Research Article

Determination of elemental composition of volatile organic compounds from Chinese rose oil by spectral accuracy and mass accuracy

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Elemental composition determination of volatile organic compounds through high mass accuracy and isotope pattern matching could not be routinely achieved with a unit-mass resolution mass spectrometer until the recent development of the comprehensive instrument line-shape calibration technology. Through this unique technology, both m/z values and mass spectral peak shapes are calibrated simultaneously. Of fundamental importance is that calibrated mass spectra have symmetric and mathematically known peak shapes, which makes it possible to deconvolute overlapped monoisotopes and their ^{13}C-isotope peaks and achieve accurate mass measurements. The key experimental requirements for the measurements are to acquire true raw data in a profile or continuum mode with the acquisition threshold set to zero. A total of 13 ions from Chinese rose oil were analyzed with internal calibration. Most of the ions produced high mass accuracy of better than 5 mDa and high spectral accuracy of better than 99%. These results allow five tested ions to be identified with unique elemental compositions and the other eight ions to be determined as a top match from multiple candidates based on spectral accuracy. One of them, a coeluted component (Nerol) with m/z 154, could not be identified by conventional GC/MS (gas chromatography/mass spectrometry) and library search. Such effective determination for elemental compositions of the volatile organic compounds with a unit-mass resolution quadrupole system is obviously attributed to the significant improvement of mass accuracy. More importantly, high spectral accuracy available through the instrument line-shape calibration enables highly accurate isotope pattern recognition for unknown identification. Copyright © 2011 John Wiley & Sons, Ltd.

The determination of elemental compositions (DEC) of volatile organic compounds can be accomplished through two basic approaches. One approach is to use the unit-mass resolution quadrupole-based GC/MS (gas chromatograph/ mass spectrometry) followed by library search[1–3] and another approach relies on high mass accuracy achieved by high resolving power accurate mass instruments such as double-focusing magnetic sector,[4] time of flight (TOF),[5] Fourier transform ion cyclotron resonance (FTICR),[6] and Orbitrap.[7] The former enjoys great popularity among the majority of GC/MS users because the quadrupole GC/MS is easy to use, inexpensive, and highly reliable; however, this unit-mass resolution instrument approach suffers from a lack of high mass accuracy and spectral accuracy which are necessary to determine the elemental composition of unknowns in many challenging cases. These cases include ambiguous library search results due to similar match values, non-searchable chemical ionization mass spectra, true unknowns not represented among the available library spectra, and composite spectra acquired during coelution of different compounds. Although these difficult DEC problems can be resolved by the latter approach with high mass accuracy

through high resolving power mass spectrometers, these instruments come with high cost to purchase and maintain and are not as user-friendly as the quadrupole instruments; therefore, it is desirable to perform DEC on a unit-mass resolution quadrupole instrument, if possible.

In a conventionally calibrated unit-mass resolution mass spectrometer, achievable mass accuracy typically does not allow elemental composition determination. The major reasons for the lack of mass accuracy are twofold. First, the mass spectral peak shape is asymmetric and distorted. As a result, it is difficult to obtain the exact center of the peak for accurate mass measurement. Second, by the definition of unit-mass resolution, the monoisotope peak (A) overlaps its ^{13}C-isotope peak (A + 1), which also hinders accurate mass determination. Early attempts to achieve DEC on a unit-mass resolution quadrupole GC/MS platform were made for identification of uncommon plant metabolites by improved mass accuracy and the patterns of isotope peak intensity ratios.[8] In this current presentation, the application of a novel approach to determining elemental compositions of volatile organic compounds with a unit-mass resolution quadrupole mass spectrometer is described. This is based on high spectral accuracy and mass accuracy achieved through unique instrument line-shape calibration technology as reviewed extensively in a recent feature article in *Analytical Chemistry*.[9] Briefly, the instrument line-shape calibration provides comprehensive mass spectral calibration not only on exact m/z values, but, more importantly, on the mass spectral

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peak shape as opposed to conventional mass spectral calibration performed on *m/z* values only. Consequently, the calibrated spectra have mathematically well-defined and symmetrical peak shapes, which allow mathematical separation of A and A + 1 peaks resulting in accurate centroiding for accurate mass measurements. In addition, the same known peak shape can be used to generate theoretical profile mass spectra to effectively match experimental spectra for DEC.

