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Detection of Diethyl Phthalate in Perfumes by Extractive Electrospray Ionization Mass Spectrometry

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Recent findings suggest that long-term exposure to diethyl phthalate (DEP), one of the widely used phthalate esters, can lead to serious health problems. Most perfumes contain non-negligible amounts of DEP. Rapid and sensitive detection of DEP in perfumes is thus of increasing importance. A novel procedure based on extractive electrospray ionization mass spectrometry (EESI-MS) has been developed for fast detection and identification of DEP in perfumes without the need for any sample pretreatment. The limit of determination for DEP in perfume was less than 100 ppb using tandem mass spectrometry on a commercial quadrupole time-of-flight mass spectrometer. The dynamic range of this method was about 4 orders of magnitude. A single sample analysis was completed within a few seconds, providing a rapid way to obtain semiquantitative information on the DEP content in perfumes. This study shows that both volatile and nonvolatile analytes (e.g., amino acids) in liquids can be directly sampled by neutral desorption, providing a convenient way for high-throughput screening of target compounds using EESI-MS.

Diethyl phthalate (DEP) is a plasticizer widely used in many industrial products, including tools, automotive parts, toothbrushes, food packaging, cosmetics and insecticides.[1,2] DEP is also widely used in the perfume industry as a vehicle for fragrances and as an alcohol denaturizing agent. Until recently it was believed that cosmetics containing phthalates pose no risks to human health or the environment. Thus, currently relatively high amounts of DEP are used in most cosmetics such as perfumes. DEP concentrations higher than a few percent occur in many products available on the market. In a recent survey by Greenpeace, DEP was found in 34 out of 36 perfumes tested.[3] The highest levels of DEP were detected in Eternity by Calvin Klein (2.2% (w/w)), Iris Blue by Melvita (1.1% (w/w)), and Le Male by Jean-Paul Gaultier (0.99% (w/w)). DEP concentrations in perfumes have not been regulated by existing legislation because they were believed to have low overall toxicity.[4,5] Recent findings, however, contest their safety.[6−16] Studies on rats have shown that upon long-term exposure, DEP can be a reason for reproductive failure.[6,7,9,12,13] Reduced neurotransmitter activity due to water contamination with DEP was observed in adult male fishes.[10,15] Recently, DEP was also shown to be a possible promoter of ocular damage in animals.[16] Besides animal experiments, developmental and reproductive toxicity of DEP is suggested by recent human studies.[17,18] In 2005, the European Union banned the use of six phthalates including DEP in children's products.[19] When applied to skin, DEP rapidly penetrates it and becomes widely distributed around the body following each exposure.[20] This renders a perfume that contains DEP potentially hazardous.

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Many techniques including chromatography,[21−23] optical spectroscopy,[24,25] ion mobility spectrometry,[26] and mass spectrometry[27−32] have been used for detection of DEP in various samples. Because of the complexity of the real samples, a sample cleanup procedure was usually required for most techniques in previous studies. Chromatographic techniques such as GC and HPLC are conventionally used to identify phthalate esters in cosmetic products.[33,34] A single HPLC/GC run typically takes approximate 30 min. In addition, sample pretreatment may be required, especially for sensitive detection (e.g., extraction, preconcentration). However, when one has to process a large number of samples (e.g., in quality control laboratories), high throughput may become of major importance. An appropriate analytical tool for practical sample analysis must meet the demanding requirements for high throughput, high sensitivity, and specificity since the concentration of DEP as well as the sample composition varies over a wide range.

