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EVALUATION OF ION TRAP MASS SPECTROMETRY FOR  
THE DETERMINATION OF AMBIENT NICOTINE\*

Marcus B. Wise, Cecil E. Higgins,  
Ralph H. Ilgner, and Michael R. Guerin  
Organic Chemistry Section  
Analytical Chemistry Division  
Oak Ridge National Laboratory  
P.O. Box 2008, MS-120  
Oak Ridge, TN 37831-6120

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A thermal desorption unit has been interfaced directly with a Finnigan Ion Trap mass spectrometer (ITMS) for the identification and quantification of trace organics in air. No chromatographic separation of the desorbed constituents is performed prior to introduction into the mass spectrometer. Instead, positive identification of a compound is made based on its collision induced dissociation (CID) tandem (MS/MS) mass spectrum. Using this technique, as little as 50 pg of a constituent desorbed from a resin trap can be characterized and quantified with a sample turnaround time of only 2-3 minutes.

This technology has recently been evaluated for the determination of ambient nicotine. Equilibrium concentrations of nicotine ranging from approximately 1  $\mu\text{g}/\text{m}^3$  to 300  $\mu\text{g}/\text{m}^3$  in air were generated by the controlled smoking of 1R4F filtered Kentucky Reference Cigarettes in a laboratory equipped for the study of environmental tobacco smoke (ETS). Samples were collected on resin traps 3 in. long x 0.25 in. diam containing a 1 in bed of Tenax. For comparison, simultaneous samples were collected on glass fiber filters treated with 4%  $\text{NaHSO}_4$  for analysis by gas chromatography. Sampling flow rates through the Tenax traps ranged from 30-50 ml/min and sampling times varied from 1-20 min. Analyses were performed by flash heating the Tenax traps at 450 watts for 10 seconds while purging with helium at a flow of 20 ml/min. The effluent was admitted directly into the ITMS through an open-split interface with a split ratio of approximately 100:1. Isobutane chemical ionization was used to generate protonated nicotine at 163 daltons which was subsequently fragmented by CID to generate characteristic MS/MS ions at 84, 106, 120, and 132 daltons. Quantification was performed by summing the integrated ion intensities for these ions and comparing the response with a standard working curve generated using authentic nicotine. The linear range of the working curve was from 300 pg-50 ng of desorbed nicotine and the correlation coefficient for the working curve was 0.9996. Total analysis time was less than 10 min per sample including calculations and the results of the ITMS method compared favorably with the treated filter GC method.

### Introduction

Because nicotine is a tobacco specific compound and is present in large quantities in tobacco smoke, it is commonly used as a marker for assessing human exposure to environmental tobacco smoke (ETS). As a result, a number of methods have been developed for the sampling and quantification of ambient nicotine. Analytical methodology typically involves either thermal desorption or solvent elution of trapped nicotine from resin tubes or glass fiber filters followed by gas chromatography (GC)

with a nitrogen specific detector (1,2). We report the use of direct thermal desorption combined with ion trap mass spectrometry (ITMS) for the rapid determination of ambient nicotine.

Although quadrupole ion traps have existed for many years, the technology has only recently advanced to a point at which they are practical for use as routine mass spectrometers (3). Several important features of ion traps include the ability to perform selective chemical ionization, selective ion ejection or ion storage, daughter ion tandem mass spectrometry (MS/MS), and positive or negative ion detection. As a result of the ability to generate, store, and detect ions in the same region of space, the detection limits which can be achieved with ion traps are typically better than those of quadrupole or sector mass spectrometers. Further, the ion storage capability enables full scan daughter ion MS/MS spectra to be generated with very high efficiency. By combining selective chemical ionization with tandem mass spectrometry, a high degree of compound specificity can be achieved, even when working with complex mixtures such as ETS. This enables targeted compounds in a mixture to be rapidly determined without the use of prior chromatographic separation or significant sample preparation.

The use of resin beads, such as Tenax, for trapping and concentrating airborne constituents is well established and is commonly employed for air sampling purposes. The adsorbed components are typically eluted from the trap by heating the resin bed while simultaneously purging with an inert gas such as helium. This process is typically performed in conjunction with some type of sample focusing and then followed by analysis using gas chromatography or combined gas chromatography/mass spectrometry (GC/MS). As an alternative, we have recently developed instrumentation and experimental methods for the determination of trace organics in air using direct thermal desorption ITMS, thus eliminating the need for sample focusing and gas chromatography. Full scan daughter ion MS/MS spectra have been generated on as little as 50 pg of a desorbed compound in the presence of numerous other constituents. Application of this technology to the determination of ambient nicotine appears to show tremendous promise as a rapid and reliable analytical tool. Because of the excellent detection limits that can be achieved with thermal desorption ITMS, sampling volumes and times can be significantly reduced making it possible to acquire larger numbers of samples in field studies.

