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ScienceDirect
International Journal of Mass Spectrometry 259 (2007) 57–64
International Journal of Mass Spectrometry
www.elsevier.com/locate/ijms

GC/MS on an LC/MS instrument using atmospheric pressure photoionization

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Received 9 June 2006; received in revised form 7 July 2006; accepted 10 July 2006
Available online 23 August 2006

Abstract

Atmospheric pressure (AP) GC/MS was first introduced by Horning et al. [E.C. Horning, M.G. Horning, D.I. Carroll, I. Dzidic, R.N. Stillwell, Anal. Chem. 45 (1973) 936] using ^{63}Ni as a beta-emitter for ionization. Because, at the time special instrumentation was required, the technique was only applied with consistency to negative ion environmental studies where high sensitivity was required [T. Kinouchi, A.T.L. Miranda, L.G. Rushing, F.A. Beland, W.A. Korfmacher, J. High Resolut. Chromatogr., Chromatogr. Commun. 13 (1990) 281]. Currently, AP ion sources are commonly available on LC/MS instruments and recently a method was reported for converting an AP-LC/MS ion source to a combination AP-LC/MS:GC/MS source [C.N. McEwen, R.G. McKay, J. Am. Soc. Mass Spectrom. 16 (2005) 1730]. Here, we report the use of atmospheric pressure photoionization (APPI) with GC/MS and compare this to AP chemical ionization (APCI) GC/MS and electron ionization (EI) GC/MS. Using a nitrogen purge gas, we observe excellent chromatographic resolution and abundant molecular $M^{+\bullet}$ and MH^+ ions as well as structurally significant fragment ions. Comparison of a 9.8 eV UV lamp with a 10.6 eV lamp, as expected, shows that the higher energy lamp gives more universal ionization and more fragment ions than the lower energy lamp. While there are clear differences in the fragment ions observed by APPI-MS versus EI-MS, there are also similarities. As might be expected from the ionization mechanism, APPI ionization is similar to low energy EI. These odd electron fragment ions are useful in identifying unknown compounds by comparison to mass spectra in computer libraries.

Keywords: Photoionization; Atmospheric pressure ionization; Gas chromatograhy; Liquid chromatography; Mass spectrometry

1. Introduction

On joining Professor Hunt's laboratory, I had the opportunity to work with a new high-resolution mass spectrometer (AEI MS-9) that was equipped with one of the first commercial chemical ionization (CI) sources. Anytime a new ionization method is introduced into mass spectrometer it becomes an exciting time for research because the utility is largely unexplored. So it was in the days of CI when we were trying various reagent gases in an effort to improve analysis methods for specific kinds of compounds. One such reagent gas was nitric oxide [4]. Unfortunately, my instrument shift was after the nitric oxide experiments and invariably the filament would burn out. In those days, changing a filament was an ordeal that required making gold seals and hoping you had done an adequate job so that the instrument would actually achieve vacuum. It would be hours before any experiments could be done. Out of necessity, I built a discharge tube into a CI ion source that enabled CI without use of a filament. Unlike a heated filament, the discharge tube was robust to oxidizing gases [5]. The discharge worked well with the chemical ionization source but was unnecessary for most reagent gases and never received much attention. At about the same time, Professor Horning's group reported on a new atmospheric pressure ion source that used ^{63}Ni beta emission to produce ions [1]. Unlike the CI case, discharge ionization when introduced to APCI was a considerable improvement, but even though Horning's group interfaced APCI MS to both GC and LC the technique was only rarely used because it required instrumentation that was not commercially available [6–8]. It was not until the introduction of electrospray ionization (ESI) that liquid introduction APCI and thus LC/MS flourished [9].

Liquid introduction APCI MS was necessary because ESI was not sensitive with low polarity compounds and even fails to ionize certain compound classes. APCI extended the range

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doi:10.1016/j.ijms.2006.07.004

of low polarity/low-mass compounds that were amenable to LC/MS analysis but compound types still exist that are either insensitive or do not ionize with this liquid introduction method. Thus, photoionization (PI) was introduced to extend the range of compounds which can be ionized in LC/MS [10,11]. APCI as an LC/MS ionization method is limited in the compounds that can be analyzed because of the solvent load in the ion source which, due to a series of ion–molecule reactions, form protonated solvent clusters (e.g., $(H_2O)_nH^+$). Thus, only compounds more basic than the solvent clusters are ionized in liquid introduction APCI. Photoionization in the absence of dopants, ionizes the analyte directly by absorbing a photon and releasing an electron. Because of the low energy relative to the ionization (IP) of the analyte, the radical cation thus formed is fairly stable, but in the presence of a high concentration of solvent will charge exchange with compounds which have lower IP or abstract a hydrogen atom from solvent and impurity molecules to form the MH^+ ion. The MH^+ ion will survive only if it does not undergo collisions with more basic solvent molecules or impurities to which it can transfer the proton and become neutral. The other problem with PI as an ionization method for LC/MS is that solvent reduces sensitivity [12,13]. For this reason dopants, such as toluene are commonly used to enhance PI sensitivity in LC/MS applications [14].