To facilitate high-throughput mass spectrometric analysis, techniques such as desorption electrospray ionization (DESI),[35−37] desorption atmospheric pressure chemical ionization (DAPCI),[38−41] direct analysis in real time (DART),[36,41−44] atmospheric-pressure solids analysis probe (ASAP),[45,46] and thermal desorption atmospheric pressure chemical ionization (TD-APCI) [47,48] have been used for fast detection of analytes on solid surfaces. Besides some common advantages of these ambient ionization techniques, each one has unique features for specific analytical applications. Liquid samples can be analyzed by these techniques but require sample pretreatment. For example, dilute urine dried on a paper surface[49] can be examined by DESI. Similar to DESI, other techniques such as DART, ASAP, and TD-APCI analyze liquid samples indirectly. Usually, deposition of the sample on a solid surface and solvent volatilization is employed as a sample preparation step. In DART, TD-APCI as well as ASAP, the solvent evaporation can be shortened to 2−3 min by heating the sample surface to a high temperature (e.g., 250−450 °C). However, such a high temperature results in fast degradation of sensitive compounds, and thus the mass spectrum of a sample can be significantly changed. This renders data interpretation difficult, especially for analysis of heat sensitive samples such as perfumes.

Liquids, gases, suspensions, and aerosol samples can be directly analyzed by extractive electrospray ionization (EESI)[36,50−62] mass spectrometry without any sample pretreatment. With the use of a neutral desorption (ND) device,[36,53,54] analytes such as metabolites, active drug components, explosives, and chemical pollutants can be liberated from virtually any type of surface for subsequent EESI analysis. Recently we demonstrated that ND-EESI-MS enables rapid classification of perfumes without any sample pretreatment.[63] Perfumes are complex liquid samples, which are composed of fragrant essential oils, aroma compounds, fixatives, and alcohol matrixes. Note that many ingredients in perfumes are heat sensitive and degrade quickly when heated to

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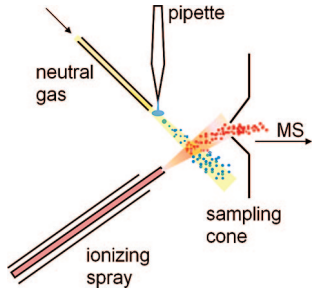

Figure 1. Schematics of the experimental setup where liquids are sampled directly by gentle neutral desorption for EESI-MS detection.

a temperature higher than 200 °C.[64] In conventional desorption sampling, it takes only ~2−3 min for a perfume deposited on a solid substrate to dry. The speed is not a serious problem in most applications. However, it is necessary to improve the throughput and to simplify the data interpretation when a specific analyte (such as DEP) in a large number of complex samples (such as perfume products) must be rapidly screened. Herein we extend EESI-MS to rapid detection and identification of DEP directly from liquid perfume samples, without any sample pretreatment.

EXPERIMENTAL SECTION

The key part of the experimental setup is schematically shown in Figure 1. A pipet tip (Gilson, France) filled with 1 μL of a perfume was exposed to a gentle stream of nitrogen gas (100~400 L/h) coming out from a Teflon tube with a 7 mm inner diameter. The pipet tip was 2 cm away from the sampling cone of the ESI source (Z-spray, Micromass, U.K.). The sample was desorbed and then transported from the pipet tip by the neutral nitrogen gas flow. Perfume droplets thus produced were ionized by the EESI source using a solvent mixture (methanol/water/acetic acid 40%/40%/20%), infused at a flow rate of 5 μL/min. The experiments were run in the positive ion detection mode on a commercial electrospray ionization (ESI) quadrupole time-of-flight (Q-TOF) mass spectrometer (QTOF Ultima, Micromass, Manchester, U.K.). Briefly, the capillary voltage was 3 kV and the cone voltage was 40 V. Other parameters were default values of the instrument. No further optimization was performed.

For DEP identification, tandem mass spectrometry was used. Ions of m/z 223 corresponding to protonated DEP ions were isolated in an rf hexapole and then subjected to collisions with buffer gas molecules in the collision cell. Fragments as well as nondissociated parent ions were then detected by the TOF analyzer. Collision energy was set to 10 units on the QTOF software. This allowed observing the parent ion and two major fragments at m/z 177 and m/z 149. These three peaks were finally used to identify DEP in perfume samples.

The Mass Lynx 4.0 software (Waters, Manchester, U.K.) was used for the QTOF-MS experiments. A detailed procedure for background subtraction in a QTOF instrument has been described elsewhere.[65] The mass spectra were typically accumulated for about 5−10 s, the single scan time being 0.5 s.

