Studies on the Positive-Ion Mass Spectra from Atmospheric Pressure Chemical Ionization of Gases and Solvents Used in Liquid Chromatography and Direct Liquid Injection

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Detailed studies have been made using different source gases and solvents in a Micromass Quattro mass spectrometer under positive ion atmospheric pressure chemical ionization conditions. The major background ions from nitrogen, air, or carbon dioxide were investigated by tandem mass spectrometry, followed by similar studies on solvents commonly employed in normal- and reversed-phase high-performance liquid chromatography, namely, water-acetonitrile, acetonitrile, and dichloromethane, with nitrogen, air, or carbon dioxide; hydrocarbon solvents were studied using nitrogen. Spectra were interpreted in terms of the gases, solvents, and their impurities. The acetonitrile spectra provided clear evidence for both charge exchange and proton transfer, the former being facilitated by the introduction of some air into a flow of nitrogen. Radical cations of acetonitrile dimers, trimers, and tetramers were observed, as were protonated dimer and trimer species. Examination of the analytical response of four polycyclic aromatic hydrocarbons in various hydrocarbon solvents, with nitrogen gas, showed that the sensitivity of detection for an analyte and its ionization mechanism are dependent on both the analyte structure and the solvent, with pyrene showing the highest sensitivity, phenanthrene and fluorene being intermediate, and naphthalene having the lowest sensitivity. The degree of protonation followed the same trend. Signal intensity and degree of protonation were dependent on the alkane solvent used, with isooctane providing the best overall sensitivity for the sum of protonated molecules and molecular ions. The ions observed in these studies appeared to be the most stable ions formed under equilibrium conditions in the source.   (J Am Soc Mass Spectrom 2004, 15, 311–324) © 2004 American Society for Mass Spectrometry

The most suitable mass spectral ionization technique for many high-performance liquid chromatographic (HPLC), supercritical fluid chromatographic (SFC), or direct liquid injection analyses is atmospheric pressure chemical ionization (APCI) which is now generally available on all types of mass spectrometers. The technique has been reviewed in some detail [1–4]. The facility with which APCI can lead to ionization of polar compounds, without interference from the overwhelming dominance of air and solvent species, is impressive [5]. Not only is ionization highly efficient [6], but the internal energy of ions emerging from atmospheric pressure sources can be modified using the large number of collisions in this type of source [5, 7].

However, APCI-MS sensitivity for less polar molecules such as polycyclic aromatic hydrocarbons (PAHs) is relatively poor. PAHs form an interesting group of materials because of their well-known effects on health and the challenges involved with their analysis. Most PAH-containing matrices are very complex mixtures containing low concentrations of individual components, suitable standards are often unavailable and alkylated or high-mass PAHs may have many isomers. Common analytical methods employ a gas chromatograph coupled to a mass spectrometer operating in the electron ionization mode (GC/MS), but the success of this technique is limited by the complexity of the samples and by the maximum mass of PAHs that can be passed successfully through a gas chromatographic column. Special techniques are continually being developed to alleviate some of these problems [8–10].

By contrast, HPLC or SFC offer some advantages over GC, such as simpler sample preparation, the possibility of better separation of isomers in some cases, and the possibility of analyzing less volatile, high molecular mass PAHs. A significant disadvantage lies in the fact that the resolution of current LC columns is
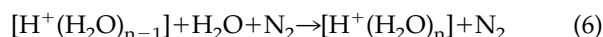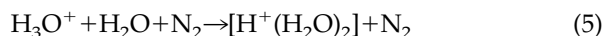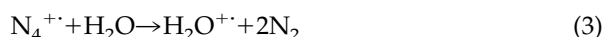
not as high as that of capillary GC columns [4, 11, 12]. APCI-MS is one of the most suitable methods for the detection of PAHs when HPLC or SFC is employed, even though sensitivity is poor (especially for PAHs with lower molecular masses), and is dependent on the solvent used for the HPLC analysis [11, 12]. A better understanding of the processes occurring during ionization under typical analytical conditions might lead to improvements in sensitivity, especially since PAHs are known to ionize by both charge exchange and proton transfer [11, 12].

Early work on the reactions occurring in an APCI source was reviewed by Carroll et al. [13]. These authors had worked with a source in which the corona discharge needle could be moved between 0.5 and 4.0 mm with respect to the source aperture. Using nitrogen gas containing low concentrations of water they observed ions formed in the plasma by a corona discharge, which could be rationalized on the basis of the following equations. The mixture of ions observed depended directly on the distance of the corona needle from the source aperture.

$$N_2 + e^- \rightarrow N_2^{+\cdot} + 2e^- \tag{1}$$

$$N_2^{+\cdot} + 2N_2 \rightarrow N_4^{+\cdot} + N_2 \tag{2}$$

$$N_4^{+\cdot} + H_2O \rightarrow H_2O^{+\cdot} + 2N_2 \tag{3}$$

$$H_2O^{+\cdot} + H_2O \rightarrow H_3O^+ + HO\cdot \tag{4}$$

$$H_3O^+ + H_2O + N_2 \rightarrow [H^+(H_2O)_2] + N_2 \tag{5}$$

$$[H^+(H_2O)_{n-1}] + H_2O + N_2 \rightarrow [H^+(H_2O)_n] + N_2 \tag{6}$$

The formation of water clusters when a corona discharge occurs in air having normal humidity levels has been known for many years [14] and has more recently been studied in detail by Kebarle and coworkers [15, 16]. These authors used a Sciex TAGA 6000E (Concord, Ontario, Canada) mass spectrometer designed for the analysis of contaminants in air and equipped with a corona needle which was operated at a constant current (2.0 μA) and which could be moved over a distance of 5 to 25 mm from the sampling orifice. Analytes were ionized, depending on their proton affinities, by ion-molecule reactions involving proton transfer from clusters formed as in eq. 5 and 6. Sunner et al. found that heating the air in the source to 200 °C dramatically increased the sensitivity of a weak Brønsted base such as anthracene to protonation from the proton-water clusters. Otherwise, the system was not useful for the detection of PAHs in air [16]. These studies were essentially based on ion-molecule reactions between gas-derived ions and analyte molecules. They involved the use of humid, ambient air and very limited volumes of solvent which makes them poor models for an APCI source attached to an HPLC

column or for direct liquid injection of samples. In this case, a solvent flow of 1 mL min^{-1} typically generates a copious volume of gas when vaporized (approximately 29 L h^{-1} at 25 °C and one atmosphere pressure, assuming an ideal gas and a solvent with M.W. = 50 g mol^{-1} and a density of 1.0 g cm^{-3}). Therefore, solvent flows may dramatically change the gas-phase ion chemistry of an APCI source such as those described above.

Indeed, solvents have been shown to participate in ion-molecule reactions with analytes. Benzene is ionized to its molecular ion and also shows an ion at m/z 156, namely the complex ion $[C_6H_6 + C_6H_6^{+\cdot}]$ [13]. The benzene molecular ion will ionize samples of a lower ionization energy (IE) via charge exchange, although it can also function as a proton donor towards strong Brønsted bases such as amines [13]. The chemistry occurring in an APCI source can be complex and may be reflected in the observation of secondary ions, rather than the ions formed directly in the corona discharge as was first recognized by Shahin [14]. Given a sufficient distance between the corona needle and the sampling cone, the ions observed from an APCI source in general reflect equilibrium conditions, in contrast to those from a traditional chemical ionization (CI) source, which in general reflect kinetic conditions [2, 13, 17].

Chloroform is neither easily ionized nor protonated (see Table 1). With the source at 200 °C, Carroll et al. observed ions at m/z 93 in the APCI mass spectrum of chloroform, which indicated proton-bound dimers of ethanol, $[H^+(EtOH)_2]$ [13]. Ethanol is normally used to stabilize chloroform and ions directly arising from chloroform itself were not observed. It has also been recognized that the effective temperature of the APCI source affects the distribution of ions actually observed, especially the distribution of cluster ions [3]. A further example of chemistry involving a solvent came from a study of the hydrocarbons isooctane and commercial hexanes [18]. The authors proposed that isooctane and hexanes are ionized directly by the corona discharge or by charge exchange with $N_4^{+\cdot}$ to yield fragment ions such as $C_4H_8^{+\cdot}$ and $C_4H_9^+$, the predominant species in the spectrum of isooctane. The latter ion is likely the t-butyl cation. Other fragment ions formed are $[M - CH_3]^+$ (only for isooctane) and $[M - H]^+$. The $[M - H]^+$ ions, suggested to be formed by hydride abstraction from the parent molecules by $C_4H_9^+$, produced the predominant peak in the APCI spectrum of hexanes. Of relevance to the present study, Carroll et al. showed that PAHs in the absence of solvent or in the presence of benzene yielded molecular ions by charge exchange. When the solvent was changed to isooctane, PAHs formed protonated molecules with anthracene being detectable at a level of about 1 ppb [18].

