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New Developments in SPME, Part 1: The Use of Vapor-Phase Deprotonation and On-Fiber Derivatization with Alkylchloroformates in the Analysis of Preparations Containing Amphetamines

ABSTRACT: Due to their high polarity and low vapor pressure, most amine salts of amphetamine-type drugs are not directly amenable to headspace recovery using solid-phase microextraction (SPME). Described in this article is a simple vapor-phase procedure for the conversion of solid drug salt samples into their free bases by the use of triethylamine. This process can be conducted simultaneously with headspace SPME, the outcome being that solid drug salts can be sampled directly for GC-MS without the need for dissolution and chemical processing. Potential applications for this methodology include the noninvasive recovery of drug traces from objects such as banknotes and garments.

This new process for recovery of amphetamine-type drugs has been combined with on-fiber derivatization using alkylchloroformates. This extra step was included to improve the chromatographic performance of analytes and allow for the resolution of drug enantiomers.

KEYWORDS: forensic science, SPME, amphetamine-type drugs, on-fiber derivatization, drug profiling, drug intelligence, chloroformates

Solid-phase microextraction (SPME) is now an important technique for a wide range of analytical applications, including forensic drug chemistry. As reported previously by us (1,2) and Koester (3), SPME combined with GC-MS is ideally suited to the gathering of intelligence, to comparison with putative source material, and to the generation of evidence as to the route of manufacture of amphetamine-type drugs. This involves generation of "impurity profiles" or "fingerprints" relating to amphetamine congeners such as manufacturing by-products and precursors.

Although the scope of SPME is extremely wide, some practical limitations to its application should be considered. For example, simple headspace SPME is not an efficient method for the recovery of amphetamines present as their salts. If low limits of detection are required, the amphetamines must first be converted into their volatile free bases. Although effective, conversion to the free base is somewhat tedious and might not always be appropriate, i.e., when the task is to screen large garments or seizures of money for the presence of drug traces.

In relation to the gas chromatographic analysis of amines in general, these substances are quite active, and as a consequence dirty split liners and chromatographic columns can have an adverse impact upon the chromatography of amines. Moreover, when amines are encountered in mixtures with other reactive compounds such as aldehydes or ketones, condensations can take place upon injection, resulting in the generation of artifacts such as imines. In relation to the examination of illicit drug preparations for the presence of manufacturing by-products and precursors, these phenomena might generate misleading chromatograms no matter what injection technique (e.g., liquid phase or SPME) is employed.

It was decided to explore techniques that might address these particular problems and thereby expand the scope of SPME as applied to forensic drug analysis.

Firstly, it was decided to explore the possibility of developing a method for deprotonation of amine salts that does not involve conventional solution-phase acid-base chemistry and has the capability for integration with SPME. The aim of this investigation was to develop a sensitive, streamlined, one-step alternative to aqueous swabbing operations for the screening of garments, apparatus, documents, and banknotes for the detection of any amphetamine drugs in their salt form as well as their "profiling" congeners.

Secondly, it was felt that SPME in combination with derivatization offers some advantages over standard methodologies for a number of reasons. Derivatization is a useful way in which active compounds such as amphetamine-type drugs can be rendered less active and prone to condensation, thereby improving their chromatography and reducing the occurrence of artifacts. Moreover, derivatization increases the molecular weight of the analyte, and, in the case of amphetamine-type drugs especially, this leads to an increase in the amount of information present in the electron impact mass spectral fragmentation pattern. Finally, derivatization offers a scope for the resolution of the optical isomers of amphetamines.

In principle, derivatization-SPME can be performed in three modes: sequential derivatization, where the analyte is mixed with

the derivatization reagent and then after an appropriate time the derivatized analyte is recovered by SPME; and two on-fiber modes whereby the analyte and the derivatization reagent are mixed within the SPME fiber. Instead of the sequential technique, it was decided to pursue on-fiber derivatization-SPME, as it was felt that this approach would consume less derivatization reagent and have more to offer in terms of recovery- and time-efficiency. On-fiber derivatization-SPME involves exposing the fiber to the analyte, then exposing it to the derivatization reagent before desorption in the usual fashion (4–7). In this way, derivatization might take place immediately on the fiber or within the injection port. According to Koster (8), it is also possible to rearrange the sequence of events so that the fiber is exposed to the derivatizing reagent before the analyte. Not only might this alternative mode of on-fiber derivatization-SPME be a more time-effective solution, it might offer better limits of detection in the case of low-molecular-weight analytes. If derivatization takes place within the fiber, and if the fiber is loaded with derivatization reagent before it is exposed to the analyte, then the situation might arise whereby the analyte becomes "trapped" on the fiber. Essentially, the equilibrium between the analyte external to the fiber and the analyte within the fiber will be perturbed towards the latter because the analyte is in its derivatized form in the fiber, and it will have a lower vapor pressure. This phenomenon was observed by Koster (8).

