

Development and Application of a Milli-Whistle for Use in Gas Chromatography Detection

Cheng-Huang Lin,* Chien-Hung Lin, Yi-Shiuan Li, and Yi-San He

Department of Chemistry, National Taiwan Normal University, 88 Sec. 4, Tingchow Road, Taipei, Taiwan

A simple milli-whistle was developed for the use in GC (gas chromatography) detection, in which, compared to a thermal conductivity detector (TCD), 1 order of magnitude superior sensitivity can be obtained. The milli-whistle can be connected to the outlet of a GC capillary. The gas and makeup gas passing through the capillary produces a sound as it passes through the milli-whistle (i.e., the gas of the GC eluate). The sound can easily be detected by a microphone, which, after a Fourier transform (FT) by means of a LabVIEW (Laboratory Virtual Instrumentation Engineering Workbench) built-in program, a very sharp frequency peak (full width at half-maximum, ~ 1.6 Hz) can be simultaneously observed. As a result, GC elutes can be qualitatively determined on the basis of their retention times, and a quantitative analysis can be achieved on the basis of the frequency shifts. When the makeup and carrier gases used were nitrogen, in the case of gas samples, including hydrogen, helium, argon, and carbon dioxide, the limits of detection were found to be $\sim 3 \mu\text{L}$ /each injection; in the case of liquid samples, including methanol, cyclohexane, tetrahydrofuran, hexane, and acetone, the limits of detection were determined to be $\sim 10 \mu\text{g}$ /each injection, respectively. When the gases were changed to hydrogen, the limits of detection were dramatically improved. When acetone was selected as the model sample, a linear relationship was found in the range of 0.2–200 μg /injection.

A variety of different detectors are currently used in gas chromatography (GC), and each has a unique advantage and disadvantage regarding sensitivity, precision, and simplicity of use. Raymond P. W. Scott summarized at least 20–30 types of chromatographic detectors in his book in 1996.¹ Among these detectors, GC/MS (gas chromatography/mass spectrometry) is undoubtedly the most popular and well-developed, but flame ionization detector (FID),^{2–5} thermal conductivity detector

(TCD),^{6–8} and electron-capture detectors (ECD)^{9,10} are also frequently used. In addition to these, several unique detectors have also been developed, such as the sonar detector¹¹ and surface acoustic wave (SAW).^{12–15} The physical characteristics of a jet-edge-resonator whistle, high frequency whistles, were reported in 1953 but were not specifically used for GC separations.¹⁶ An ultrasonic gas chromatograph effluent detector was described in 1964, which functioned by means of a “sound-cell”, where two identical transducer mounts and a Teflon sound tube were used.¹⁷ Herein, we report on the design and construction of a milli-whistle, a simple, new type of GC detector, for the first time, which is based on frequency shifts generated when the analyzed gas passes through the whistle. Since the temperature of a GC oven and the flow rate of the carrier gas can be controlled very precisely, a sound wave generated from the milli-whistle can be observed as a single peak at a specific frequency, after Fourier transform. Qualitative analyses can be performed on the basis of retention times corresponding to various analytes, while the concentration levels of the GC elutes can be determined on the basis of frequency shifts. In this study, five different gases (H_2 , He, O_2 , Ar, and CO_2) and five commonly used organic solvents (methanol, acetone, hexane, tetrahydrofuran, and cyclohexane) were selected as models. Details of the experimental conditions and the relationship between frequency shifts and sample injection volume are reported.

EXPERIMENTAL SECTION

Reagents. All of the ultrapurified gases (>99.99%) were obtained from Fong-Ming Industrial (Taiwan). These included hydrogen, helium, nitrogen, oxygen, argon, carbon dioxide, and synthetic air. Hexane (liquid chromatography grade, 98.1%) was

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* Corresponding author. E-mail: chenglin@ntnu.edu.tw.

