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High throughput analysis of atmospheric volatile organic compounds by thermal injection – isothermal gas chromatography – time-of-flight mass spectrometry

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ABSTRACT

Sixty one volatile organic compounds (VOCs) from a standard gas mixture were separated via isothermal gas chromatography coupled with time-of-flight mass spectrometry (GC–TOFMS) in a ~35 s separation time window (~45 s separation). The VOCs in the standard gas mixture were selected based on the EPA TO-15 methodology. The high throughput separation was achieved with a relatively high total peak capacity (n_c~114), by simultaneously minimizing both on-column and off-column peak width broadening. The on-column contributions to peak width broadening were minimized by taking into account and applying GC separation theory for the selection of column dimensions and carrier gas flow rate conditions. Both fast cryogenic focusing and re-injection of compounds (implemented via a commercially available thermal modulator and referred to herein as *thermal injection* (TI) and fast TOFMS detection (100 scans/s)) were applied to reduce off-column sources of peak width band broadening (sometimes referred to as off-column band broadening). Cryogenic focusing during TI and minimal band broadening-based dilution during separation resulted in preconcentration factors for the detected peaks ranging from 78 (1,4-dichlorobenzene) to 420 (propylene). Since the injected volume for preconcentration was 500 μl, and based on the detected noise levels at selected *m*/*z* for each analyte compound, the concentration limit of detection (LOD) ranged from 67 ppbv (parts per billion by volume) for propylene, to 4 ppbv for freon-12. While application of standard VOC analysis conditions leads to separation times typically ranging from ~30 to 50 min, the isothermal GC–TOFMS method reported herein represents a 40-fold improvement in analysis time while maintaining peak capacity and detection sensitivity that is comparable to traditional GC–MS VOC analysis.

1. Introduction

Gas chromatography coupled with mass spectrometry (GC–MS) is a widely practiced chemical analysis technique, in particular for the analysis of volatile organic compounds (VOCs) in ambient air. Ambient VOCs are important in a variety of fields (atmospheric chemistry, industrial hygiene, defense, etc. [1–3]). Because ambient VOCs have both anthropogenic and natural sources, they are often implicated in causing adverse effects on both human health and the environment. Additionally, ambient VOCs are often present at low concentration levels, making enrichment prior to separation and detection an important step in the chemical analysis process with the goal of achieving a concentration limit of detection (LOD) in the parts-per-billion (by volume, ppbv) range [4]. VOC measurements are also often used to understand time-dependent processes, and therefore, may require high temporal resolution via frequent sampling. Minimization of the total analysis time for the analytical technique is an important challenge to address, and improvement would be welcome [5].

As a benchmark for comparison, it is useful to summarize standard methodologies that have been developed for determination of VOCs in air, such as EPA methods TO-1, TO-14A, TO-15, and TO-17 methods. These EPA standard VOC analysis methods call for either cryogenic or adsorbent-based focusing prior to separation, and suggest usage of long (50 m) and wide bore (200–300 μm inner diameter (i.d.)) columns, with relatively thick stationary phase films (1 μm) operated at temperature program rates of 8 °C/min and an outlet carrier gas flow rate range from 1 to 3 ml/min [4,6–8]. The result is separation times ranging from 30 to 50 min, LODs ranging from 0.02 ppbv (ethylbenzene) to 0.19 ppbv (3-methylhexane), with the MS in full scan mode, and average peak widths at the base of ~12 s. These peak widths result in a separation peak capacity production of ~5 peaks/min

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and total peak capacities, n_c, ranging from ~150 to 250 [2,5]. These quantitative peak capacity metrics are based upon only the separation time and do not take into account the GC oven cool down, which can add several minutes to the total analysis time of standard temperature programmed methods.

GC instrumentation has evolved through the decades to address the general elution problem (GEP), resulting in temperature programming being the common practice to provide sufficient peak capacity for separations of samples containing compounds with a wide range of boiling points. However, there are applications for which temperature programming may not be the best solution given desired analysis goals. For example, with on-line process analysis applications, isothermal GC is preferably practiced to provide a simpler, more robust chemical analyzer than a temperature programmed GC analyzer [9]. Indeed, the use of a temperature program requires that the oven cool down between sample injections, often adding 5–10 min to the total analysis time (with conventional ovens). For situations where high throughput analysis is desired and the samples may not be too complex (e.g., often the case for ambient VOC analysis), isothermal GC may be a more appropriate strategy, eliminating the need for an oven cool down step.