The original APCI GC/MS introduced by Horning et al., only found its niche in the negative ion mode where sensitivity was an important factor [2,15,16]. The likely reason that APCI GC/MS only found limited application was that GC/MS with electron ionization (EI) and CI were already commercially available techniques and an atmospheric pressure ion source required special pumping and a custom instrument. Times change and now because of the success of LC/MS, API-MS instruments are commonly available and many of these instruments have MS^n and/or high mass resolution and accurate mass measurement, capabilities that are not as common with GC/MS instruments. In a recent publication, we re-introduced APCI GC/MS but on instruments built for LC/MS [3]. Therefore, it is now possible to obtain LC/MS and GC/MS spectra on the same instrument. Ionization can be either positive or negative and all of the features available with the instrument, such as MS/MS and accurate mass measurement can be used with either separation method.

APCI ionization of a GC effluent is more inclusive than LC/MS of the same volatile components because of the absence of solvent [3]. Nevertheless, residual water vapor and contaminants still reduce the compound types that are observable if ionization is done in air. This can be partially circumvented by sweeping the source with a clean dry purge gas (e.g., N_2 from a liquid source). Under these conditions, most compounds that fail by ESI analysis can be successfully run by APCI GC/MS with improved chromatographic resolution and ionization sensitivity relative to either APCI or APPI LC/MS. In addition, a GC can now be interfaced to any LC/MS instrument so that GC/MS quantitation can be achieved using reaction ion monitoring on an MS/MS instrument or accurate mass measurement can be obtained by interfacing the GC to a high resolution instrument. However, there are disadvantages in using APCI GC/MS, such as the inability to use library search routines to identify unknown compounds and the inability to ionize certain classes of compounds. It would also be valuable to have available an API ionization method that is inclusive of all compounds that elute from a GC.

Gas chromatography (GC) has used photoionization (PPD) detectors for years and it would seem natural to interface such a detector to atmospheric pressure mass spectrometry. Revelski et al. did just that by building an APPI source for a Finnigan model 4021 mass spectrometer [17]. In this work, fragmentation was not observed and the method was shown to be useful in the analysis of a wide array of compound types including alkanes, alcohols, esters and amines. We demonstrate that a commercial photoionization source built for LC/MS applications can be interfaced to a GC with only modest modifications. Thus, in this work, we come full circle from the early days in Dr. Hunt's laboratory and explore the application of photoionization for atmospheric pressure GC/MS on an LC/MS instrument.

2. Experimental

All AP mass spectra were obtained on a Waters Corporation (Beverly, MA) Micromass Qtof I mass spectrometer modified as previously described for API GC/MS operation [3]. APPI GC/MS was achieved by replacing the APCI discharge needle and 'fishbowl' cover with the Syagen Photomate® (Syagen Technology, Tustin, CA) photoionization cover and lamp used in LC/MS operation. The Syagen 10/10.6 eV UV lamp was replaced with a 9.8 eV lamp for some studies. A Hewlett Packard 6890 series GC (Agilent Corporation, Wilmington, DE) with autosampler was interfaced to the PI source with a heated transfer line as previously described [3]. Samples were separated using a 30 m J & W Scientific (Folsom, CA) DB-5 HS column held at 60 °C for 1 min, then programmed at 15 °C/min to 250 °C and held for 5 min. The helium flow rate was set at 1.5 cm^3/min and the injector temperature was 250 °C. The heated transfer line was maintained at 290 °C. The electron ionization GC/MS results were obtained on an Agilent 5975 XL Mass Selective Detector with a 30 m Restek (Bellefonte, PA) RTX-1 column.

All chemicals reported in Table 1 were obtained through VWR International (Weat Chester, PA) and used without further purification. The perfume sample is of unknown origin and was diluted with methylene chloride before injection into the GC. The EPA 8270 MegaMix™ sample was obtained from Restek Corporation and was diluted with methylene chloride to ca. 50 ppm/component before analysis.

Table 1
Compounds present in Fig. 2

(1) 2-Hydroxyacetophenone	(*m*/*z* 136)
(2) 3-Nitrobenzyl alcohol	(*m*/*z* 153)
(3) Octanoic acid	(*m*/*z* 144)
(4) 2-Isobutylthiazole	(*m*/*z* 141)
(5) 6-Undecanone	(*m*/*z* 170)
(6) *n*-Butrophenone	(*m*/*z* 148)
(7) 2-Nitrophenyl octyl ether	(*m*/*z* 251)