Eighteen fragrances by different brands were examined on DEP content: “Weekend” by Burberry, “Relaxing fragrance” by Shiseido, “Be delicious” by DKNY, “Beautiful” by Estee Lauder, “Hugo XY” by Hugo Boss, “le Male” by Jean Paul Gaultier, “ETH Zurich 150” by Givadaun, “Bright Crystal” by Versace, “Option” by Nova, “CK One” by Calvin Klein, “Miss Dior” and “Midnight Poison” by Christian Dior, “Clinique Happy for Men” and “Clinique Happy Heart” by Clinique, “Opium”, “Opium Shanghai”, and “Opium Impereale” by Yves Saint Laurent, and “White Musk” (Eau de Toilette) by The Body Shop.

DEP (>99.5% purity) was purchased from Fluka (Switzerland). Chemicals such as methanol and acetic acid were bought from Fluka (Switzerland) with the highest purity grades available. The water used was deionized water, available in house at ETH. To minimize the background signal of DEP, plastic material was avoided completely for handling the reagents. The only exception was a plastic pipet tip (D10, Gilson, France) used to deliver perfume samples to neutral desorption EESI. These pipet tips were made from pure, translucent polypropylene. No additives are used in their production. No background level change was observed when glass tips were used instead, in agreement with the presumed absence of DEP in these tips. Therefore, cheap replaceable plastic tips were used in all the experiments, which is also beneficial for high-throughput analysis. For quantitative analysis, perfumes were diluted with ethanol 1000 times to minimize matrix effects, followed by a standard addition analysis using DEP.

Safety Recommendations. Latex powder-free gloves were used in all the experiments in order to avoid undesirable exposure of skin to solvents. It is recommended to use an exhaust vent over the nebulization area in order to reduce exposure to inhalation of fumes and prevent substantial DEP deposition in the ion source area.

RESULTS AND DISCUSSION

Rapid Screening of DEP by EESI-MS. In our previous study on perfumes, neutral desorption was carried out from samples deposited on a smelling strip.[63] The analytes in the perfume were then sampled to the EESI source by neutral desorption after the strip had dried. However, for rapid analysis of liquid samples, especially in cases where only a particular compound is of interest, neutral desorption from a liquid hanging droplet is a more straightforward sampling method, and facilitates high-throughput analysis by eliminating the step to deposit and dry the sample on a surface. Also, sensitive detection from a substrate surface (e.g., paper) can be complicated because of adhesion of DEP as well as other components to the surface. Stronger nitrogen gas flows would then be required to release analytes from the surface. This, however, would result in a decreased residence time of the desorbed neutrals inside the ionizing plume, yielding lower overall sensitivity.

With the use of a gentle gas flow (as shown in Figure 1), the hanging perfume droplet was nebulized and the resulting aerosol was transferred into an ESI plume for ionization. Figure 2 presents EESI-MS fingerprints of three different fragrances (“le Male” by Jean Paul Gaultier; “Hugo XY” by Hugo Boss, and “Natural fragrance” by Shiseido) within the m/z 100−300 range. As can be seen, several peaks are commonly present in all the three mass spectral patterns. These signals typically correspond to the generally used essential fragrance compounds in the perfume industry, such as limonene (m/z 137) and citronellol (m/z 157);