To partially offset the loss in peak capacity for an isothermal separation (relative to a temperature programmed separation of equal time), maximizing the generation of peak capacity requires careful attention to minimizing peak broadening due to the injection, separation, and detection processes to produce narrow peaks. The detected peak width is the result of both on-column contributions (due to the separation processes) and off-column contributions (due to non-separation processes, i.e., injection, detection, electronics, dead volumes, etc). This has led to the development of a wide variety of techniques for minimizing peak broadening due to injection via the production of narrow injection pulses (reports range from fluid logic gates to micro gas valve inlets to high speed diaphragm valves [9–16]). As mentioned above, cryogenic focusing to preconcentrate compounds with subsequent thermal desorption via commercial systems is a standard technique for producing peaks ~12 s wide [5]. Reports of fast thermal desorption systems, capable of producing peak widths at the base ranging from 11 ms to 500 ms wide, function by cryogenically focusing the entire sample in a small volume by heating at high rates, addressing the constraints of commercial thermal desorption systems [17–22]. Unfortunately, most of these thermal injection systems have not been subjected to development and commercialization, remaining firmly in the realm of research reports. As we recently reported [23], one can readily apply a commercially available thermal modulator, designed initially for use in a comprehensive two-dimensional gas chromatography instrument (GC × GC) [24–27] to cryogenically focus and reinject sample in a narrow band pulse onto the single GC column. Such a system should, in principle, benefit from high peak capacity production, due to the narrow peaks generated by thermal injection while simultaneously providing low LODs facilitated by preconcentration.

Short separation run times and narrow peaks demand a detector that is designed to minimize off-column broadening due to a sufficiently small detector volume and an adequate sampling frequency of the peak. For these reasons the FID and TCD are most often the detectors chosen for fast GC [14,17]. For many analyses, the extra selectivity provided by MS detection is very advantageous, since the FID and TCD are univariate detectors. Of the varieties of MS available, TOFMS is recognized as well-suited for the detection of temporally narrow GC peaks because it is inherently non-mass-scanning, and is thus able to collect a complete mass spectrum in as little as 100 μs, though most reports combining fast GC with TOFMS detection have been demonstrated with simple mixtures containing no more than 10 compounds [28]. Additionally the non-scanning nature of the TOFMS also means it does not suffer from the skew problems associated with scanning MS designs (e.g., the quadrupole MS), making post run spectral deconvolution less problematic [29].

Since thermal injection produces narrow injection pulses, and the TOFMS is capable of detecting narrow peaks, it is desirable to maintain the narrowness of the peaks between these two steps of the analysis by minimizing the on-column broadening due to the isothermal GC separation process. It is also necessary to work within the parameters established by the hardware constraints of the instrumentation. These two issues are addressed by selecting column and instrument parameters via in-house GC separation modeling software described in previous reports [14,23,30] and based on the work of Snijders et al. [31,32]. This modeling software allows for both the prediction of the instrumental requirements for operating a column of given dimensions at or near the optimum linear flow velocity of the carrier gas prior to performing any experiments, and also, the subsequent comparison of the theoretical modeling to the peak width band broadening obtained from experimental results.

In this report, separation modeling is initially used to select column dimensions and experimental parameters given the practical constraints of combining thermal injection with GC–TOFMS, referred to as TI–GC–TOFMS (Agilent 6890 GC – LECO Pegasus III TOFMS instrumental platform), and a desired separation run time that would be conducive for high throughput analysis. Unlike our previous work utilizing the thermal modulator for TI [23] the column was operated isothermally and isobarically for the GC separation of a standard VOC mixture. For these studies each analyte compound was nominally ~1 ppmv in the VOC test gas mixture. The contribution of the thermal modulator (from the LECO instrument) to the peak width was then evaluated from the widths and retention times obtained. Though the band broadening introduced by the thermal modulator was more significant than our in-house built device for TI [21], the commercial availability and robustness of the thermal modulator made it more suitable to demonstrate TI in high throughput situations. Next, the potential peak capacity for this instrumental platform is modeled using the given experimental parameters. Finally, the preconcentration performance of TI was evaluated in terms of injected concentration LODs and preconcentration factors.

2. Experimental

2.1. Theoretical considerations for experimental design

In-house developed GC separation modeling software is used to predict the peak band broadening due to the separation processes on the column alone, the separation run time, and the total peak capacity for a given set of column dimensions (length and column inside diameter, i.d.) and outlet carrier gas flow rates. Extending the findings of a previous report [23] to isothermal conditions, balanced by the available column head pressure, the desired separation run time, and the boiling point and polarity range of compounds in the sample, led to the selection of a 100 μm i.d. column with a stationary phase thickness of 0.1 μm and operated at a volumetric outlet flow rate of ~1 ml/min for this report. Based on our separation modeling, a 7.5 m, 100 μm i.d. column, operated at ~1 ml/min and 80 °C, while keeping the column head pressure at ~80 psi absolute (psia), should produce a separation time of ~35 s while remaining well within the capabilities of the electronic pressure controller (EPC) of the GC which was limited to 115 psia. For these separation conditions,

Table 1
Compounds in VOC test mixture, with their GC–TOFMS data.