This article investigates the application of SPME and on-fiber derivatization using alkylchloroformates to the qualitative analysis of amphetamine-type drugs. Alkylchloroformates [1] (see Fig. 1) were chosen as derivatization reagents for this study because they appeared to offer some useful characteristics, as observed by Ugland (9). Firstly, they are quite reactive towards amines, but are relatively inactive towards water, alcohols, and other oxygen-based nucleophiles. As a consequence, alkylchloroformates offer the very practical advantage of being applicable to the derivatization of amines present in wet or moist evidentiary material. They also promise greater selectivity in the derivatization of ambient molecules such as ephedrine, which yields mixtures of single and double derivatives with derivatization reagents such as anhydrides. In addition, many different alkylchloroformates are commercially available, offering the forensic chemist some control over the molecular weight and chromatographic retention of the derivative. Finally, optically active chloroformates are also commercially available, so the possibility exists for chromatographic resolution of drug enantiomers without the need for the chiral stationary phases (10). Alkylchloroformates react with amines to yield carbamates (also known as urethanes) [2] as indicated in Fig. 1.

This article also explores the usage of triethylamine in the vapor phase as a reagent for the conversion of amphetamine-type drug salts in the solid phase into their free bases. This process generates a rich headspace of the drug.

Materials and Methods

Reagents

Ethyl chloroformate [3], n-butyl chloroformate [4], (−)-menthyl chloroformate [5], and triethylamine were purchased from Aldrich Chemical Co. Inc. (Milwaukee, WI).

Equipment

Gas Chromatography/Mass Spectrometry—GC-MS analyses were performed on a Hewlett Packard 5890A chromatograph using a ZB-1 column (30 m by 0.25 μm by 0.5-μm fused silica) with a Hewlett Packard 5971 series mass selective detector operating in the EI mode (70 eV) at a temperature of 310°C. The scanning range was 35 to 350 Da at a rate of 2.2 scans/s, and a maximum sensitivity autotune was used routinely. Helium was employed as the carrier gas at 20 psi, which corresponded to a carrier gas linear velocity of 31.3 cm/s at 100°C. The injector temperature was set at 250°C, and the splitless mode was used. Oven settings were 100°C held for 3 min, with a ramp of 40°C/min up to 280°C maintained for 2.5 min.

SPME—All fibers and SPME holders were purchased from Supelco (Bellefonte, PA). The following fiber coatings were used: 100-μm polydimethylsiloxane (PDMS), 65-μm PDMS/divinylbenzene (DVB), 85-μm polyacrylate, 75-μm carboxen/PDMS, 65-μm carbowax/DVB, 50-μm DVB/carboxen/PDMS, 30-μm DVB/carboxen/PDMS. Unless specified otherwise, all experiments described below utilized 85-μm polyacrylate-coated fibers.

On-Fiber SPME Derivatization Experiments

On-Fiber SPME Derivatization of Drugs in Aqueous Media—SPME of analytes and their derivatization were conveniently performed in 2 mL of GC autosampler vials equipped with Teflon-backed elastomeric septum crimp caps. The needle of the SPME "syringe" is easily capable of puncturing these caps.

The SPME fiber was placed into a solution of the analyte as its hydrochloride salt in water (typically 1 mL of 1 μg/mL solution in a GC vial) for 1 min. After that time, the fiber was withdrawn and exposed to the headspace above the chloroformate (10 μL in a GC vial) for 30 s. The fiber was then desorbed in the injection port of

[3] R= ethyl
[4] R= n-butyl
[5] R= (-)-menthyl

[6] R"=H, R' = $C_6H_5CH_2CHCH_3$, R=ethyl

[7] R"=H, R' = $C_6H_5CH_2CHCH_3$, R=n-butyl

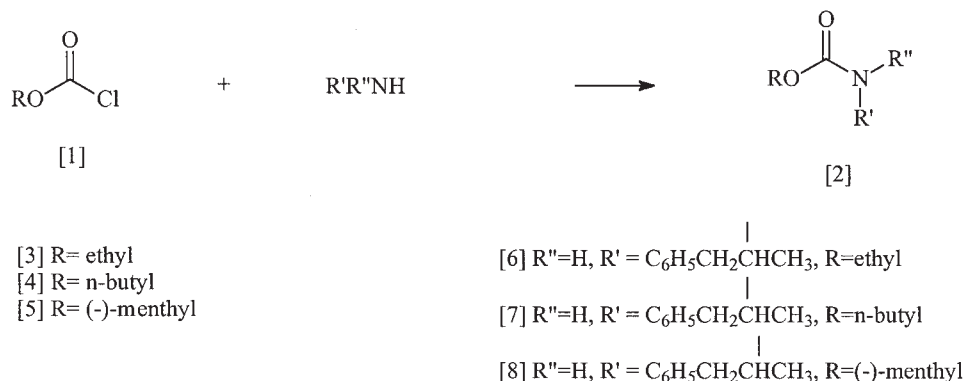[8] R"=H, R' = $C_6H_5CH_2CHCH_3$, R=(-)-menthyl

FIG. 1

the GC. The reverse process, where the fiber was exposed to the derivatizing reagent first, then exposed to the solution of the analyte, also was found to be effective.

Vapor-Phase Deprotonation and SPME Derivatization of Methylamphetamine Hydrochloride—Triethylamine (2 μL) was applied to the inside surface of a crimp cap GC vial containing approximately 1 mg of methylamphetamine hydrochloride; the triethylamine does not have to wet the powder. The arrangement was allowed to equilibrate for 5 min before exposing an SPME fiber to the headspace for 1 min. After that time, the fiber was removed, placed into the headspace of a vial containing ethyl chloroformate (10 μL) for 30 s, then desorbed in the injection port of the GC-MS.

