



# Direct detection of aromatic amines and observation of intermediates of Schiff-base reactions by reactive desorption electrospray ionization mass spectrometry

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## ABSTRACT

The fast, sensitive detection for 6 aromatic amines and direct observation of intermediates of Schiff-base reactions were achieved through reactive desorption electrospray ionization mass spectrometry (reactive DESI-MS). Pure acetone was electrosprayed to impact the aromatic amines on the paper, allowing two reactions, a proton-transfer reaction and a Schiff-base reaction, to occur in these experiments. The former was used to detect the aromatic amines, and the protonated analytes generated were selected for the qualitative and quantitative analysis. The false-positive signals were excluded by tandem mass spectrometry. For the 6 analytes, linear signal responses were obtained, and each had a dynamic range of 5 orders of magnitude. The relative standard deviation (RSD) and limit of detection (LOD) for all the measurements were in 1.5–5.3% and 0.03–0.2 pg/mm<sup>2</sup> range, respectively. The latter is a nucleophilic addition reaction that occurred between the aromatic amines and the acetone. The carbinolamine intermediates of these reactions were directly detected and identified by reactive DESI-MS. The data show that reactive DESI-MS is not only a reliable, sensitive tool for chemical analysis, but also a valid and promising method for studying organic reactions simultaneously, especially for heterogeneous reactions that occurred at a solution/solid interface.

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## 1. Introduction

The unmatched abilities to detect, count, and characterize atoms and molecules make mass spectrometry (MS) a powerful and widely applicable analytical technology [1] for chemical analysis and also studying organic reactions [2]. Recently, a contemporary revolution occurred in MS with the introduction of new members to both the APCI and ESI families [3] of direct sampling desorption/ionization (DI) techniques [1], now known collectively as ambient mass spectrometry [3–6]. These techniques are different from the traditional atmospheric pressure ionization (API) sources, and they can be employed to analyze samples directly in their native status without sample pretreatment. The first landmark technique of ambient mass spectrometry is desorption electrospray ionization (DESI), which has become one of the most important DI techniques. Typical applications of DESI-MS include explosive detection [7,8], natural product analysis [9–11], pharmaceutical quality control [12–16], and tissue imaging [17–19]. The detection of trace analytes is an important part of DESI-MS, and the samples can be either solid or liquid mixtures. The spray solvent

is usually a methanol/water (1:1) mixture, and sometimes a little acid is added. In reactive DESI [20], instead of spraying only solvent on the sample surface, reagents are added into the solvent to react with the targeted compounds, and thus the selectivity and ionization efficiency of the analytes containing specific functional groups can be greatly improved by particular ion/molecule reactions [21,22]. For the detection of explosives on surfaces [20], the sensitivities for trinitrohexahydro-1,3,5-triazine (RDX) and octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX) were enhanced by adding chloride or trifluoroacetate (TFA) to the spray solvent. It was shown that when alkylamine was in the DESI spray solution, the sensitivity for artesunate molecules exposed on the tablet surface was increased 170-fold more than reagent-less DESI [23]. For imaging mass spectrometry, lipid alterations in injured rat spinal cord were mapped by reactive DESI-MS [24]. Reactive DESI-MS is also a useful tool for investigating the trace reactions: redox reactions [25], complex formation [23,26], chemical bond-forming reactions [21,22,27–29] and bimolecular reactions [30]. Because ambient mass spectrometry can provide transient detection to organic reactions [31], the detection of transient species in ultra-fast reactions can be achieved by reactive DESI-MS. For example, Zare et al. detected reactive intermediates formed in the secondary microdroplets on the millisecond timescale [32,33] and provided an extra case of DESI-MS for studying mechanisms of chemical reactions.

The class of aromatic amines has a special place among the chemical carcinogens, in terms of extent of use available scientific knowledge.