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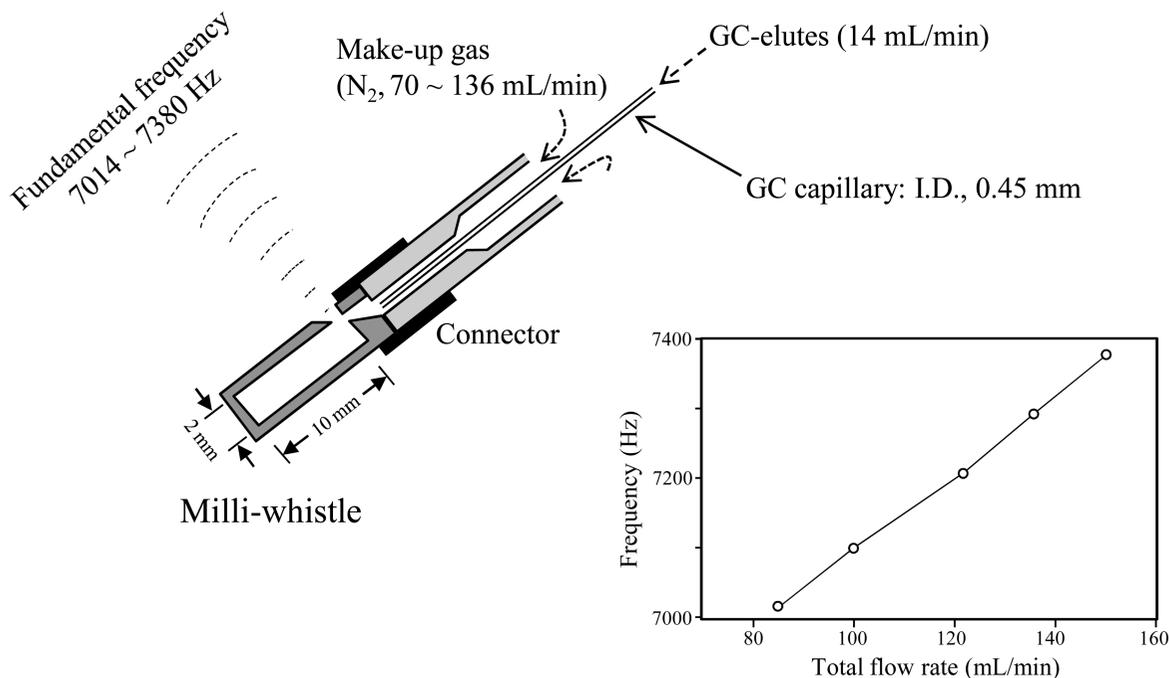


Figure 1. Schematic diagram of the milli-whistle used in this study. The relationship between flow rate and produced frequency is shown on the right side.

purchased from Mallinckrodt Baker (USA). Tetrahydrofuran (THF) and cyclohexane (liquid chromatography grade, 99.7%) were purchased from Alps Chem. Co., Ltd. (Taiwan); methanol and acetone (spectrophotometric grade, 99.9% and 99+ %, respectively) were obtained from ACROS (Belgium). All other chemicals were of analytical grade and were obtained from commercial sources.

Apparatus. A gas chromatograph (GC 5890; Hewlett-Packard, Avondale, PA) equipped with a DB-VRX column (30 m × 0.45 mm × 1.4 μm) was used in this study; nitrogen or hydrogen was used as the makeup and carrier gas, respectively. A thermal conductivity detector (Hewlett-Packard) was also used for comparison. The milli-whistles were made of brass and were 2 mm in diameter and 6–25 mm in depth; a microphone (PCB Piezotronics, Inc.; Model 426E01; detectable range: 6.3–125 000 Hz) was used to acquire the sound. Both devices were located inside a stainless vacuum chamber (I.D./depth, 4 in./10 cm), which was used as a sound insulation chamber. The sampling rate of the microphone was set at 20 000 Hz, and all of the collected data were used for Fourier transformation; the sampling rate for the chromatogram was 5 points/sec. A magnetic injector, as described in a previous study, was used for pressurized gas injection.¹⁸ A cylinder injector (1.0 μL) was also used for liquid injection. A data acquisition system (NI PXI 1042Q; National Instruments, USA), equipped with a PXI 6221 device and a PXI-4461 device, was used to acquire real-time data from the microphone. A LabVIEW 9 (Laboratory Virtual Instrumentation Engineering Workbench) program built-in Fourier transform function was used for real-time sound frequency monitoring.

