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Preparation, Delivery, and Evaluation of Picomole Vapor Standards

DUANE A. ROGERS

*DU/EMF Laboratory
Joint Base Andrews, Maryland*

KEVIN J. JOHNSON

*Navy Technology Center for Safety and Survivability
Chemistry Division*

CHRISTOPHER J. KATILIE

*Nova Research, Inc.
Alexandria, Virginia*

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14. ABSTRACT A method is described for the modification and use of a gas chromatograph heated inlet for the preparation of trace vapor reference standards. A conventional GC-MS is used to validate the prepared vapor standards and an evaluation is provided on the reproducibility of replicate measurements made from a single sample as well as individual measurements made between replicate samples. The described method is applied to the preparation of single component trace organic vapors, complex vapor mixtures (containing >10 components over a concentration range spanning four orders of magnitude), and low vapor pressure analytes, which are solids under ambient conditions (e.g., ferrocene). Results demonstrate delivery of picomole quantities of single component organic vapors with a reproducibility of ca. 1% RSD.					
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Introduction

Analytical trace chemical standards are a necessary component in the development of sensors, canine training aids[1-4], laboratory or field-based analytical equipment [1, 5, 6], or characterization of new analytical technology [7]. The complexity of vapor samples needed for these applications vary significantly in composition. For example, canine training aids for explosives, narcotics, or cadavers should not necessarily be a single chemical (e.g. trinitrotoluene, tetrahydrocannabinol, or cadaverine). Rather, the training aid should reflect the complex chemical signature of the material for which training is being conducted. In such situations, the active ingredient is often one of the least volatile components and potentially present in the lowest concentration [3, 8]. In contrast, early development and characterization of sensor materials often requires single component vapor standards to avoid convoluting nonspecific responses [9-12]. Unavailability of a vapor standard for the compound of interest often forces researchers to compromise and use a simulant [13, 14].

While liquid standards for thousands of chemicals are readily available, certified vapor standards are often difficult to obtain. No doubt, one of the greatest challenges with trace vapor standards is consistent production and a reliable means to transport and deliver the vapor to the analytical system being evaluated. Certified gas mixtures and permeation tubes can often be obtained from commercial suppliers for compounds that are widely available and that have relatively high vapor pressures [15]. However, because certified gas mixtures are often pressurized to thousands of kPa, compounds with low vapor pressures are generally avoided to prevent condensation within the gas cylinder. In the case of permeation tubes, long stabilization times, on the order of hours to days, are often necessary to reach a steady emission rate [16]. In this work a means for preparing trace vapor standards in-house is described along with a vapor delivery system.

To generate small quantities of organic vapors, a gas chromatograph was modified to vaporize small injections of analytical standards and transfer the vapor into 100 mL canisters. Aliquots of vapor could then be extracted from the canister through the use of a 6-port valve and sample loop and then analyzed or used as needed. Even though much of this discussion will focus on single component standards in a helium buffer gas, mixtures of volatile organic compounds (VOC) can also be generated by injecting a preformulated liquid mixture of the necessary components. As will be demonstrated, analytes that are solids at room temperature but have a relatively high vapor pressure (e.g. ferrocene) can be dissolved in solvent and then later separated from the solvent based on differences in vapor pressures. In the case of ferrocene, for example, solid crystals are dissolved in methylene chloride and the mixture is then vaporized in a GC inlet. The analyte-solvent vapor mixture is then cryogenically trapped in the inlet, allowing the solvent to be desorbed and discarded prior to desorbing the analyte, if desired. When the analyte is desorbed and transferred to a transport vessel the vessel pressure can be optimized to keep the analyte in the gas phase.

For the purpose of this discussion, samples will be discussed in terms of quantity rather than concentration. Certainly it is often desirable to generate a constant stream of VOCs at a particular concentration, however, this work focuses on the preparation and delivery of discrete VOC aliquots. Through the use of a 100 μ L sample loop, portions of the vapor contained within the 100 mL canister can be reproducibly extracted and used. With this approach, a small initial liquid injection (10 μ L- 250 nL) can be vaporized and stored. At a later date, a small portion of the vapor standard can be reliably extracted and delivered to provide < 20 picomoles of analyte.

Experimental

Sample Preparation

To generate small quantities of organic vapors, an Agilent 7890A GC was modified to vaporize small injections of analytical standards and transfer the vapor into a 100 mL canister. Aliquots of vapor could then be stored, transported, and utilized as needed. Specifically, an Agilent automatic liquid sampler (ALS model 7683B; Santa Clara, CA USA) was used to inject small volumes (10 nL to 10 μ L) of commercially obtained liquid standards (CAS numbers provided in Table 1) into a standard Agilent 7890A GC split/splitless inlet held at 250°C with a splitless liner (model 5188-6568; Agilent Technologies, Santa Clara, CA USA). To reduce sample losses in the inlet, the septum purge was turned off, the outlet capped, and the inlet was set to splitless mode at 20 psig. Upon injection, vapor generated in the inlet is swept from the inlet by a helium carrier gas flow. This flow is directed through a short length (ca. 4 cm) of deactivated 200 μ m ID fused silica capillary (part No. 25737, Supelco Co., St. Louis, MO USA) into a 6-port valve (part No. 20584; Restek, Bellefonte, PA USA) located inside the GC oven that is held at 100°C. The temperature of the oven and inlet can be adjusted to accommodate less volatile analytes. The vapor is then directed through a 10 cm length of 1/16 in. O.D. (ca. 1.59 mm) 304 grade stainless steel tubing with siltek/sulfinert coating, to reduce sample losses (part No. 22505, Restek U.S., Bellefonte, PA, USA), and into a 100 mL Entech MinicanTM with siltek/sulfinert coating (model No. MC100SQT, Entech Instruments Inc., Simi Valley, CA USA) by way of a siltek/sulfinert coated Micro-QTTM quick connect valve (part No. 30-22300, Entech Instruments Inc., Simi Valley, CA USA). After an injection, sample and carrier gas were allowed to pass into the MiniCanTM for 2 minutes before the canister was disconnected and the 4-port valve was switched from “Fill Mode” (Figure 1a) to “Flush Mode” (Figure 1b.) The 2 min. fill time is used to flush remnants of the sample from the inlet into the canister and to pressurize the canister to a 103.4 kPa (15 psig). When the 4-port valve is in “Flush Mode” carrier gas flows through the heated inlet at ca. 150 mL min⁻¹ into an evacuated 1 L ballast canister, while the dead volume of the quick connect is evacuated with a turbomolecular vacuum pump.