Several papers have been published on the analysis of PAHs using HPLC combined with APCI-MS [12, 19, 20] using Sciex API-III triple quadrupole mass spectrometers fitted with heated nebulizer APCI interfaces. It was found that PAHs with higher molecular masses showed predominantly proton transfer especially when

Table 1. Ionization properties of PAH analytes, gases, solvents, and intermediates

Species	Ionization Energy (eV)[ac]	Proton Affinity (kJ mol^{-1})[bc]
Fluorene	7.89	832
Naphthalene	8.14	803
Phenanthrene	7.89	826
Pyrene	7.41	869
Ammonia	10.0	854
Carbon dioxide	13.8	541
Nitrogen	15.6	494
Oxygen	12.1	421
Water	12.6	695
Acetic acid	10.7	784
Acetone	9.7	812
Acetonitrile	12.2	779
1.3-Butadiene	9.1	783
Chloroform	11.4	647
Cyclohexene	8.9	785
Dichloromethane	11.3	—
Dimethyl ether	10.0	792
Ethanol	10.5	776
Methanol	10.9	754
2-Methylpropene	9.2	802
1-Propanol	10.2	787
Propene	9.7	752

[a]From Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *J. Phys. Chem. Reference Data* **1988** 17, *Suppl. 1,* 40–646.
[b]From Hunter, E. P.; Lias, S. G. *J. Phys. Chem. Reference Data* **1998,** 27, 413.
[c]Some data also from Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *Ion Energetics Data* in *NIST Chemistry WebBook, NIST Standard Reference Database Number 69,* Linstrom, P. J.; Mallard, W. G., Eds. March 2003. National Institute of Standards and Technology, Gaithersburg MD, 20899 (http://web-book.nist.gov).

the eluent stream, if nonaqueous, was doped with a low concentration of water. These authors also used high-purity air as the nebulizing gas, with nitrogen as the desolvating curtain gas. It should be noted that, in contrast to CI mass spectrometry in which a wide range of gases and gas combinations have been studied [2], spectra using APCI have been acquired only with nitrogen or air in the gas streams [13, 19].

Other workers using a VG (Micromass) Platform LC/APCI-MS system carried out reversed-phase HPLC and likewise observed the heavier PAHs as protonated molecules but found no specific correlations between protonation versus charge exchange with respect to the structure, ionization energies or proton affinities of the PAHs [11, 21]. These authors observed the greatest sensitivity when the HPLC eluent was acetonitrile, but a five- to tenfold drop in response on addition of 5% water to the acetonitrile, and a smaller but significant drop in sensitivity on addition of 25% dichloromethane to the acetonitrile. At best, they estimated a detection limit for the protonated molecule of dibenzo[*a,l*]pyrene

($C_{24}H_{14}$) of 200 pg (on column injection) in the single ion monitoring (SIM) mode. They used nitrogen in both the bath and sheath gas flows, but did not comment on the nebulizer gas.

The present study was undertaken in order to investigate the analysis of non-polar compounds such as PAHs using a commercial mass spectrometer and ion source under common liquid introduction conditions, since the instruments and/or sample introduction methods used by others may not correspond closely to those commonly in use [11, 12, 15, 22]. The solvents (HPLC grade) were chosen to be those commonly used and available commercially. A number of gases were employed to evaluate their effect on analytical sensitivity. Detection limits for some compounds, especially non-polar species, have been found to be poor and optimization of detection has been complicated by an incomplete understanding of the chemistry occurring in the APCI plasma and the possibility that instrumental artifacts are involved. This study describes an attempt to gain an understanding of the fundamental chemistry in the liquid-introduction APCI plasma of a Micromass system, using PAHs as a tool to assist the study, and can be divided into three parts, beginning with an examination of ions produced by different gases, without solvents. This is followed by an examination of the use of different gas flows in the APCI source coupled with three solvent systems of different polarity typically used in reversed-phase HPLC. The paper concludes with a study of hydrocarbon solvents typically used in normal-phase HPLC and some solutions of PAHs in these hydrocarbons.

Experimental

Solvents and Gases

The solvents cyclohexane and isooctane (Fisher, Nepean, Ontario, Canada), *n*-pentane (Caledon, Georgetown, Ontario, Canada), hexanes (HPLC grade mixed C₆ hydrocarbons, Van Waters and Rogers, Montreal, Canada), *n*-hexane (BDH), *n*-octane (Phillips, Bartlesville, OK), *n*-heptane and *n*-nonane (Aldrich, Oakville, Ontario, Canada) and dichloromethane (DCM, HPLC grade, ACP Chemicals, St. Leonard, Canada) were distilled before use. Acetonitrile (MeCN, HPLC grade, Caledon) was used as received and deionized water was used as obtained from a Barnstead (Fisher, Nepean, Ontario, Canada) NANOpure purifier. The acetonitrile-water solvent mixture was made from acetonitrile and deionized water, each 50% by volume. Dimethyl ether (Matheson, Whitby, Ontario, Canada), acetone (Aldrich), 2-butanone (BDH) and acetic acid (BDH) were dissolved in water to make solutions (ca 1 mg/mL) for introduction into the APCI source.

The following compressed gases (contained in tanks), air (water <10 ppm, referred to as T-air), nitrogen (99.999%, water <3 ppm, referred to as T-nitrogen), oxygen (99.6%, water <10 ppm), carbon dioxide (99.9%,
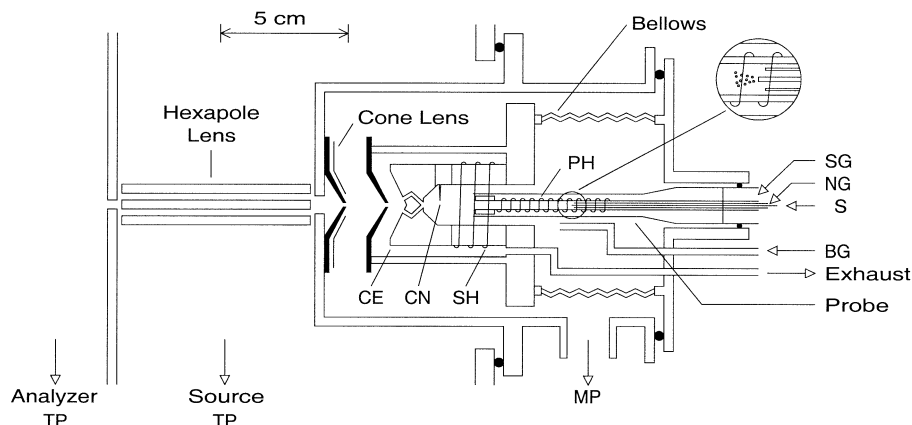
Figure 1.   The Micromass Quattro APCI source and probe used in this study: SG = sheath gas, NG = nebulizer gas, S = solvent or sample, BG = bath gas, PH = probe heater, SH = source heater, CN = corona needle, CE = counter electrode with pepper pot, MP = mechanical rotary oil pump, TP = turbomolecular pump.

water <25 ppm), carbon monoxide (99.5%, water <5 ppm), hydrogen (99.95%, water <30 ppm), and methane (99.5%, water <150 ppm), were obtained from Praxair. Compressed argon was purchased from Liquid Carbonic. Compressed air was also obtained from the building supply (referred to as B-air) and was filtered to remove water, particulates, and oil droplets. Nitrogen was also obtained from evaporation of liquid nitrogen stored in a 160-L pressurized, stainless steel Dewar. Generally, the liquid nitrogen was obtained by in-house fractionation of liquified air in a Philips nitrogen liquifier and is referred to as D-nitrogen.

Samples of the PAHs—naphthalene (Fisher), phenanthrene (Anachemia, Montreal, Canada), fluorene and pyrene (Aldrich)—were used as received, with stock solutions (10 mM) being prepared in each solvent.

Mass Spectrometry

Mass spectra were obtained with a Micromass Quattro triple quadrupole mass spectrometer running under MassLynx V2.1 software and equipped with a Quattro APCI source. The APCI source, Figure 1, uses a "pepper pot" counter electrode [1] and three separate, concentric gas streams. The nebulizer gas flows past a thin silica capillary containing the solvent and breaks that flow into a stream of fine droplets which are vaporized by heat from the probe heater in an alumina tube. The sheath gas flows over the outside of this heater, is thus itself heated, but it also cools the probe sheath. The nebulizer and sheath gases are mixed at the tip of the probe. The bath gas flows along the walls of the source and mainly prevents analytes or solvents from depositing on these relatively cool surfaces. The ionizing plasma is formed at the tip of the corona needle near the pepper pot counter electrode. The gases and ions, after passing through the counter electrode, are sampled by two cones, the region between which is differentially

pumped by rotary vacuum pumps. The ions are finally guided into the analyzer through a hexapole lens. The assembly of the corona needle, the counter electrode, and the first skimmer cone is mounted on a bellows which allows some vertical movement between the first and second skimmer cones. Other than this movement, all other components, including the corona needle, are fixed in position.

