}{}} \rightarrow \overset{NC}{\underset{Nu}{}}\overset{}{\underset{CN}{}} \rightarrow$$

$$\rightarrow \overset{NC}{\underset{Nu}{}}\overset{}{\underset{CN}{}}_n \quad (9)$$
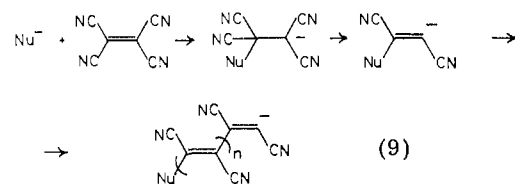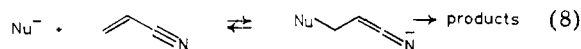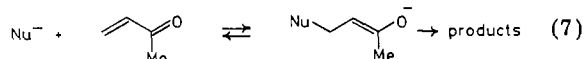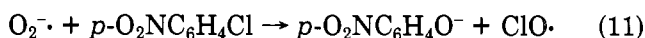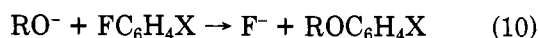
Neither adducts nor their decomposition products were detected in the ICR cell for these reactions. Perhaps no reaction occurred, or perhaps the negative ions formed were not stable enough for detection.

Unlike methyl vinyl ketone and acrylonitrile, tetracyanoethylene forms particularly stable negative ions;[25] this molecule should thus provide an excellent substrate for the detection of nucleophilic addition reactions. Tetracyanoethylene reacts with a number of nucleophiles to form detectable adducts, and these adducts react further, causing anionic polymerizations.[26] The reaction sequence is shown in eq 9. The initial adduct eliminates cyanogen to yield a species which in turn reacts with tetracyanoethylene. This sequence is repeated a number of times to form a final ion in which the value of n depends on the particular nucleophile used. For example, for a cell pressure of 1×10^{-5} torr and an Nu^- transit time of 1×10^{-3} s, $n = 1$ when Nu $= CF_3CO_2$. When Nu $= (NC)_2C=\overset{-}{C}(CN)$ [the $(M-CN\cdot)$ ion from tetracyanoethylene], $n = 3$ and the reaction sequence constitutes the most complex anionic polymerization yet observed by ICR spectrometry.
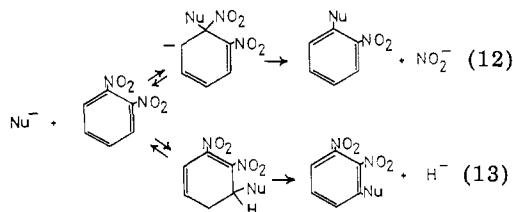
Aromatic Nucleophilic Substitution. An investigation of aromatic nucleophilic substitution in the gas phase would be valuable, since in solution such reactions take a number of pathways.[27,28] For example, nitrobenzene gives either ortho or para substitution

depending upon both nucleophile and solvents.[29] o-Dinitrobenzene[28] and p-dinitrobenzene[30] undergo replacement of a nitro group, whereas m-dinitrobenzene loses either a nitro or the 2-H substituent.[31] Evidence for the intermediacy of Jackson–Meisenheimer σ complexes[30,32-34] and radical anions[35] has been found in such reactions.

Previous studies of aromatic nucleophilic substitution in the gas phase have generally been restricted to halide displacement (and related reactions), particularly with alkoxide anion nucleophiles,[36,37] and to the development of oxygen[38,39] and chloride[40] negative ion chemical ionization mass spectrometry. To date, no really clear mechanistic picture can be drawn from this work except that such gas-phase reactions are considerable faster than those observed in solution[36,37] and that the intermediacy of Jackson–Meisenheimer complexes best rationalizes the formation of some products, e.g., in the reaction sequences 10[37] and 11.[38]

$$RO^- + FC_6H_4X \rightarrow F^- + ROC_6H_4X \quad (10)$$

$$O_2^-\cdot + p\text{-}O_2NC_6H_4Cl \rightarrow p\text{-}O_2NC_6H_4O^- + ClO\cdot \quad (11)$$