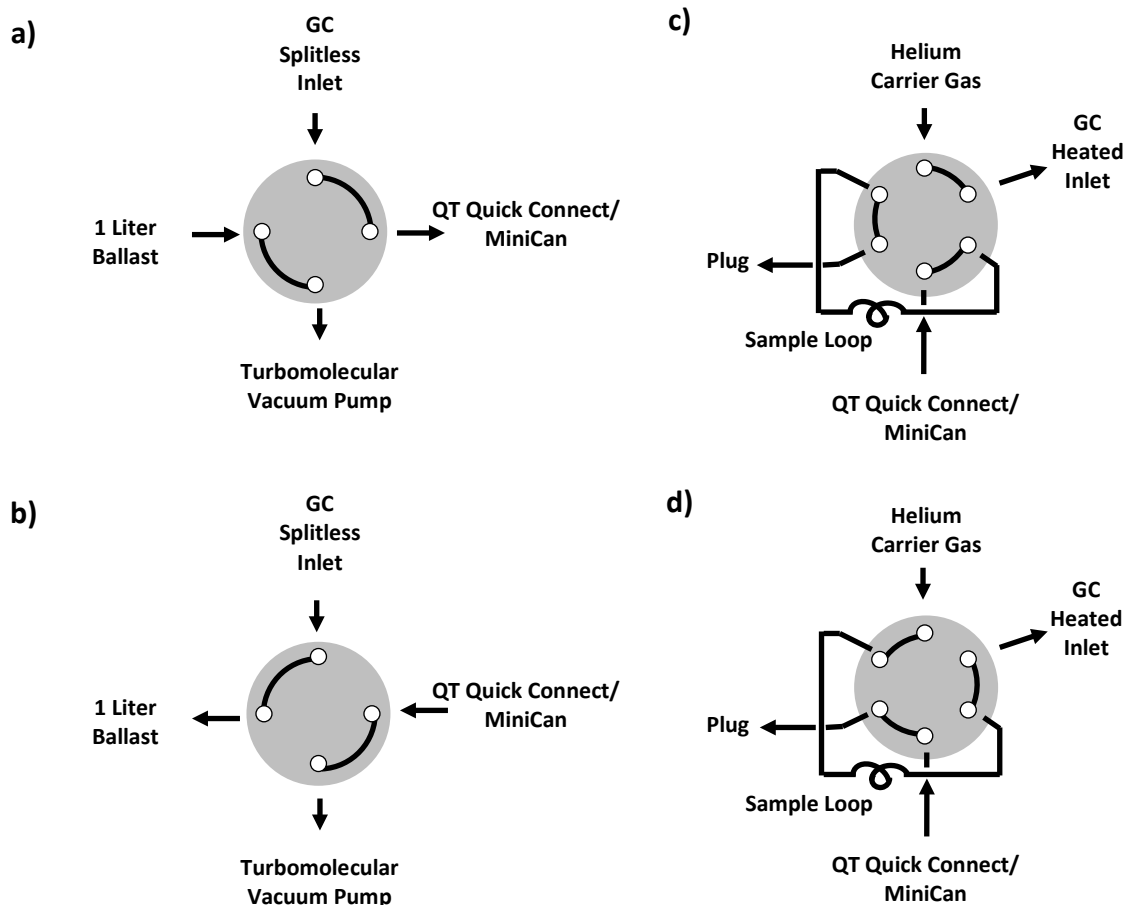


Figure 1: Valve layout for (a) 4-port sample preparation in "fill" mode (b) 4-port sample preparation in "flush" mode (c) 6-port vapor sample introduction in "sample load" mode and (d) 6-port vapor sample introduction in "sample inject" mode.

As is shown in Figure 2, longer fill times can be used to reach higher pressures, but to maintain a positive gas flow into the canister, and reduce diffusion losses, a 2 min. fill time was used. Alternatively, the GC inlet pressure can also be varied to select a pressure in the transfer vessel.

To generate an analytical vapor of ferrocene, 1 μL of 0.2 M ferrocene, dissolved in methylene chloride, was injected into a cryogenically cooled GC inlet (model No. CIS-4, GERSTEL GmbH & Co. KG, Mülheim an der Ruhr, Germany) onto a GC inlet liner filled with 8 mg of Tenax sorbent held at -100°C . The temperature was subsequently increased to 0°C to vaporize the solvent and the inlet solvent-vent mode was engaged at 500 mL min^{-1} with the 4-port valve directing the flow into a 1 L ballast container for 4 minutes. After the solvent was removed the temperature was ramped to 200°C at $12^{\circ}\text{C min}^{-1}$ and the 4-port valve was actuated to direct the vapor flow into a 100 mL canister for 2 min.