Compound	Quantitative mass channel	t_R (s)	Original conc. C_{inj} (ppmv)	Peak height (au)	Sensitivity (au/ppmv)	$3\sigma_{Noise}$ (au)	C_{peak} LOD (ppbv)
Propylene	39	9.07	1.06	200	190	13	67
Freon-12	85	9.09	1.04	5200	5000	21	41
Chloromethane	52	9.17	1.05	1600	1500	17	11
Freon-114	85	9.17	1.04	5200	5000	22	4
Vinyl chloride	62	9.23	1.05	1000	980	21	20
1,3-Butadiene	39	9.27	1.06	660	630	15	22
Bromomethane	94	9.39	1.06	1100	1100	19	17
Chloroethane	64	9.44	1.05	670	640	14	20
Ethanol	31	9.44	0.91	1900	2100	20	10
Acrolein	56	9.59	1.10	400	370	20	50
Acetone	43	9.63	1.03	3500	3400	17	5
Freon-11	101	9.61	1.10	4300	3900	18	4
Isopropyl alcohol	45	9.64	1.05	2900	2800	15	5
1,1-Dichloroethene	96	9.83	1.05	1100	1100	19	17
Carbon disulfide	76	10.05	1.03	3200	3100	19	6
Methylene chloride	49	9.90	1.06	1600	1600	23	14
Freon-113	101	9.85	1.02	2700	2700	18	7
trans-1,2-dichloroethene	61	10.16	1.01	2200	2100	18	8
1,1-Dichloroethane	63	10.16	1.02	2400	2300	21	9
methyl-*tert*-butyl ether	73	10.18	1.03	2600	2600	21	8
Vinyl acetate	86	10.26	1.01	230	230	15	66
Methyl ethyl ketone	43	10.45	1.04	3400	3300	17	5
cis-1,2-Dichloroethene	61	10.62	1.03	2100	2000	19	9
Hexane	57	10.47	1.04	1100	1000	19	18
Chloroform	83	10.76	1.03	2600	2500	18	7
Ethyl acetate	43	10.60	1.03	3300	3200	17	5
Tetrahydrofuran	42	10.95	1.05	1100	1000	20	18
1,2-Dichloroethane	62	11.24	1.03	2300	2200	21	9
1,1,1-Trichloroethane	97	11.24	1.01	2500	2500	16	6
Benzene	78	11.50	1.03	2300	2200	19	9
Carbon Tetrachloride	117	11.57	1.00	2100	2100	16	8
Cyclohexane	56	11.59	1.03	940	920	19	20
1,2-Dichloropropane	63	12.27	1.03	1100	1100	23	20
Trichloroethylene	95	12.30	1.01	1400	1400	21	15
Bromo-dichloromethane	83	12.45	1.01	2300	2300	19	8
1,4-Dioxane	88	12.46	1.01	730	720	19	26
Methyl methacrylate	69	12.38	1.00	960	960	17	18
Heptane	43	12.13	1.03	1200	1200	17	14
Methyl isobutyl ketone	43	13.27	1.00	2700	2700	17	6
cis-1,3-Dichloropropene	75	13.33	1.06	1400	1300	17	12
trans-1,3-Dichloropropene	75	14.12	1.07	1500	1400	16	11
1,1,2-Trichloroethane	97	14.47	1.01	1100	1000	16	16
Toluene	91	14.44	1.03	2100	2000	18	9
Methyl butyl ketone	43	15.10	1.05	2800	2700	16	6
Dibromo chloromethane	129	15.68	1.02	1500	1500	17	11
1,2-Dibromoethane	107	16.27	1.02	1600	1600	17	11
Tetrachloroethylene	166	16.50	1.01	900	890	18	20
Chlorobenzene	112	18.74	1.04	1700	1600	18	11
Ethylbenzene	91	19.73	1.03	2300	2200	18	8
p-Xylene	91	20.33	1.01	3700	3700	19	5
m-Xylene	91	20.33	1.01	3700	3700	19	5
Bromoform	173	21.80	1.01	1100	1100	18	17
Styrene	104	22.20	1.03	940	920	19	20
o-Xylene	91	22.48	1.04	2000	200	19	9
1,1,2,2-Tetrachloroethane	83	24.00	1.04	2000	1900	18	9
4-Ethyltoluene	105	31.00	1.01	1700	1700	19	11
1,3,5-Trimethylbenzene	105	31.80	1.02	1700	1600	19	11
1,2,4-Trimethylbenzene	105	36.30	1.02	1500	1400	19	13
1,3-Dichlorobenzene	146	38.75	1.01	1300	1300	19	15
Benzyl chloride	91	40.20	1.01	1100	1100	19	17
1,4-Dichlorobenzene	146	40.04	1.00	1300	1300	19	14

modeling indicated that the peak widths at the base (assuming only on-column broadening for the moment) should be ~88 ms at the beginning of the separation, and ~500 ms at the end (i.e., at ~35 s). In the absence of off-column peak broadening, the theoretical total peak capacity for the isothermal separation was determined to approach 100 peaks at unit resolution. Based on the insight provided by the modeling effort, we experimentally studied these column conditions to demonstrate the separation of a standard VOC mixture.

2.2. Samples and reagents

A standard mixture containing 61 of the 104 volatile organic compounds (VOCs) listed in EPA method TO-15 at a concentration of ~1 ppmv in nitrogen gas (Spectra Gases, Branchburg, NJ) was used in this study as an example of ambient and indoor air quality analysis. The list of total compounds in the mixture appears in Table 1, along with each compound's nominal concentration, retention time and the mass channel used for quantification.

Retention time and quantitative mass channels were determined by comparison to library spectra and visual deconvolution of overlapping peaks.