### Experimental Methods

Ion trap experiments were performed with a Finnigan MAT ion trap mass spectrometer equipped with two 360 l/sec turbomolecular pumps, an electro-polished vacuum chamber, a capillary restrictor open-split interface, and batch inlets for chemical ionization reagent gas and calibration compounds. In addition, this instrument has hardware for selective mass storage, positive or negative ion detection, and an auxiliary frequency synthesizer for MS/MS parent ion dissociation. The instrument is controlled by an IBM PC-AT computer using software supplied by the manufacturer.

The thermal desorption apparatus used for these experiments was designed and constructed by the authors specifically for use with the ITMS and is shown schematically in Figure 1. This system uses resin traps 3 in. long x 0.25 in. diam packed with a 1 in. bed of Tenax. A septum is mounted in the cap of the desorber body to enable direct injection of standards into the ITMS.

Atmospheres of ETS were generated in a 52 m<sup>3</sup> laboratory at Oak Ridge National Laboratory which has been modified and equipped for this purpose. Exhaust fans provide air circulation and an air exchange rate of approximately 2.4 changes per hour. Instruments in this laboratory enable monitoring of CO and CO<sub>2</sub> levels, nitrogen oxide levels, and respirable suspended particulate matter (RSP) concentrations. Simulated ETS (dilute sidestream smoke) was generated in our laboratory by the controlled smoking of 1R4F filtered Kentucky reference cigarettes using an ADL-II smoking machine. The mainstream particulate matter was trapped on a Cambridge filter pad and the mainstream gas phase smoke was collected in a Tedlar bag. The cigarettes were smoked using standard FTC conditions and only sidestream smoke only was allowed to escape into the air during puffing. The concentration of ETS was controlled by varying the number of minutes between puffs. For the generation of high levels of ETS, a single cigarette was also allowed to continuously smolder in

the ETS laboratory in addition to the cigarette smoked using the ADL-II. Samples were collected only after the atmosphere had equilibrated as indicated by the concentration of RSP.

Three replicate samples of ETS were collected using Tenax traps for the ITMS study and simultaneously using 37 mm diam Pallflex teflon coated glass fiber filters treated with 4% NaHSO<sub>4</sub> for comparative analysis by a standard GC method (1). Sampling rates for the Tenax traps varied from approximately 50-75 ml/min using low volume sampling pumps and rates for the Pallflex filters varied from approximately 8-25 l/min using high volume sampling pumps. Total sample volumes varied from 0.05-8 l for the Tenax traps and 8-70 l for the treated filters. The total sampling time was the same for both the Tenax traps and the filters in order to minimize effects resulting from changes in the ETS atmosphere with time. After completion of the sample collection, the Tenax traps were stored in 40 ml screw top glass vials and sealed with teflon lined caps until analysis. The treated filters were folded and stored in 1 dram vials which were also sealed with teflon.

The Tenax traps were analyzed by direct thermal desorption into the ITMS. Experimental conditions for the desorption included a heating time of 10 seconds, 450 watts of heater power, and a helium purge flow of approximately 20 ml/min. Effluent from the traps was admitted into the ITMS through the open split interface with an estimated split ratio of approximately 100:1. The maximum temperature of the Tenax traps was approximately 220°C and was reached approximately 30 seconds after the heater was turned on. In order to minimize deposition of nicotine inside the open-split interface and mass spectrometer, the interface was maintained at 200°C and the ITMS analyzer cell was maintained at 100°C.

Selectivity for nicotine was accomplished by using a combination of isobutane chemical ionization and daughter ion MS/MS. The isobutane pressure was maintained at  $5 \times 10^{-6}$  torr and the chemical ionization reaction time was 50 msec which efficiently produced protonated nicotine at a mass of 163 daltons. Collisional dissociation (using helium collision gas) of the protonated nicotine (163 ion) resulted in characteristic daughter ions at 84, 106, 120, and 132 daltons. Quantification was performed by integrating and summing the areas of the desorption profiles for each of the characteristic ions for nicotine. A typical desorption profile is shown in Figure 2 and demonstrates the selectivity that can be achieved using MS/MS (daughter ion at 84 daltons) as well as the narrow desorption profiles that can be generated with the experimental apparatus. In order to check the efficiency of the desorption process, a second heating of the Tenax traps was performed at approximately 4 min and less than 5% of the nicotine was found to remain.