Headspace Deprotonation and SPME Derivatization of Simulated Methylamphetamine Hydrochloride Traces on Bank Notes— A solution of methylamphetamine hydrochloride in water (1 μL, 1 mg/mL concentration) was spotted onto filter paper, and the treated section of paper was excised with the aid of a hole punch. The disk was placed into a 20-mL glass container equipped with a plastic lid. A small hole, just big enough to accommodate the SPME needle, was pierced through the lid. Approximately 10 μL of triethylamine was applied to the inside surface of the container, the hole in the lid sealed up with adhesive tape, and the container left for approximately 5 min for the contents to equilibrate. The SPME fiber was then exposed to the headspace of the container for 1 min, after which time it was exposed to the headspace above the chloroformate (10 μL in a GC vial) and then thermally desorbed in the injection port of the GC-MS.

Headspace Deprotonation and SPME Derivatization of Simulated Methylamphetamine Hydrochloride Traces on Bank Notes (Absorption Kinetics and Limits of Detection)—Six disks of paper, each treated with methylamphetamine hydrochloride (1 μg), were prepared as above. The disks were subjected to headspace deprotonation (as above), and each headspace was extracted over a different time frame (1, 2, 5, 10, 20, and 80 min). After the extraction period the fiber was placed into the headspace above ethyl chloroformate (10 μL) for 30 s, then thermally desorbed in the injection port of the GC-MS. The level of analyte recovery for each absorption time was calculated simply by measuring the methylamphetamine chromatographic peak areas.

A stock solution of methylamphetamine hydrochloride in water (1 mg/mL) was serially diluted with water to yield solutions of the drug, ranging in concentration from 100 μg/mL to 10 ng/mL. Aliquots of these solutions (10 μL) were applied to filter paper pieces that were then placed in 1-L cans. Triethylamine (10 μL) was applied to the inside surface of the cans, which were then sealed and left to equilibrate for approximately 20 min. Headspace inside the cans was sampled for 20 min by placing the SPME fiber through small holes in the lids. Any recovered methylamphetamine was then derivatized by placing the fiber into the headspace of a vial containing ethyl chloroformate (10 μL) for 30 s. Desorption into the GC-MS then followed in the manner described above. The limit of detection for derivatized methylamphetamine was judged to be the point when the intensity of the 58 and 130-Da ions extracted from full-scan data at the appropriate retention time achieved a value three times greater than the peak-to-peak background noise.

Recovery of Drug Traces from a Rubber Glove—In order to compare the performance of vapor-phase deprotonation followed by on-fiber SPME derivatization against conventional liquid-phase techniques for the recovery of drug traces, the two techniques were applied to a rubber (latex) glove seized from a clandestine laboratory.

The glove was placed into a Cryovac Bag, triethylamine (10 μL) was applied to its inside surface, a SPME fiber exposed to the headspace for 1 h inside surface, a SPME fiber was exposed to the headspace for 1 h and then exposed to the headspace above ethyl chloroformate for 30 s before being analyzed by GC-MS.

The conventional recovery undertaken involved three separate swabbing operations, each performed on about 30% of the glove surface: one used a swab moistened with water that was then extracted with water, the aqueous solution then being basified and extracted into isooctane; the second used a swab moistened with methanol that was then extracted with methanol; and the third used a swab moistened with methanol that was extracted with methanol, the extract then being blown to dryness, basified, then extracted with isooctane. GC-MS analysis of the three swabbing products followed.

Cleaning of SPME Fibers

No special routine cleaning protocol was followed. Instead, the fiber was left in the injection port after thermal desorption for the entire chromatographic run, or at least 10 min. If this procedure was followed, carryover was effectively eliminated.

Results and Discussion

As expected, methylamphetamine easily generated carbamate (urethane) derivatives [6–8] upon reaction with simple *n*-alkylchloroformates (see Fig. 1) under all the extraction conditions described in the Materials and Methods section. Analogous derivatives would be expected from other primary and secondary amphetamine-type drugs. Figure 2 shows the mass spectrum of the derivative produced by the reaction between methylamphetamine and ethylchloroformate; proposed structures for fragment ions are given.

However, upon treatment with alkylchloroformates, both pseudoephedrine and *N,N*-dimethylamphetamine yielded unusual derivatives. In the case of pseudoephedrine, only a single equivalent of chloroformate underwent addition. However, instead of the expected carbamate [9], a compound identified as 3,4-dimethyl-5-phenyl-2-oxazolidinone [10] (based on its mass spectral fragmentation pattern) was obtained. As depicted in Fig. 3, we believe the oxazolidinone arises through an internal nucleophilic attack by oxygen upon the carbamate carbonyl moiety. Although the product derived from ephedrine was not the one expected, it nevertheless is a useful derivative as it is stable, chromatographs without tailing, and yields a characteristic fragmentation pattern (see Fig. 4).