The liquid delivery system (unless otherwise noted) consisted of an LC-10AT*VP* HPLC pump (Shimadzu, from Mandel Scientific, Guelph, Ontario, Canada) and a Model 7125 injector (Rheodyne, from Supelco, Oakville, Ontario, Canada). All tubing connections were made with 1/16" o.d. polyetheretherketone (PEEK) tubing. The tubing and solvent bottles used for experimentation were dedicated to one solvent to prevent cross-contamination. Flushing between solvent changes was done with general-use tubing, solvents, and solvent bottles. Gases were distributed by a system built in-house (see Figure 2) which allowed for fine control and
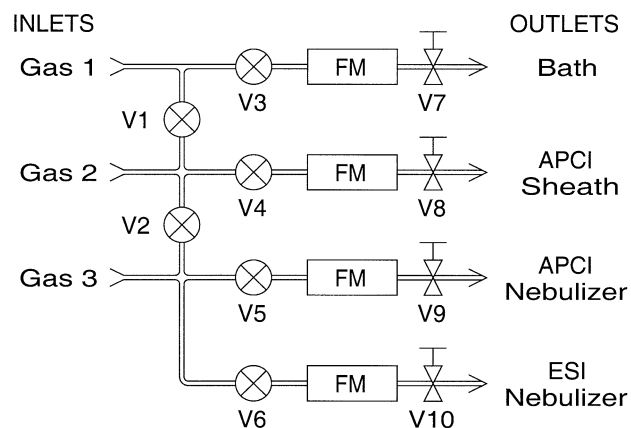

Figure 2.   A block diagram of the gas distribution system used in this study: V1–V6 = on/off toggle valves, V7–V10 = metering valves, FM = rotameter flow meter.

flow measurement of all gases and for different combinations of gases to be used in any of the nebulizer, sheath or bath gas streams.

Regular operating parameters (unless otherwise noted) were: corona voltage = 4.0 kV (4.5 kV for DCM), cone voltage = 22 V, source temperature = 120 °C (100 °C for hexanes), probe temperature = 350 °C; bath gas flow = 300 sLph (standard liters per hour), sheath gas flow = 300 sLph, nebulizer gas flow = 30 sLph; solvent flow rate = 0.200 mL min^{-1}; sample injection volume = 200 μL. A mass spectral range from m/z 5–300 was scanned over a period of 1.0 s. Spectra were averaged and smoothed using the MassLynx software.

Experiments with a Gas Flow but No Solvent Flow

The solvent line to the probe was disconnected and plugged to prevent entry of laboratory air. Between each experiment, the source cone and pepper pot were thoroughly cleaned. With D-nitrogen flowing through the gas lines, the probe and source were heated to 500 and 190 °C, respectively, for 30 min. to remove any adsorbed species. The source and probe were then cooled to running conditions (above) and the analysis was initiated. When switching to different gases, care was taken to purge all traces of the previous gases from the gas distribution system. The plasma was allowed to stabilize for a ten-min period after the introduction of a new gas. All analyses were performed in triplicate.

Experiments With Gases and Solvents

As in the gas studies above, the probe and source were heated to remove any adsorbed solvent or analyte species. General-use tubing and solvent bottles containing the solvent to be studied were attached to the HPLC pump, the lines were purged, and the solvent was allowed to flow to waste through the tubing at 2 mL min^{-1} for 5 min. Solvent-dedicated bottles and tubing were then installed, the solvent was again flushed through all tubing at 2 mL min^{-1} for 5 min. The pump was connected to the APCI probe, the flow of solvent initiated, and the solvent background acquired under the conditions described above. This was repeated twice, after which the source gas composition was changed. All gas combinations were examined with a single solvent before switching to the next solvent. When switching solvents, the above sequence of steps was repeated.

Alkane Solvent Studies

Solvent spectra were acquired using 1.0-s continuum scans. PAHs were observed using single ion monitoring (SIM) with 0.25-s dwell times at m/z 128 and 129 (naphthalene), 166 and 167 (fluorene), 178 and 179 (phenanthrene), 202 and 203 (pyrene), and cone voltages of 30 and 50 V. Thirty scans of background were acquired, the sample was injected, and acquisition was continued for twenty scans after the total ion signal returned to baseline. The background spectrum was obtained by averaging scans 5–25, the sample spectra were averaged and background corrected. Both the total signal intensity (the sum of the response in counts of the background-corrected protonated molecule and molecular ion) and the ratio of the intensity of the protonated molecule (the intensity of the [M + 1] peak corrected for the ^{13}C isotopes in the molecular ion) to that of the molecular ion were calculated for each species in each solvent.

Studies On the Structures of Ions

Detailed studies were carried out on selected, major ions observed from one of T-air, carbon dioxide, or D-nitrogen in the gas streams; studies were also done on acetonitrile, primarily using nitrogen gas, but in one case with T-air in the nebulizer and nitrogen in the other streams. The identities of selected ions in the gas and solvent backgrounds were confirmed by doing tandem mass spectrometry on ions at the same m/z values obtained from known compounds, under the same CID conditions. Studies on ions from acetonitrile and from solutions of reference compounds were made by infusion or flow-injection techniques using a syringe pump with a flow of 20 μL min^{-1} with sufficient gas flows to produce a stable ion beam. Cone voltages between 10 and 30 V were used, the first giving a significant number of proton-containing cluster ions. Tandem mass spectrometry was carried out on mass-selected ions using a series of collision energies ranging from 5 to 30 eV (laboratory frame, in increments of 5 eV). The argon collision gas pressure was adjusted to reduce the precursor ion signal to 25–50% of its original value.

Results and Discussion

Studies with Different Source Gases

Preliminary experiments were conducted using nitrogen, air, oxygen, carbon dioxide, carbon monoxide, methane and hydrogen in all gas streams, together with a reference mixture of several polycyclic aromatic compounds (PACs) dissolved in acetonitrile. These experiments showed that the type of gas employed had a significant impact on the signal intensity and the protonation versus charge exchange ratio of the analytes. It was apparent that methane and hydrogen gave poor sensitivity and little protonation of the analytes. This is in marked contrast to their behavior as chemical ionization reagent gases. The use of hydrogen gas resulted in probe cooling, source heating and damage to the corona needle. No useful analytical benefits were apparent from the use of oxygen or carbon monoxide. Hence, with no apparent advantages and significant dangers inherent in their use, no further experiments were done with methane, hydrogen, oxygen or carbon monoxide.
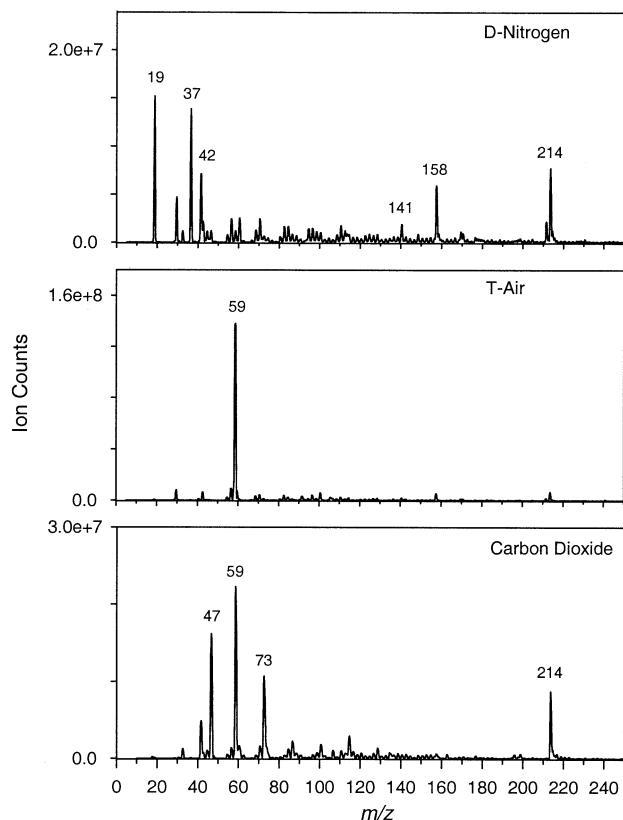
Figure 3. Positive-ion APCI spectra of the gas flows only for D-nitrogen, T-air and carbon dioxide—see Experimental section for conditions.