There have been reports[10–14] on DEC for volatile organic compounds with unit-mass resolution GC/MS data through this unique calibration method. This paper describes such application with explicit details from experimental design to data interpretation. Elemental composition determination will be demonstrated through examples of volatile organic natural products from Chinese rose oil including a challenging case where an unknown compound could not be identified by GC/MS and library search because of its weak mass spectral signals and coelution with a major component.

EXPERIMENTAL

The Chinese rose oil of the KuShui type was manufactured and provided by Maolin Rose Industrial Development Company, Ltd. (Yongdeng, Gansu, China) and was used without further purification before analysis by a GC/MS 7890A/ 5975 C system from Agilent Technologies (Santa Clara, CA, USA). Containing over 130 components, this complex natural product was separated using a DB-1701 column, 60 m long, 0.25 mm i.d., 0.25 μm film thickness, from Agilent Technologies; a starting temperature of 60 °C, held for 1 min, ramped to 270 °C at 2 °C min^{-1}, and held for 10 min. For the separation of coeluting components, a 2D GC/GC/MS system was used. This 2D system consists of an Agilent 7890A gas chromatograph, an Agilent 7890A/5975 C GC/MS system, and a Gerstel (Germany) 2D GC/GC interface that transfers a portion of eluate from the first GC system to the second GC for further separation. The first GC separation used a GC column and operating conditions identical to those described in the above GC/MS analysis. For the second-dimension GC/MS separation, a CP-Wax 57CB column, 25 m long, 0.25 mm i.d., 0.2 μm film thickness, from Varian (Walnut Creek, CA, USA), was employed with temperature programming starting at 40 °C, held for 5 min, ramped at 3 °C min^{-1} to 220 °C, and held for 5 min. The injection port temperature for both GC/MS and GC/GC/MS systems was maintained at 250 °C.

GC/MS data were acquired in a **Raw Scan** (profile, 10 measures per mass spectral peak) **Acq. Mode** with the **Threshold** set to 0, a scan range of 50 to 500 *m/z* units, and a sampling rate of 2^3, which results in 1.66 spectra per second. GC/GC/MS data were acquired in the centroid mode (**Scan Mode**) with the **Threshold** set to 150, a scan range of 18 to 300 *m/z* units, and a sampling rate of 2^3.

Mass spectral instrument line-shape calibration and DEC were performed with *MassWorks* version 3.0 (Cerno Bioscience, Danbury, CT, USA), a post-data acquisition software. For all the compounds under study, search parameters for DEC were selected with few constraints to mimic real unknown identification situations. Although primary elements for most of essential oils are C H O, the search conducted here

also included N. Unless specified otherwise, the lower bound of elements was set to zero, whereas their upper bound was selected to be the maximum that depends on elements used and the nominal mass of a compound to be searched. For example, the upper bound for C in an unknown with a nominal mass of 240 Da is 240/12 = 20, the nominal mass of the compound (as determined by the *m/z* value of the molecular ion peak) divided by the nominal mass of C. Additional search parameters included double-bond equivalent values from −1 to 50, mass tolerance of 10 mDa, electron state as 'odd' for the molecular ions and 'both' for fragments.

A mass spectral database search was conducted with NIST Mass Spectral Search Program version 2.0 (NIST, Gaithersburg, MD, USA) against the NIST/EPA/NIH Mass Spectral Database version 2.0 f.

RESULTS AND DISCUSSION

Essential oils are usually manufactured by a steam-distillation process from plants such as flowers, seeds, roots, and leaves. Depending on the variation of climates or processing conditions, the essential oils produced from the same area may appear to be the same, but they can have different chemical compositions.[15] For the purpose of quality control,[16,17] it is necessary to establish a GC/MS profile for each batch of essential oils. As a popular essential oil embraced by both domestic and foreign customers, Chinese rose oil is widely used as an additive for flavors, fragrances, cosmetic products, food, and medicines. Mandatory quality assessment for each batch of the rose oil is carried out by GC/MS and library search in this laboratory before the material can be purchased. Whereas GC/MS analysis followed by library search has been recognized as a method of choice for such analysis, DEC for its components does serve as an orthogonal confirmation. More importantly, DEC is a valuable tool to help identify any unknown that cannot be determined by a conventional GC/MS library search.