3. Discussion and results

In an APCI GC/MS source using a nitrogen purge gas, the primary ionization event is loss of an electron from N_2 to form a radical cation [3]. This $N_2^{+\bullet}$ radical cation in a nitrogen atmosphere forms $N_4^{+\bullet}$, which in turn reacts with trace levels of water to form through ion-molecule reactions H_3O^+ ions. Because of the high frequency of collisions at atmospheric pressure, H_3O^+ will react further with trace water or impurities to form either protonated water clusters or protonated impurity molecules. Only under very dry and clean ion source conditions is it possible in APCI to obtain molecular radical cations by charge exchange with $N_2^{+\bullet}$ or $N_4^{+\bullet}$. It is also these dry and clean conditions that reduce formation of protonated water clusters so that ionization of analyte is through reaction with the more acidic H_3O^+. Under these conditions, APCI ionizes a wider array of volatile and semivolatile compound types than APCI LC/MS. On the other hand, photons in photoionization sources have too low an energy to ionize either nitrogen gas (IP = 15.6 eV) or water vapor (IP = 13.2) but are absorbed by volatile organic compounds with loss of an electron and thus direct formation of a radical cation. The odd-electron radical cation that is produced is of low energy and some survive to be detected. Collision of the odd-electron ion with water vapor, impurities or with neutral analyte can result in abstraction of a hydrogen atom to form an MH^+ ion. If sufficient energy is available, the radical cation can fragment in an analogous manner to low-energy electron ionization.

In APPI GC/MS photons interacting directly with gaseous analyte produces an ionization event only if the photon energy is above the ionization potential of the analyte molecules. Therefore, photoionization is a selective process depending on the photon energy. Photoionization lamps are available with energies of 8.3–11.7 eV. The lowest energy lamp will be most selective and the 11.7 eV lamp will be more universal and produce the most fragment ions. Typically in mass spectrometry applications, 9.8–10.6 eV lamps are used and ionize most efficiently those compounds with the lowest ionization potential (IP). For hydrocarbon based structures, electron-donating groups lower the IP and electron withdrawing groups increase the IP as is illustrated by toluene (IP = 8.83), benzene (IP = 9.25) and nitrobenzene (IP = 9.94). Compounds containing hetroatoms, such as organosulfur or organophosphorus will generally have IPs low enough to be ionized. The ionization efficiency for VOCs using PI is generally in the order aromatics and iodine compounds > olefins, ketones, ethers, amines and sulfur compounds > esters, aldehydes, alcohols and aliphatics. Thus, one would expect that highly unsaturated compounds would be highly sensitive by photoionization but not necessarily by APCI. On the other hand, aliphatic compounds with functional groups capable of protonation by H_3O^+, such as saturated esters, acids, aldehydes or alcohols would be expected to be less sensitive with low eV lamps than with APCI discharge ionization.

In order to look at the differences in API GC/MS with discharge ionization versus photoionization, mixtures of selected compounds as well as a perfume sample and Restek's EPA 8270 Megamix™ were run by both techniques and compared. To determine that comparisons are valid, a reproducibility study was undertaken using a Restek EPA 8270 Megamix™ sample diluted in acetonitrile and injected using a GC auto-sampler. The results from two of a series of chromatograms run consecutively are shown in Fig. 1 for APPI GC/MS and demonstrate good reproducibility. Comparable results were obtained for APCI GC/MS (results not shown). Fluctuations in peak abundances were noted because the GC peak widths for many compounds were narrow (<1.5 s at half height) relative to the available spectral acquisition rate (2 acquisitions/s). These fluctuations were generally smaller than the ionization differences of interest in this study.

A most important difference was observed between APCI and APPI ionization for GC analysis. Whereas, APCI after a

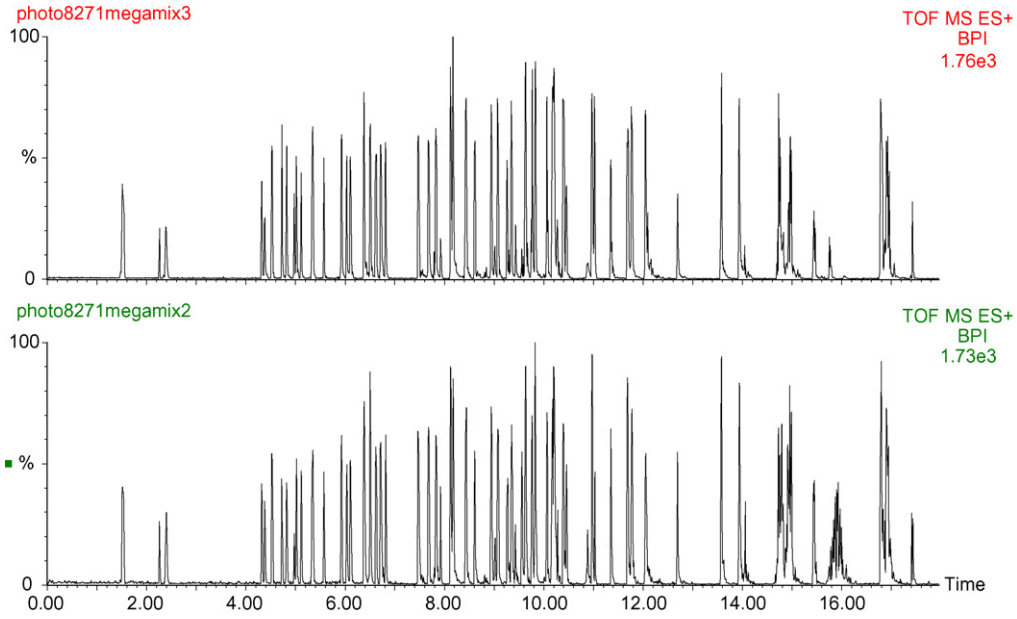

Fig. 1. Consecutive base peak mass chromatograms from a reproducibility study using Restek's EPA 8270 Megamix™ by 10/10.6 eV APPI GC/MS.