RESULTS AND DISCUSSION

Milli-Whistle/GC System. Figure 1 shows a schematic diagram of the milli-whistle system used in this study. The milli-

whistle/GC system consists of a commercial GC oven, a magnetic injector, the sound insulation chamber, a temperature sensor, the milli-whistle, and the microphone receive/record devices. The magnetic injector (an in-house fabricated microcontrol valve) was prepared by modifying a standard pulse nozzle, as described in a previous report.¹⁸ The injection volume of the pressurized sample was adjusted by changing the background pressure, the inner diameter of the capillary, the capillary length, and the injection time. During regular operation at a background pressure of 3 kg/cm², the injection volume of gas and liquid sample can be readily controlled in the range of 3–90 μL and 40–280 nL/each injection, respectively (linear relationships, both $R^2 = 0.9990$). In this study, hundreds of whistles were examined, and after evaluating them, a small whistle (I.D., 2 mm; depth, 10 mm) was selected as the model whistle. The relationship between flow rate and the produced frequency is shown in the right side of Figure 1. When nitrogen was used as the carrier gas (flow rate, 14 mL/min) associated with makeup gas (70–136 mL/min), the milli-whistle produces frequencies in the range of 7014–7380 Hz. The frequency of the sound shifts when the flow rates of makeup/carrier gases, temperature, or the amount of analytes change.

Quantitative Analysis Based on Frequency Shifts. It is well-known that if humidity and temperature are neglected, a closed pipe (i.e., the milli-whistle) will have an approximate resonance of

$$f = v/4(L + 0.4d) \quad (1)$$

where f , v , L , and d are the frequency, the speed of sound, the depth, and the diameter of the closed pipe, respectively. The approximate speed of sound can be calculated from

$$v = (\gamma RT/M)^{1/2} \quad (2)$$

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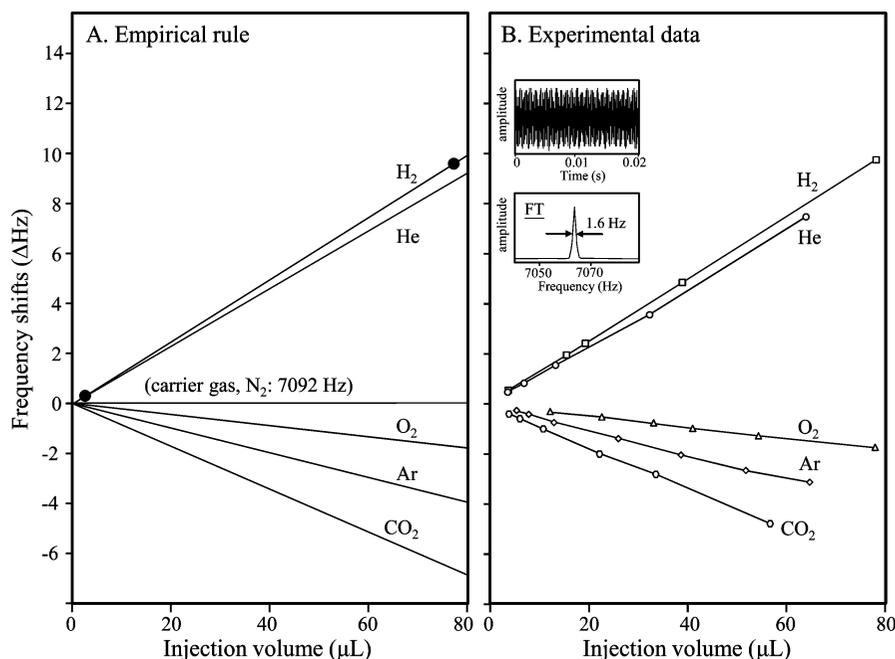


Figure 2. Empirical relationship between frequency shifts (ΔHz) and various gas injection volumes (A, empirical; B, experimental data). The inset shows a spectrum of the real-time sound frequency and the identical spectrum after Fourier transform. GC conditions: inlet temperature, 35 °C; the column oven, 35 °C for 5 min without temperature programming. Head pressure, 15 psi. Make-up/carrier gas (N_2), 125/14 $\text{mL}\cdot\text{min}^{-1}$.