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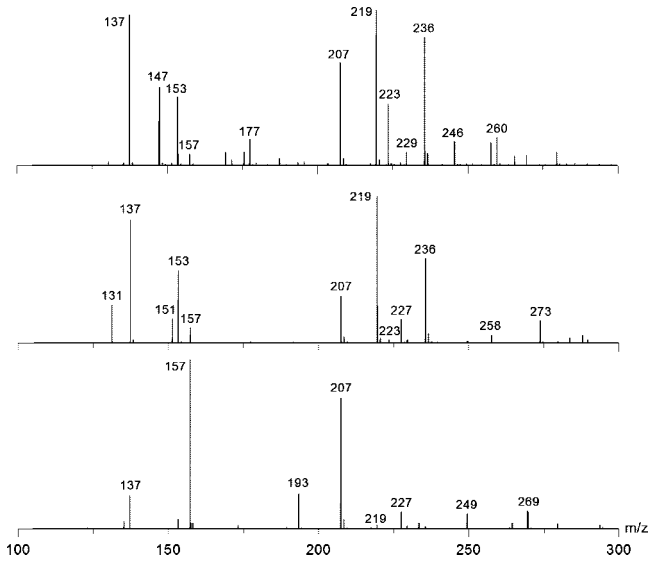

Figure 2. Chemical fingerprints of three famous fragrances, recorded in the positive ion detection mode by EESI-MS. Top, "le Male" by Jean Paul Gaultier; middle, "Hugo XY" by Hugo Boss; bottom, "Natural fragrance" by Shiseido.

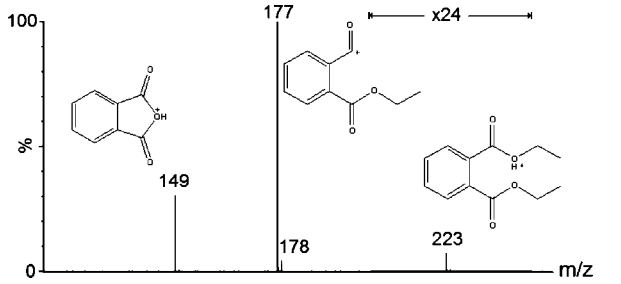

Figure 3. MS/MS spectrum of DEP recorded using ND-EESI-MS.

both of them showed up as protonated molecules in the EESI-MS spectra. However, even though these compounds occur in all the three perfume samples, their relative abundances are very different (e.g., citronellol and limonene). This is obvious from the different relative peak intensities for the corresponding compounds in the mass spectra. Some signals, on the other hand, occur only in particular fragrances (e.g., m/z 246 in "le Male"). The signal at m/z 223 is abundant in the EESI-MS fingerprint for "le Male" perfume, noticeable in "Hugo XY" and was not detected in "Natural fragrance". In order to judge whether this signal comes from protonated DEP species or some other compound with the same molecular weight, its MS/MS spectrum should be compared to the reference MS/MS spectrum of pure DEP. Figure 3 shows an EESI-MS/MS spectrum of authentic DEP (1 ppm in ethanol). One can see protonated DEP ions at m/z 223 as well as the first and the second fragment at m/z 177 and m/z 149, respectively. Figure 3 shows the structures of the characteristic fragments.[66] The fragment at m/z 177 started to appear at lower CID energies than that at m/z 149, indicating that the pathway for ethanol cleavage was favored. Identical MS/MS spectral patterns of ions (m/z 223) were observed in perfume samples as well. These data confirmed the successful detection of DEP in perfumes. In order to achieve high throughput analysis, the CID energy was

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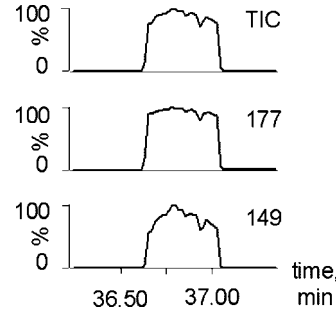

Figure 4. Ion "chromatograms" of DEP fragments and total ion current (TIC) detected by EESI-MS/MS from a "Miss Dior" perfume.

optimized to see both characteristic fragments simultaneously (CID energy was 10 units in the QTOF software).