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Aromatic amines are widely used as raw materials and at an intermediate stage in the manufacturing of industrial chemicals such as pesticides, medicines, dyestuffs, polymers, surfactants, cosmetics and corrosion inhibitors [34]. They are also a common contaminant in several working environments: the chemical and mechanic industries and aluminum transformation. The relationship between arylamines and bladder cancer has been studied extensively [35]. Several analytical methods have been reported for the determination of aromatic amines. Among these methods, gas chromatography (GC) [36,37] and liquid chromatography (LC) [38,39] are common-used techniques. Capillary electrophoresis (CE) [40,41] and mass spectrometry [38] have also been employed. However, the sample pretreatment makes these methods time-consuming and laborious. Without any sample manipulation or sample-preparation steps, the ambient mass spectrometry (e.g., DESI-MS) may provide simple, high-throughput analysis for these compounds. Aromatic amines are also a reactant of a Schiff-base reaction, which is one of the most important reactions as the Schiff-base reaction has a wide variety of applications in many fields, such as in organic, biological, medicinal and analytical chemistry [42]. Snell proposed the generally accepted mechanism for this reaction [43], in which carbinolamine is the intermediate [44–46]. Several carbinolamine detection methods such as ultraviolet spectroscopy [47,48], Raman spectroscopy [49], and NMR [50–53] have been developed. All these methods have the complicated spectra, and the spectral features are easily interfered by those of the complex chemical components and/or the similar groups. While for the ultraviolet spectrometry, the evidence for the existence of the carbinolamine is indirectly obtained by the kinetic studies of the whole reaction process [54]. With the advantages of high sensitivity, selectivity and speed [1], MS is a very useful tool for studying the reaction mechanism. More importantly, MS can provide direct evidence for identifying the intermediate structure through the collision-induced dissociation (CID). Thus, ESI-MS was successfully used for the detection of carbinolamines in solution by Marquez et al. [55,56], though the detection is difficult [57] for the rapid decomposition of carbinolamines [51]. However, for heterogeneous reactions at a solution/solid interface, ESI-MS is not applicable, but such kind of reaction can be adequately investigated by reactive DESI-MS, with much shorter response time for the detection of the intermediate in a reaction [2]. Thus, in this paper the reactive DESI-MS was for the first time proposed to be used to study the Schiff-base reactions, especially for the several heterogeneous reactions. In addition, the simultaneous quantitative analysis of aromatic amines does not need sample pretreatment, which is necessary for the previous methods mentioned above.

In this study, pure acetone was used as the spray solvent and the reagent in reactive DESI-MS. The aromatic amine solutions were deposited on the paper. On the surface occurred two reactions: (1) the proton-transfer reaction, and (2) the Schiff-base reaction. The former reaction adds a proton to the aromatic amines similar to the traditional ESI-MS spray solvent. The aromatic amines were detected in this mode and the LOD is acceptable. In the latter reaction, the intermediates were observed directly and were proved to be the covalent carbinolamines by tandem mass spectrometry.

## 2. Materials and methods

### 2.1. Instrumental setup (DESI-MS)

All reactive DESI experiments were carried out using a commercial linear ion trap mass spectrometer (LTQ-XL, Finnigan Scientific, San Jose, CA) with a home-built DESI source. It consists of an inner capillary (fused silica, 100  $\mu\text{m}$  i.d., 190  $\mu\text{m}$  o.d.) for delivering the spray solvent and an outer capillary (stainless steel, 0.01 in. i.d., 1/16 in. o.d.) for delivering the nebulizing gas. The vertical distance between the sprayer tip and the sample surface was 2 mm. The horizontal distance between the sprayer and the inlet of the mass spectrometer was 4 mm. The angle between the sprayer and the paper surface was 45°. The

spray voltage was +3.5 kV. The nebulizing gas ( $\text{N}_2$ ) pressure was 1.4 MPa. Pure acetone was used as the electrospray solvent, and its flow rate was 5  $\mu\text{L}/\text{min}$ . The temperature and the voltage of the heated capillary of the LTQ instrument were maintained at 275 °C and 20 V, respectively. The tube lens voltage was 110 V. The default voltages for the conversion dynode, the detectors and the ion guide system were used without optimization. CID was performed with 20–32% (manufacturer's units) collision energy to the precursor ions, which were isolated with a mass window width of 1.6  $m/z$  units. A Mathieu parameter  $q_z$  value of 0.25 was used during collisional activation. Positive ion detection mode was used for all the experiments. The Xcalibur software from Finnigan was used to control the instrument and to process the data.