This is in contrast to useful results that have been obtained from some of these gases as reagents in CIMS [23].

More detailed studies were therefore carried out using nitrogen, air or carbon dioxide in all three gas streams of the Quattro APCI source, but with no liquid stream being present. Typical spectra are shown in Figure 3 (note the sensitivity differences in these spectra).

Both D-nitrogen and T-nitrogen gave essentially the same spectra, with some modest variations between batches; thus only the D-nitrogen results are reported here. Ions at m/z 19, 37, and 42 were the predominant low-mass ions at a cone voltage of 20 V. The first two ions can reasonably be assigned to protonated water $[H_3O]^+$ and the proton-bound dimer $[H^+(H_2O)_2]$. Despite the specifications for T-nitrogen having < 3 ppm water, these spectra demonstrated clearly that the ions observed in this system are in agreement with those postulated in eqs 4 and 5. The third ion was shown by MS/MS experiments to be protonated acetonitrile, $[MeC\equiv NH]^+$, since the only fragment ion observed was at m/z 15. At low cone voltages, an ion at m/z 60 was found, which was shown by MS/MS to be the proton-bound adduct between water and acetonitrile. There was no evidence that the ion at m/z 42 was N_3^+, as postulated by earlier workers [13, 24]. Horning's group

[13] observed N_3^+ as a relatively minor ion when the distance between the corona needle and the sampling cone was 0.5 mm. These conditions do not apply to the Quattro APCI source, as discussed later. The protonated acetonitrile molecule and other minor ions observed probably reflect the composition of the ambient air used to produce the liquified nitrogen, an operation performed in-house, since acetonitrile may be a ubiquitous contaminant in air [25]. Finally, a minor ion at m/z 61 was regularly found to be present in the D-nitrogen and this was shown to be from protonated acetic acid, $[MeC(OH)_2]^+$. Comparison of the MS/MS spectrum from this ion with that from acetic acid also showed ions at m/z 46 and 43. Formation of protonated ions from a compound such as acetic acid is feasible, given its proton affinity, listed in Table 1, along with the ionization properties of other compounds found in these studies.

The major ion observed using air in the gas streams appeared at m/z 59, usually accompanied by some protonated water cluster ions. There was also a significant, yet unsurprising, difference between T-air and B-air, with the former giving primarily a single ion, but the latter showing a spectrum with many ions, including those from water and hydrocarbons. This background contamination of B-air was of such a magnitude that the results were not deemed sufficiently useful to warrant reporting. It should be noted that, according to specifications, T-air may contain three times the amount of water as T-nitrogen. The ion at m/z 59 must contain either one or two oxygen atoms, or two nitrogen atoms. The latter is highly unlikely, thus possible ions are $C_3H_7O^+$ or $C_2H_3O_2^+$. Studies using MS/MS on protonated molecules from a range of compounds produced an excellent match between the ion at m/z 59 and protonated acetone (fragment ions at m/z 44, 43, 41, and 31), as shown in Figure 4.

Intensities of the major ions observed from carbon dioxide (Figure 3) varied with the grade of gas employed. The ions typically appeared at m/z values of 73, 59, and 47 for the less expensive grade. These ions can be attributed to protonated oxygen-containing species. Again, studies on reference compounds provided good evidence that the observed ions were from protonated 2-butanone, acetone, and dimethyl ether, respectively. The MS/MS spectrum from m/z 73 gave major ions at m/z 58, 55, 45, and 43, which was complementary to those from m/z 59, whereas the ion at m/z 47 fragmented to m/z 31, 29, and 15. In order to place this work in perspective, a higher quality grade of carbon dioxide (99.99%, water <5 ppm) was also checked. The total ion current (TIC) of this gas was two orders of magnitude lower than that of the other gases studied, as expected for a purer gas. The major ions were at m/z 61 and 47, which were shown by MS/MS to be derived from protonated ethyl methyl ether and dimethyl ether, respectively. As with the other gases, no ions directly attributable to the gas molecules were observed.

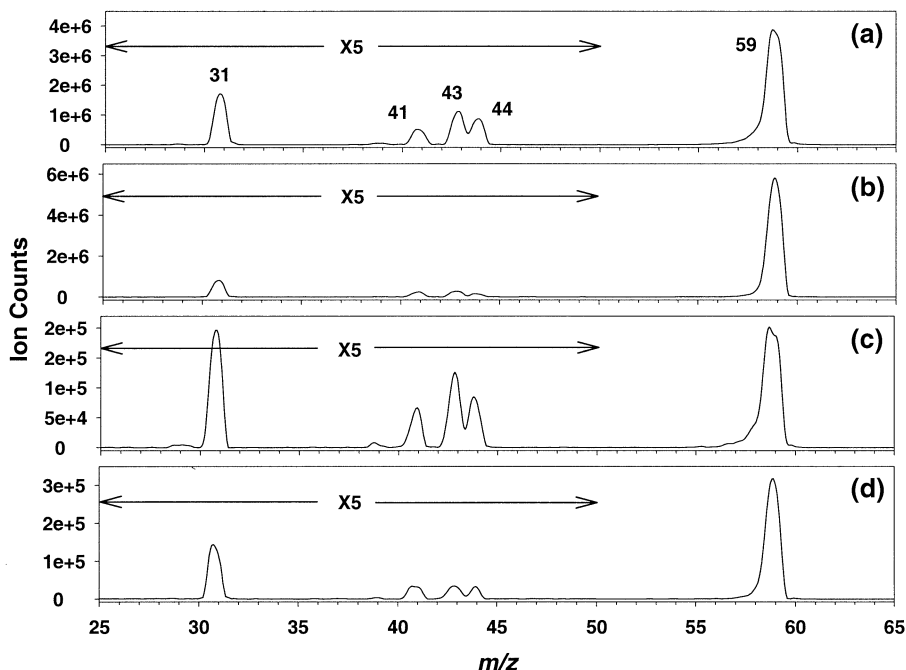A reasonable explanation of these results is that

Figure 4. APCI MS/MS fragment ion spectra (cone voltage = 20) of m/z 59 parent ions: (**a**): From acetone, with 20 eV CID; (**b**): From acetone, with 15 eV CID; (**c**): From T-Air, with 20 eV CID; (**d**): From T-Air, with 15 eV CID.

equilibrium conditions are present in the Quattro APCI source [17] leading to the observation of the most stable ions being formed from the species having the highest proton affinity (PA) present [26] (see Table 1). The ions observed are derived from trace constituents of the gas. Similar results have been observed in the work of Donò et al. as they studied both positive and negative ion APCI spectra of moist air [27].

All three spectra in Figure 3 and those for B-air and T-nitrogen (not shown) contain ions at m/z 214, 158, and 141 (with approximately the same intensity from spectrum to spectrum) which are due to a compound that apparently is linked to the Quattro APCI probe. The intensity of the ions was a function of the temperature of the probe at a given cone voltage. The m/z values of these ions, together with their isotope cluster ratios, suggested a sulfur-containing nitrogenous compound. Tandem mass spectrometry on the ion at m/z 214 gave fragment ions at m/z 158, 141, 77, 57, 55, 43, and 41 all of which were also observed at comparable intensities in the MS/MS spectrum of a sample of *N*-butylbenzene-sulfonamide, synthesized in the regular manner from benzenesulfonyl chloride and 1-butanamine. The origin of this compound is not clear, although it is used as a plasticizer for polyamides [28] and an ion at m/z 214 has been observed as a contaminant in water [29].

Studies With Polar Solvents

These studies were carried out in order to explore the behavior of three solvents which are commonly used for reversed-phase HPLC separations, namely acetoni-trile-water, acetonitrile, and dichloromethane. The positive ion APCI spectra from these solvents are presented in Figures 5, 6, 7, and 8 in which each solvent system was studied using D-nitrogen, T-air and carbon dioxide, respectively, in the gas streams. Except in the case of acetonitrile, results with T-nitrogen were very similar to those with D-nitrogen and hence are not reported. Spectra of acetonitrile using different gas streams showed a tantalizing level of complexity and were studied in detail, as is discussed later. Spectra from the use of B-air suffered from a high level of background ions and are also not reported.

As expected, the spectra of acetonitrile-water (Figure 5) were found to be dominated by the protonated molecule at m/z 42 $[CH_3CNH]^+$ and the proton-bound adduct at m/z 60, $[CH_3CN + H_2O + H^+]$, although the relative intensities of these ions were dependent on the gases in the source. Also present in all spectra were ions at m/z 18 and 19, which can be ascribed to NH_4^+ and H_3O^+ respectively, together with the ions arising from the APCI probe contamination (m/z 214 and its fragment ions).