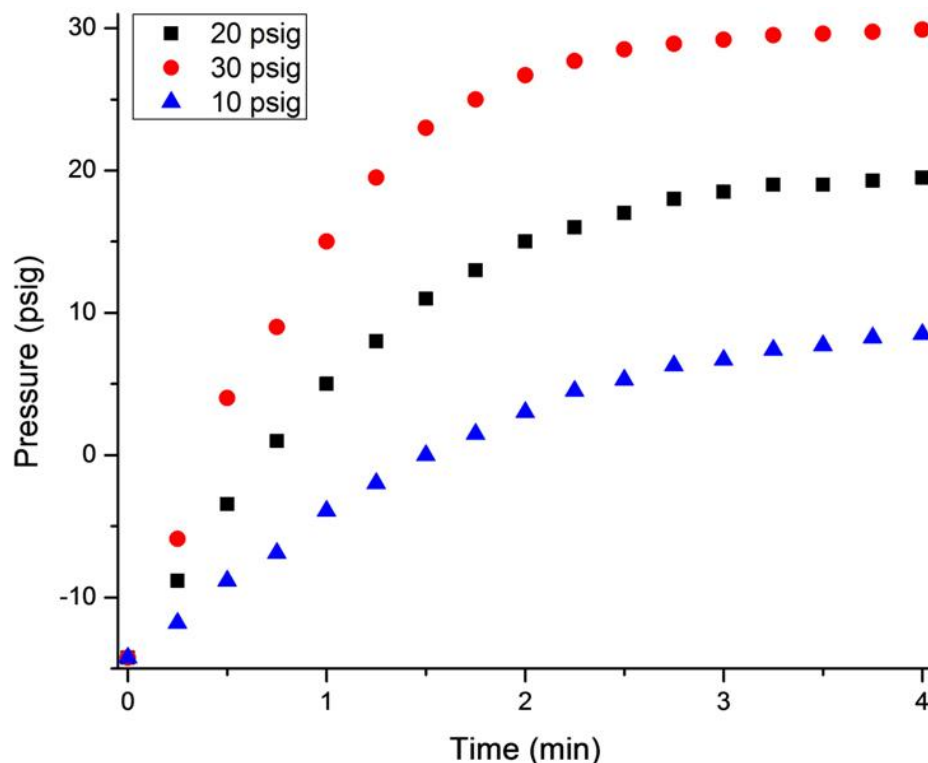


Figure 2: Plot of canister pressure as a function of fill time and inlet pressure. A 100 mL EntechTM MiniCanTM was filled with inlet helium pressures of 10, 20, and 30 psig.

With the Agilent 7683B ALS, liquid volumes as small as to 10 nL could be injected and vaporized with the use of an SGE 500 μ L syringe (part No. 000415, SGE Analytical Science, Victoria, Australia). For small injections, the precision of sample delivered to the 100 mL canister became limited by the precision of the injection at volumes $< 100 \mu$ L, shown in Figure 3. For injection volumes of 10 nL, only the syringe needle is filled with sample. Consequently, it is not possible to visually identify the presence of bubbles in the syringe and abort the injection, as can be done with larger injection volumes. No doubt, injection reproducibility is affected by sample viscosity and transfer efficiency from the needle to the splitless liner. In this work a 1 sec. viscosity delay was found to be adequate for pure dodecane, which was considered a worst case, and was therefore used on all samples. Injection volumes up to 30 μ L could be used through the use of a 100 μ L syringe, but longer washout times were necessary.

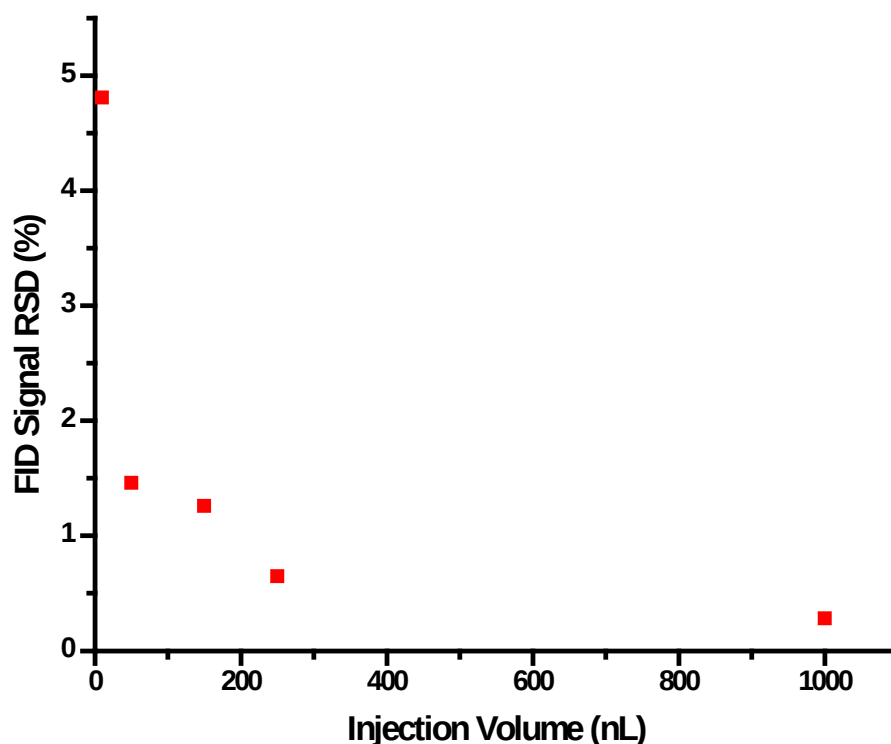


Figure 3: Plot of injection precision as a function of injection volume measured for hexane with an Agilent 7683 ALS and flame ionization detector. Injection volumes $< 1 \mu\text{L}$ were obtained with a $500 \mu\text{L}$ SGE syringe. Precision for $1 \mu\text{L}$ injections with a $10 \mu\text{L}$ syringe is 0.28%.