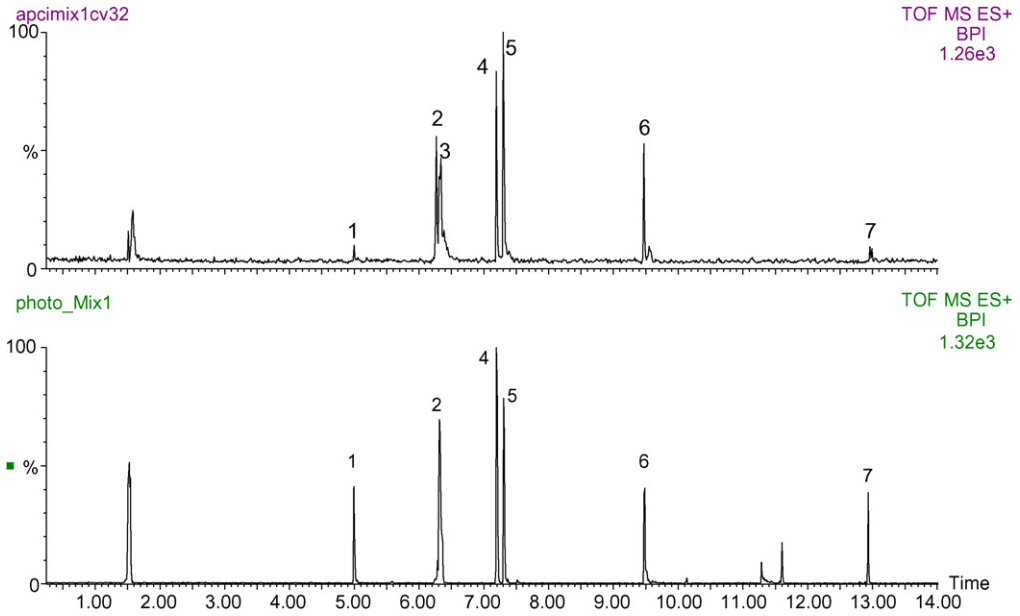

Fig. 2. Base peak mass chromatograms of a comparison of APCI (top) to APPI 10/10.6 eV (bottom) for the ionization of a seven compound mixture: (1) 2-isobutylthiazole, (2) 2-hydroxyacetophenone, (3) octanoic acid, (4) *n*-butyrophenone, (5) 6-undecanone, (6) 3-nitrobenzyl alcohol, (7) 2-nitrophenyl octyl ether.