The spectra of acetonitrile using different source gases (Figure 6) were significantly different. The ion at m/z 42, $[CH_3CNH]^+$, was the base peak when the gas streams contained one of D-nitrogen, T-nitrogen (not shown) or carbon dioxide. By contrast, when the gas streams contained T-air, the predominant ion was a trimeric species at m/z 124, with the ion at m/z 82 (a dimeric species) being also significant. In one experiment, D-nitrogen generated in-house was unavailable and use of a commercial supply (Air Liquide, Dart-mouth, Canada) led to much lower intensities of the
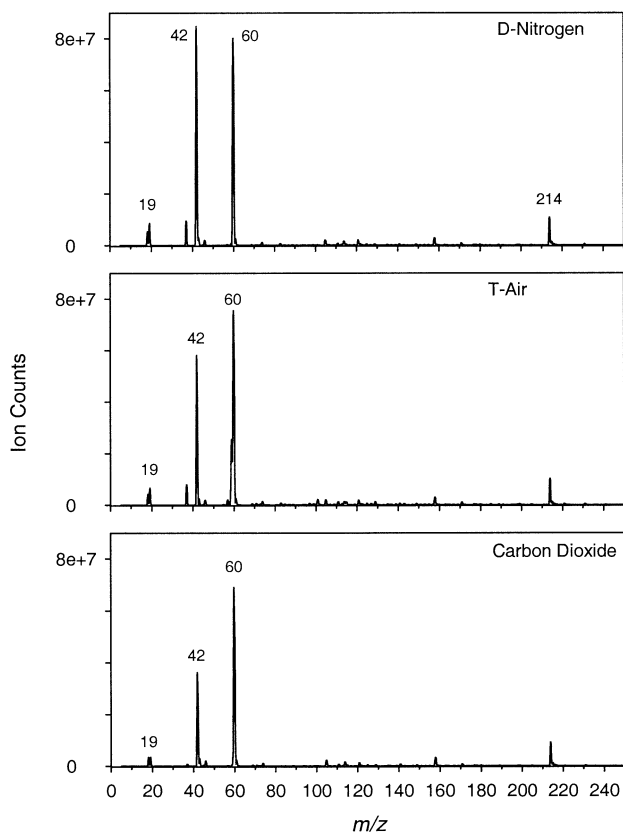
Figure 5. Positive-ion APCI spectra of water-acetonitrile (1:1) with gas streams of D-nitrogen, T-air and carbon dioxide—see Experimental section for conditions.
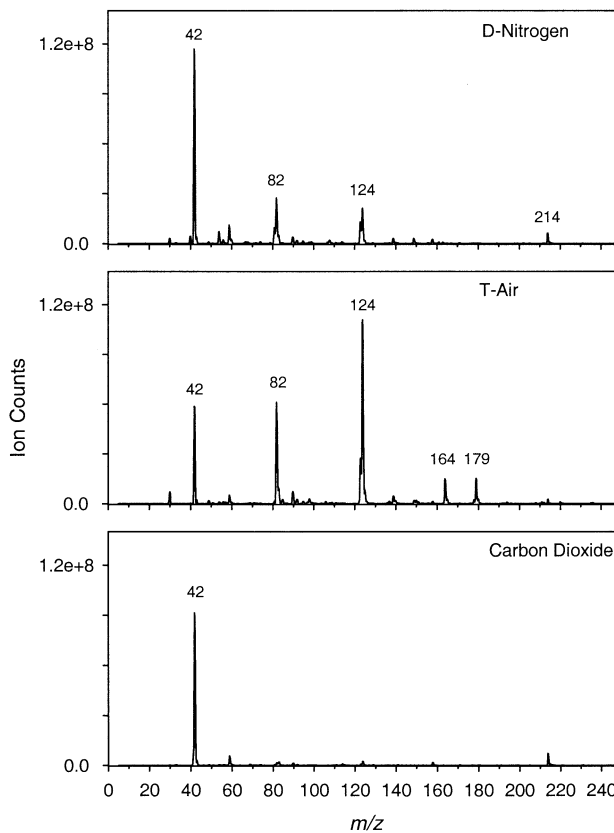

Figure 6. Positive-ion APCI spectra of acetonitrile with gas streams of D-nitrogen, T-air and carbon dioxide—see Experimental section for conditions.

ions at m/z 123/124 and 82/83 being observed, in comparison to those shown in Figure 6. It was found that the intensities of these four ions could be dramatically enhanced by introducing T-air into the nebulizer gas stream, with nitrogen from the commercial (Air Liquide) supply in the bath and sheath gas streams, as shown in Figure 7. These experiments provided two valuable pieces of information, namely that fractionation of oxygen from nitrogen using the in-house Philips nitrogen liquifier is apparently incomplete and that the nitrogen labeled "D-nitrogen" in this work in fact contains some level of oxygen which is not important when the material is used for cooling purposes, but is significant when chemical reactions can occur, such as in an APCI source. The second piece of information is that charge exchange in the Quattro APCI source can be facilitated by mixing other gases, such as oxygen, with nitrogen in the source. Oxygen has a lower ionization energy than nitrogen (see Table 1) and may promote charge exchange. This may have mechanistic implications, as discussed later.

The spectra shown in Figure 7 illustrate some apparently unexplored areas of the chemistry of ions derived from acetonitrile in an APCI source. At low cone voltages (5 V), the ions at m/z 83 and 123 in the clusters at m/z 82/83 and 123/124 predominate, whereas at

higher voltages (25 V) the predominant ions shift to m/z 82 and 124, with the crossover being around 15 V. The composition of these ions was studied using MS/MS techniques. The ion at m/z 83 could be shown to be a protonated dimer of acetonitrile, $[(CH_3CN)_2 + H]^+$, since it fragmented cleanly to a single ion at m/z 42, even at a collision energy as low as 5 eV (laboratory frame). The ion at m/z 82, by contrast, began to fragment into ions at m/z 42 and 41 at a collision energy of 10 eV; at 15 eV the two ions were clearly defined and were present in a ratio of about 2:1, respectively. Thus, the ion at m/z 82 is a complex of acetonitrile with its radical cation, $[(CH_3CN)_2]^{+\cdot}$. To our knowledge, this radical cation complex has been little studied [30–32] and has not been reported previously from an APCI source.

Understanding the structures of the heavier cluster ions proved to be more challenging. The ion at m/z 124 fragmented to give primarily m/z 42, but with minor amounts of both m/z 82 and 83; all three ions appeared at low collision energies. The fact that the intensity of the ion at m/z 124 remains relatively constant while that of m/z 123 decreases with increasing cone voltage (Figure 7) can be interpreted that the ion is *not* the proton-bound trimer of acetonitrile, $[(CH_3CN)_3 + H^+]$ in which a proton is complexed by the nitrogen atoms from three acetonitrile molecules (**a**, see Scheme **1**). The intensities of typical proton-bound dimers and trimers, such as the
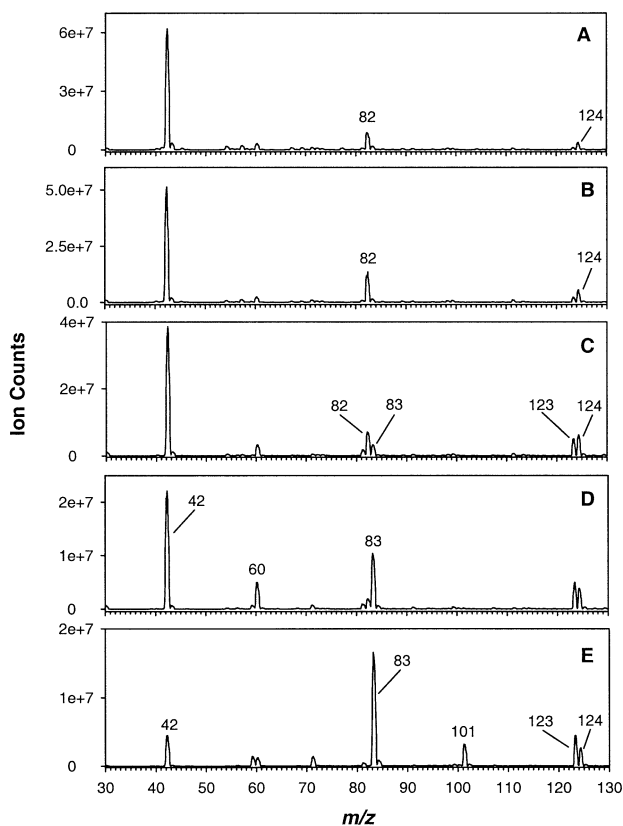
Figure 7. Positive-ion APCI spectra of acetonitrile with nitrogen (bath and sheath) and T-air (nebulizer): (**A**): Cone voltage = 25; (**b**): Cone voltage = 20; (**c**): Cone voltage = 15; (**d**): Cone voltage = 10; (**e**): Cone voltage = 5.