EESI-MS/MS spectra of 18 perfume samples were obtained under the same conditions to identify the DEP content. DEP was detected in 13 out of the 18 samples (detected in "Weekend", "Beautiful", "Hugo XY", "le Male", "ETH Zurich 150", "Bright Crystal", "Option", "CK One", "Miss Dior", "Clinique Happy for Men", "Opium", "Opium Shanghai", "Opium Impereale"; not detected in "Natural fragrance", "White Musk", "Midnight Poison", "Be delicious", and "Clinique Happy Heart"). For these samples MS/MS spectral patterns of m/z 223 ions were identical to that of authentic DEP. DEP was found in abundance in perfume products for both men and women. The highest detected signal was from '"le Male" by Jean Paul Gaultier. According to the Greenpeace Survey, this fragrance holds about 1% DEP (w/w).[3] Most products designed for men contained a measurable percentage of DEP. Also, our observations indicate a huge variation of DEP content in perfumes, supporting the recent results from the Greenpeace survey.[3] Recent findings suggest that DEP is more toxic to males by causing reproductive failure,[6,7,9,12,13] thus it is of greater concern for men to avoid using perfume products containing high amounts of DEP.

It is worth noting that for the samples that we examined the chemical and detector noise level was always negligible compared to the detected signals from DEP in perfumes. This means that we did not meet any borderline case when the DEP signal was around the detection limit, there was either an easily seen signal or no signal at all. Typical ion current profiles of the two major DEP fragments for "Miss Dior" perfume are presented in Figure 4. The plateau region in the profile corresponds to the time when the perfume was being sampled for EESI analysis. Notably, the ion current responded rapidly to the presence of perfume samples. For example, the 90% signal raise time was less than 1 s for the fragment of m/z 177, and after a measurement time of ~0.5 min, the signal dropped down to the noise level in about 0.8 s when the pipet with a perfume sample was moved away. Note that the full scan time was 0.5 s for this experiment, i.e., the signal responded within two scans. In none of the experiments performed was any sample carryover observed. Therefore, the analysis speed is largely dependent on the measurement time, which can be shortened to less than 1 s using a fast scan mode. For the current setup, the speed is essentially limited by the sample delivery. In our experiments, the perfume samples were delivered manually using a pipet; it took about 1~3 s for each sample loading. Clearly, this simple method enables high-throughput detection of DEP.

Taking advantage of the unique design of EESI, ion/molecule reactions can be easily implemented in the ionization process. It was found that DEP formed ionic sodium adducts (m/z 245) rather than protonated molecules when a diluted sodium chloride solution (1 ppm) was electrosprayed in the EESI source. This information can enhance the specificity of DEP detection from complex perfume samples. When the sodium content was decreased down to the low parts per billion range, both of the sodium adducts and the protonated molecules of DEP were simultaneously observed in the EESI-MS spectra. Cationization of DEP can provide a better sensitivity, probably due to higher affinity of DEP to sodium ions compared to protons. This is also supported by the CID experiments of DEP sodium adducts, which gave no fragments with the possible highest energy for collisions in our QTOF instrument, showing the stability of the DEP sodium adducts. Thus, a reliable identification without resorting to tandem MS can be done from a high precision mass measurement experiments of the parent ions by using FTICR[67] or Orbitrap[68] analyzers, both of which feature very high mass accuracy.

Also, it is well-known that the CID fragment of DEP at m/z 149 is characteristic for other phthalates as well.[66] Therefore, surveying all parent ions of this fragment could be informative of other closely related phthalates present in a perfume sample. This can be easily achieved by neutral-loss scan available in a number of tandem mass spectrometers, e.g., triple-stage quadrupoles.[69] Therefore, this method can be potentially extended to fast screening of any phthalic acid in perfume products.