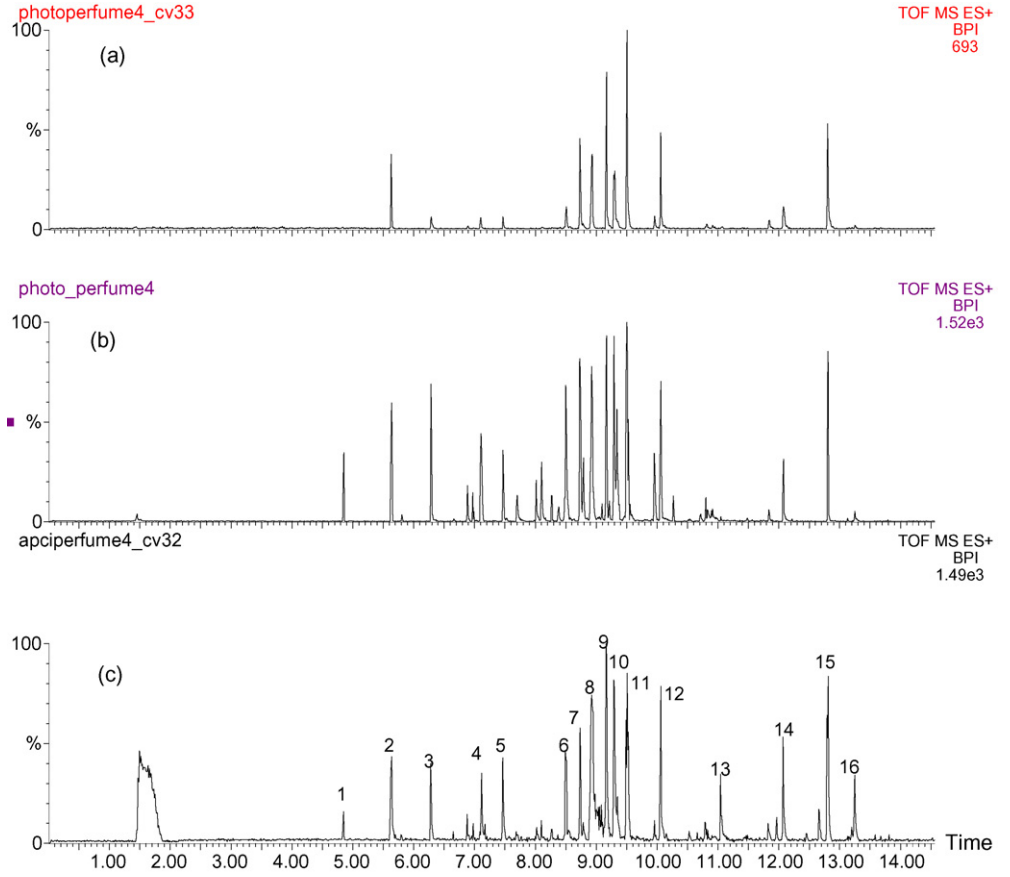

Fig. 3. Base peak mass chromatogram of a perfume analysis by: (a) 9.8 eV APPI-GC/MS, (b) 10/10.6 eV APPI GC/MS and (c) APCI GC/MS: (1) rose oil, (2) linalool, (3) $C_{14}H_{12}$, (4) geraniol, (5) dimethyl-2,6-octadien-1-ol, (6) vanillin, (7) ionone, (8) coumarin, (9) cetone, (10) dimethoxypropenylbenene, (11) isomethylionine, (12) diethylphthalate, (13) methyltetradecanoic acid, (14) methylpentadecanone, (15) musk ketone, (16) civetone.

changeover from LC/MS operation required overnight to reduce background to an acceptable level, APPI had sufficiently low background ions for immediate operation. Even after extensive use, there remains a background in the APCI ionization mode that can obscure trace components if background subtraction is not employed. Therefore, APPI has the distinct advantage that even small peaks can be observed in the total ion current or base peak chromatograms without need of background subtraction. Rapid turnaround between LC/MS operation and API GC/MS operation is significantly improved with photoionization. This is an interesting outcome because APPI appears to be a more universal ionization method than APCI but produces less background. It is possible that the discharge desorbs surface species that remain on the ion source surfaces during photoionization.

A synthetic mixture made of the compounds shown in Table 1 was run by APCI and APPI GC/MS using the same concentration sample and identical conditions except for the mode of ionization. As can be seen in Fig. 2, except for octanoic acid (3), all of the compounds provided a better signal to noise using PI with the dual 10/10.6 eV lamp. 2-Isobutylthiazole (1) and 2-nitrophenyl octyl ether (7) were significantly more sensitive by PI. On the other hand, using the 9.8 eV lamp, nitrobenzyl alcohol (2), which has an ionization potential of 9.94 eV was not observed and isobutylthiazole (4) as well as nitrophenyl octyl ether were of much lower intensity. As expected, the lower energy PI lamp is more selective but also produces little fragmentation suggesting that a dual lamp source using 10.6 and 9.8 eV PI lamps could be a useful feature.

A perfume sample offers a more complex mixture to judge the differences between APCI and APPI GC/MS (Fig. 3). The APCI chromatogram (Fig. 3c) shows an increased background level relative to the PI chromatograms as noted above. This sample was also run by EI GC/MS to produce a total ion chromatogram that was similar to the API results. Accurate mass from the APCI GC/MS data and a NIST library search of the EI GC/MS data were used to identify most components in the perfume. Interestingly, the sensitivity of the three techniques as determined by the signal to noise ratio for equal sample amounts injected with equivalent split ratios was similar for the best ionized compounds. Fig. 3a shows the APPI GC/MS results using the 9.8 eV lamp. Clearly, for some compounds in this mixture PI is less sensitive than APCI (Fig. 3c). Methyltetradecanoic acid and civetone cannot be identified in the PI mass spectrum as was the case for phenylethyl alcohol. Geraniol and dimethyl-2,6-octadien-1-ol are alcohols with two un-conjugated double bonds and both are observed by PI (9.8 eV) but with lower sensitivity