2.3. Instrumentation

All experiments were performed using a commercially available GC × GC–TOFMS instrument modified for TI and isothermal GC–TOFMS analysis, employing an Agilent 6890 N gas chromatograph (Agilent Technologies, Palo Alto, CA) coupled to a Pegasus III TOFMS and utilizing liquid nitrogen cooled thermal modulator (LECO, St. Joseph, MI), as shown in Fig. 1. A 7.5 m × 100 μm column with a standard 0.1 μm film SPB-5 stationary phase (poly(5% diphenyl/95% dimethyl siloxane), Supelco, St. Louis, MO) was used for the separation. The inlet and capillary transfer line were both set to 200 °C, while the modulator block was set to 50 °C higher than the oven temperature (130 °C). The TOFMS ion source was set to 225 °C and a mass spectrum was collected every 10 ms (mass channels 12–502 m/z). The oven was held at 80 °C and the column head pressure was held at 80 psia throughout the entire run time.

To use the thermal modulator for TI onto the single column of a GC–TOFMS (Fig. 1), the column head was inserted backwards, through the top of the modulator block (in the second oven), down past jet 2, then past jet 1 and out the bottom of the modulator block before being connected to the instrument inlet, such that the modulator stages are in the same order relative to the column flow as for normal GC × GC operation. The section of column between the stock inlet and the thermal modulator, essentially acts as short capillary transfer line coated with stationary phase. This could potentially lead to separation of the compounds prior to injection on the separation column and cause the injection system to be biased towards low boiling point compounds. This is mitigated by introducing the sample to the instrument at the beginning of the 45 s modulation period, giving the high boiling point compounds sufficient time to travel from the inlet to the first cryogenic focusing liquid nitrogen jet. To further minimize compound discrimination, this section of column could in principle be replaced with an integrated deactivated guard column, 500 μl of the standard gas test mixture was transferred from the canister to the GC inlet via a regulator set to 19 psia and a gas tight syringe (Hamilton Company, Reno, NV). Sample was introduced to the instrument inlet ~90 s (two modulation periods) after the initiation of the method (to both ensure freshly cooled nitrogen would be used to cryogenically focus the sample and to allow extra time for any high boiling point compounds from the previous run to elute from the column) giving a total analysis time of ~180 s (four modulation periods) for each sample. In principle, both of these issues could be mitigated (and analysis time reduced) by further development of the instrument and method. Improved modulator control software could reduce this sampling time to a much shorter time as it only needs to be long enough to ensure complete cooling of the thermal injector and cryogenic focusing of the sample. Either increasing the oven temperature, or a back flush step could be implemented to clean the column between runs. With these improvements and utilization of the dead time for separation, the total analysis time could be reduced to ~45 s. In this study, a 45 s modulation period and 2 s hot pulse were used, along with the default jet timing, to ensure complete sample transfer to the separation column.

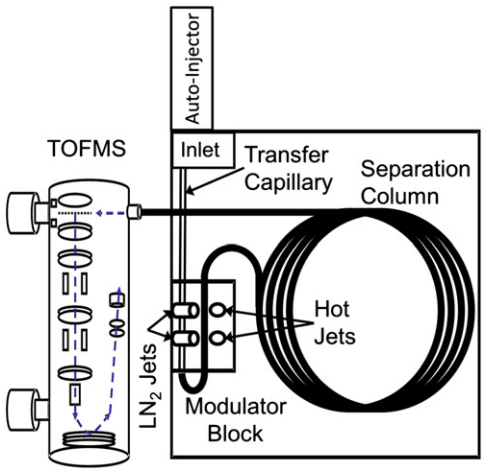

Fig. 1. Schematic of TI–GC–TOFMS instrument (thermal injection onto a single column, using a modified LECO GC × GC–TOFMS instrument upgraded with the commercial thermal modulator). The head of the column is inserted through the thermal modulator and then attached to the stock inlet, before being connected to the TOFMS via a heated transfer line. The section of column between the stock inlet and the thermal modulator essentially acts as a short capillary transfer line. The default timing of the hot and cold jets is used with 45 s modulation period and 2 s hot pulse to produce a narrow pulse of sample on the separation column.

3. Results and discussion

To visualize the GC separation, the analytical ion chromatogram (AIC) was constructed by summing the signal from the selected mass channels for each compound listed in Table 1. The resulting separation is provided in Fig. 2(A) and demonstrates that ~40 s was required for the elution of benzyl chloride (the most retained analyte compound). Use of the AIC is preferred over the TIC since many of the lower m/z channels in the TIC were obscured by permanent atmospheric gases, e.g., nitrogen, oxygen, argon, and carbon dioxide that accompanied each injection. It is evident from the chromatogram in Fig. 2(A) that the majority of compounds in this test mixture, separated at 80 °C, elute early in the separation. To highlight the peak capacity and resolving power provided by the separation conditions in this early time window, a detail of the first 3 s of the chromatogram is presented in Fig. 2(B). From the AIC it appears as though there are only 16 compounds in this time window, with peak widths at the base ($W_b = 4\sigma$) ranging from 115 ms to 150 ms. In this region of the chromatogram the benefit provided by the TOFMS selectivity is apparent in Fig. 2(C), where the two-dimensional (2D) plot of mass channel as a function of retention time allows visual evidence of 29 compounds, instead of what appears to be only 16 in Fig. 2(B). These 29 compounds were readily quantified using selected m/z (see Table 1), as will be described later herein.