Confirmation of selected compounds

Chinese rose oil is a very complex natural product. It contains over 130 volatile organic compounds that are separated and detected through capillary GC/MS, as shown in Fig. 1. In spite of positive identification for most of the components by a library search, it is desirable to boost the confidence of the identification by independent confirmation through DEC. This is demonstrated through 13 selected ions at different retention times during the separation of the rose oil mixture.

The first step to perform DEC in a quadrupole GC/MS system is to create the instrument line-shape calibration with calibration standards of either perfluorotributylamine PFTBA[10–13] or user-selected compounds.[14] In this analysis, four compounds from the mixture that have been unambiguously identified previously[18] were conveniently employed as internal calibration standards because they have decent signal-to-noise ratio and sufficient mass range coverage for the ions of interest. These compounds produce ions with *m/z* values of 139, 218, 296, and 352 that have elemental compositions of $C_9H_{15}O$, $C_{15}H_{22}O$, $C_{21}H_{44}$, and $C_{25}H_{52}$, respectively. It is important to point out that in this unique calibration, in addition to the exact *m/z* value of the

calibration ions, the isotope distribution information of each calibration standard is also taken as input for calibration calculation. This is illustrated by the calibration standard
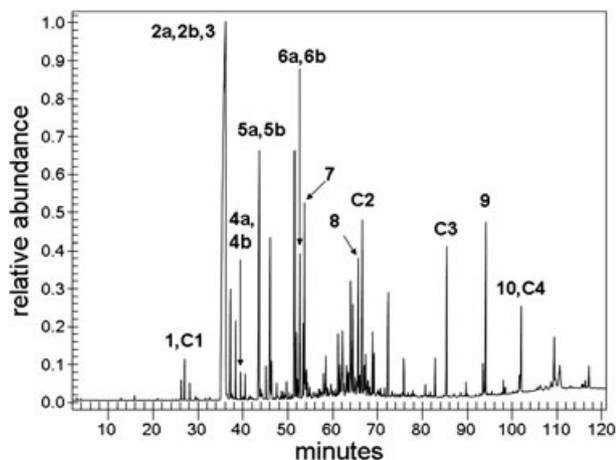
Figure 1. TIC of Chinese rose oil separated by GC/MS. Identified molecular ions or fragments are labeled as 1 to 13 and calibration standard ions are labeled as C1 (rose oxdide-CH$_3$), C2 (γ-cadinen-15-al), C3 (heneicosane), and C4 (pentacosane) with m/z values of 139, 218, 296, and 352 respectively.

$C_{15}H_{22}O$ (Fig. 2(a)). Its entire isotope profile is highlighted in the gray area which was automatically defined by the left and right edges. Based on theoretically calculated and experimentally measured spectra, this calibration effectively transforms the distorted raw spectrum (dotted line) into a symmetrical and mathematically well-defined calibrated one (bold solid line). To report the calibration performance, mass accuracy and spectral accuracy for all calibration standards were calculated as shown to be less than 1 mDa and better than 99%, respectively (Fig. 2(b)), indicating ideal calibration. The second step is to apply the calibration to raw data files to perform accurate mass measurements and exact isotope modeling. As the last step, a DEC is performed by both high mass accuracy and spectral accuracy.

The calibration significantly improved mass accuracy to a low mDa level, making it possible to obtain unique elemental composition for such low molecular weight volatile organic compounds by DEC.[19] For example, five ions with m/z 324, 323, 198, 156, and 138 were found to have high mass accuracy of less than 5 mDa and to be identified with unique elemental compositions of $C_{23}H_{48}$, $C_{23}H_{47}$, $C_{13}H_{26}O$, $C_{10}H_{20}O$, and $C_{10}H_{18}$, respectively, as shown in Table 1. However, more often than not, multiple elemental compositions will result from a DEC with the used search conditions. The correct elemental composition can be further identified with the aid of spectral accuracy.