Reactions between Nu^- (Nu = Cl, Br, I, and NO_2) and nitrobenzene yield adducts of low abundance; our studies[41] have therefore utilized substituted nitrobenzenes which produce more stable adducts. In a typical experiment, Nu^- (Nu = Cl or NO_2) reacts with o-dinitrobenzene to form (at least) two intermediates, the major one corresponding to the Jackson–Meisenheimer complex shown in sequence 12, the other form-

$$Nu^- + \overset{NO_2}{\underset{NO_2}{}} \rightleftharpoons \overset{Nu}{\underset{}{}}\overset{NO_2}{\underset{NO_2}{}} \rightarrow \overset{Nu}{\underset{}{}}\overset{NO_2}{\underset{}{}} \cdot NO_2^- \quad (12)$$

$$\rightleftharpoons \overset{NO_2}{\underset{Nu}{}}\overset{}{\underset{H}{}} \rightarrow \overset{NO_2}{\underset{Nu}{}}\overset{NO_2}{} \cdot H^- \quad (13)$$

ing by attack at C-3 and/or C-4 (C-3 is shown in sequence 13, but we cannot distinguish between attack at C-3 or C-4). Evidence for sequence 12 comes from the mutual coupling of Cl^- and NO_2^- (i.e., a cyclotron ejection experiment shows that an alteration in the translational energy of Cl^- affects the yield of NO_2^-),

(24) V. C. Trenerry and J. H. Bowie, *Aust. J. Chem.*, submitted for publication.

(25) C. E. Brion and L. A. R. Olsen, *Int. J. Mass Spectrom. Ion Phys.*, **9**, 413 (1972), and references cited therein.

(26) J. H. Bowie, *Aust. J. Chem.*, **30**, 2161 (1977).

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and from the detection of neutral chloronitrobenzene formed in the reaction. In the latter experiment, the reaction is carried out for some period (say 30 min) under conditions of static pressure, and the neutrals formed are detected by the more sensitive positive ion spectrum.[42] Detection of smaller amounts of a chlorodinitrobenzene in the reaction suggests the operation of sequence 13.

Monosubstituted nitrobenzenes react with Cl^- to give adducts which, surprisingly, increase to intensity (i.e., become more stable) as the electron-donating character of the substituent increases. Using nitroanisoles and dialkylnitroanilines, we have been unable to find any evidence to substantiate substitution of Cl^- at either the carbon bearing the nitro group or at that bearing the other substituent. The possibility of substitution at other positions (cf. sequence 13) is at present being examined by determination of deuterium isotope effects. Clearly, more work with other substrates and other nucleophiles will be necessary before any generalization can be made concerning the mechanisms of nucleophilic aromatic substitution in the gas phase.

Anions Produced by Negative Ion Chemical Ionization. Many studies of anionic substitution in the gas phase have, to date, been restricted to the use of even-electron ions produced mainly by the fragmentation of low-energy molecular anions. The recent development of negative ion chemical ionization mass spectrometry as an analytical technique[43] has led to the discovery of certain anions[44] and radical anions[45] not available by conventional ionization. The most important of these ions result from the proton abstraction reaction which occurs between HO^- (formed from N_2O and CH_4) and any organic substrate which contains at least one "acidic" hydrogen substituent.[44] For example, acetone gives the ambident species $MeCOCH_2^-$. ICR studies with ions of this type could lead to interesting analogies with solution chemistry.

Basicities toward Trimethylsilicon Cations. Unquestionably, the most important application of ICR spectrometry in the last decade has been its use for the determination of gas-phase basicities and acidities.[3] The best known examples concern amines[46] and alcohols.[47] The basicities of amines in the gas phase mirror theoretical predictions[46] (e.g., $Me_3N > Me_2NH > MeNH_2 > NH_3$), whereas the sequence in solution is different and depends upon the solvent.[48] The acidities of alcohols in the gas phase (e.g., t-BuOH > i-PrOH > EtOH > MeOH > H_2O) are the reverse of those found in solution.[47] The ICR experiments used for this type of study involve proton-transfer reactions with either positive ions[49] or negative ions[50] and as such give relative scales of proton basicity and acidity.