We now provide some insight into the fundamentals of the observed peak width band broadening for this relatively fast isothermal GC–TOFMS separation. Excluding off-column sources of peak width band broadening, the on-column band broadening, H, for an analyte with a retention factor of k as derived by Golay is given by

$$H = \frac{2D_{G,o}jf}{\bar{u}} + \frac{1+6k+11k^2}{96(1+k)^2}\frac{d_c^2\bar{u}f}{D_{G,o}j} + \frac{2kd_f^2\bar{u}}{3(1+k)^2D_L} \quad (1)$$

where k is the retention factor of the analyte, d_c is the i.d. of the capillary, d_f is the thickness of the stationary phase film, $D_{G,o}$ is the diffusion coefficient of the analyte in the gas phase at the outlet of the column, j and f are gas compression correction factors, D_L is the diffusion coefficient of the analyte in the stationary phase, and $\bar{u}$ is the average linear velocity of the carrier gas. Since H is quantitatively the length variance per column length, L, of the analyte peak on-column, the appropriate translation to the detected peak width (4σ) in units of time under

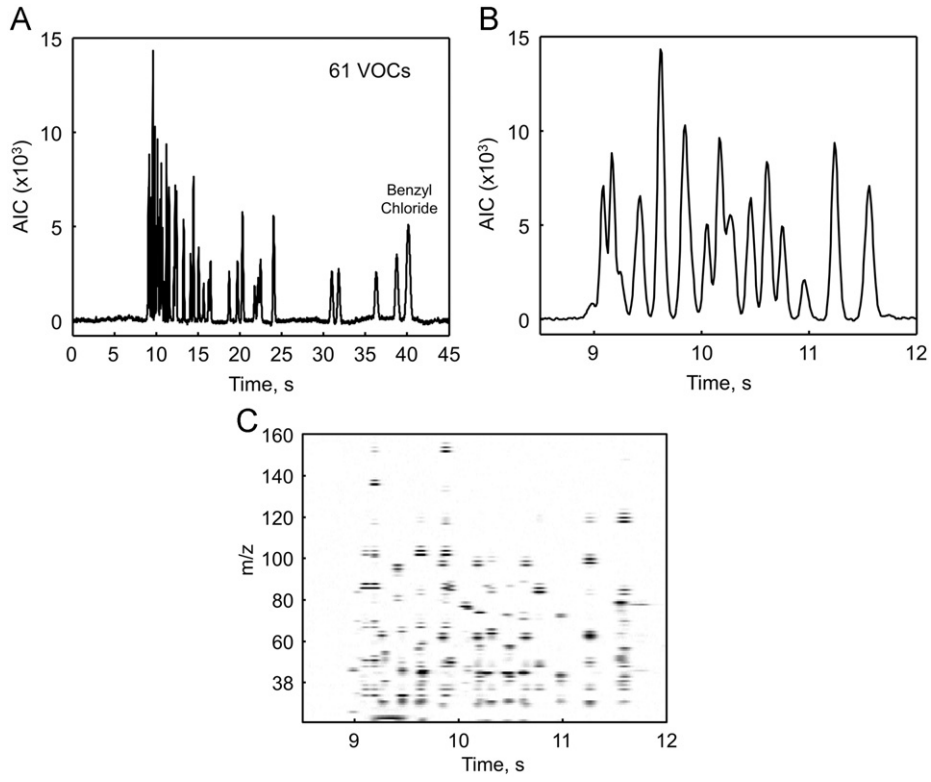

Fig. 2. Separation of a VOC test mixture (Table 1) utilizing TI for sample introduction to a 7.5 m SPB-5 column (100 μm i.d.) primary separation column. Both the column head pressure (80 psia) and the oven temperature (80 °C) were held constant throughout the run. (A) Plot of analytical ion chromatogram (AIC is the sum of mass channels for each compound listed in Table 1) gives an overview of the separation. Retention order is given in Table 1. (B) Detail window of the AIC between 9 and 12 s, where 16 peaks appear to be partially resolved. (C) 2D plot of all mass channels for the time window in (B) demonstrates the added selectivity provided by the TOFMS and provides evidence for 29 VOCs (instead of 16 peaks) in this region of the chromatogram.

isothermal conditions, W_b, is given by [14],

$$W_b = 4\left(\frac{2D_{G,o}jf(1+k)^2t_o^2}{L^2} + \frac{\left(1+6k+11k^2\right)d_c^2 f t_o}{96D_{G,o}j} + \frac{2kd_f^2 t_o}{3D_L}\right)^{1/2} \quad (2)$$

where t_o is the carrier gas dead time for the separation conditions. A linear relationship between peak width and retention factor k is anticipated for isothermal open-tubular capillary GC indicative of separation and overall peak broadening conditions dominated by the middle "mass transfer in the mobile phase" term of the Golay equation (specifically the $11k^2$ portion of the middle term, which in practice makes W_b sufficiently linear with k per Eq. (2)).