Sample Delivery/Validation

To validate the quantity of analyte in the canisters a sulfinert-coated 6-port valve (Part No. 20585; Restek, Bellefonte, PA USA) with a gas sample loop was used to sample a small fraction of the vapor in the canister (Figure 1c) and inject it (Figure 1d) into an Agilent 6890 gas chromatograph with 5975 mass selective detector (Agilent, Santa Clara, CA USA). Measured signals were compared to a GC-MS calibration curve established with conventional liquid injections. To deliver a small aliquot of vapor from the MiniCanTM transfer vessel to the GC inlet, the sample loop was first evacuated with a ballast canister and then filled with sample from a MiniCanTM. A 10 sec. equilibration time was allowed to pressurize the loop to the pressure of the canister. The 6-port valve was then actuated to sweep sample from the loop into the GC carrier stream and inject it into a cryo-cooled inlet system (model No. CIS-4, GERSTEL GmbH & Co. KG, Mülheim an der Ruhr, Germany). The use of a 6-port valve and evacuated sample loop in this fashion offers a means to reliably sample and deliver aliquots of vapor from MiniCansTM to other analytical applications. The cooled inlet could be operated at a constant temperature (e.g. 250°C) to emulate a standard GC inlet or cryogenically cooled to trap sample vapor on a sorbent bed. When cryogenically cooled, the cooled inlet can preconcentrate vapor sample and subsequently inject it onto the GC column by rapidly increasing the inlet temperature

($\leq 12^{\circ}\text{C min}^{-1}$). Through the use of a ramp-and-hold temperature program the CIS-4 can be used to separate analytes which might otherwise coelute.

Canister Cleaning

It was found new MiniCansTM were contaminated with small amounts (ca. nanomoles) of chemical standards from the manufacturer. These chemical standards are used by the manufacturer to evaluate the efficacy of the sulfinert coating and to certify the canister's performance. A cleaning procedure was therefore developed to remove this contamination in new canisters as well as to clean used canisters so they could be reused. To clean the canister a vacuum manifold was constructed of 2 inch (ca 5.08 cm) OD stainless steel connected to an oil-free scroll pump (Triscroll 600, Varian, Lexington, MA USA) by way of a brass bellows vacuum valve (Part No. BFLM-K40, Duniway Stockroom Corp., Mountain View, CA USA). A scroll pump was used rather than a mechanical roughing pump to prevent oil mist contamination. When a contaminated transfer vessel was connected to the manifold, by way of a Micro-QTTM quick connect valve (part No. 30-22300, Entech Instruments Inc., Simi Valley, CA USA), the vacuum valve was closed isolating the manifold from the vacuum pump. The manifold was then pressurized to several hundred Torr of ultra-high purity (UHP) nitrogen. The nitrogen valve would subsequently be closed and the vacuum valve opened to evacuate the manifold along with the attached canisters to $< 10^{-5}$ Torr. The cleaning manifold was eventually expanded to 30 canisters so that the cleaning step did not limit the preparation of samples. Typically the manifold pressure would be cycled from ca. 1500 Torr (absolute pressure) to 10^{-3} Torr six times to reduce remnants of preceding samples below the detection limit of the analysis technique (ca. 1 picomole). This cleaning procedure could easily be expanded to include heating of the canisters during the flush-and-fill cycles, although it was evaluated here at ambient temperature.

To evaluate the cleaning procedure, a canister was injected with 1.25 ng of dodecane dissolved in methylene chloride (1 μL total injection volume). Vapor was sampled from the canister with a 100 μL loop. As is shown in Figure 4, the amount of VOC present in the canister is significantly reduced after each flush-and-fill cycle. Expectedly, the rate at which an analyte is depleted from the canister is dependent on its vapor pressure. Consequently, methylene chloride is reduced below the detection limits of the GC-MS in three cycles and dodecane is depleted after four cycles. It appears the first flush-and-fill cycle removes more analyte from the canister than subsequent cycles. This observation suggests that analyte is adhered to the canister walls even in an evacuated (i.e. low pressure) environment. The additional fill cycles no doubt introduce turbulence within the vessel capable of overcoming these wall effects. Because these samples may be used on instruments more sensitive than GC-MS, six cleaning cycles were typically used to reduce contamination below the femtomole-level limit of detection seen with conventional GC-MS instrumentation.