### 2.2. Materials and reagents

Aniline (AR) was purchased from Fuchen Chemical Reagent Factory (Tianjin, China). The 2-aminonaphthalene, 2,4,5-trimethylaniline, 4-chloroaniline and 4-chloro-2-methylaniline (HPLC-grade) were purchased from Dr. Ehrenstorfer GmbH (Augsburg, Germany). 2-Nitroaniline (98%) was purchased from Alfa Aesar China (Tianjin) Co., Ltd. (Tianjin, China). Acetone (AR) was purchased from Zhongtian Chemical Co., Ltd. (Wuhan, China). Ethanol (AR) was purchased from Hengxing Chemical Preparation Co., Ltd. (Tianjin, China). Filter papers were purchased from Hangzhou Special Paper Co., Ltd. (Hangzhou, China).

### 2.3. Samples

Each of the 6 aromatic amines was dissolved in ethanol to prepare working solutions ( $1 \times 10^{-4}$  g/mL to  $1 \times 10^{-8}$  g/mL). Filter paper was cut into 5 cm  $\times$  1 cm pieces as the substrate. For each experiment, a 1  $\mu\text{L}$  sample solution was deposited onto the filter paper, and the solution formed a sample spot about 10 mm<sup>2</sup>.

## 3. Results and discussion

### 3.1. Sample blank

For this reactive DESI experiment, pure acetone was used as the reagent and spray solvent to replace the commonly-used methanol/water (1:1) mixture. The mass spectrum of the background was recorded without sample introduction (see Fig. 1). The generator of the primary ions of DESI is the electrospray (ESI), which is suitable and very effective for analyzing polar compounds and the signal intensity will be stronger with the increasing of the polarity. Though the polarity of acetone is weaker than methanol and water, the signal intensity is still strong under the optimal conditions (as shown in Fig. 1). The two obvious peaks at  $m/z$  59 and  $m/z$  117 are originated from the protonated acetone and the protonated acetone dimer, respectively. The higher intensity of the protonated acetone dimer ( $m/z$  117) may be caused by pure acetone. These two kinds of ions can provide enough primary ions for further analysis of the aromatic amine samples. In the spectrum, there are other peaks with relatively high intensities, such as the ion of  $m/z$  99,  $m/z$  124,  $m/z$  157 and  $m/z$  173, etc. These peaks may be generated from the background of airborne compounds, and fortunately, no interference is observed.

### 3.2. The main reactions occurred in reactive DESI experiments

After the introduction of 6 aromatic amine samples (about 10 ng/mm<sup>2</sup>), the full scan spectra were obtained immediately and were shown in Fig. 2. In each spectrum, the base peak is the protonated molecule of the corresponding aromatic amine, such as the ions of  $m/z$  94 in Fig. 2(a). The two main types of primary ions are protonated acetone and their dimers (Fig. 1), so the protons are

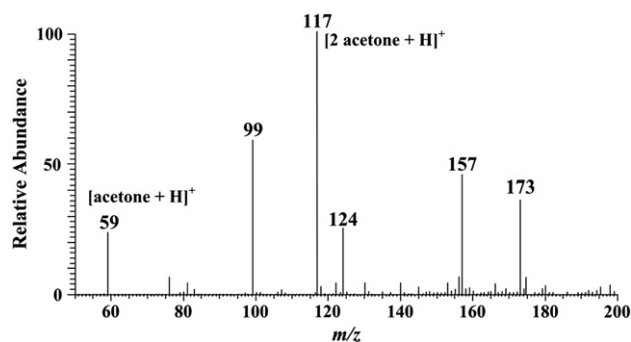


Fig 1. The spectrum of the background recorded by reactive DESI-MS.

transferred from these primary ions to the target analytes. The ions in the form of  $[M + H]^+$  were generated. Proton affinities (PA) are commonly used to assess whether or not a proton-transfer reaction is likely to be spontaneous [58]. In this study, the proton-transfer process would occur if the aromatic amines have a larger PA than acetone. The proton affinity of aniline is 882.5 kJ/mol [59], which is greater than that of acetone (812 kJ/mol [59]), thus a proton will transfer spontaneously from protonated acetone to aniline.