As a means of evaluating the contribution of TI (using the thermal modulator for injection onto the primary column) to the band broadening of each peak, the peak width and retention time data obtained from the 7.5 m × 100 μm i.d. column were plotted, W_b as a function of k in Fig. 3, with a best fit line resulting in a slope of 0.11 and a coefficient of determination R^2 of 0.988, hence supporting the assertion that the $11k^2$ term dominates the k dependency in Eq. (2). As k approaches zero in Fig. 3 (analyte compounds that elute in this region are nearly unretained), W_b approaches a y-intercept value of 100 ms (FWHM of ~60 ms). Based on in-house modeling of GC separations [14,23,30], a nearly unretained peak (such as propylene) eluting under these conditions should have a W_b of 88 ms, which is reasonably close the observed value of 100 ms. The discrepancy of 100 ms versus 88 ms suggests that the off-column sources of band broadening (injection, detection, dead volumes, etc) are increasing the width of early eluting compounds by ~14% relative to the theoretical value.

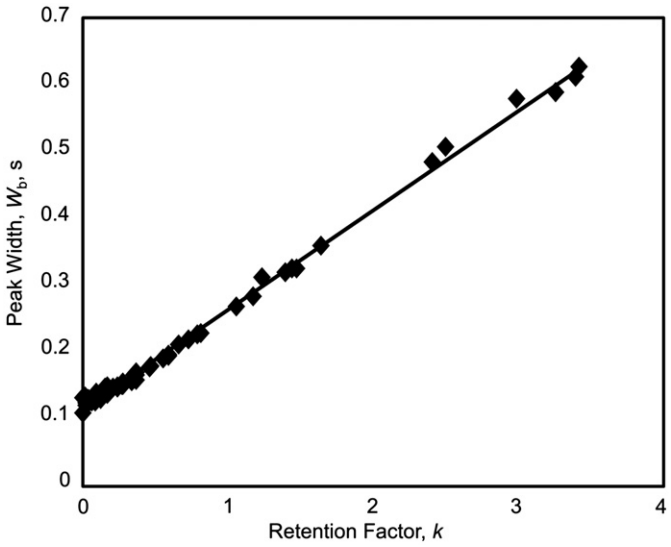

Fig. 3. GC peak width at the base (4σ), W_b, versus the retention factor, k, using all VOCs from Table 1.

To gain a better understanding of the potential benefit toward optimizing total peak capacity offered by implementing TI, an isothermal chromatogram with peaks of equivalent area was simulated based on the experimental data in Figs. 2 and 3 and presented in Fig. 4. Note that the simple, conventional peak capacity equation (i.e., $n_c=(t_R-t_o)/W_b$, where t_R is the retention time of the last eluting peak) does not provide an adequate metric for isothermal GC separations due to the dependence of W_b on the retention factor in Eq. (2). Therefore, retention times were

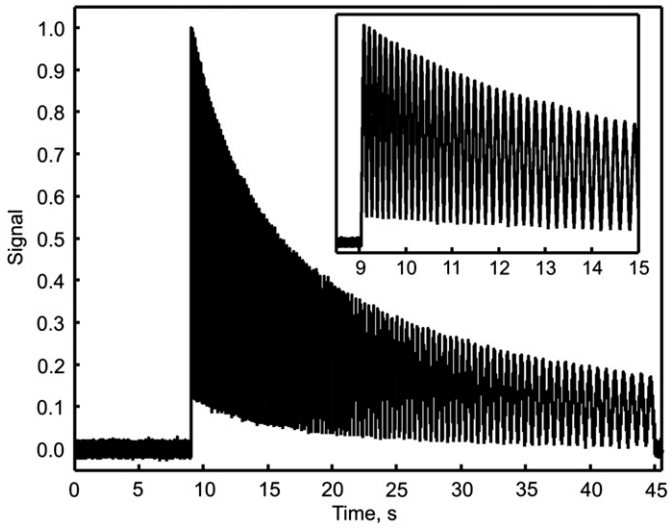

Fig. 4. Simulated isothermal chromatogram in which all peaks have equal area and are at unit resolution. The simulation is based on the data from Figs. 2 and 3. Inset details a smaller time window (9–15 s) and highlights the potential peak capacity available at the beginning of an isothermal separation under conditions applied in this report.

calculated such that adjacent peaks were separated by unit resolution ($R_s=1$) throughout the separation. This was accomplished by applying the following recursive equation for resolution between successive peaks

$$R_s = \frac{t_{R,n}-t_{R,n-1}}{0.5(W_{b,n}+W_{b,n-1})} = 1 \quad (3)$$

The relationship between k, where $k=(t_R-t_o)/t_o$, and W_b defined in the previous paragraph (and illustrated in Fig. 4) was substituted for both $W_{b,n}$ and $W_{b,n-1}$ in Eq. (3). Rearrangement of Eq. 3 gave a linear equation for retention times of successive peaks (and $R_s=1$) with a slope equal to 1.02 and a y-intercept equal to –0.04, allowing the iterative calculation of retention times based on the measured dead time, $t_{R,(n=0)}$. These retention times were used to calculate peak widths from the experimentally observed linear relationship between k and W_b per Eq. (2) and Fig. 3. Individual Gaussian peaks of equivalent area were modeled based on these peak widths, then concatenated and smoothed to give a continuous chromatogram. Finally, simulated white noise was added resulting in the model chromatogram shown in Fig. 4. For a separation time window of ~35 s (similar to that of the VOC standard mix chromatogram) the peak capacity n_c is 114, with the last peak having a k just above 3. For these separation conditions, the peak height decreased by a factor of ~6 between the first and last peak, since the peak width increased by a factor of ~6. The inset in Fig. 4 is a detail of the first 6 s of the modeled chromatogram and emphasizes that the majority of the separation peak capacity is produced early in the separation time where it is most useful for this mixture of VOCs. Since the separation is isothermal there is no need to wait for the oven to cool down and the dead time may be used as separation time for applications in which multiple samples need to be analyzed in succession.