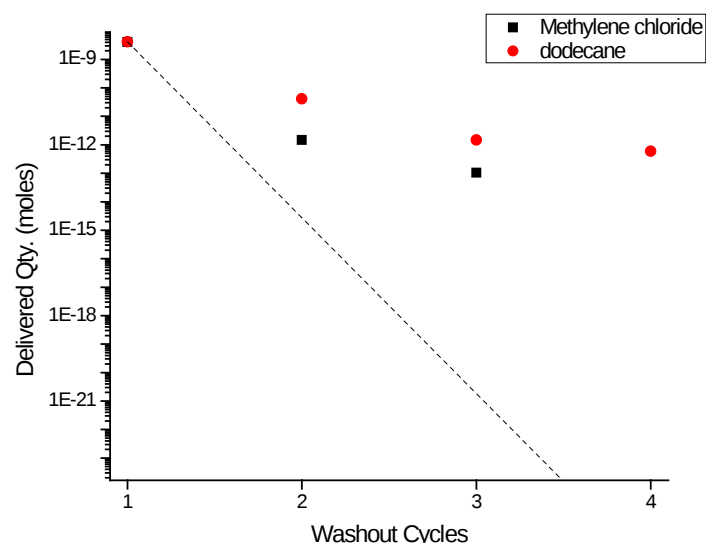


Figure 4: Plot showing the average amount of recovered methylene chloride (■) and dodecane (●) recovered from three canisters after a flush-and-fill cycle. The first point for both compounds overlap at ca. 4.0×10^{-9} moles. After three and four flush-and-fill cycles the recovered amount of methylene chloride and dodecane fell below the detection limit of the GC-MS, respectively. The dashed line represents the theoretical amount of analyte that would be present in the vial after each wash cycle if no wall effects were present.

Results and Discussion

Effect of aliquot volume

As discussed previously, precision of measurements made between multiple canisters can be limited by injection volume. The obvious means to reduce error associated with canister preparation is to take replicate aliquots from a single canister. However, reproducibility of aliquots taken from a single canister can become limited when removing large aliquots relative to the total volume of the transfer vessel. For large sample aliquots each measurement can remove a significant amount of material from the canister and simultaneously reduce the canister pressure. Consequently, after multiple measurements from a single canister, the total amount of material in the canister is reduced and the amount of material available to fill subsequent sample loops is also reduced. The situation is further complicated because with the removal of subsequent aliquots, the pressure in the canister is decreased. For analytes that are initially near their equilibrium vapor pressure in the canister, or which may be adsorbed on the interior surface of the canister, the reduction of canister pressure can increase the vapor pressure and consequently increase the quantity of available analyte in the canister.

In Figure 5, multiple aliquots are taken from a single 100 mL transfer vessel. Integrated GC-MS signals for aliquot volumes of 10, 100 and 1000 μL are shown for replicate vessels containing 15.6 micromoles of methylene chloride and 5000 μL aliquots taken from replicate vessels containing 4.4 micromoles of dodecane. Because of the high vapor pressure of methylene chloride, dodecane was used with the 5000 μL sample loop to prevent overloading the GC column.