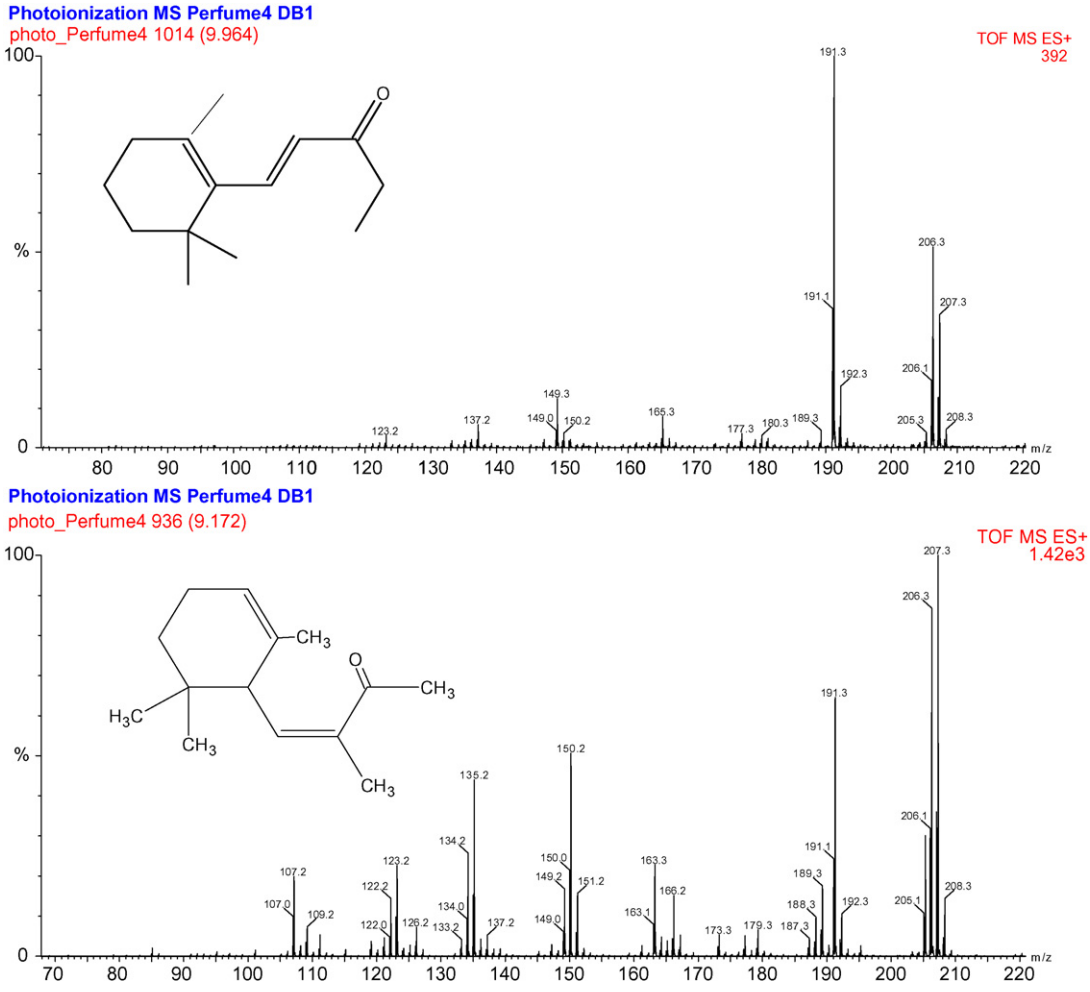

Fig. 4. Mass spectra of isomers of methyl-ionone using 10/10.6 eV APPI.

than APCI. Linalool, a very similar structure has excellent sensitivity by PI. Compounds, such as vanillin and ionone, which have conjugated ketone functionality as well as coumarin with a conjugated ester group ionize with good sensitivity by PI. Clearly, small structural differences can make significant relative differences between APCI and 9.8 eV PI ionization. On the other hand, the 10/10.6 eV PI lamp gave nearly universal ionization for this sample (Fig. 3b).

In contrast to the results reported by Revelsky et al., APPI (10/10.6 eV) under the conditions used here produces significant fragmentation for the compounds in this mixture. For example, methyl ionone produces an APPI mass spectra (Fig. 4) similar in many respects to the 70 eV electron ionization mass spectrum (Fig. 5) but very different from the APCI spectrum (not shown). Note that because of significant MH^+ ion formation, the isotope ratios for the $M^{+\bullet}$ ions in APPI will be unreliable. The fragment ions produced by 10/10.6 eV PI are the energetically more favorable high-mass fragments that have more structural significance than the low-mass fragmentation that often dominates 70 eV electron ionization spectra. Because in APPI-MS, the molecular weight can be known unambiguously (abundant $M^{+\bullet}/MH^+$), it is possible to reduce a computer assisted library search can be reduced to only those compounds in the library having the correct molecular weight. With high performance mass spectrometers, accurate mass measurement can be used to further reduce the library to those compounds having the correct elemental compositions. Searching this reduced library for compounds with the most matching fragment ions to those observed in the APPI mass spectra, regardless of ion abundance, provides, at worst, a list of closely related compounds. A search of the ionone mass spectrum by molecular weight or by elemental composition and then by the PI fragment ions, produces closely related structures. At least for the compound types in this mixture, 10.6 eV PI provides fragment ions that can be used to search commercial electron ionization libraries and thus aid in compound identification.