where γ , R , T , and M are the heat capacity ratio (air, 1.4), the molar gas constant (8.31 $\text{J}/\text{K}\cdot\text{mol}$), absolute temperature in degrees Kelvin, and molar mass (air, 28.8×10^{-3} kg/mol), respectively. Hence, at room temperature, the relationship between the depth of closed pipes and frequencies generated can be derived from the relationship below

$$f = (\gamma RT/M)^{1/2}/4(L + 0.4d) \quad (3)$$

On the basis of this equation, when a closed pipe (I.D., 2 mm; depth, 10 mm) is used at 25 °C, the empirical frequency should be ~ 8021 Hz (in air). However, the milli-whistle produces frequencies in the range of 7014–7380 Hz, which indicates that appropriate experimental factors are needed to modify the eq 3. As a result, it can be concluded that when a stream of gas, including sample gas/carrier gas and makeup gas, passes through the whistle, a sound is produced and its frequency can be calculated by the followed equation.

$$f = \alpha \sqrt{\frac{\gamma RT}{\left(1 - \frac{V_s}{V_m + V_c}\right) \times 2\Delta t \times M_c + \frac{V_s}{V_m + V_c} \times M_s}} \quad (4)$$

Herein, α is the modifying factor acquired from experimental data. T and Δt are the inside temperature of the sound insulation chamber and the experimentally determined peak width of the sample, respectively. V_s , V_m , and V_c are the volumes of sample gas, makeup gas, and carrier gas; M_c and M_s are the molar mass of the carrier and sample gas, respectively. Figure 2A shows the empirical relationship between frequency shifts (ΔHz) and various gas injection volumes (0–80 μL for hydrogen, helium, oxygen,

argon, and carbon dioxide, respectively); makeup/carrier gas was nitrogen which produces a fundamental tone at 7092 Hz. The molecular weights of hydrogen and helium are lower than the carrier gas (N_2), so that the frequencies observed are higher than that of the carrier gas (N_2), whereas gases with molecular weights higher than N_2 would produce lower frequencies. When the experimental factors (α) for hydrogen, helium, oxygen, argon, and carbon dioxide were set at 0.94, 0.96, 0.64, 0.41, and 0.57 (in Figure 2A), respectively, compared to the experimental data (as shown in Figure 2B), we found that they match each other perfectly. For example, in the case of hydrogen, the line in Figure 2A was derived for the case where α , Δt , T , V_m , and V_c were 0.94, 5.7 s, 25 °C, 125.5 mL, and 14 mL, respectively. Assuming that the injection volumes of hydrogen are 4 and 78 μL (indicated as “●” symbols), the calculated results should be 7092.05 and 7101.76 Hz, respectively. The values are nearly identical to the experimental data (7092.05 and 7101.79 Hz, as shown in Figure 2B, H_2 line). The detected frequency shifts are completely consistent with the empirical predictions, suggesting that the milli-whistle/GC system functions very well. It can, therefore, be concluded that, in the case of a gas sample, if α values can be determined under various conditions, quantitative analyses can be performed quickly. The limits of detection of the five model gases were in the range of 3–5 μL /each injection. The inset in Figure 2B shows a spectrum of real-time sound frequency and the same spectrum after Fourier transform. The narrow width (fwhm, 1.6 Hz) indicates that the milli-whistle/GC system also provides for high spectral resolution. On the other hand, the milli-whistle/GC system can also be used for the analysis of liquid samples. Figure 3 shows the relationship between liquid injection volumes (nL) and frequency shifts (ΔHz) for five common organic solvents, i.e., cyclohexane, tetrahydrofuran, hexane, and acetone, respectively. In this case, due to the

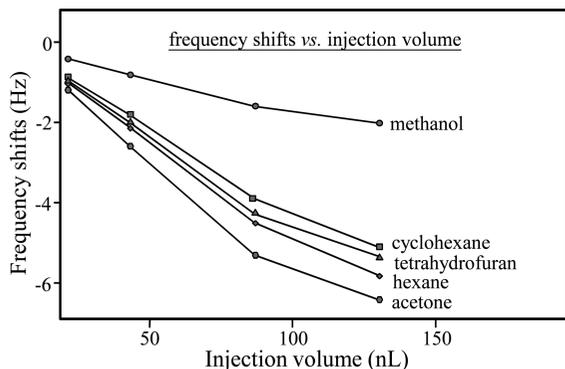


Figure 3. Relationship between liquid injection volumes (nL) and frequency shifts (Δ Hz) for five common organic solvents, including methanol, cyclohexane, tetrahydrofuran, hexane, and acetone, respectively. GC conditions: inlet temperature, 180 °C; the column oven, 80 °C for 5 min without temperature programming. Head pressure, 15 psi; makeup/carrier gas (N_2), 115/14 mL \cdot min $^{-1}$.