A nine point standard curve was generated for nicotine by injecting 1  $\mu$ l aliquots of nicotine standards directly into the thermal desorber apparatus through the septum port and into a glass liner. The thermal desorber was then flash heated using the same conditions that were used for the Tenax traps. The concentration of the nicotine standards varied from 300 pg/ $\mu$ l - 500 ng/ $\mu$ l in methanol.

The treated Pallflex filters were analyzed by extraction of the nicotine followed by gas chromatography with nitrogen specific detection. The extraction procedure included the addition of 100  $\mu$ l and 2 ml of 5N NaOH solution to the filter pad followed by 10 min of shaking. A 500  $\mu$ l volume of ammoniated heptane containing 20 ng/ $\mu$ l of quinoline was added as an internal standard and the sample was shaken another 10 min. After phase separation, the heptane layer was analyzed for nicotine by direct (splitless) injection of 5  $\mu$ l aliquots onto a 6 ft 0.25 in. diam column packed with 10% Carbowax and 2% KOH on 80-100 mesh chromasorb WAW. The injector temperature was 200°C, detector temperature was 250°C, and the oven temperature was programmed from a starting temperature of 70°C to 190°C at a rate of 24°C/min with no initial hold and a final hold time of 5 min. Helium pressure at the inlet was 30 psi and the signal from the nitrogen specific detector was output to a Maxima chromatography workstation for data collection and manipulation. A four point standard curve was generated for 0.3-20 ng/ $\mu$ l in ammoniated heptane having the same concentration of quinoline as an internal standard. Actual concentrations of ambient nicotine were calculated by dividing the absolute quantity of nicotine determined by the volume of air sampled.

## Results

The standard working curve generated for nicotine using the thermal desorption ITMS method was found to be linear from 300 pg-50 ng of desorbed nicotine and the correlation coefficient was 0.9996 as shown in Figure 3. Significant deviation from linearity was observed at levels above 100 ng of desorbed nicotine due to overloading of the ITMS analyzer with too many ions. Relative standard deviations for replicate injections of the standard solutions varied from 2-17% and the RSD for replicate thermal desorptions of nicotine from Tenax traps varied from 14-26%. No internal standards were used for any of the ITMS measurements. The total time per sample analysis was typically less than 10 min including the time required for calculations. Actual generation of the thermal desorption profile and collection of the MS/MS spectra was less than 5 minutes per sample.

A comparison of the results for both the thermal desorption method and the treated filter GC method is shown in Table 1. The calculated ambient nicotine concentrations varied from <1 ug/m<sup>3</sup> - 360 ug/m<sup>3</sup> which encompasses the range expected to be encountered in actual ETS measurements. Good agreement was obtained between both methods except for the measurements at the highest nicotine concentration. It should be noted, however, that the concentration calculated by the ITMS method was based on 3 significantly different volumes of air sampled, giving absolute quantities of nicotine desorbed ranging from 9-40 ng. The calculated air concentration of 360 ug/m<sup>3</sup> was therefore determined using three significantly different points on the calibration curve with an RSD of less than 15% suggesting that this value may be more accurate than that generated by the treated filter method.

## Conclusion

Direct thermal desorption ITMS can be used as a rapid and specific method for the determination of ambient nicotine. Detection limits are comparable to or better than can be achieved with other standard methods and total analysis time is less than 10 min with no sample preparation or internal standards required. Because of the excellent detection limits of the method, it should be possible to sample 1 l or less of air and still maintain the sensitivity required for field measurement of ambient nicotine at levels down to 1 ug/m<sup>3</sup> or less.

In addition to the ability to monitor nicotine in ETS, the same methodology should be applicable to the measurement of other possible markers and compounds of interest in ETS. For instance, pilot studies have shown that it is possible to desorb and detect ng quantities of compounds such as 4-amino biphenyl and diethyl N-nitrosoamine using the method described above. Finally, recent studies in our laboratory have also shown that with minor modifications to the open-split interface of the ITMS, it is possible to use the ITMS in a "sniffer" mode for real time monitoring of volatile constituent in air. This could be particularly useful for the characterization of ETS atmospheres and direct determination of the concentration of ETS markers. Because of the simplicity and small size of the ITMS instrumentation, it may be possible to develop an instrument for field use in the near future.

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