We have undertaken a program to investigate relative basicities of organic molecules toward species other than the proton. We first chose silicon. Let us assume that two related bases X and Y react (through a lone pair of electrons on the basic center) with Me_3Si^+ to form two adducts Me_3SiX^+ and Me_3SiY^+. If Y can displace X from Me_3SiX^+ (eq 14) but X cannot displace Y from

$$Me_3SiX^+ + Y \rightarrow Me_3SiY^+ + X \qquad (14)$$
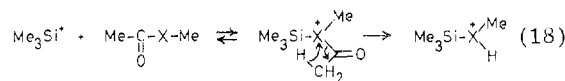
$$Me_3SiY^+ + X \nrightarrow Me_3SiX^+ + Y \qquad (15)$$

Me_3SiY^+ (eq 15), then Y is a stronger silicon base than X. The reaction sequence is determined by the cyclotron ejection technique, and consecutive pairs of experiments then reveal the relative basicity scale.[51] We have obtained the following silicon-basicity scales (basicity decreasing) for alcohols and ketones:[52] t-BuOH > i-PrOH > cyclopentanol $\approx$ n-PrOH > EtOH > MeOH; t-BuCOMe > i-PrCOMe > EtCOMe > Me_2CO $\approx$ cycloheptanone $\approx$ cyclohexanone > cyclopentanone > cyclobutanone.

Acyclic ketones follow the general trend that as alkyl groups attached to the carbonyl carbon become more substituted, the carbonyl oxygen becomes more basic toward Me_3Si^+. Cyclic ketones become less basic as the ring size decreases. Alcohols follow a similar pattern; i.e., elaboration of the alkyl group, particularly at the α carbon, makes the alcohol a stronger silicon base. This is also the direction of increasing gas-phase basicity of alcohols toward the proton.[53] This correspondence between proton and silicon basicity must mean that a major factor influencing the trend in silicon basicity is the ion-induced dipole interaction between the oxonium center (of the adduct) and the polarizable alkyl group. The greater the polarizabiltiy of the alkyl group, the larger will be the ion-induced stabilizing interaction.

This method can also be used for certain other organic molecules including aldehydes, esters, and lactones, but it is *not* applicable to all organic bases. Some adducts appear to be too stable to undergo the displacement reaction (e.g., those formed between Me_3Si^+ and amines), whereas for others, both reactions 14 and 15 are observed (e.g., Me_3Si^+ and nitriles). We are searching for other reference acids to overcome these problems.

The Me_3Si^+ species is also an excellent reagent for examining the basicities of alternative sites in ambient neutral bases. As an example, it is known that the trimethylsilyl cation forms 16 and 17, respectively, with

$$Me_3Si^+ + Me-\underset{O}{\overset{\|}{C}}-X-Me \rightleftharpoons Me_3Si-X\underset{H}{\overset{+}{\underset{CH_2}{\diagdown}}}{=}O \longrightarrow Me_3Si-X\overset{+}{\diagdown}\underset{H}{\overset{Me}{}} \qquad (18)$$

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(52) These reactions were carried out under the following conditions: 70 eV, transit time $(Me_3Si^+) = 2 \times 10^{-3}$ s, tetramethylsilane pressure 1 $\times 10^{-6}$ torr; the pressure of the two alcohols (or ketones) was adjusted so that the two adduct peaks were obtained in a 1:1 ratio. The cell pressure was 3×10^{-5} torr.

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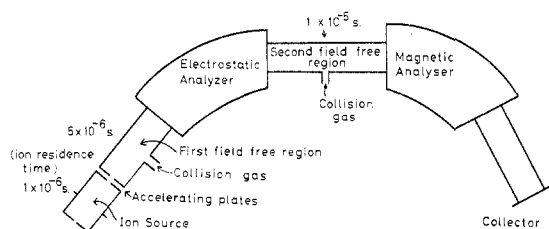
Figure 2. Schematic diagram of a double focussing mass spectrometer of conventional geometry. The Adelaide instrument is an Hitachi Perkin-Elmer R.M.U. 6D mass spectrometer, operating typically at an electron energy of 70 eV, an accelerating voltage of −3.6 kV, sample pressure of 2×10^{-6} torr in the source, and a collision gas (nitrogen) pressure of 1×10^{-5} torr in the appropriate field free region.
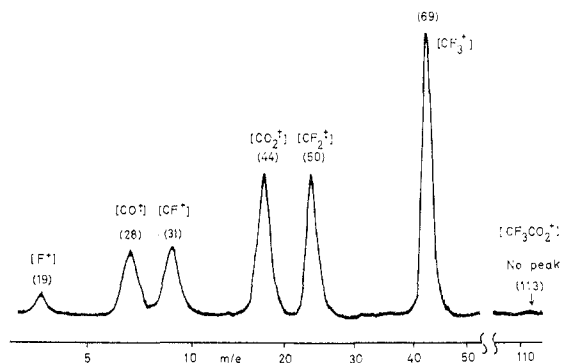

Figure 3. Dissociative charge-inversion spectrum derived from the $CF_3CO_2^-$ ion of $(CF_3CO)_2O$. Decompositions occurring in the second field-free region; magnetic field scan. Peaks are shown with the conventional masses in brackets. Experimental conditions as recorded in the legend to Figure 2.

ethers[54] and ketones,[51] but at which oxygen of a simple ester will it react? The adduct formed between Me_3Si^+ and methyl acetate (X = O) eliminates ketene, hence the reaction sequence is that shown in (18).[55] Reaction sequence 18 also occurs if S-methyl thioacetate (X = S) is used as the ambident base.