N,N-dimethylamphetamine [11], a tertiary amine, cannot yield a carbamate derivative. However, although on-fiber derivatization of pure *N,N*-dimethylamphetamine using ethylchloroformate resulted in the detection of the unchanged drug in abundance, a small amount of a derivative was detected. The derivative was identical in all respects to that produced by the reaction between methylamphetamine and ethyl chloroformate [6]. According to Prager (11), phenylchlorothionoformate is capable of dealkylating tertiary amines, and both Pelander (12) and Herraez-Hernandez (13) report that chloroformates bring about *N*-demethylation of tertiary amine drugs. We propose that the derivative obtained from *N,N*-dimethylamphetamine arises through an analogous mechanism, which is depicted in Fig. 5. This finding suggests that chromatographic data should be interpreted with caution if there is any possibility that an analyte is a tertiary amine.

Derivatization can be achieved readily on the SPME device. The best SPME stationary phase in terms of absolute recovery of
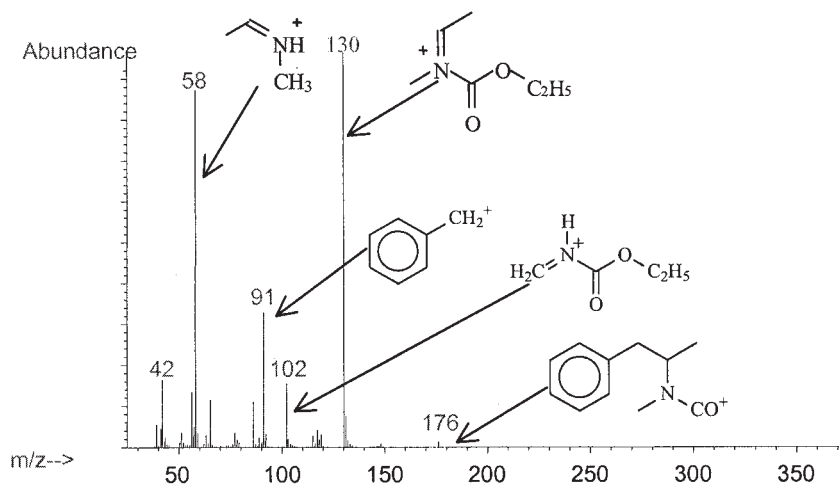
FIG. 2—*Mass spectrum for the product of reaction [6] between methylamphetamine and ethylchloroformate. Structures for the major fragment ions are given; the molecular ion (221Da) is of extremely low abundance.*
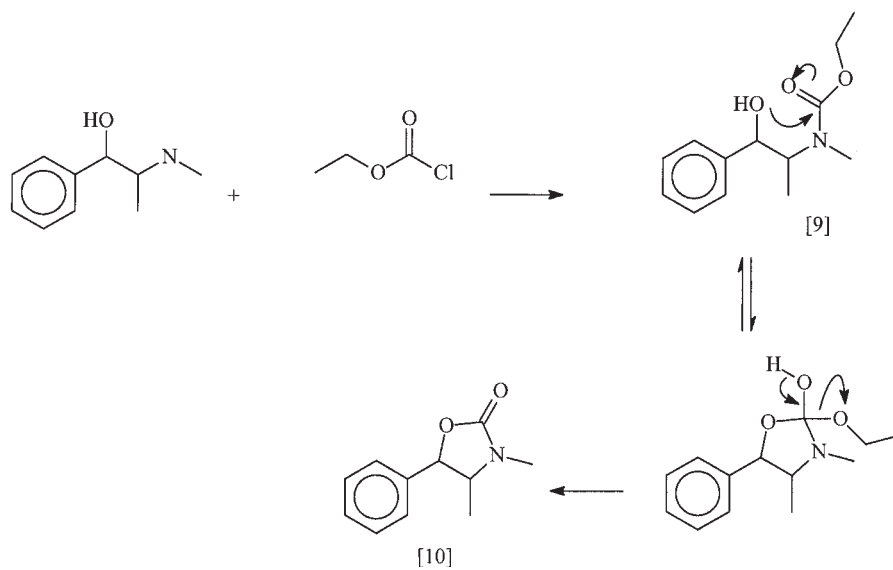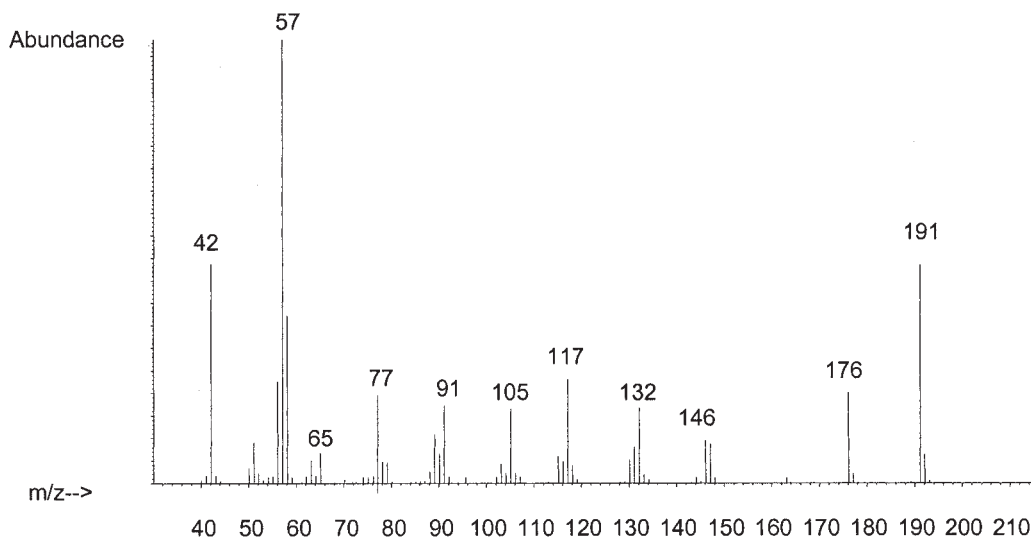