RT Window	Formula Entry	Net Formula	Mono Isotope	Centroid	Left Edge	Right Edge
0: Scans 12426–12438	C15H22O	C15H22O	218.1671	218.3351	216.623	220.672
1: Scans 16052–16065	C21H44	C21H44	296.3443	296.5748	294.553	298.992
2: Scans 4794–4818	C9H15O	C9H15O	139.1123	139.2151	135.927	143.112
3: Scans 19236–19272	C25H52	C25H52	352.4069	352.6813	350.947	353.971

Net Formula	Mono Isotope	Closest Centroid	ΔM (mDa)	ΔM (ppm)	Spectral Accuracy (%)
C15H22O	218.1671	218.1673	0.22	1	99.6
C21H44	296.3443	296.3445	0.2	0.7	99.6
C9H15O	139.1123	139.1126	0.28	2	99.2
C25H52	352.4069	352.4073	0.4	1.1	99.3

Figure 2. (a) Instrument line-shape calibration inputs and (b) instrument line-shape calibration results.

Spectral accuracy is a measure of similarity between the calibrated and calculated spectra. A rigorous mathematical description can be found elsewhere.[9] This new metric has proved to be very effective for the identification of unknown compounds even for data with high mass accuracy from a high resolving power instrument. For example, in elemental composition searching with a mass tolerance of 2 ppm and elements of C, H, N, O, S, and Cl, the spectral accuracy can remove 99% of the false positives for ions with mass larger than 900 Da.[20] Such powerful selectivity has also been found to be beneficial to the DEC for the volatile organic compounds from the Chinese rose oil (Table 1). The results of DEC for eight ions show multiple elemental composition candidates. Without additional chemistry constraints such as upper limits of the elements or limits of elemental types, it will be very difficult to determine which one is likely to be correct. Fortunately, mass spectrometric measurements do carry unique isotope pattern information as fingerprints for each compound in addition to high mass accuracy. This practice has been employed to determine the number of Cl and/or Br or C atoms in a given ion by simple visualization or simple isotope ratio calculation for many years. With the line-shape calibration and this sophisticated computer program, this manual and rudimentary method is replaced by highly accurate isotope pattern recognition to determine unknown elemental composition. Indeed, the eight ions achieved the best spectral accuracy and had their correct elemental composition identified as a top match. For example, having a total of six elemental compositions resulting from the DEC (Table 2), the ion with *m/z* 164 was correctly identified as having the elemental composition $C_{10}H_{12}O_2$ based on the best spectral accuracy of 99.6%. As shown by the overlay of the calibrated spectrum (dotted line) and the theoretically calculated spectrum (bold solid line) in Fig. 3, the nearly perfect fit is made possible by the instrument line calibration which allows both the calibrated and calculated spectra to be described by the same peak shape functions.[9] Results from the same search, on the other hand, showed the elemental compositions of $C_6H_8N_6$ and $C_5H_{12}O_4N_2$ had relatively poor matches against calibrated spectra with spectral accuracy of 98.6% and 97.5%, respectively. Their obvious mismatches can be observed in the overlays in Fig. 3.

Identification of coeluted components

The rose oil is such a complex mixture, and its components could not be completely separated even by capillary GC with a 2-h temperature gradient analysis because some of the compounds in this natural product have very similar molecular weights and molecular structures. Sometimes a dominant component has an overwhelming signal that is retained in a column for a long time and masks other components. The very large chromatographic peak appearing with a retention time of 36 min represents exactly such a component. Identified

Table 1. Identified molecular ions or fragments of selected components from the Chinese rose oil