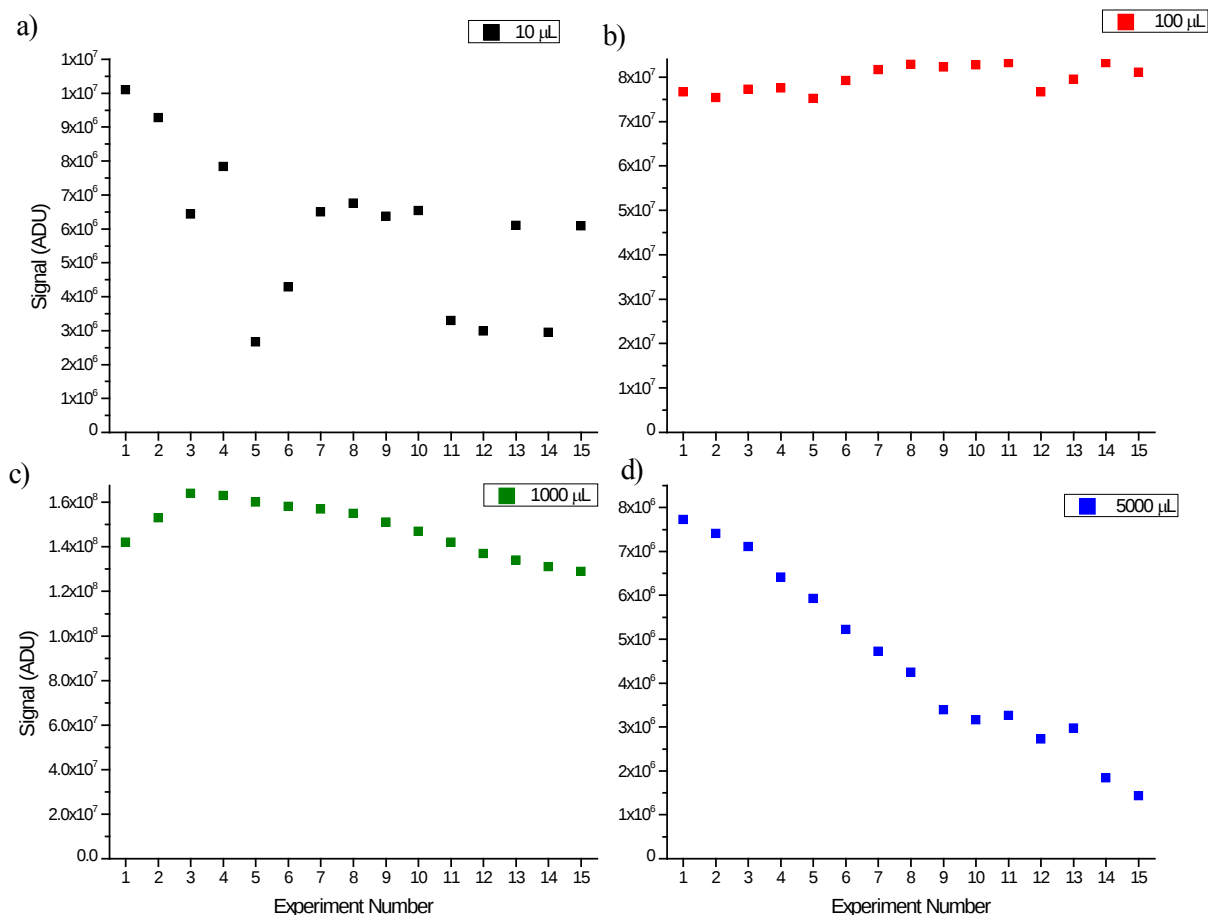


Figure 5: Reproducibility of integrated GC-MS signals for multiple aliquots taken from a single 100 mL MiniCanTM. Aliquot (i.e. sample loop) volumes of (a) 10 μL , (b) 100 μL and (c) 1000 μL are shown for methylene chloride and (d) shows data for 5000 μL dodecane vapor. To highlight relative reproducibility, each volume is shown on a separate plot.

In the case of 10 μL sample loop, reproducibility over 15 measurements was 36% RSD, with average recovery efficiency, corrected for sample loop volume, of $< 1\%$. Replicate measurements show a stochastic pattern without a discernible trend. These poor results are attributed to poor loading of the sample loop. Because the transfer vessel pressure is used to fill the sample loop, and the small inner diameter of the sample loop results in a small pressure drop, sample is inefficiently transferred into the sample loop. The 100 μL demonstrates reproducibility over 15 measurements of 3.9% RSD and a transfer efficiency of $13\% \pm 0.5\%$. It

should also be noted that the first 5 measurements made from the 100 mL canister have an RSD of 1.3%. In Figure 5b a slight upward trend can be seen after the fifth 100 μ L aliquot is removed from the canister. Similarly the first three 1000 μ L aliquots shows an upward trend. This upward trend is attributed to a reduced pressure in the canister and a resulting higher vapor pressure. This pattern is much more noticeable for the 1000 μ L (Figure 5c) sample loop where the measured signal trends upwards for the initial three measurements before eventually falling off. The downward trend in the latter experiments is attributed to sample depletion in the canister. As expected, this depletion phenomena is even more apparent in the 5000 μ L (Figure 5d) sample loop experiment.

It should be noted that while the percent recovery for these samples is low ($\leq 13\%$), the precision of the 100 μ L sample loop indicates sample losses, and ultimately the quantity extracted and delivered, can be corrected for. Thus, multiple aliquots of sample can be reliably delivered from a single canister and the delivered quantity can be calibrated.

Complex vapor mixtures

As has been previously mentioned, it is often necessary to generate complex vapor mixtures to mimic real-world samples. To evaluate the performance of the described system to generate vapor mixtures varying in chemical composition and concentration, two mixtures were gravimetrically prepared and loaded into MiniCansTM. Results from the analysis of the mixtures are provided in Table 1. To avoid chemical reactions in the liquid phase prior to vaporization, each mixture was prepared immediately (i.e. < 2 hrs) before the sample was prepared.

The samples were initially measured with a 100 μ L sample loop, but to measure the low end of the concentration range, a second measurement was made with a 5 mL sample loop. Percent recovery was calculated for each analyte accounting for the sample loop volume. The amounts delivered for the various analytes varied from 10^{-8} to 10^{-11} moles. When the 5 mL sample loop was used, a calculated 10^{-6} moles was delivered for the most abundant two analytes in either mixture. However, the limited dynamic range of the GC-MS prevented the quantitation of this concentration range. It should be noted that even though a two step (100 μ L and 5 mL sample loop) validation is necessary to cover the six-decade dynamic range of the complex mixture sample, this is a limitation only of the analysis technique and not the sample preparation method.

With the notable exception of (–)-carvone, measurements showed good vial-to-vial reproducibility with relative standard deviations $\leq 10\%$. The percent recovery varied from 35-21% and 54-20% for the first and second mixtures, respectively. There is not a clear connection between an analyte's chemical class and its percent recovery. For example, in the second mixture, n-octane and dodecane represent the high and low ends of the percent recovery scale (i.e. 52.3% and 21.8%, respectively). The greatest sample loss is attributed to wall effects within the canister. It is suspected that the differences in recovery are due to a combination of vapor

pressure, concentration, and chemical class. A single parameter does not account for the differences. Based upon these results, artificial vapor mixtures can be prepared in house to accurately represent the natural headspace of real-world materials.

Table 1: List of analytes in two representative complex vapor mixtures and values describing recovery efficiency. Values identified with an asterisk (*) were measured with a 100 μ L sample loop and all others were measured with a 5 mL sample loop. Relative standard deviations were determined from single measurements from three separately prepared MiniCansTM.