FIG. 3

FIG. 4—*Mass spectrum for the product of reaction [10] between pseudoephedrine and ethylchloroformate.*
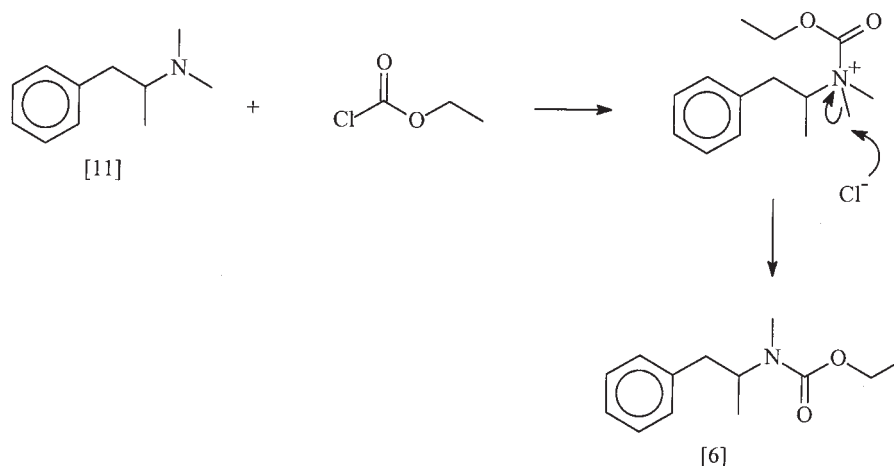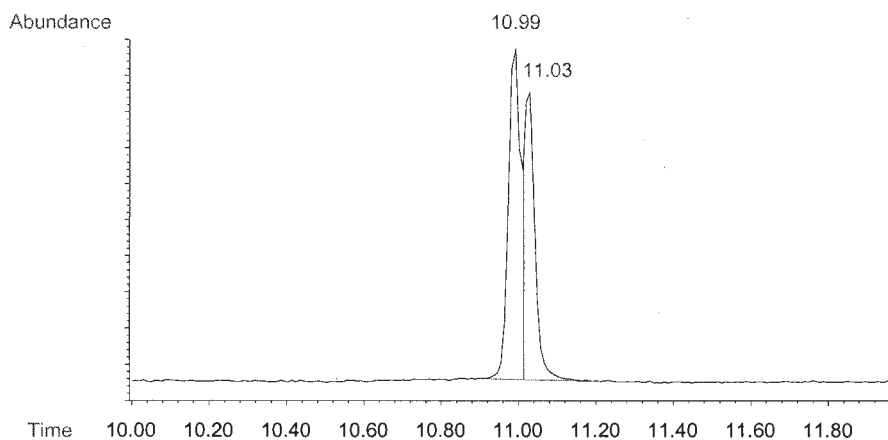
FIG. 5

FIG. 6—*Total ion chromatogram depicting the separation of the two derivatives of racemic amphetamine prepared using (−)-menthylchloroformate. The derivative arising from L-amphetamine eluted first.*

analyte was found to be the 65-μm-thick film of carbowax/divinyl benzene, with the 85-μm polyacrylate phase second best. The former phase, however, was found to be very delicate and prone to "stripping," and the silica fibers themselves were also quite weak. These comments also apply to partially bonded Stableflex CW/DVB fibers; the same phenomena have been reported by Wittmann (14). Consequently, all results described in this paper were obtained using the polyacrylate-coated fiber, which was much more robust in all regards.

Although it is common to basify aqueous solutions of amphetamine-type drugs prior to extraction (see Jurado (4), for example), our results indicate SPME of methylamphetamine or pseudoephedrine followed by on-fiber derivatization can be quite readily achieved using dilute (<1 mg/mL) aqueous solutions of their hydrochloride salts. Conversion of these drugs to their free base is therefore not a necessity for SPME to be effective. Each of the simple n-alkylchloroformates functioned equally well; the only practical feature to favor one reagent over another was the retention time of the derivatives formed. (−)-Menthylchloroformate yielded two diastereomeric derivatives upon reaction with a racemic mixture of amphetamine and just one with d-amphetamine hydrochloride. Although the GC column used did resolve the mixture of diastereomeric derivatives, baseline separation was not achieved (see

Fig. 6); the mass spectral fragmentation patterns of the two derivatives were identical.

The recovery of methylamphetamine from an aqueous solution of its salt was followed over a period of 60 min. As can be seen from Fig. 7, after 20 min the amount of drug recovered did not rise appreciably. At this time, minimum limits of detection will be realized; however, the graph also shows that if maximal recovery is not required, then an extraction time as short as 1 min can be used in the interests of time efficiency.