Peak number	Name	Elemental composition	Rt (min)	Monoisotope (Da)	Mass error (mDa)	Mass error (ppm)	Spectral acuracy (%)	Rank/ Total
1	Rose oxide ($M^{+\cdot}$)	$C_{10}H_{18}O$	27	154.1358	5.5	35.5	99.3	1/2
2a	Citronellol ($M^{+\cdot}$)	$C_{10}H_{20}O$	36.1	156.1514	3.0	19.3	99.5	1/1
2b	Citronellol ($M^{+\cdot}$-H_2O)	$C_{10}H_{18}$	36.1	138.1409	−4.3	−31.5	99.2	1/1
3	Nerol ($M^{+\cdot}$)	$C_{10}H_{18}O$	36.1	154.1358	11	69.8	97.9	1/2
4a	2-Undecanone ($M^{+\cdot}$)	$C_{11}H_{22}O$	39.5	170.1671	5.5	32.1	99.6	1/2
4b	2-Undecanone ($M^{+\cdot}$-CH_3)	$C_{10}H_{19}O$	39.5	155.1436	4.5	28.9	98.7	1/4
5a	Phenethyl acetate ($M^{+\cdot}$)	$C_{10}H_{12}O_2$	43.5	164.0837	2.1	13.0	99.6	1/6
5b	Phenethyl acetate ($M^{+\cdot}$-CH_3)	$C_9H_9O_2$	43.5	149.0603	2.1	13.8	99.2	1/8
6a	Citronellyl acetate ($M^{+\cdot}$)	$C_{13}H_{26}O$	52.6	198.1984	3.8	19.0	99.3	1/1
6b	Citronellyl acetate ($M^{+\cdot}$-CH_3)	$C_{12}H_{23}O$	52.6	183.1749	3.7	20.1	99.5	1/3
7	β-Caryophyllene ($M^{+\cdot}$)	$C_{15}H_{24}$	53.6	204.1878	4.0	19.6	97.1	1/3
8	Z,Z-Farnesol ($M^{+\cdot}$)	$C_{15}H_{26}O$	65.7	222.1984	4.3	19.2	99.0	1/4
9	Tricosane ($M^{+\cdot}$)	$C_{23}H_{48}$	94	324.3756	3.5	10.8	99.8	1/1
10	Pentacosane ($M^{+\cdot}$-C_2H_5)	$C_{23}H_{47}$	102	323.3678	0.7	2.1	97.6	1/1

Table 2. Elemental composition determination results for *m/z* 164

Row	Elemental composition	Monoisotope	Mass error (mDa)	Mass error (ppm)	Spectral accuracy (%)
1	$C_{10}H_{12}O_2$	164.0837	2.1	13.0	99.5
2	$C_6H_8N_6$	164.0810	−0.6	−3.4	98.1
3	$C_5H_{12}O_4N_2$	164.0797	−1.9	−11.5	96.0
4	$C_4H_{12}O_3N_4$	164.0909	9.3	56.9	95.8
5	$CH_8O_2N_8$	164.0770	−4.6	−27.9	94.6
6	H_8ON_{10}	164.0883	6.7	40.6	94.4

as citronellol ($C_{10}H_{20}O$) by a search of the NIST08 Mass Spectral Database using the NIST MS Search Program and confirmed by DEC, this component has an elution time of over 1.2 min and is the most abundant compound in the mixture, accounting for about 50% of the total oil. By careful examination of the range from m/z 150 to 156 in the spectrum of citronellol from the rose oil (Fig. 4), two ions are obviously observed; one with m/z 152 and the other with m/z 154. Based on common decomposition pathways of molecular ions, the ions with m/z 152 having 4 m/z units less than the molecular ion of citronellol (m/z 156) are unlikely fragments from the citronellol. Likewise, the ions with m/z 154 probably do not result from a loss of two hydrogen radicals or a molecule of hydrogen from citronellol, which is a primary alcohol. The mass spectra of most aliphathic alcohols with four or more atoms of carbon do not exhibit a molecular ion peak.[21] Citronellol is unusual in this respect, and there is no reason to think that the fragmentation of citronellol molecular ions would produce $[M-2]^{+\cdot}$ ions. These arguments are consistent with the appearance of the NIST library spectrum of pure citronellol, which does not exhibit any peaks at m/z 152 and 154; therefore, these ions must represent unknown
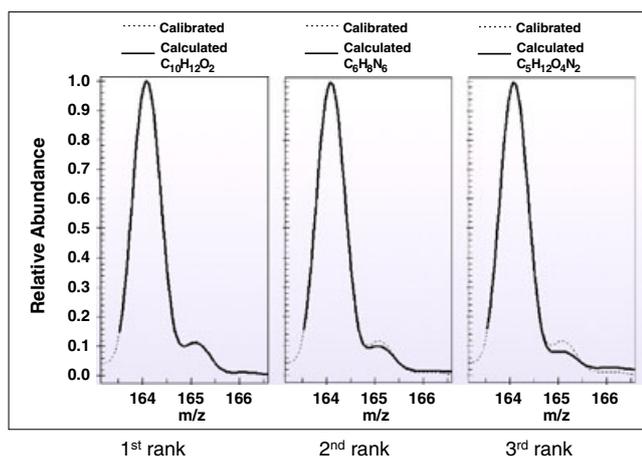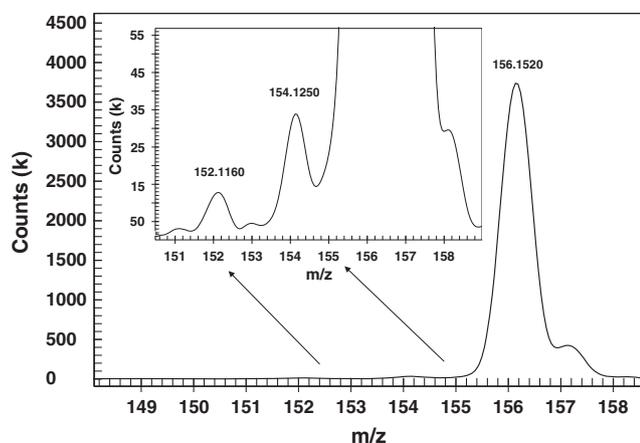
components which coeluted with citronellol. Due to the fact that these two components completely overlapped with citronellol, it is difficult to perform deconvolution and identify them using library search methods.