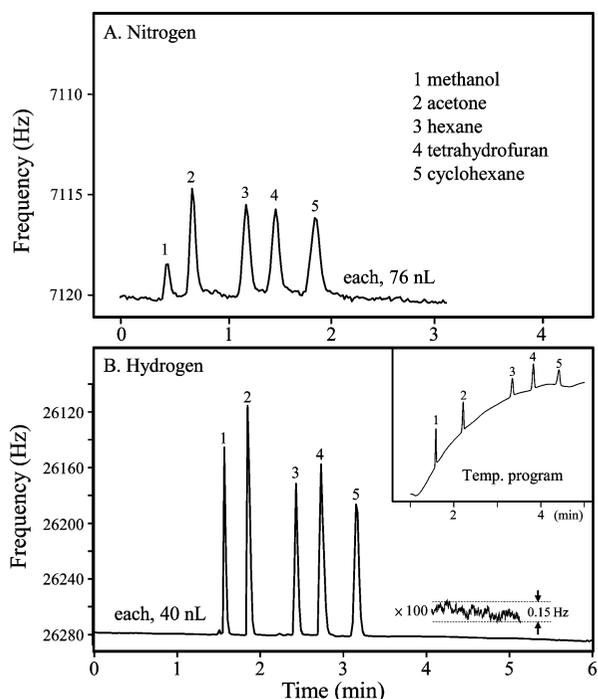


Figure 4. Typical GC/MS chromatograms for five organic solvents based on the milli-whistle/GC system. Make-up and carrier gases: A, nitrogen; B, hydrogen. Peaks, 1–5: methanol, acetone, hexane, tetrahydrofuran, and cyclohexane, respectively. GC conditions: column, DB-VRX column; inlet temperature, 150 °C; the column oven, 80 °C for 5 min without temperature programming. Flow rates: A (N_2), makeup gas/carrier gas, 140/14 mL \cdot min $^{-1}$; B (H_2), makeup gas/carrier gas, 280/6.8 mL \cdot min $^{-1}$. Inset in B, data was obtained by a temperature programming: the column oven was held at 40 °C for 0.5 min, then programmed from 40 to 70 at 10 °C/min, and held for 2 min.

coefficients of expansion (liquid to gas phase), the densities and boiling points of the five solvents are different, and as can be seen, there is no linear relationship between them. In the other words, the frequency shifts are more difficult to predict, compared to a gas. The limits of detection for the five organic solvents were in the range of 10–15 μ g. In order to compare the efficiency of the milli-whistle/GC system when a different gas is used, Figure 4A,B shows the results obtained when nitrogen and hydrogen, respec-