Extraction of pseudoephedrine took at least twice as long to achieve a maximum. As indicated in Fig. 8, blank solutions yielded very clean chromatograms.

SPME over 20 min followed by on-fiber derivatization for recovery of methylamphetamine or pseudoephedrine from aqueous solutions of their salts results in detection limits of about 100 ng/mL and 1 μg/mL, respectively.

The situation where methylamphetamine salt is present as a trace on banknotes, clandestine laboratory "recipes," garments, etc. was replicated by spotting trace quantities of the drug onto filter paper. It was found that methylamphetamine hydrochloride traces on filter paper could be converted into their free base using triethylamine vapor. In free base form, methylamphetamine forms a rich headspace that can be readily extracted using SPME and simply
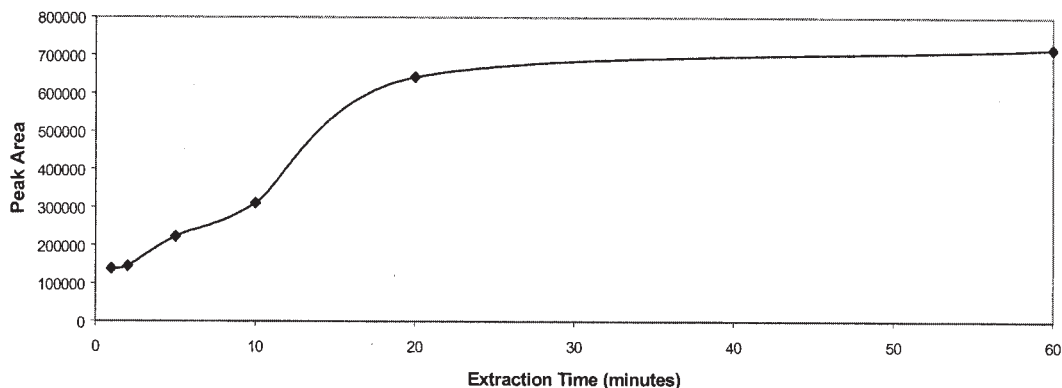
FIG. 7—*Plot of extraction time versus peak area for recovery of methylamphetamine from an aqueous solution of its hydrochloride salt (1 mL, 1 μg/mL concentration).*
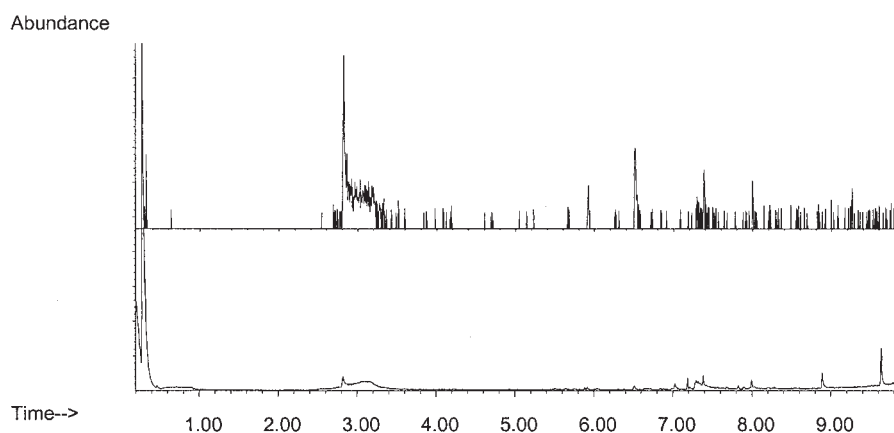

FIG. 8—*Total ion chromatogram resulting from extraction of blank water. The inset is an extracted ion chromatogram plotted for the most abundant ion present in the mass spectrum of the derivative of methylamphetamine (^{130}Da). The maximum abundance of the ions recorded in the extracted ion chromatogram was about 400.*

derivatized thereafter using any of the chloroformates referred to above. Although triethylamine is a tertiary amine and therefore undergoes dealkylation in the presence of chloroformates, the carbamate produced is quite volatile and does not interfere with the chromatography of amphetamine derivatives. The use of pyridine for vapor-phase deprotonation was investigated, but it was found to be less effective than triethylamine. As indicated in Fig. 9, SPME of methylamphetamine from headspace above paper takes a relatively long time to equilibrate at room temperature; however, about 25% of maximum recovery appears to be reached within only 5 min. The limits of detection for methylamphetamine recovered from headspace for 20 min and detected as its ethyl carbamate derivative were reached when 10 ng were applied to paper that was contained in a 1-L vessel. In the Australian context in relation to currency, this performance limitation is acceptable as there is negligible "background contamination" of notes.

Detection limits did not appear to be related to the sequence in which recovery and derivatization took place. It would therefore appear that derivatization does not take place on the fiber, but in the injection port of the GC. This was confirmed in an experiment where the SPME fiber was exposed sequentially to the headspace above the methylamphetamine free base for 1 min, then headspace above ethylchloroformate for 1 h, then headspace above *n*-butyl chloroformate before desorption. Under these conditions, both ethyl and *n*-butylcarbamate derivatives were detected in good

yields (Fig. 10). If derivatization took place on the fiber, then it is reasonable to believe that the *n*-butylcarbamate derivative would not be detected. As the analyte is not "trapped" on the fiber in its less volatile, derivatized form, an important contamination issue in casework arises. It has been found that if headspace recovery of amphetamines takes place before absorption of the derivatization reagent, there is a significant opportunity for underivatized amphetamine to desorb into the vial containing the derivatization reagent. Any subsequent absorption from that vial will result in carryover of amphetamine. We therefore recommend that the vial containing derivatization reagent be used only once, then disposed of.