Possible Sampling Mechanism. In this study a neutral gas flow was used in order to sample a drop of liquid to EESI analysis. This approach is analogous to the technique introduced earlier for sampling analytes deposited on a solid surface known as "neutral desorption".[36,53,54,65] For consistency with these earlier studies, we also use the term "neutral desorption" here when referring to the sampling method. The mechanism of analyte liberation from the bulk liquid, however, may be different. Since DEP is a semivolatile compound, we believe that two processes contribute to the sample desorption−transportation process. The first is a simple evaporation assisted by the neutral gas flow, which delivers gas-phase DEP molecules into the surrounding air. The second mechanism is a process based on nebulization of the sample liquid. In this process, small neutral droplets are produced first with the assistance of the desorption gas beam, by disruption of the liquid surface. These droplets are carried by the neutral desorption gas, moving toward to the EESI source in the air. They form an aerosol containing both droplets with dissolved DEP and DEP vapor produced by normal evaporation. The aerosol is transported to the EESI region for extractive electrospray ionization, and finally partially solvated DEP species are ionized. An important difference between these two mechanisms is that droplet formation does not require the analyte to be volatile. Figure 5 shows an EESI mass spectrum of arginine dissolved in water (100 μM). The spectrum was recorded under the same experimental conditions that were used for DEP detection. Arginine is a nonvolatile amino acid. No signal could be detected when the

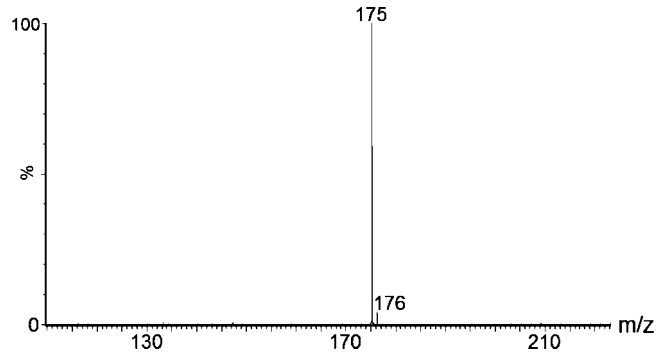

Figure 5. A mass spectrum of arginine in aqueous solution recorded using ND-EESI.

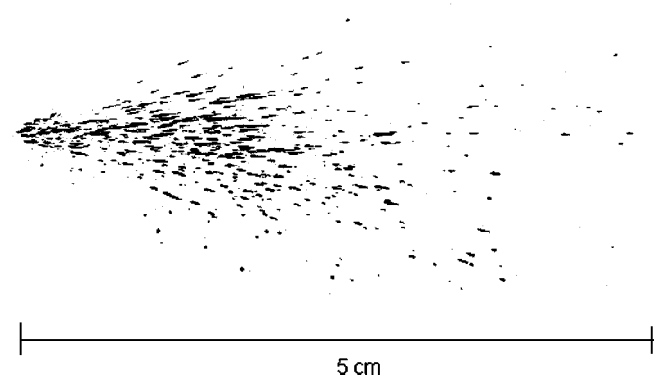

Figure 6. Aerosols produced by neutral desorption from a droplet of ethanol solution of rhodamine 6G. The fine droplets were recorded using a piece of white paper, which was placed parallel to the gas flow direction. The distance from the pipet tip to the paper surface was 5 mm. The color is due to deposition of rhodamine molecules on the paper surface. The extension of the plume was about 5 cm. The sample volume in the pipet was 2 μL. The neutral desorption gas flow was 400 L/h.

neutral desorption gas was off. This demonstrates that even nonvolatile samples can be transported from the liquid by neutral desorption. Further, we carried out a test experiment in which neutral desorption was performed on rhodamine 6G (1 mM in ethanol) under the same conditions used for perfume analyses. Figure 6 shows aerosol droplets of the rhodamine 6G solution after deposition on a piece of white paper. As rhodamine 6G is a typical nonvolatile compound, the essential factor contributing to its extraction from a large droplet on the pipet tip was aerosol generation induced by the neutral gas flow.