We now consider the performance of this instrumental platform for providing sensitive analytical results. LODs for each in the VOC test mixture were determined using the most sensitive (and sufficiently selective) mass channel (m/z) for each compound in the test mixture. The injected concentration LODs were calculated by dividing the detected noise (for a time interval that represents the analyte peak width) by the analyte sensitivity for a given compound in the test mixture. For the LOD calculation $3\sigma_{Noise}$ was defined as three times the standard deviation of the detected signal collected over a time interval equal to W_b at the beginning of the chromatogram for the specified mass channel of the particular compound. For example, the detected noise for propylene was 13 au (arbitrary units), collected using m/z 39 (per Table 1), for a time interval of 0.10 s (per Table 2). Additionally, the sensitivity was determined using the m/z providing the largest peak height (peak concentration, C_{peak}), divided by the original injected concentration of the compound in the VOC test mixture, C_{inj}. The results of the LOD calculations are summarized

Table 2
Compounds in VOC test mixture with their detected peak width information and preconcentration factor, P, applying Eq. 8.

VOC	W_b (s)	$W_{b,vol}$ (μl)	P
Propylene	0.10	2.0	420
Freon-12	0.13	2.3	370
Chloromethane	0.13	2.3	370
Freon-114	0.12	2.2	380
Vinyl chloride	0.12	2.2	390
1,3-Butadiene	0.11	2.1	400
Bromomethane	0.12	2.3	370
Chloroethane	0.12	2.2	380
Ethanol	0.12	2.2	380
Acrolein	0.12	2.2	380
Acetone	0.12	2.3	370
Freon-11	0.12	2.2	390
Isopropyl alcohol	0.12	2.3	380
1,1-Dichloroethene	0.12	2.3	380
Carbon disulfide	0.13	2.4	360
Methylene chloride	0.13	2.5	350
Freon-113	0.12	2.2	390
trans-1,2-Dichloroethene	0.13	2.3	360
1,1-Dichloroethane	0.13	2.4	360
Methyl-*tert*-butyl ether	0.12	2.3	370
Vinyl acetate	0.13	2.2	380
Methyl ethyl ketone	0.14	2.6	330
cis-1,2-Dichloroethene	0.14	2.6	330
Hexane	0.14	2.5	340
Chloroform	0.14	2.5	340
Ethyl acetate	0.13	2.4	350
Tetrahydrofuran	0.14	2.6	330
1,2-Dichloroethane	0.14	2.6	320
1,1,1-Thrichloroethane	0.14	2.6	330
Benzene	0.15	2.7	320
Carbon tetrachloride	0.15	2.7	320
Cyclohexane	0.15	2.7	310
1,2-Dichloropropane	0.16	2.9	300
Trichloroethylene	0.16	2.9	290
Bromo-dichloromethane	0.16	2.9	290
1,4-Dioxane	0.16	3.0	280
Methyl methacrylate	0.15	2.8	300
Heptane	0.15	2.8	300
Methyl isobutyl ketone	0.17	3.2	270
cis-1,3-Dichloropropene	0.17	3.2	270
trans-1,3-Dichloropropene	0.19	3.4	250
1,1,2-Trichloroethane	0.19	3.5	250
Toluene	0.19	3.4	250
Methyl butyl ketone	0.21	3.8	220
Dibromo chloromethane	0.21	3.9	220
1,2-Dibromoethane	0.22	4.0	210
Tetrachloroethylene	0.22	4.0	210
Chlorobenzene	0.26	4.8	180
Ethylbenzene	0.28	5.1	170
p-Xylene	0.31	5.6	150
m-Xylene	0.31	5.6	150
Bromoform	0.31	5.7	150
Styrene	0.32	5.8	150
o-Xylene	0.32	5.8	150
1,1,2,2-Tetrachloroethane	0.35	6.5	130
4-Ethyltoluene	0.48	8.8	96
1,3,5-Trimethylbenzene	0.50	9.2	93
1,2,4-Trimethylbenzene	0.58	10.4	82
1,3-Dichlorobenzene	0.59	10.9	78
Benzyl chloride	0.62	11.5	74
1,4-Dichlorobenzene	0.61	11.0	78

in Table 1. The injected concentration LODs range from 4 ppbv (Freon-12) to 67 ppbv (propylene), and exhibited no discernible relationship to retention time. Based on the relationship between chromatographic peak width and retention time that governs isothermal GC separations, as is evident in Fig. 3, it might be expected that early eluting compounds would have lower LODs than later eluting compounds. Absence of this relationship is primarily due to the differing sensitivities of the TOFMS mass channels and partly by the high density of compounds toward the beginning of the separation, which required the selection of less sensitive, but more selective mass channels for some compounds (e.g., propyl benzene and chloromethane), in contrast to the low density of analytes eluting toward the end of the separation, allowing for selection of the most sensitive mass channel (e.g., benzyl chloride and styrene).