Figure 8. Positive-ion APCI spectra of dichloromethane with gas streams of D-nitrogen, T-air and carbon dioxide—see Experimental section for conditions.

ions at m/z 65 and 97 from methanol decrease very rapidly with increasing cone voltage, the latter not being observed above 10 V. Hence, we suggest that the ion at m/z 124 is described by Structure **b**, although it is possible that some fraction of the ions at m/z 124 have structure **c** and that the ion at m/z 83 could exist as both Structures **d** and **e**.

The ion at m/z 123 fragmented to give initially only m/z 82 (beginning at 10 eV) with the ions at m/z 41 and 42 appearing at energies above 20 eV, thus providing evidence that m/z 123 is a radical cation containing three acetonitrile units which can be described by Structures **f–h**, with **i** as a reasonable structure for the ion at m/z 82. Fragmentation pathways are outlined in Scheme **1** and these were deduced from a full set of both fragment- and precursor-ion spectra. These experiments provide a clear insight into the rich chemistry of the ionization processes occurring in this APCI source.

The mixture of radical cations and protonated molecules shown in Scheme **1** can be expected to be formed by in-source collisions involving nucleophilic attacks of neutral acetonitrile molecules on either the radical cation of acetonitrile or on its protonated molecule. The formation of a radical cation complexed to a neutral molecule in an APCI source has been precedented by Horning's group in the case of benzene (vide supra)
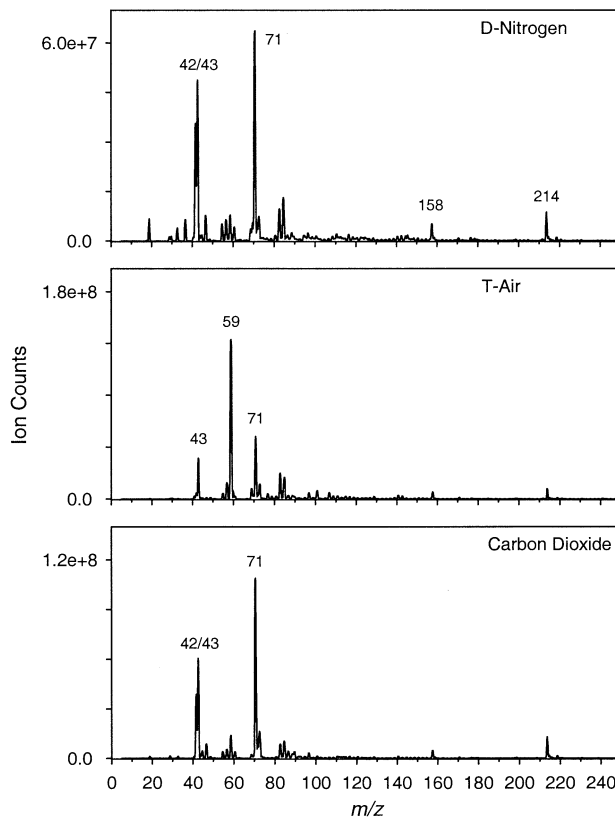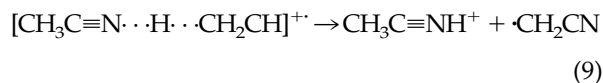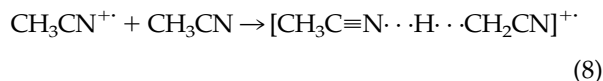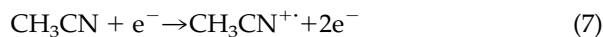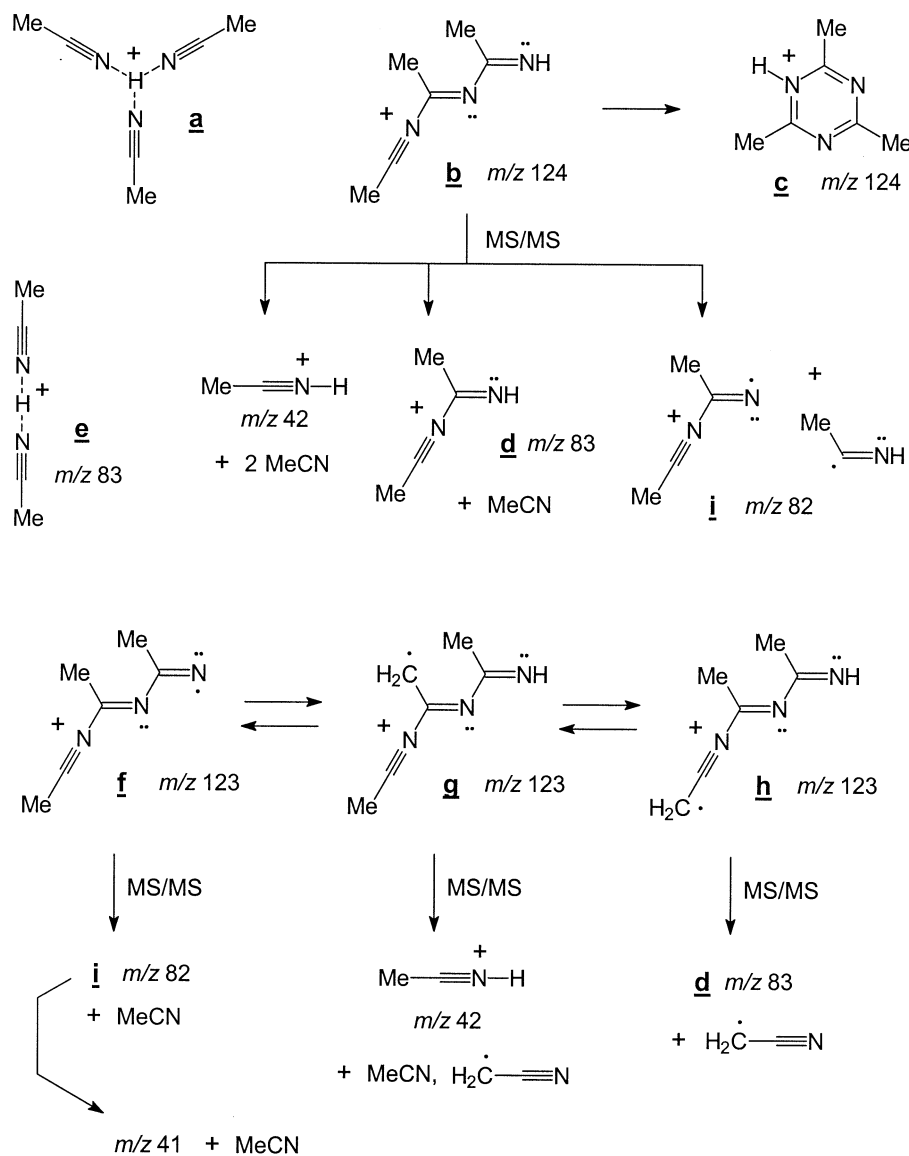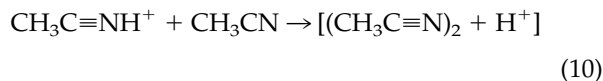
[13]. We suggest that the ionization of acetonitrile (eq 7) proceeds to the radical cation as the neutral molecule passes through the corona discharge, but also that charge exchange between neutral acetonitrile and ionized oxygen or nitrogen species is possible (see Table 1 for ionization energies). The acetonitrile radical cation could cluster with neutral molecules (eq 8) which could fragment to give protonated acetonitrile (eq 9). However, clustering can also occur with geometries other than that implied by eq 8, leading to other species, as outlined in Scheme **1**. The abundances of the various acetonitrile dimer and trimer species would obviously depend on the lifetime of the various species in the source, on their internal energies, the energy transferred during in-source collisions and on the kinetics of the processes outlined in eqs 7–10. The process described in eq 9 has been found to be exothermic by 322 kJ mol^{-1} [31].

$$\text{CH}_3\text{CN} + e^- \rightarrow \text{CH}_3\text{CN}^{+\cdot} + 2e^- \tag{7}$$

$$\text{CH}_3\text{CN}^{+\cdot} + \text{CH}_3\text{CN} \rightarrow [\text{CH}_3\text{C}{\equiv}\text{N}\cdots\cdot\text{H}\cdots\cdot\text{CH}_2\text{CN}]^{+\cdot} \tag{8}$$

$$[\text{CH}_3\text{C}{\equiv}\text{N}\cdots\cdot\text{H}\cdots\cdot\text{CH}_2\text{CH}]^{+\cdot} \rightarrow \text{CH}_3\text{C}{\equiv}\text{NH}^+ + \cdot\text{CH}_2\text{CN} \tag{9}$$

a

b *m/z* 124

c *m/z* 124

MS/MS

e *m/z* 83

Me—≡N—H *m/z* 42 + 2 MeCN

d *m/z* 83 + MeCN

i *m/z* 82

f *m/z* 123 ⇌ **g** *m/z* 123 ⇌ **h** *m/z* 123

MS/MS | MS/MS | MS/MS

i *m/z* 82 + MeCN

Me—≡N—H *m/z* 42 + MeCN, $H_2\dot{C}$—≡N

d *m/z* 83 + $H_2\dot{C}$—≡N

m/z 41 + MeCN

Scheme 1

$$CH_3C \equiv NH^+ + CH_3CN \rightarrow [(CH_3C \equiv N)_2 + H^+]$$

(10)

The gas molecules in the source appear to play a role in the ionization process, but can also contribute to collisional cooling and to declustering of ion complexes, which must contribute to the different spectra observed. Apparently, carbon dioxide is more effective in declustering the ions than are nitrogen or oxygen (Figure 6), but overall, a complex set of processes takes place in the Quattro APCI source.