The third sample is Restek's EPA 8270 megamix (Fig. 1), which is composed primarily of aromatic compounds. As can be seen in the inset of Fig. 6b, dichlorophenol gives excellent mass spectra by APPI, even using the 9.8 eV lamp, but is not observed by APCI at the concentration used in this study. Chloronapthalene, trichlorobenzene, hexachlorobu-

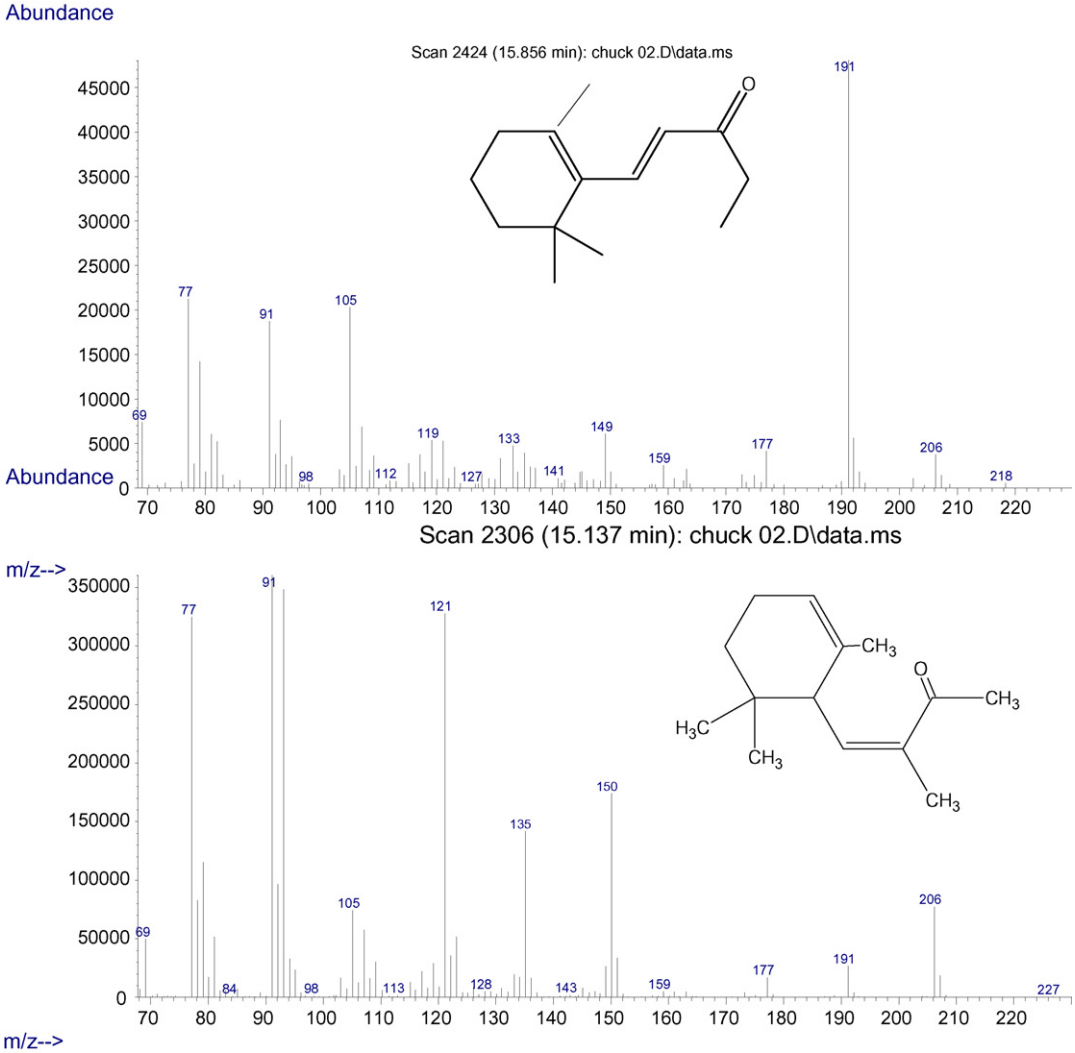

Fig. 5. Mass spectra of isomers of methyl-ionone using electron ionization.