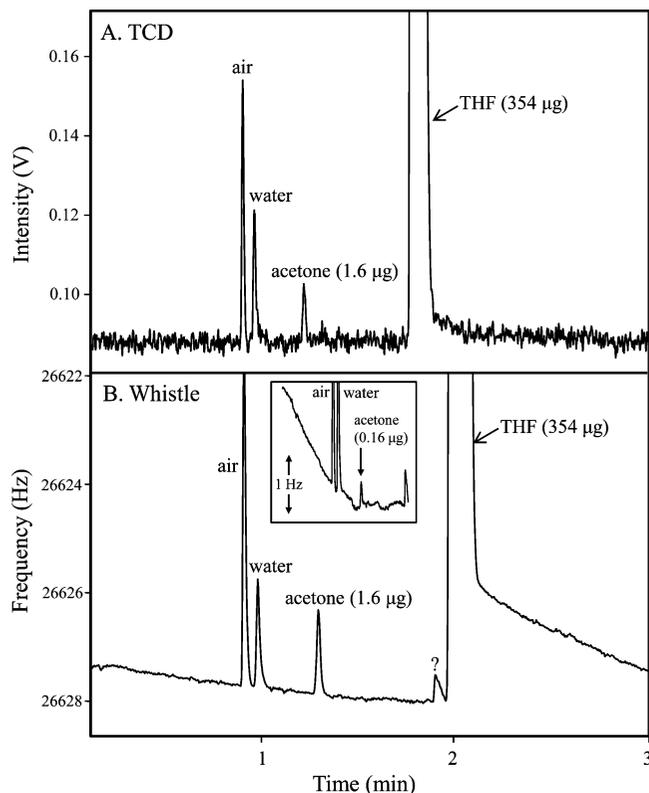


Figure 5. (A) TCD; (B) the milli-whistle. Typical GC/MS chromatogram for a test sample (a 5 μ L sample of acetone was added to 995 μ L of THF) with a 0.4 μ L injection (acetone, 1.6 μ g) by sandwich injection mode; inset, acetone, 0.16 μ g. Make-up and carrier gas: H_2 . GC conditions: A, inlet temperature, 150 °C; the column oven, 80 °C for 5 min without temperature programming. TCD detector, 220 °C. Head pressure, 4 psi; reference gas, 8 mL/min; carrier gas, 6.8 mL. B (H_2), makeup gas/carrier gas, 280/6.8 mL \cdot min $^{-1}$.

tively, are used. In Figure 4A, a GC chromatogram of a mixture of the five solvents (v/v: 1/1) is shown using nitrogen gas; the injection volume for each sample was 76 nL. The findings show that the molecular weight of methanol is close to nitrogen but much smaller than the others, and as a result, a weaker peak was obtained. Instead of nitrogen, the makeup/carrier gases were changed to hydrogen, and the results are shown in Figure 4B. The findings show that the peak intensities were dramatically improved when hydrogen was used; the fundamental frequency was changed to \sim 26 280 Hz. It should be noted that the background noise (the spectrum above the GC chromatogram, expanded by 100-fold) is only \sim 0.15 Hz, indicating that the milli-whistle/GC system also provides a high degree of stability. A very important criteria for a GC detector is how it performs under conditions of temperature programming. The inset (in Figure 4B) shows the result obtained when a temperature program was applied. Herein, the column oven was held at 40 °C for 0.5 min, then programmed from 40 to 70 at 10 °C/min, and held for 2 min (makeup/carrier gas: hydrogen, flow-rate 280/6.8 mL \cdot min $^{-1}$). In this case, the five peaks are located on the background baseline with almost the same intensity (frequency change); the retention time is longer, but the separation efficiency becomes better. In this case, a background subtraction is recommended.

Application. In order to evaluate the performance of the milli-whistle/GC system, the results were compared to data obtained using a thermal conductivity detector (TCD). As shown in Figure

5A, using a TCD, a test sample (a 5 μL sample of acetone was added to 995 μL of THF), with a 0.4 μL injection (the mass of acetone, 1.6 μg) by the sandwich injection mode (air–sample–air) was examined. The intensity (mV) change for acetone was found to be 0.02 V. The THF solvent generates a large peak; water (impurity in the solvent) and air peaks are also observed. However, the retention time is too short to permit the separation of nitrogen and oxygen. In contrast to this, as shown in Figure 5B, when the milli-whistle detector was used in conjunction with hydrogen as the makeup/carrier gases, the frequency change for acetone was found to be 1.6 Hz. The S/N (signal-to-noise) ratio of the baseline is much better than that of a TCD. When the test sample (acetone) was further diluted to 1/10 with THF, acetone could be detected at levels as low as $\sim 0.1 \mu\text{g}$ (S/N ratio = 3; as shown in the inset in Figure 5B.) Furthermore, a linear relationship was found in the range of 0.2–200 μg /injection for the milli-whistle system, whereas it was in the range of 2–100 μg /injection for the TCD used in this study. Thus, on the basis of direct comparisons, we concluded that the sensitivity of the milli-whistle detector indeed is superior to that of a TCD.

CONCLUSION

In this study, we describe the development of a novel GC detector based on detecting frequency shifts using a milli-whistle.

The detected frequency shifts for various gases were in good agreement with empirical values. It is noteworthy that qualitative analyses can be performed on the basis of frequency shifts. Some additional efforts remain in terms of improving the limit of detection, including the use of a smaller whistle (to decrease the use of makeup gas) and the use of a lock-in amplifier. Since the capability of the milli-whistle/GC system in terms of sensitivity is superior to a regular TCD, it would be very useful in analyzing samples that are difficult to detect by mass spectrometry or by a flame ionization detector. The present method is simple, is consistent with green chemistry, and has the potential for use in practical analyses.

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