Results from the use of dichloromethane in the liquid stream of the probe were more complex, as shown in Figure 8 (note the sensitivity differences in these spectra). There was no evidence for any ions containing chlorine, which was also the observation in the case of the APCI-MS of chloroform [13]. However, recent work

by Paradisi and her group [27, 33] on the positive ion APCI mass spectra of chloroethanes showed a rich ion chemistry with a range of chlorine-containing ions being formed. These workers used a Fisons (Micromass) TRIO 1000 II spectrometer with a different design of APCI source than used in the Quattro, but with vapors of the chloroethanes being introduced into a gas flow of air. They used no solvent stream.

The spectrum of dichloromethane obtained in this work using D-nitrogen in the gas streams showed major ions at *m/z* 71 and 43. In T-air the major ions appeared at *m/z* 71, 59, and 43, whereas in carbon dioxide the pattern was quite similar to that of D-nitrogen. In the case of chloroform, the principal species was the proton-bound dimer of ethanol but none of the ions observed in the spectra from dichloromethane can be rationalized as a proton-bound dimer. The Aldrich
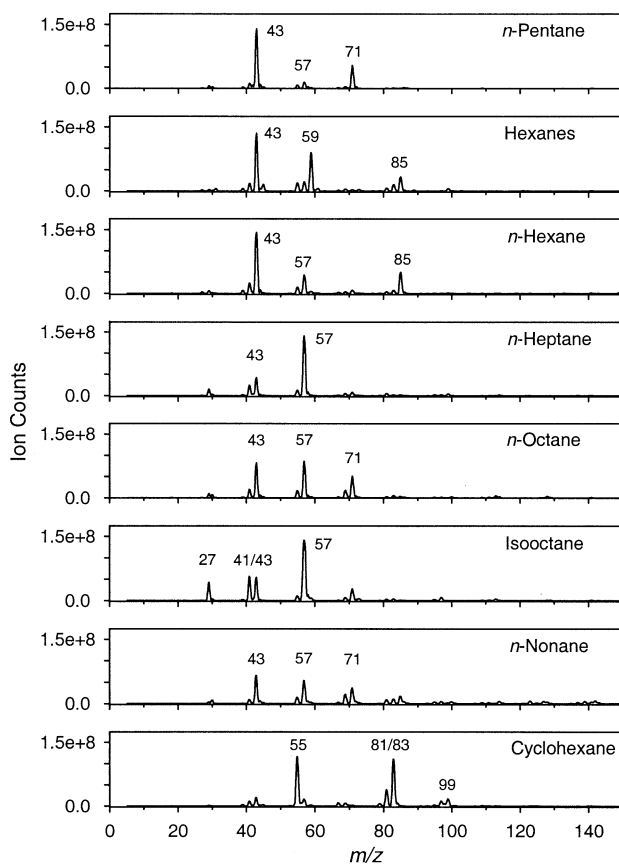
Figure 9. Positive-ion APCI spectra of *n*-pentane, hexanes, *n*-hexane, *n*-heptane, *n*-octane, isooctane, *n*-nonane, and cyclohexane with D-nitrogen in all gas streams—see Experimental section for conditions.

Company catalog lists dichloromethane as containing "50–150 ppm of hydrocarbon stabilizer", which would account for the ions at *m/z* 71 ($C_5H_{11}^+$) and 43 ($C_3H_7^+$). These ions would be expected from, for example, isopentane which has a lower IE than dichloromethane (Table 1) and would thus dominate the spectrum.

In the case of dichloromethane with T-air in the gas streams, MS/MS on the base peak at *m/z* 59 was consistent with that from acetone so in this case an ion from an oxygenated species in the gas streams with a low IE and a high PA dominates the spectrum.

Studies With Hydrocarbon Solvents

Alkane solvents are important in chemical analysis both as extraction reagents and as normal-phase chromatographic eluents. We have studied the positive ion APCI mass spectra obtained from a range of hydrocarbon solvents (C_5–C_9) commonly used for these purposes. The spectra are presented in Figure 9. We have also measured the response of a standard mixture of PAHs in this series of solvents. All measurements were done using only D-nitrogen in all gas streams.

Carroll et al. found that the APCI mass spectra of hexanes and isooctane derived from a corona discharge

showed $[M - H]^+$ and *m/z* 57, $C_4H_9^+$, respectively, as the predominant ions [18]. Work by Bell et al. has also shown the importance of $[M - H]^+$ and $[M - 3H]^+$ ions in the APCI mass spectra of alkanes generated by a corona discharge and monitored by ion mobilities [34].

In the present work, all hydrocarbons with the exception of cyclohexane gave either *m/z* 43 ($C_3H_7^+$) or *m/z* 57 as the base peak. There was no evidence for the presence of molecular ions although the ionization energies of the hydrocarbons are all much lower than, for example, that of acetonitrile. Only *n*-pentane, hexanes, *n*-hexane, and cyclohexane showed significant $[M - H]^+$ ions, with both hexanes and cyclohexane showing significant $[M - 3H]^+$ ions. Examination of the spectra in Figure 9 shows that losses of the neutral species C_2H_4 or C_3H_6 from the $[M - H]^+$ ions are apparently preferred. It has been postulated that the $[M - H]^+$ ions are formed by hydride transfer from molecules to a $C_4H_9^+$ cation [2, 18]. It is also theoretically feasible that N_2H^+, a strong Brønsted acid, could be formed, as shown in eq 11. However, since this reaction involves a collision between two radical cations, its cross section should be low and it should not play a significant role in subsequent protonation processes.

$$C_6H_{14}^{+\cdot} + N_2^{+\cdot} \rightarrow C_6H_{13}^+ + N_2H^+ + 6.8eV \qquad (11)$$
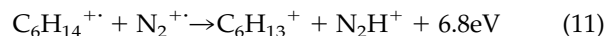
The spectra obtained in the present work are generally similar to the limited data reported previously, although more fragmentation was observed [18, 34]. The base peak in the spectrum of cyclohexane, *m/z* 55, was presumably formed by loss of C_2H_4 as a neutral fragment from *m/z* 83, the $[M - H]^+$ ion. Similar neutral losses can account for all the major fragment ions and the spectra shown in Figure 9 reflect product ions after a substantial number of collisions; they do not give direct information about the primary ionization processes of small alkanes in a corona discharge. A cone voltage of 22 V gave maximum signal intensity.

The only ion that does not fit the previous analysis is that at *m/z* 59 in the spectrum of the hexanes mixture. This ion arises from an impurity which can be readily protonated (perhaps acetone). The intensity of the ion was substantially reduced after passing the hexanes through a column of chromatographic grade alumina. The behavior of the set of hydrocarbon solvents was further studied by obtaining spectra of a mixture of four PAHs, namely naphthalene, fluorene, phenanthrene and pyrene in each solvent. The total intensities of the signals from these analytes are given in Figure 10, while the ratios of protonated molecules to molecular ions are given in Figure 11.

As expected, the results show that pyrene with the lowest IE and highest PA is the most readily detected and the most readily protonated of the four PAHs tested. The converse applies to naphthalene, except in *n*-octane (there is no obvious explanation for this result). The Brønsted acidity of the isopropyl cation,
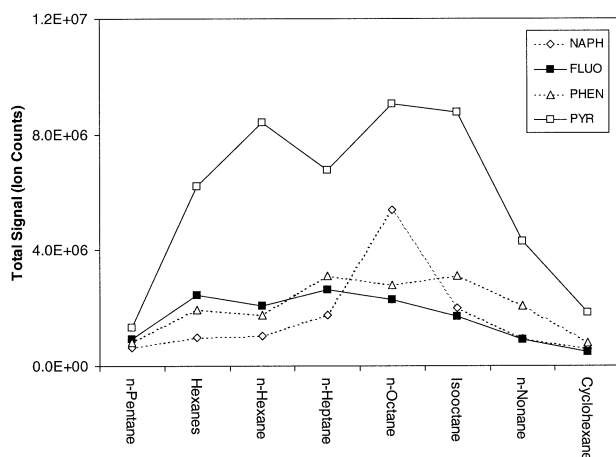
Figure 10. The total signal (sum of $[M + H]^+$ and $M^{+\cdot}$ ions, in counts) from a set of four PAHs, as a function of alkane solvent.