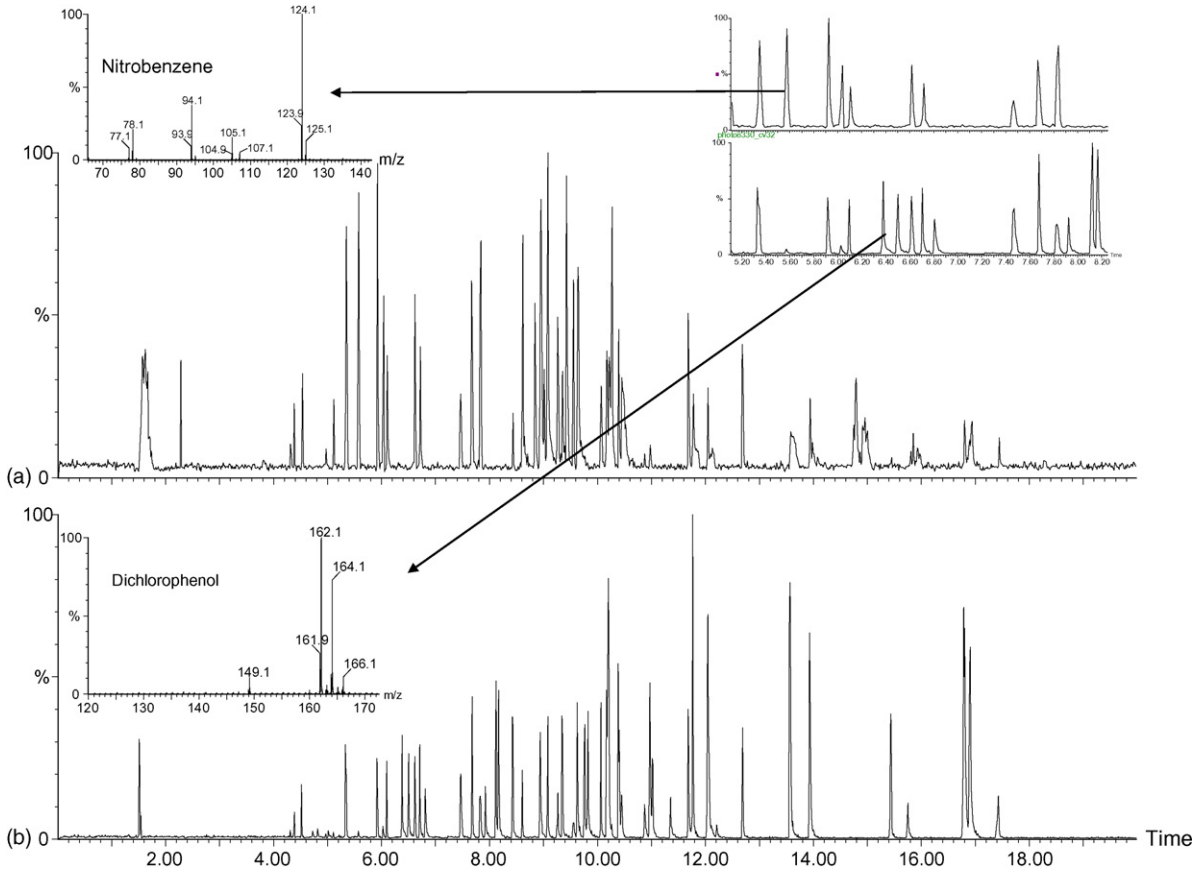

Fig. 6. Base peak mass chromatogram of a GC separation of Restek's EPA 8270 Megamix™ with (top) APCI ionization and (bottom) APPI (9.8 eV) ionization. *Insets*: Top right shows expanded region of APCI (top) and APPI (bottom) of base peak mass chromatogram. Top left shows mass spectrum of nitrobenzene obtained by APCI and bottom left shows mass spectrum of dichlorophenol obtained by APPI.

tadiene, trichlorophenol, tetrachlorophenol, pentachlorophenol, hexachloropentadiene bromodiphenyl ether and hexachlorobenzene are other compounds readily observed in APPI MS but not present in the APCI GC/MS base peak chromatogram for this sample. As seen in the inset of Fig. 6a, nitrobenzene (IP = 9.94 eV) is not observed in the 9.8 eV APPI chromatogram, but is easily observed with APCI. All components observed by EI GC/MS of this mixture were also observed by positive ion 10/10.6 eV APPI GC/MS.

4. Conclusion

API GC/MS using an LC/MS API ion source has been reported using APCI ionization [3]. Here, we show that atmospheric pressure photoionization (APPI) has significant advantages as an ionization source for gas chromatography. The initial ionization event is production of an odd-electron radical cation as in electron ionization. As has been reported previously [17], sufficient odd-electron molecular ions survive to be readily detected. In addition, hydrogen atom abstraction by the molecular radical cation during the frequent collisions at atmospheric pressure produces protonated molecular ions (MH^+). We show here that low energy PI (9.8 eV) can be used as a more selective ionization method and one in which abundant $M^{+\bullet}$ and MH^+ are produced. Higher energy PI (10.6 eV) is an almost universal ionization method that also produces abundant $M^{+\bullet}/MH^+$ ions for the compounds reported here, and for many of the compounds studied, also produced structurally important fragment ions. The fragment ions produced in PI primarily result from prompt decomposition of the molecular radical cation to produce a subset of the fragment ions observed in 70 eV electron ionization. Fragment ions arising from MH^+ decomposition are also observed. The combination of an easily recognized molecular ion and fragment ions that appear in mass spectral libraries, provides an opportunity to use electron ionization library search routines for compound identification or confirmation. Additionally, many LC/MS instruments have accurate mass capabilities so that a further restriction that can be applied to a library search is the elemental formula. The use of photoionization for atmospheric pressure GC/MS appears to provide a middle ground between the advantages of chemical ionization and those of electron ionization. For the compound types in this study, the sensitivity appears similar to EI GC/MS, but further work is required to determine the limits of detection of this method and its value as a quantitative tool.

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