The elemental compositions of these two ions can be determined by accurate mass measurements and an elemental composition search. Note that high intensities (3 700 000 counts) of the peak at m/z 156 resulted in high mass accuracy of 3 mDa and spectral accuracy of 99.5% (Table 1), but the signal strength for both m/z 152 and 154 is much less, at about 15 000 and 35 000 counts, respectively, which are less than 1% of that of the m/z 156 peak. Due to such drastically low signals, the mass accuracy and spectral accuracy for m/z 152 and 154 are inevitably compromised. As a result, DEC for these two components employed more relaxed mass tolerance and more restrictive elemental upper bounds than those used for other compounds. With modified mass tolerance of 15 mDa and the upper bounds for elements O and N set to 3, quite specific DECs for the two components were obtained. The ion with m/z 152 was determined exclusively as $C_{10}H_{16}O$, whereas two elemental compositions, $C_{10}H_{18}O$ and $C_8H_{14}ON_2$, were found to be possible candidates for the ion with m/z 154. Further analysis by GC/GC/MS was needed to positively confirm the elemental composition of the ion with m/z 154. As shown in Fig. 5(a), the second dimension of GC successfully separated the component producing the ion with m/z 154 from the major component represented by the ion with m/z 156 and that eluted from the first GC column over a retention time range of 35.0 to 36.1 min. The identity of the ion with m/z 154 was found to be nerol ($C_{10}H_{18}O$) as the first hit in a search of the NIST08 Database using the NIST MS Search Program (Fig. 5(b)) with a Match Factor of 881 and Reverse Match Factor of 909.

Figure 3. Three overlays of calculated spectra and calibrated spectra for m/z 164. The correct compound was identified as number one hit with the best spectral accuracy of 99.6%.