$C_3H_7^+$, is higher than that of the *t*-butyl cation, $C_4H_9^+$, the species presumed to be the ions at *m/z* 43 and 57, respectively (see Table 1). It might be argued, therefore, that *n*-pentane, the solvent producing the greatest relative proportion of ions at *m/z* 43, should show the highest relative amount of proton transfer versus charge exchange. Experimentally, proton transfer, in general, is more favorable in *n*-hexane and isooctane, not pentane.

For the case of cyclohexane, based simply on the Brønsted acidities of the two predominant cations [*m/z* 83 ($C_6H_{11}^+$) and 55 ($C_4H_7^+$)], it could reasonably be expected that this solvent should promote charge exchange ionization of the PAHs in the mixture. Also, comparison of the IE values for cyclohexane versus the PAHs would lead one to expect a facile charge exchange. Cyclohexane does have the best relative charge exchange of all solvents, except nonane, for all compounds (Figure 11). However, it does not strongly
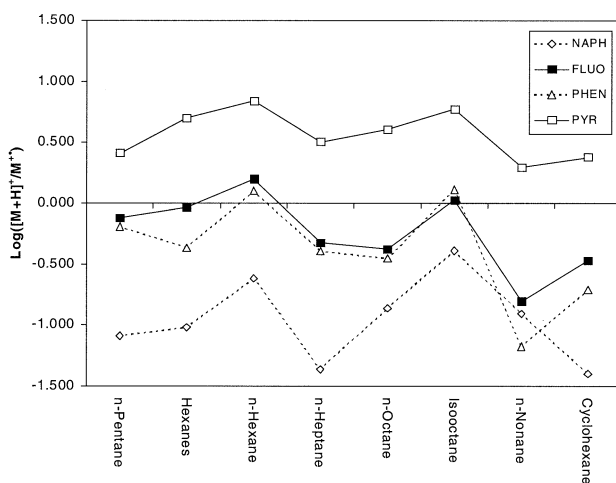

Figure 11. The log of the ratio of the counts for $[M + H]^+$ (protonation) to those for $M^{+\cdot}$ (charge exchange) for four PAHs, as a function of alkane solvents.

promote charge exchange, since it has one of the lowest overall sensitivities of all the solvents (Figure 10).

We have attempted to correlate the intensities of ions observed in the spectra of the PAH solutions in the hydrocarbons with the background ions from the solvents and also with a broad range of solvent properties, including IE, PA, surface tension, viscosity, and energy to vaporize a constant volume of solvent flow. Furthermore, although the solvents were distilled before use, the work described above shows how minor impurities can affect the intensity of the ions observed. No obvious correlations between variables in this study became apparent, which suggests that the ionization processes in the APCI source are complex and involve many variables.

Conclusions

These experiments have provided some insight into the processes occurring in the Micromass Quattro APCI source under conditions approximating those often found in HPLC and direct liquid injection analyses. It appears that the spectra produced may be highly dependent on the construction of a given ion source. The APCI source used by Horning's group consisted of a single heated gas flow together with a heated liquid stream which passed through a corona discharge directly next to the sampling aperture [13]. The Sciex TAGA 6000 APCI source used in Kebarle's laboratory sampled an air stream which passed through a corona discharge, the distance of which to the sampling orifice could be varied. An inner ion source cavity had pure nitrogen as a bath gas flowing through it in a direction counter to the movement of ions towards the mass analyzer [15]. The Quattro source uses three concentric heated gas streams in line with the heated liquid stream and the movement of ions. An important difference between this source and those of earlier workers [13, 15] is that the "atmospheric pressure" part of this source is sealed and is at a slight positive pressure, with the excess gas escaping from an exhaust tube. Thus, the gaseous environment of the source is fully dependent on both the solvents used and on the gases admitted into the source through the three gas flows. It is not open to the atmosphere in the same way as some other sources.

With a distance of over 25 mm between the corona needle and the sampling cone in the Quattro APCI source, which includes passing through the "pepper pot" counter electrode, ions at atmospheric pressure can undergo many collisions. The residence time in an Extrel APCI source is $\sim 10^{-4}$ s [35], much longer than in a typical CI source [2]. Kebarle and coworkers [15] were able to vary the distance between the corona needle and the sampling cone over a range of 5–25 mm. At a distance of 15 mm, they estimated the residence time of a typical cluster ion to be of the same magnitude, $\sim 10^{-4}$ s [15]. The residence time in the Micromass Quattro source, based on the volume between the corona needle

and the first skimmer cone and the gas flow rates, is ~0.03 s. Horning's source allowed for movement of the corona needle only between 0.5 and 4 mm from the sampling aperture, thus producing ions with much less time to equilibrate [13]. The ions observed depended on the corona needle distance. Another difference that might affect the ions observed is that in some instruments the corona needle current is controlled whereas in others the voltage is controlled, which may lead to differences in the corona discharge. In the Quattro APCI source the voltage is controlled and there is no provision for measuring the current flowing through the corona needle.

The rate constants for electron transfer between energetic radical cations and PAH molecules should be high. Some fraction of the PAH molecules could also be ionized directly as they pass through the corona discharge, producing relative yields of PAH molecular ions that are reasonably independent of solvents. Likewise, proton transfer between Brønsted acids with an adequately low PA to a typical PAH should be fast [2]. A problem may occur when the value of ΔPA between the species is low, in which case proton transfer may be so slow as to lead to few protonated molecules. This must be largely a function of solvent, especially for species such as proton-bound dimers of water or acetonitrile. Examination of the data in Figures 10 and 11 bears this out for hydrocarbon solvents (but not necessarily for other types of solvents), namely that it is the much increased level of protonation, in for example isooctane, that accounts for most of the changes in signals of the PAHs. In general when comparing different hydrocarbon solvents, the degree of protonation is far more variable than the level of charge exchange.

Many molecules are ionized preferentially by proton transfer in the APCI ion source, mechanisms for proton transfer in nitrogen or air (eqs 1–6) being well established. However, ionization to produce molecular ions, in addition to or in place of proton transfer, can also occur. It can occur by direct ionization in the corona discharge, by charge exchange with other radical ions, or conceivably by interactions with metastable species. We have found evidence for the importance of radical cation formation in the case of acetonitrile; this type of ionization also applies to naphthalene in most of the solvents studied. Enhancing charge exchange, e.g., by adding air to one of the nitrogen gas streams, may prove to be useful in developing analytical methods for weakly basic compounds using APCI-MS. The previously well-documented mechanisms invoked the hydronium ion as the primary reactive species for the APCI source [2, 3]. We have observed little evidence for significant concentrations of hydronium ions under the conditions which we have studied, but rather have observed various species which are weaker Brønsted acids than the hydronium ion, indeed hydronium ions may be unimportant for protonation reactions under these conditions. We also noted that the introduction of

any significant concentration of water into the Quattro APCI source reduced the total ion count.

Overall, it appears that spectra from the Quattro APCI source reflect equilibrium conditions with ions having time for many collisions. The protonated ions appearing in a spectrum are those having the lowest energy, having been formed from species with higher proton affinities. Typically, these appear to be from impurities in the gas or liquid streams, but total removal of which would most likely be very difficult and hence impractical for normal operations. Charge transfer between species is governed by the initially formed ions being able to collide with species having lower ionization energies, which is a complex function of both the solvent and the source gases. In general, the number and types of ions produced in an APCI source depend on many variables and may bear no obvious relation to the background ions produced by the solvent or source gases used.

In a more practical vein, this study indicates that the use of more "exotic" and dangerous gases such as methane or carbon monoxide offers no advantage over the more commonly available gases, nitrogen, air and carbon dioxide. Care should be exercised in the use of gases produced in-house unless these are rigorously purified (although an oxygen impurity in a nitrogen supply may be beneficial). Obviously, air should not be used with highly flammable solvents. Finally, for the analysis of PAHs and similar compounds by APCI-MS in a hydrocarbon solvent, there appear to be large differences in sensitivity between solvents which should behave similarly with regard to chromatography. Isooctane and *n*-hexane provided the best overall sensitivity for the sum of protonated molecules and molecular ions of the compounds studied; pentane and cyclohexane should be avoided.

Acknowledgments

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