Sensitivity and Dynamic Range. In order to determine the sensitivity of the detection, a sample that did not produce any DEP signal ("White Musk" Eau de Toilette) was spiked with DEP (Note that "White Musk" Eau de Toilette is a fragrance different from "White Musk" Eau de Parfum examined by Greenpeace[3]). In the MS/MS experiments, the characteristic fragments (i.e., m/z 177, 149) of DEP could be simultaneously detected starting from a concentration of 100 ppb (w/w) DEP in the perfume. The total amount of DEP was quite low since only 1 μL of solution was used. The detection limit was about 10 times lower when DEP was diluted in a pure alcohol, e.g., methanol or ethanol, rather than a complex perfume matrix. This finding suggests that even though perfumes largely consist of alcohols, the neutral desorption efficiency depends on the viscosity of a particular perfume sample. We also noticed that maximum yields of the first and the second

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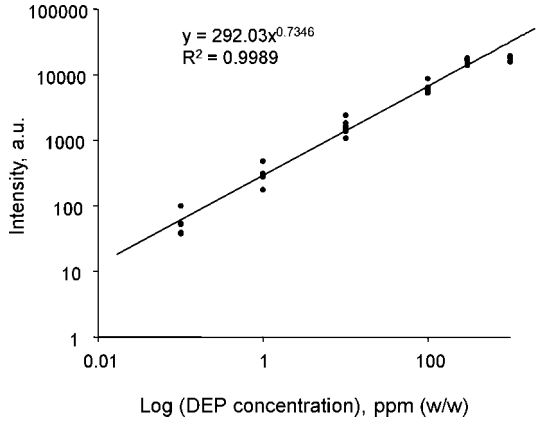

Figure 7. Dependence of the MS/MS signal intensity at *m/z* 177 on DEP concentration in ethanol.

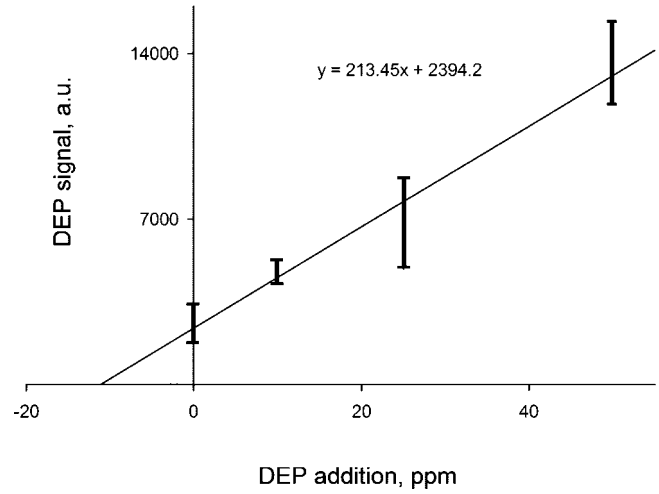

Figure 8. Quantification of the DEP content in "le Male" perfume using standard addition. The sample was diluted 1000 times in ethanol to make sure the response was linear. Signals were recorded from the diluted sample spiked with 10, 25, and 50 ppm of DEP along with a nonspiked sample. Concentration of DEP in the diluted sample was extracted by extrapolating the linear fit to the *x* axis ($213.45x + 2394.2 = 0$, $x = 11.2$ ppm). The number thus obtained was multiplied by 1000 to give the actual concentration of DEP in the nondiluted sample. The error bars show the standard deviation of the mean value of six measurements for each standard addition.

fragments occur at different collisional energy values. For example, the fragment at *m/z* 177 could be detected alone with a much higher intensity than when both fragments at *m/z* 177 and 149 showed up (as shown in Figure 3). In order to increase the sensitivity of the method, one can detect specific fragments at different CID energy values. The detection limit can thus be lower than 100 ppb in cases where the fragment *m/z* 177 is known to be exclusively derived from DEP, and then only this fragment can be used for quantification.

Another factor limiting the sensitivity rather than the methodology itself was chemical noise in the mass spectrometer. Phthalates are widely used in the production of PVC and other plastics as plasticizers. Such additives are not chemically bound to the polymer, i.e., they are continuously released into the ambient air or leached out.[70] This makes phthalic acid esters ubiquitous contaminants. For example, they can be extracted from the ESI source plastic tubing by the solvents used.[71] Also, the solvent itself can be contaminated by phthalates because of their leaching from plastic containers.[72] For most MS instruments, gases such as sheath gas are supplied through plastic tubes. As plastic materials commonly contain phthalates, DEP can be desorbed by the nitrogen gas flowing through the tubing and then delivered to the ionizing region. It was impossible to replace all the tubes used in our instrument, i.e., further attempts to eliminate the chemical background due to DEP would require a complete redesign of the ESI source. Fortunately, as typical DEP signals from perfume samples are relatively high, it was not necessary to get an absolutely clean background signal for screening of DEP in perfume samples.