Figure 4. Mass spectra of coeluted compounds citronellol, nerol, and α-citral.
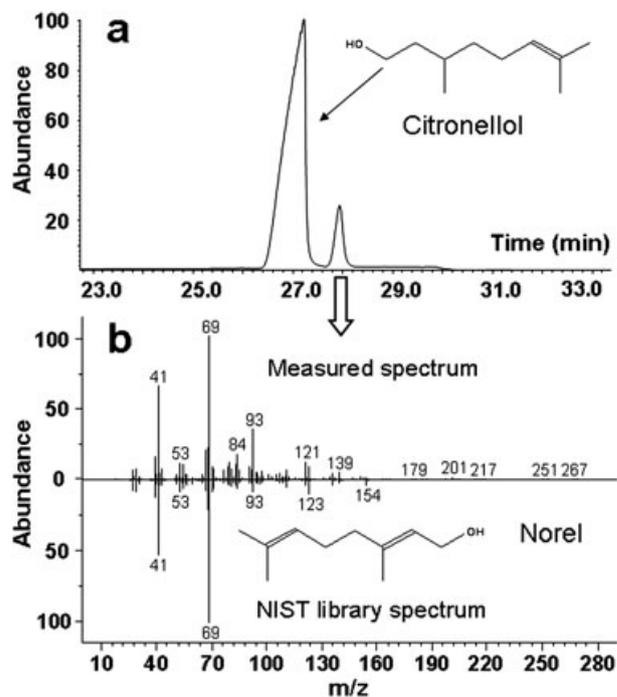
Figure 5. TIC of GC/GC/MS for separated components of citronellol and nerol (a), averaged experimental spectrum of nerol without background subtraction (b, top), and NIST08 Database library spectrum of nerol (b, bottom).

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Further work would be necessary to make an unambiguous composition of the compound represented by the $C_{10}H_{16}O$ elemental composition. Examination of the multiple spectra for nerol in the NIST08 Database showed the peak at *m/z* 152 did not represent a fragment of the molecular ion peak of nerol.

CONCLUSIONS

Enabled by instrument line-shape calibration technology, the most accessible unit-mass resolution quadrupole mass spectrometers can achieve sufficient high mass accuracy to become new players for DEC. As demonstrated in the data analysis for volatile organic compounds in the Chinese rose oil, five ions were uniquely identified and the rest of the ions were found to be consistently the highest ranked possibility based on spectral accuracy. These results show that the quadrupole systems are capable of performing elemental composition determination for volatile organic compounds and can be used for other unknown identification both in GC/MS and LC/MS (liquid chromatography/mass spectrometry).

The capability for the quadrupole systems to perform DEC is not merely an economic alternative to high-resolution instruments for many applications. For DEC, the quadrupole systems do have unique advantages over high resolving power mass spectrometers such as TOF. With TOF systems, in order to achieve high mass accuracy and normal isotope patterns, the signal strength needs to be constantly controlled to ensure that no signal saturation occurs. On the other hand, the quadrupole systems typically have an excellent dynamic range that allows routine and robust accurate mass measurements as well as high-fidelity isotope patterns to be obtained. This is especially important when the automatic elemental composition determination process is considered. The high tolerance for detector saturation in the quadrupole systems facilitates direct integration across an LC/MS peak followed by DEC. Conversely, this automatic process is often not feasible because it is necessary to manually select scans to avoid saturated signal in TOF systems.

The high mass accuracy of the quadrupole systems achieved by the calibration technology certainly plays a significant role in DEC by reducing the number of possible candidates of elemental composition that must be considered. More importantly, the enhanced spectral accuracy allows highly accurate isotope pattern matching between calibrated and calculated spectra because both of them are profile spectra and described by the same mathematical function. This high-performance isotope matching makes it possible to take full advantage of molecular fingerprint information for DEC. The current technology combining high mass accuracy with high spectral accuracy represents the most advanced approach to elemental composition determination.