Analyte	CAS No.	Vapor Pressure (Pa)	Quantity Delivered (moles)	Percent Recovery (%)	RSD (%)
Diethyl ether	60-29-7	567	$3.97 \times 10^{-8} *$	34.9*	2.65
Methyl tert-butyl ether	1634-04-4	251	$2.35 \times 10^{-8} *$	34.5*	7.12
Tetrahydrofuran	109-99-9	152	6.58×10^{-7}	31.2	7.00
1,2-Dichloroethane	107-06-2	83.9	3.87×10^{-7}	28.6	3.51
Trichloroethene	79-01-6	72.4	2.26×10^{-7}	28.9	3.29
2,5-Dimethylfuran	625-86-5	57.1	1.33×10^{-7}	30.2	2.93
n-Propyl acetate	109-60-4	35.2	7.51×10^{-8}	29.3	6.49
Toluene	108-88-3	27.7	4.47×10^{-8}	31.1	3.27
nonanal	124-19-6	0.532	3.13×10^{-8}	28.0	14.7
Ethyl isobutyrate	97-62-1	21.6	1.45×10^{-8}	32.6	8.92
Ethylbenzene	100-41-4	9.21	8.31×10^{-9}	32.8	8.41
1,7-Octadiene	3710-30-3	22.5	4.74×10^{-9}	31.8	10.7
Styrene	100-42-5	6.21	2.77×10^{-9}	31.9	9.59
Amyl acetate	628-63-7	3.93	1.57×10^{-9}	31.4	11.2
1,2,4-Trimethylbenzene	95-63-6	1.92	1.16×10^{-9}	32.1	9.39
n-Butylcyclohexane	1678-93-9	1.22	5.04×10^{-10}	32.2	10.6
Phenol	108-95-2	0.614	2.86×10^{-10}	25.3	13.4
Camphor	76-22-2	0.225	1.61×10^{-10}	29.2	8.86
(-)-Carvone	6485-40-1	0.0656	9.68×10^{-11}	21.7	20.7
Ferrocene	102-54-5	0.0075	5.58×10^{-11}	22.8	3.41
Dimethyl sulfide	75-18-3	647	$3.89 \times 10^{-8} *$	24.0*	7.85
Carbon disulfide	75-15-0	352	$2.64 \times 10^{-8} *$	26.8 *	5.60
2-Methylfuran	534-22-5	176	1.75×10^{-8}	21.0	3.85
n-Hexane	110-54-3	151	1.15×10^{-8}	22.0	2.31
2-Propanol (Isopropanol)	67-63-0	81.3	7.25×10^{-9}	25.3	2.82
2,2,3-Trimethylbutane	464-06-2	90	4.44×10^{-9}	22.0	4.28
3-Methylthiophene	616-44-4	23.8	1.41×10^{-7}	51.7	1.20
Dodecane	112-40-3	0.2	8.33×10^{-8}	21.8	8.43
n-Octane	111-65-9	14.2	4.90×10^{-8}	52.3	5.33
4-Vinylcyclohexene	100-40-3	12.7	2.85×10^{-8}	53.0	6.84
n-Dibutyl ether	142-96-1	1.84	1.67×10^{-8}	20.5	8.81
N,N-dimethylmethanesulfonamide	918-05-8	7.1	9.32×10^{-9}	53.6	3.88
2,4-Dithiapentane (bis(methylthio)methane)	1618-26-4	5.71	5.28×10^{-9}	39.9	7.44
1-Octanal	124-13-0	2.07	2.75×10^{-8}	47.3	14.31
Benzaldehyde	100-52-7	0.974	9.34×10^{-10}	48.4	8.48
trans-Decahydronaphthalene	493-02-7	0.735	4.35×10^{-10}	48.7	8.34
Acetophenone	98-86-2	0.299	2.61×10^{-10}	43.2	10.91
Naphthalene	91-20-3	0.159	1.14×10^{-10}	39.2	9.02

Preparation of low volatility vapor standards

Even though much of this discussion has focused on vapors of analytes that are liquids at ambient pressure and temperature, additional measures can be taken to generate vapor standards of analytes which are solids (e.g. ferrocene, TNT, cocaine, etc.). These analytes are often of particular interest as training aids and sensor evaluation. To generate vapor standards of this type, solid chemical standard is dissolved in a low boiling point solvent (e.g. methylene chloride or acetone) and injected onto a cryogenically cooled GC inlet. A temperature program can then be crafted to thermally desorb the solvent and the analyte of interest at different times. This approach benefits from selecting a solvent with the lowest possible boiling point, while maintaining chemical compatibility with the analyte of interest.

To demonstrate this approach, 1 μL of 0.2 M ferrocene, dissolved in methylene chloride, was injected into a cryogenically cooled GC inlet held at -100°C . The temperature was subsequently increased to 0°C to vaporize the solvent with the 4-port valve directing the column flow into a 1 L ballast (Figure 1a). After the solvent was removed the inlet temperature was ramped to 200°C and the 4-port valve was actuated to direct the vapor flow into a 100 mL canister. The vapor was then collected and evaluated as previously described.

In the described experiment, a 5 mL aliquot of the MiniCansTM vapor was sampled and measured, delivering 19 picomoles of ferrocene (

Table 2). For the GC-MS used in this work, the limit of quantitation for ferrocene is 10 picomoles, however, smaller sample loops could be employed to deliver smaller quantities for more sensitive detection schemes. For example, the 100 μL loop, which provided the most reproducible results in other experiments, would deliver ca. 380 femtomoles of analyte. It should also be noted that the solvent, methylene chloride, was not completely eliminated, but it was reduced to only 25% that of ferrocene. This experiment was repeated with three separate injections into separate canisters and each canister was analyzed. It is noteworthy that the relative standard deviation of ferrocene measured between three separate MiniCansTM was only 1.0%. The higher RSD for methylene chloride along with the small amount delivered suggests that a trace quantity of solvent was trapped with the ferrocene in the cryogenic inlet. During the initial temperature ramp to drive off the solvent, solvent trapped as inclusions in the ferrocene would not have been vaporized.

Table 2: Table of measured compounds and corresponding relative standard deviations (N=3) for a vapor sample prepared by thermal solvent extraction of 1 μL of 0.2 M ferrocene dissolved in methylene chloride.