Quantitative Determination of DEP. Since perfumes are complex samples, it is necessary to exclude false positive signal by using tandem mass spectrometry to utilize the major fragments for quantitative and qualitative analysis. Figure 7 shows the dependence of the MS/MS signal intensity of the fragment at *m/z* 177 on the DEP concentration in ethanol. The response curve was an exponential, with a linearity coefficient $R^2 = 0.9989$ in a doubly logarithmic representation, showing a dynamic range of 4 orders of magnitude. The figure suggests a detection limit far below 100 ppb; however, as discussed above, it is difficult to obtain a clean background. The quantitative signal response is also dependent on the matrixes of the samples. For most commercial perfume products, the major matrix is ethanol. However, as mentioned above, the same amount of DEP spiked into a DEP-free perfume matrix and into pure ethanol gave quite different signal levels. In order to overcome this matrix effect, standard addition was used for quantifying DEP in perfume samples.[73] Moreover, perfume samples were diluted in pure ethanol to make sure that the signal response would be linear, which is not the case for high DEP concentrations, as shown in Figure 7. Dilution was continued until the S/N ratio for the DEP signal was below 100, which represented a good compromise between sufficient sensitivity and elimination of matrix effects. The diluted solution was then spiked with known amounts of DEP (standard additions). Six independent measurements were made for each standard addition to record a response curve. The latter was extrapolated to give the unknown concentration of DEP in a perfume sample as shown in Figure 8 for "le Male". The same procedure was used for quantitative analysis of DEP in "CK One". Concentrations obtained were 1.1 ± 0.3% (w/w) for DEP in "le Male" and 0.28 ± 0.09% for "CK One". The same fragrances were studied in the Greenpeace survey,[3] and the DEP content reported was 0.99% and 0.11% for "le Male" and "CK One" accordingly. This reasonably good agreement suggests that our method can also be used for rapid semiquantitative analysis of the DEP content in perfumes.

CONCLUSIONS

Neutral desorption of liquid perfume samples using a gentle gas beam for rapid extractive electrospray ionization was dem-

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onstrated. The concept of neutral desorption sampling was extended for application to liquid samples for the first time. A novel method was established to semiquantitatively detect the content of DEP in various perfumes by tandem EESI-MS. DEP is a phthalate that is potentially toxic to humans but is still widely used in industry and in many products. Many countries are starting to regulate DEP contents in products such as toys. However, many perfume products contain significant amount of DEP, which requires a sensitive and easy-to-implement method for rapid screening of perfumes that may contain notable amounts of DEP. With the use of the method reported here, no sample pretreatment is required for perfume analysis, and a single sample analysis can be completed within a few seconds. The limit of determination for DEP in perfume was on the order of 100 ppb with tandem mass spectrometry. This method provided a dynamic response range about 4 orders of magnitude, providing a rapid way to obtain semiquantitative information on DEP in bulk perfume analyses. Furthermore, our experimental data show that both volatile and nonvolatile analytes in complex liquid samples can be directly sampled by neutral desorption. This sampling method provides a high duty cycle of analysis since absolutely no sample pretreatment is required. Because the liquid sample can be delivered quickly using cheap disposable devices such as pipets, this method is a convenient way for high-throughput screening of target compounds in liquid samples. For applications in which trace amounts of analytes need to be continuously monitored, the classic configuration of EESI using two spray beams[50,58,59] is probably preferable, because it enables online, real time monitoring of complex samples with ease. However, when high-throughput analysis is required (e.g., identification of hazardous species in bulk commercial products on the market), our novel sample delivery method becomes particularly useful.

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