As alluded to in previous articles (1–3), SPME followed by GC-MS is ideally matched to the task of "profiling" illicit preparations for the purpose of intelligence gathering, source comparison, and generating evidence as to the route of manufacture. Key profiling congeners of amphetamines are ketones, alcohols, pyrimidines, aldehydes, and substituted naphthalenes of medium molecular weight and relatively high vapor pressure. As reported by Koester (3), recovery of these compounds by SPME is particularly efficient, even in comparison to well-established liquid-liquid extraction procedures such as the UN method (15). Koester also reported that SPME was capable of extracting methylamphetamine, albeit with low sensitivity, from headspace above powder samples containing methylamphetamine salt. Whether the methylamphetamine recovered actually arose from the salt itself or from free base residues in
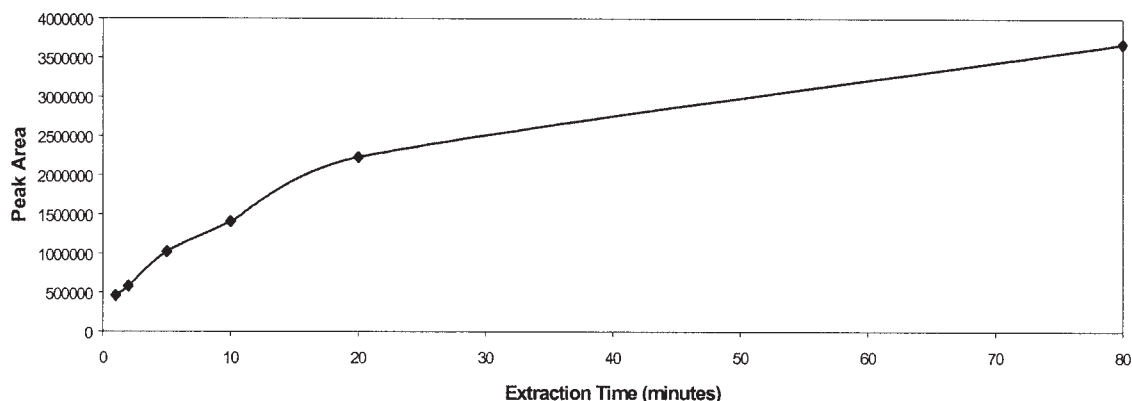
FIG. 9—*Plot of extraction time versus peak area for headspace recovery of methylamphetamine from a solution of its hydrochloride salt (1 μL, 1 mg/mL concentration) applied to filter paper and using vapor-phase deprotonation and on-fiber derivatization.*
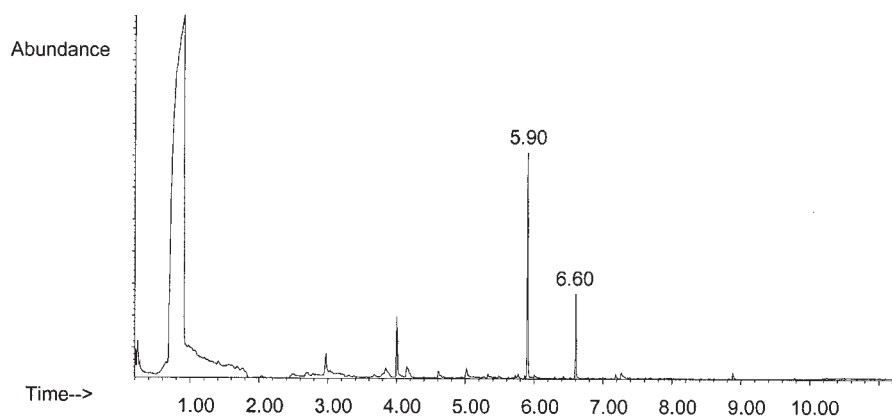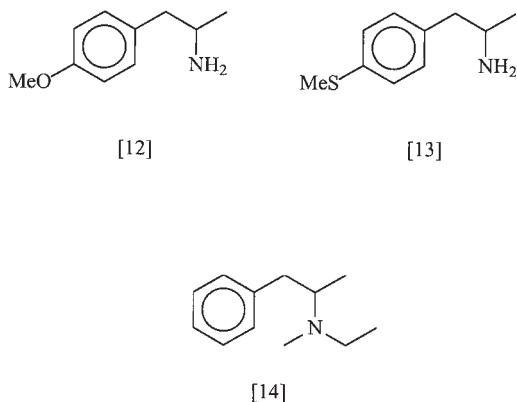

FIG. 10—*Total ion chromatogram resulting from the exposure of a SPME fiber to the headspace above methylamphetamine free base, then to the headspace above ethylchloroformate, then to the headspace above n-butylchloroformate. The two major peaks (5.90 and 6.60 min) are due to the ethyl and n-butyl derivatives respectively; the two minor peaks at about 3 and 4 min are due to carbonic acids arising from the derivatization reagents, and the large peak near to 1 min is due to the derivatization reagents. Traces of carbonic acids were routinely detected in derivatization experiments.*

the powder is not immediately apparent. Work by us (1,2) has indicated that 4-methoxyamphetamine [12] and 4-methylthioamphetamine [13] could not be recovered from the headspace above salts of these drugs using SPME (see Scheme 1 below).