	Quantity Delivered (moles)	RSD (%)
methylene chloride	5.0×10^{-12}	21.0
ferrocene	1.9×10^{-11}	1.01

Conclusions

A simple modification to a standard Agilent GC-MS has been described that allows for the generation of trace vapor standards. The described apparatus allows for vapor standards to be transferred to canisters such as the Entech MiniCanTM which can then be transported or stored for later use. Canisters used in this work were 100 mL silanized stainless steel MiniCansTM but larger or smaller canisters could be substituted to change analyte concentration in the final transfer vessel and ultimately the final quantity delivered. No doubt, the surface-to-volume ratio of the canister would influence wall effects observed in this work. Work performed at the US Naval Research Laboratory utilized only a portion of the canister volume allowing multiple measurements to be taken from a single canister, and small discrete aliquots of sample to be measured with precisions of 1% RSD for many analytes. The apparatus described permits vapor samples to be tailored for a single component present in a buffer gas or a complex mixture of compounds. Trace quantities (i.e. $\leq$ picomole) of low vapor pressure analytes can be delivered with the described technique with precision between replicate canisters of ca. 1.0% RSD.

A clear benefit of the described approach is the flexibility it offers. For example, the quantity of delivered sample can be tailored by changing the sample loop volume, and the selection of buffer gas is only limited by its compatibility with the GC pneumatic system used to fill the canister. Moreover, multiple valves can be assembled in series with different volume sample loops to allow the addition of a larger volume of low vapor pressure analyte to a small volume of high vapor pressure analyte. In this way gas mixtures can be prepared online and unrestricted by the vapor pressure of any one analyte in a single canister. Based upon the results described here, artificial vapor mixtures can be reliably prepared in house to accurately represent the natural headspace of real-world materials.

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References

1. Macias, M.S., et al., *Detection of piperonal emitted from polymer controlled odor mimic permeation systems utilizing Canis familiaris and solid phase microextraction-ion mobility spectrometry*. Forensic Sci. Int., 2010. **195**(1-3): p. 132-138.
2. Hoffman, E.M., et al., *Characterization of the volatile organic compounds present in the headspace of decomposing human remains*. Forensic Sci. Int., 2009. **186**(1-3): p. 6-13.
3. Harper, R.J., J.R. Almirall, and K.G. Furton, *Identification of dominant odor chemicals emanating from explosives for use in developing optimal training aid combinations and mimics for canine detection*. Talanta, 2005. **67**(2): p. 313-327.

4. Moore, S., W. MacCrehan, and M. Schantz, *Evaluation of vapor profiles of explosives over time using ATASS (Automated Training Aid Simulation using SPME)*. Forensic Science International, 2011.
5. Shoeib, M., K.A. Brice, and R.M. Hoff, *Airborne concentrations of toxaphene congeners at Point Petre (Ontario) using gas-chromatography-electron capture negative ion mass spectrometry (GC-ECNIMS)*. Chemosphere, 1999. **39**(5): p. 849-71.
6. Joshi, M., K. Rigsby, and J.R. Almirall, *Analysis of the headspace composition of smokeless powders using GC-MS, GC- μ ECD and ion mobility spectrometry*. Forensic Sci. Int., 2011. **208**(1-3): p. 29-36.
7. Murillo, M., et al., *Optimization of experimental parameters for the determination of mercury by MIP/AES*. Talanta, 2001. **54**(2): p. 389-95.
8. Bellamy, A.J. and E. Brzoska, *Contamination of explosive materials with N-methylpyrrolidin-2-one (NMP)*. J. Energ. Mater., 2003. **21**(1): p. 43-55.
9. Verma, A.L., et al., *Hydrogen peroxide vapor sensor using metal-phthalocyanine functionalized carbon nanotubes*. Thin Solid Films, 2011. **519**(22): p. 8144-8148.
10. Salehi-Khojin, A., et al., *Sensitivity of nanotube chemical sensors at the onset of Poole-Frenkel conduction*. Appl. Phys. Lett., 2010. **96**(16): p. 163110/1-163110/3.
11. Boehme, M., F. Voelklein, and W. Ensinger, *Low cost chemical sensor device for supersensitive pentaerythritol tetranitrate (PETN) explosives detection based on titanium dioxide nanotubes*. Sens. Actuators, B, 2011. **158**(1): p. 286-291.
12. Rorrer, L.C., III and R.A. Yost, *Solvent vapor effects on planar high-field asymmetric waveform ion mobility spectrometry*. Int. J. Mass Spectrom., 2011. **300**(Copyright (C) 2011 American Chemical Society (ACS). All Rights Reserved.): p. 173-181.
13. Apodaca, D.C., et al., *Detection of 2,4-Dinitrotoluene (DNT) as a Model System for Nitroaromatic Compounds via Molecularly Imprinted Short-Alkyl-Chain SAMs*. Langmuir, 2011. **27**(11): p. 6768-6779.
14. Shulman, H., et al., *Simulant explosive as training and calibration aid for peroxide-type explosives*. 2009, (Rafael Advanced Defense Systems Ltd., Israel). Application: WO. p. 16pp.
15. Scaringelli, F.P., S.A. Frey, and B.E. Saltzman, *Evaluation of teflon permeation tubes for use with sulfur dioxide*. Am Ind Hyg Assoc J, 1967. **28**(3): p. 260-6.
16. Mitchell, G.D., W.D. Dorko, and P.A. Johnson, *Long-term stability of sulfur dioxide permeation tube standard reference materials*. Fresenius' J. Anal. Chem., 1992. **344**(6): p. 229-33.