Collision-Induced Dissociations of Negative Ions

Let us now consider a quite different type of two-body reaction. In a conventional mass spectrometer, a nondecomposing anion is accelerated to a high translational energy (typically 2000 to 10 000 eV depending upon the spectrometer) as it leaves the ion source. If this accelerated anion undergoes a collision with a nonreactive neutral molecule, there is a probability that some of the translational energy of the ion will be converted into internal (mainly electronic and vibrational) energy. If this occurs, the anion must liberate excess internal energy by one of a number of processes, viz., collisional deactivation, autoionization, or a radiative process, or by some type of fragmentation. We will be concerned here with collision-induced fragmentations. Such processes may be detected in either field-free region of a double-focussing mass spectrometer (see Figure 2).
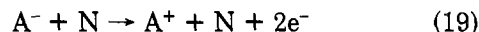
It has been known for some time that positive ions undergo fragmentation after collision with a neutral molecule.[56] This process, called collisional activation, is also important for negative ions[57] since such species, unlike positive ions, often do not have sufficient internal energy to allow any decomposition in the ion source. Collision-induced decompositions of negative ions thus yield information concerning the structure both of the anion and of the molecule that is is derived from. For example, a negative ion derived from a system containing an amide bond will only cleave at the N–C amide bond after collisional activation.[58]

Of more fundamental interest are those collision processes which induce a change in the charged state of an anion. The pioneering work of Cooks and Beynon[59] on charge exchange and charge stripping of positive ions was well under way when we commenced our

work on the charge stripping of negative ions. We have shown that any nondecomposing negative ion may be converted into a decomposing positive ion by reaction 19;[60] in general, about a 1% conversion is effected.

$$A^- + N \rightarrow A^+ + N + 2e^- \qquad (19)$$

Ions A^+, formed within 10^{-12} s of the collision process 19, are generally not stable, and peaks due to these species either are not detected or alternatively are observed in small abundance. The decomposing forms of A^+ fragment in less than 10^{-8} s to produce an intense spectrum of fragment cations.[61] These fragmentations can be measured in either field-free region, but the better resolution is achieved by measurement of decompositions occurring between the electric and magnetic sectors. In such an experiment, the electric sector transmits negative ions, but the magnet is set to accept only positive ions. A typical spectrum is shown in Figure 3.

Negative ions and positive ions, as a general rule, fragment differently, and so fragment anions often have no positive ion analogue produced by conventional ionization. The formation of positive ions by charge inversion thus allows the study of species not available by other methods,[62] e.g., the perfluoroacetate cation (Figure 3). The charge-inversion spectrum of any negative ion [e.g., $CF_3CO_2^-$ (Figure 3)] is a true fingerprint of the parent *positive* ion (e.g., $CF_3CO_2^+$), since this spectrum, at a given accelerating potential, is independent of the nature and pressure of collision gas, provided the pressure in the collision region is less than 3×10^{-5} torr.[63] As an illustration of this feature, the ortho, meta, and para isomers of $MeC_6H_4S^-$ give reproducible, but different, charge-inversion spectra.[64] The charge-inversion spectrum can also provide information about the structure of a negative ion provided that the anion does not undergo rearrangement during the collision process and that the parent positive ion does not rearrange prior to or during fragmentation.[64]

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(63) The reproducibility of the spectrum is affected if the collision gas pressure is higher than 3×10^{-5} torr. This is presumably due to both collision scattering and to the occurrence of multiple collisions.