Though the exact PA values for 2-aminonaphthalene, 2-nitroaniline, 2,4,5-trimethylaniline and 4-chloro-2-methylaniline are not available, the formation of the protonated molecules in these experiments suggests that their PA are greater than 812 kJ/mol. The upper threshold of PA for these compounds may be less than 900 kJ/mol because many small- and medium-sized organic molecules have proton affinities <900 kJ/mol [58].

Another main reaction in these experiments is the Schiff-base reaction, which contains two steps [60]: nucleophilic addition and dehydration. In Fig. 2, the two reaction steps are very obvious. The nucleophilic agents are the aromatic amines which provide lone pair electrons to attack the carbon atom of the carbonyl group on the protonated acetone. This process is shown in Fig. 2 where the addition of acetone molecule to the protonated aromatic amines in the spectrum is displayed, and the formed adduct ions are the intermediates (named carbinolamines) of Schiff-base reactions by further CID experiments. In the next step, a molecule of water was eliminated from the intermediates and the product imines were produced as the protonated molecules. The analytes 4-chloroaniline and 4-chloro-2-methylaniline contain one Cl atom in each of their molecules. The protonated molecules produce two obvious isotope peaks  $[M + H]^+$  and  $[M + H + 2]^+$  by the contribution of the isotopes  $^{35}\text{Cl}$  and  $^{37}\text{Cl}$ , respectively (such as the ions of  $m/z$  128 and the ions of  $m/z$  130 in Fig. 2(e)). The corresponding signal ratio of the two peaks is 3:1,