REFERENCES

[1] NIST/EPA/NIH Mass Spectral Database, Standard Reference Database 1, **1992**; NIST 98, Standard Reference Database 1, 1998, Standard Reference Data Program, National Institute of Standards and Technology, Gaithersburg, MD.
[2] P. Ausloos, C.L. Clifton, S.G. Lias, A.I. Mikaya, S.E. Stein, D. V. Tchekhovskoi, O.D. Sparkman, V. Zaikin, D. Zhu. The critical evaluation of a comprehensive mass spectral library. *J. Am. Soc. Mass Spectrom.* **1999**, *10*, 287.
[3] S.E. Stein. An integrated method for spectrum extraction and compound identification from GC/MS data. *J. Am. Soc. Mass Spectrom.* **1999**, *10*, 770.
[4] C.L. García, M. Becchi, M.F. Grenier-Loustalot, O. Païsse, R. Szymanskit. Analysis of aromatic sulfur compounds in gas oils using GC with sulfur chemiluminescence detection and high-resolution MS. *Anal. Chem.* **2002**, *74*, 3849.
[5] K. Qian, G.J. Dechert. Recent advances in petroleum characterization by GC field ionization time-of-flight high-resolution mass spectrometry. *Anal. Chem.* **2002**, *74*, 3977.
[6] J.E. Szulejko, T. Solouk. Potential analytical applications of interfacing a GC to an FT-ICR MS: Fingerprinting complex sample matrixes. *Anal. Chem.* **2002**, *74*, 3434.
[7] A.C. Peterson, G.C. McAlister, S.T. Quarmby, J. Griep Raming, J.J. Coon. Development and characterization of a GC-enabled QLT-Orbitrap for high-resolution and high-mass accuracy GC/MS. *Anal. Chem.* **2010**, *82*, 8618.
[8] O. Fiehn, J. Kopka, N.J. Trethewey, L. Willmitzer. Identification of uncommon plant metabolites based on calculation of elemental compositions using gas chromatography and quadrupole mass spectrometry. *Anal. Chem.* **2000**, *72*, 3573.
[9] Y. Wang, M. Gu. The concept of spectral accuracy for MS. *Anal. Chem.* **2010**, *82*, 7055.
[10] Y. Wang, H. Press. Accurate mass measurement on real chromatographic time scale with a single quadrupole mass spectrometer. *Chromatogr. Jpn.* **2006**, *27*, 135.
[11] M.C. Dancle, M. Gu, D.H. Powell. Evaluation of molecular isotope patterns for elemental composition identification on a unit resolution quadrupole mass spectrometer. Proc.55th ASMS Conf. Mass Spectrometry and Allied Topics, Indianapolis, IN, June 3–7, **2007**.
[12] J. Chen, O.D. Sparkman, M. Gu. Confident unknown identification of SVOC compounds by combining NIST library search with elemental composition determination. Proc. 57th ASMS Conf. Mass Spectrometry and Allied Topics, Philadelphia, PA, May 31–June 4, **2009**.
[13] O.D. Sparkman, P.R. Jones, M. Curtis. Anatomy of an ion's fragmentation after EI. *Spectroscopy* part I, Special Issues, May 1, **2009**.
[14] J. Chen, M. Gu, Y. Wang, D. Kuehl. Improving the confidence of unknown compound identification by first responder mobile GC/MS laboratories in time-critical environmental and homeland security incidents. *LCGC* Sept 1, **2008**.
[15] S. Zouari, N. Zouari, N. Fakhfakh, A. Bougatef, M.A. Ayadi, M. Neffati. Chemical composition and biological activities of a new essential oil chemotype of Tunisian *Artemisia herba alba*. *Asso. J. Med. Plants Res.* **2010**, *4*, 871.
[16] P. Pallado, G. Tassinato, M. D'Alpaos, P. Traldi. Gas chromatography/mass spectrometry in aroma chemistry: a comparison of essential oils and flavours extracted by classical and supercritical techniques. *Rapid Commun. Mass Spectrom.* **1997**, *11*, 1335.
[17] G.C. Galletti, M.T. Russo, P. Bocchini. Essential oil composition of leaves and berries of *Vitex agnus castus* L. from Calabria, southern Italy. *Rapid Commun. Mass Spectrom.* **1996**, *10*, 1345.
[18] W. Zhou, X.P. Zhou, G.H. Zhao, H.W. Liu, L. Ding, L.R. Chen. Studies of aroma components on essential oil of Chinese Kushui rose. *Chin. J. Chromatogr.* **2002**, *20*, 560.
[19] M.L. Gross. Accurate masses for structure confirmation. *J. Am. Soc. Mass Spectrom.* **1994**, *5*, 57.
[20] J.C.L. Erve, M. Gu, Y. Wang, W. DeMaio, R.E. Talaat. Spectral accuracy of molecular ions in an LTQ/Orbitrap mass spectrometer and implications for elemental composition determination. *J. Am. Soc. Mass Spectrom.* **2009**, *20*, 2058.
[21] J.T. Watson, O.D. Sparkman. *Introduction to Mass Spectrometry: Instrumentation, Applications, and Strategies for Data Interpretation*, John Wiley, Chichester, UK, **2007**, chap. 6.