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This technique may be also used as an aid for structure determination of molecules. A molecule may sometimes form a molecular anion which does not fragment. Alternatively, a compound which does not yield negative ions may form a stable molecular anion when an electron capture group (e.g., nitrophenyl or perfluorophenyl) is specifically built into that molecule. In neither case is structural information generally available from fragmentation data. Measurement of the collision-induced charge inversion spectrum of the molecular anion then may give useful structural information. This technique constitutes an effective marriage of negative and positive ion mass spectrometry. It has been applied to amino acids and peptides[65] and to isomer differentiation of organic compounds.[66] Cooks[66] has used HO^- negative ion chemical ionization mass spectrometry[44] to produce $[M - 1]^-$ ions from 3,4- and 2,5-dihydroxybenzoic acids and has shown that the charge-inversion spectra of these ions are significantly different.
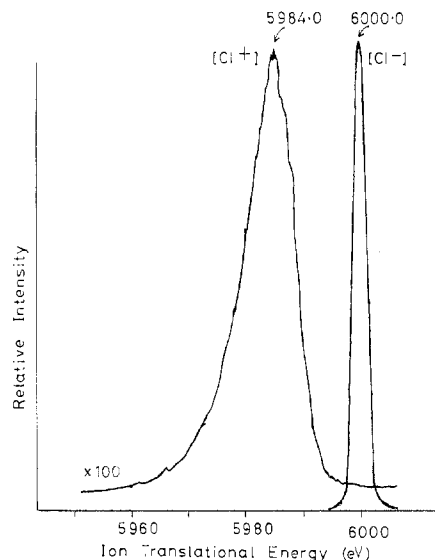
Let us consider the energetics of the charge-stripping process shown in eq 19. Although the majority of ions A^+ undergo fragmentation, in some cases peaks corresponding to A^+ are observed in small abundance.[64,65] Such peaks tend to become more pronounced as the number of atoms in the anion decrease and are most pronounced for atomic species, particularly for halogen cations from halide anions. Ions A^-, usually produced by dissociation of low-energy molecular anions, that have survived for 5×10^{-6} s in order to reach the collision region, will normally be in the electronic ground state. The energy required for the conversion A^- to A^+, assuming both ions to be in electronic ground states, will be equal to the sum of the energies necessary to remove an electron from A^- (the electron affinity, EA) and to ionize $A\cdot$ (the ionization energy, IE). The energy required to effect this transformation must originate from the translational energy of A^-.

Measurements of the differences in translational energies between A^- and A^+ have been carried out for a number of systems with use of the V.G. Micromass Z.A.B. 2F mass spectrometer at the University College of Swansea. In this instrument, the magnetic and electric sectors are arranged such that the ion beam traverses the magnetic sector first.[67] The ion kinetic (translational) energy profiles for the reaction $Cl^- \rightarrow Cl^+$ are shown in Figure 4. The energy difference ΔE between the two maxima, 16.2 ± 0.5 eV, corresponds to the calculated value of 16.6 eV = IE (13.0) + EA (3.6). A major percentage of this reaction does therefore occur through electronic ground states, but the tail of the Cl^+ peak indicates that higher levels may also be involved, even though no fine structure can be seen in the peak. An important application of this technique is that measurement of ΔE enables the estimation of electron affinity (within an accuracy of 0.4 eV), provided the value of IE is known.[68]

Figure 4. Ion translational energy spectra of Cl^- and Cl^+ for the charge-inversion reaction $Cl^- + He \rightarrow Cl^+ + He + 2e^-$. Electric sector voltage scan using MM ZAB 2F spectrometer. Experimental conditions: electron energy 50 eV, accelerating potential -6 kV, energy resolution 3000; sample CCl_4, source pressure 5×10^{-7} torr; collision gas, helium; collision cell pressure 10^{-3} torr. The peak for Cl^+ is a time-averaged signal from ten scans.

Concluding Remarks

I have described a number of different areas of research into the reactions of nucleophiles or bases in the gas phase. Further work is desirable on many of these topics, namely, the detection of reactive intermediates in organic chemical reactions, the determination of relative gas-phase basicities toward acids other than the proton, and evaluation of the relative basicities of alternative sites in ambident bases. Advances in these areas will aid our understanding of chemical reactivity. I have also shown how collisional processes involving negative ions may be used for analytical purposes, to yield information on the structural and energy characteristics of negative ions, and to provide a new method for the estimation of electron affinities.

The last few years have seen a resurgence of interest in the chemistry of negative ions, a resurgence due to a number of factors not least of which are ICR spectrometry and negative ion chemical ionization mass spectrometry. Negative ion facilities are generally available with the latest generation of mass spectrometers. It is to be hoped this will encourage more work with negative ions, hitherto normally an area accessible only to the specialist.

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