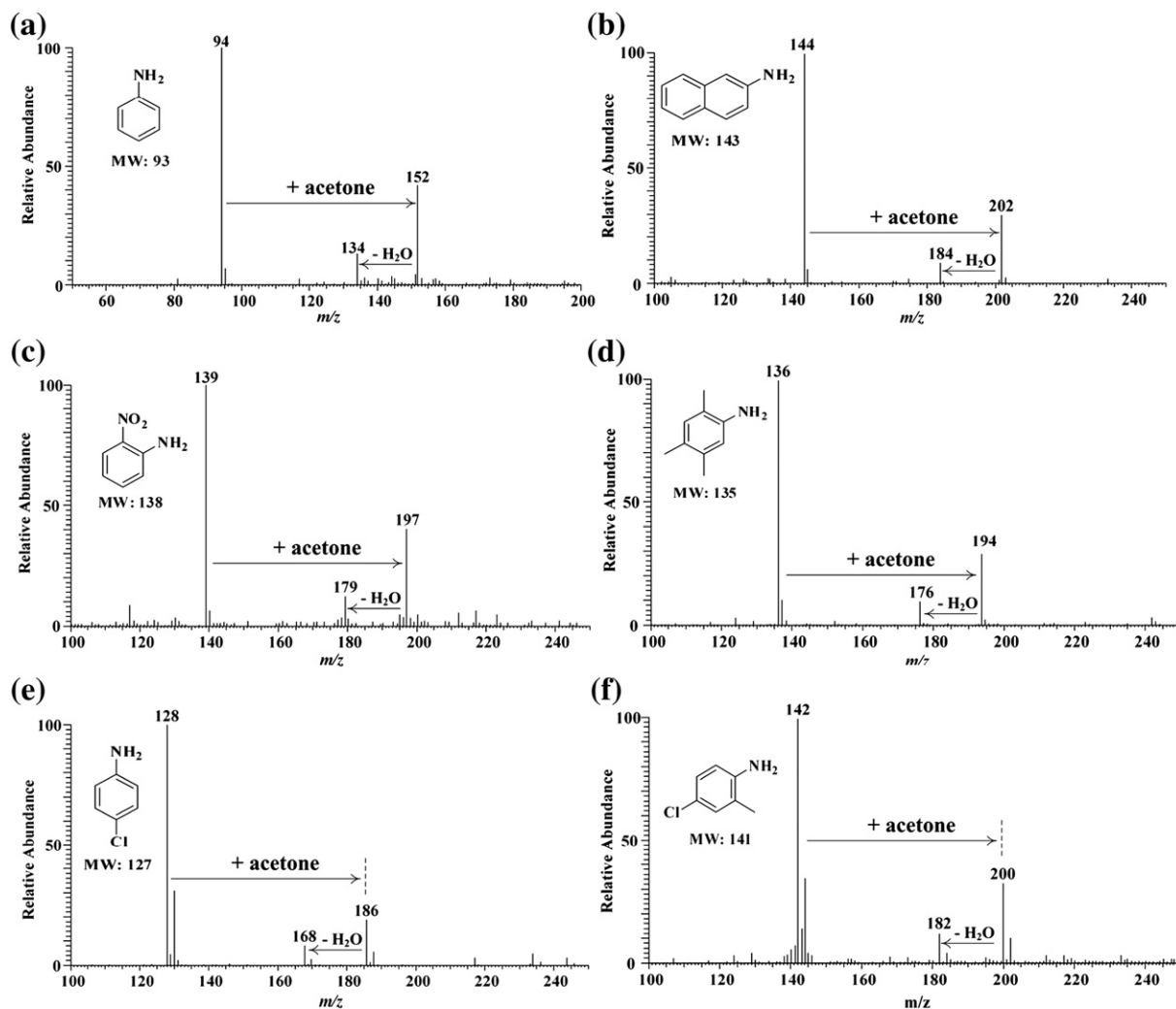


Fig. 2. DESI-MS spectra of the 6 aromatic amine: (a) aniline, (b) 2-aminonaphthalene, (c) 2-nitroaniline, (d) 2,4,5-trimethylaniline, (e) 4-chloroaniline, and (f) 4-chloro-2-methylaniline (all background subtracted).

which matches the known isotopic abundance ratio of  $^{35}\text{Cl}$  and  $^{37}\text{Cl}$ . The same signal ratio can be obtained for the intermediates and products of the Schiff-base reactions between 4-chloroaniline/4-chloro-2-methylaniline and protonated acetone (Fig. 2(e) and (f)). These data further support that the Schiff-base reaction occurred in these reactive DESI experiments.


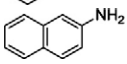
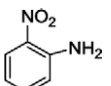
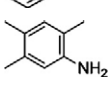
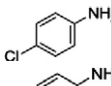
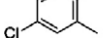
### 3.3. DESI-MS/MS analysis of aromatic amines

As indicated above, the protonated molecules of 6 aromatic amines showed obvious ion peaks on the full scan spectra, the further identification of these ions was performed by the CID experiments. The major characteristic fragment ions are shown in Table 1. For aniline, the collision energy (CE) was set at 32% to its protonated molecules ( $m/z$  94) in the CID experiment, and the main ionic fragments of  $m/z$  77, 67, and 53 were generated by the loss of  $\text{NH}_3$ ,  $\text{HCN}$ , and  $\text{CH}_3\text{CN}$ , respectively. For other aromatic amines, such as 2-aminonaphthalene, 2,4,5-trimethylaniline, 4-chloroaniline, and 4-chloro-2-methylaniline, their fragmentation pathways are in good agreement with the results obtained using DESI-MS/MS [61] or LC-ESI-MS/MS [38]. From the observation of these reactive DESI experiments, 2-nitroaniline is easily protonated and forms  $[\text{M} + \text{H}]^+$ , but its fragmentation pathway presents some differences from the other aromatic amines. During collision-induced dissociation (CID) experiments of 2-nitroaniline, the mass selected ion of  $m/z$  139 gave the fragment ions of  $m/z$  121 and  $m/z$  122 (Table 1), and the peak at  $m/z$  121 is the base peak. The ions of  $m/z$  122 are from the loss of  $\text{NH}_3$ , and the ions of  $m/z$  121 were generated by the loss of water during CID experiments. This phenomenon may be attributed to the “ortho effect” [62]. For 2-nitroaniline in this study, the two hydrogen atoms of the eliminated water molecule may come from the proton added on the nitro ( $-\text{NO}_2$ ) and original hydrogen on the amino ( $-\text{NH}_2$ ), respectively.