In any event, no matter what the actual situation is regarding the recovery of methylamphetamine, conventional SPME can at best only offer inefficient recovery of amphetamines from the headspace above preparations containing their salts. As a conse-

quence, when applied to the analysis of traces of material adhering to banknotes, etc., conventional SPME is not likely to reveal the presence of the amphetamine itself, only its volatile congeners. This technique must be supplemented with tedious swabbing and liquid-liquid extraction operations in order to detect the amphetamine. If vapor-phase deprotonation and on-fiber derivatization are used, however, SPME represents a comprehensive, "single-shot" technique that has a low limit of detection for amphetamines as well as congeners.

An example of the utility of the technique is provided by the chromatogram in Fig. 11. The chromatogram arose from vapor-phase deprotonation followed by on-fiber derivatization SPME applied to a glove seized from a clandestine laboratory. Easily detected were phenyl-2-propanone, amphetamine, methylamphetamine, and N-ethyl-N-methylamphetamine [14][3]. The advantage of the SPME-based examination of this glove is demonstrated by the fact that three different conventional, wet-swabbing operations performed on the glove did not yield any of the above substances.

[12]   [13]

[14]

Scheme 1

[3] Amphetamine and *N*-ethyl-*N*-methylamphetamine are commonly encountered in illicit methylamphetamine in South Australia produced using hydroiodic acid/red phosphorus (or equivalent) reduction. These compounds seem to arise when the precursor used is pseudoephedrine contaminated with ethanol, which itself is carried over from the process of extraction of pseudoephedrine from over-the-counter medications.
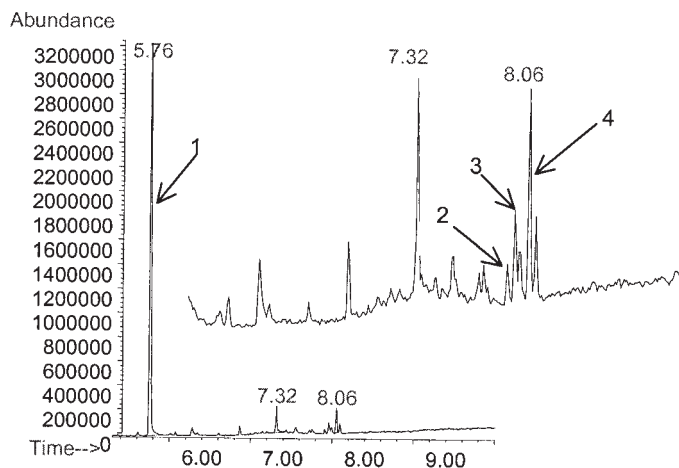
FIG. 11—*Total ion chromatogram obtained from application of vapor-phase deprotonation and on-fiber derivatization SPME to a glove seized from a clandestine laboratory, and an expanded view of the 6 to 8.5-min region (inset). Peak assignments are as follows: 1, phenyl-2-propanone; 2, amphetamine (derivative); 3, N-ethyl-N-methylamphetamine; 4, methyl-amphetamine (derivative). Early eluting peaks (not shown) originated from the derivatizing reagent.*

The work described in this paper was performed with a gas chromatograph equipped with a HewlettPackard 5971 MSD. When detection limits were assessed using a more modern Agilent 5973 MSD, detection limits at least two orders of magnitude lower were achieved in full scan mode.

Conclusions

A new development of SPME is described that allows rapid, comprehensive screening of evidentiary material for the presence of amphetamine-type drugs, their precursors, and manufacturing by-products.

The development involves vapor-phase conversion of salts of amphetamine-type drugs into their free bases using triethylamine. This process can be integrated with headspace SPME to form one step, which is immediately followed by rapid on-fiber derivatization using alkylchloroformates to yield chromatographically stable and inert derivatives.

The process has direct application in the screening of "difficult" evidentiary material such as banknotes, clandestine laboratory documents, or garments. Compared to liquid swabbing or extraction methods, such as that reported by Al Dirbashi (16) and the methods described in the Materials and Methods section in this article, the headspace method reported here is less invasive to the sample and much more convenient. In the case where a wad of banknotes is received, for example, the process can be applied to the entire seizure, saving the time and tedious effort required to swab each one (or a representative sample) with liquid and prepare liquid extracts. Detection limits achieved are quite appropriate for the task of recovering traces of drugs, and more than sufficient for screening visible quantities of powder, tablets, etc.

In addition to amphetamines themselves, the technique covers a wide range of compounds; therefore, it is well suited to intelligence gathering, source comparison, and identification of synthetic pathway. The use of (−)-menthylchloroformate allows the enantiomeric composition of preparations to be simply examined, enabling more sophisticated intelligence gathering (17) or evidence presentation, especially in those jurisdictions where drug enantiomeric composition has some bearing upon criminal proceedings.

Further work is being done to extend the techniques described in this paper.

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