Previous work has shown that the LECO thermal modulator is a highly capable technology for TI able to produce the narrow injection pulses required for fast GC, while simultaneously focusing (i.e., preconcentrating) the sample. In principle, focusing of the compounds, along with the narrowness of the peaks provided by a high efficiency GC separation, should result in a higher signal-to-noise ratio (S/N) and a lower LOD, as compared to a comparable separation without preconcentration. From a S/N perspective, the separation step and the inherent broadening processes that occur, while reducing interference between compounds, will result in some unwanted dilution. Hence, the separation step works against preconcentration to some extent. Thus, the minimization of on-column broadening due to the GC separation itself is essential, not only for maximizing separation power, but also as a means to maximize detection sensitivity. Therefore, we studied these issues for this instrumental platform.

To relate the maximum detected peak concentration, C_{peak}, to the original sample concentration, C_{inj}, in the 500 μl volume injected, $W_{inj,vol}$, and the preconcentration factor, P, we start by relating the number of moles injected, mol_{inj}, to the original concentration, C_{inj}, by

$$mol_{inj} = C_{inj}\, W_{inj,vol} \tag{4}$$

Since ~95% (assuming a Gaussian peak model for simplicity) of analyte resides within $\pm 2\sigma$ of the detected peak concentration profile, the moles of analyte detected, mol_{det}, is expressed as

$$mol_{det} = W_{b,vol}\, C_{ave} \tag{5}$$

where $W_{b,vol}$ is the volume of the detected analyte peak (and is calculated by multiplying the measured peak width at the base in time, W_b (theoretically defined in Eq. (2)), and the volumetric flow at the column outlet, F_o, (18.3 μl/s in this study). C_{ave} is the average detected analyte peak concentration, which is calculated from the maximum detected peak concentration, C_{peak}, by multiplying by 1.7 (as defined in the Gaussian peak model). Assuming mol_{inj} is equivalent to mol_{det} (and acknowledging a 5% discrepancy between mol_{inj} and mol_{det} due to the definition of Eq. (5)), we equate Eq. (4) and Eq. (5). Solving for C_{ave} gives the following expression

$$C_{peak} = \left(\frac{1.7\, W_{inj,vol}}{W_{b,vol}}\right) C_{inj} \tag{6}$$

We now define the preconcentration factor, P, as

$$P = C_{peak}/C_{inj} \tag{7}$$

Experimentally, it follows from Eq. (6) that P is obtained from Eq. (7) according to,

$$P = \frac{1.7\, W_{inj,vol}}{W_{b,vol}} \tag{8}$$

The resulting preconcentration factors are summarized in Table 1 and range from 420 for the narrowest analyte peak (propylene) to 78 for the broadest analyte peak (benzyl chloride). It is important to note that these values include all analysis steps from injection to detection. With TI–GC–TOFMS, reduction in preconcentration (compared to traditional VOC trapping systems) resulting from the relatively low sample capacity of the standard stationary phase in the modulator is offset by the narrow (and consequently high signal) peaks generated by the fast injection and maintained throughout the separation process by selection of optimal instrumental parameters within the hardware's constraints.

There are several issues to continue to address concerning the performance of this fast isothermal TI–GC–TOFMS instrument. First, the EPA TO-15 method suggests that baseline resolution (R_s=1.5) of benzene and carbon tetrachloride is indicative of acceptable chromatographic performance [4], while the fast separation we report provides a R_s=0.6 between these two compounds. However, the selectivity provided by the TOFMS compensates for the lower resolution and readily allows mathematical resolution (deconvolution) of benzene and carbon tetrachloride. Second, while the LODs achieved by the fast isothermal TI–GC–TOFMS instrument are in the ppbv range suggested by the EPA, they are significantly larger than those presented in the literature. This is primarily due to the large difference in sample volume being preconcentrated. While standard methods suggest preconcentrating up to 1.0 l aliquots of gaseous sample and the examples in the literature use 25 ml to 600 ml aliquots of sample, the LODs presented herein are calculated from preconcentration of a 500 μl sample. Future work should address this issue by exploring the ability of TI to preconcentrate larger sample volumes via an increase in the column stationary phase thickness within the TI unit.

4. Conclusions

With the LECO thermal modulator configured to provide TI onto a single column, and careful selection of column dimensions and flow conditions according to theoretical modeling, band broadening due to both injection and the column has been significantly reduced. This preserved the focusing provided by TI and resulted in preconcentration factors as high as 420. The isothermal conditions applied herein gave a GC system with relatively high total peak capacity (n_c=114 peaks at unit resolution) that suffered somewhat in practice from overlapped chromatographic peaks. Resolution of chromatographically overlapped peaks required the selectivity provided by mass selective detection and resulted in a high throughput analysis with injected concentration LODs as low as 4 ppbv.

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