### 3.4. Quantitative analysis for aromatic amines

Of the two main reactions in these reactive DESI experiments, the proton-transfer reaction shows higher ionization efficiency than the Schiff-base reaction for the aromatic amines. The signals from the protonated molecules of the proton-transfer reaction are higher than that of the Schiff-base reaction for the 6 analytes (Fig. 1), and the corresponding ions have been identified by using tandem mass spectrometry (Table 1). Thus, the protonated amines were used for

**Table 1**  
DESI-MS/MS information for 6 protonated aromatic amines.

Compound	Molecular Structure	MW, [M + H] <sup>+</sup>	CE (%)	Main fragments (MS/MS)	Neutral loss
Aniline		93, 94	32	77 67 53	$\text{NH}_3$ $\text{HCN}$ $\text{CH}_3\text{CN}$
2-Aminonaphthalene		143, 144	28	117	$\text{NH}_3$
2-Nitroaniline		138, 139	20	121	$\text{CH}_3\text{CN}$ $\text{H}_2\text{O}$
2,4,5-Trimethylaniline		135, 136	20	122 121	$\text{NH}_3$ $\text{CH}_3$
4-Chloroaniline		127, 128	20	93	$\text{NH}_3$ $3 \times \text{CH}_3$ $\text{Cl}$
4-Chloro-2-methylaniline		141, 142	28	111 107 127	$\text{NH}_3$ $\text{Cl}$ $\text{CH}_3$

MW, molecular weight; CE, collision energy; MS/MS, tandem mass spectrometry.

the quantitative analysis of the aromatic amines. Their linear dynamic ranges were obtained by depositing trace amounts of aromatic amines onto the filter papers, and showed a linear range of 5 orders of magnitude (Fig. 3). Table 2 shows the narrow RSDs for six replicates of different amounts of aromatic amines on the filter paper. Aniline showed the highest sensitivity (curve I in Fig. 3). This is probably due to its higher volatility. The LOD of aniline on the filter paper is  $0.03 \text{ pg/mm}^2$  ( $S/N=3$ ) under the experiment conditions. 2-Nitroaniline and 4-chloro-2-methylaniline have similar sensitivities, which are the lowest among the six samples. The sensitivities of the six amines are different, and the differences in sensitivity may be caused by the differences of their volatility, PA and adherence with filter paper.

The LODs in the experiments were measured by depositing a series of standard amine solutions onto filter paper when the signal intensity reached 3 times the noise level. The calculation equation used is as follows:

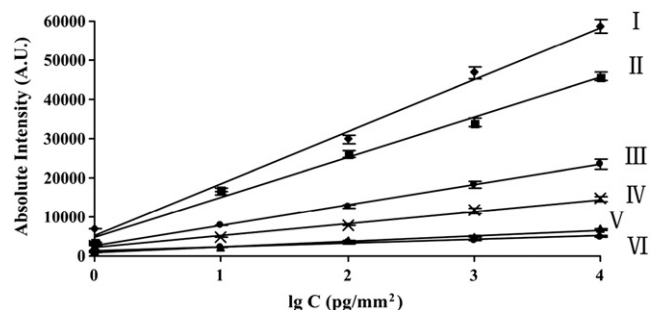
$$\text{LOD} = \frac{3\sigma c}{S}$$

where  $\sigma$  is the standard deviation of all the measurements performed on the blank sample ( $n=6$ ),  $c$  is the minimal concentration of a standard solution deposited on the filter paper to make the calibration curve, and  $S$  is the mean signal intensity value of the analyte at the concentration  $c$ . Depending on the experiment conditions, the LOD values detected for the 6 amines are in the low picogram per millimeter squared range,  $0.03\text{--}0.2 \text{ pg/mm}^2$  (Table 3), which are about 2 orders of magnitude lower than that of LC-MS [38] by comparing the results of the same analytes: 2-aminonaphthalene, 2,4,5-trimethylaniline, 4-chloroaniline and 4-chloro-2-methylaniline.

DESI-MS is highly sensitive for the detection of aromatic amines on the surface. The relatively low RSD values from the measurements are acceptable for the rapid detection. The LOD values are also desirable. Obviously, unlike traditional methods (e.g., GC-MS [37], LC-MS [38]) which need tedious sample pretreatments when aromatic amines are on a surface, DESI-MS is a high-throughput detection method. Here, the spray solvent is pure acetone, which is effective for the detection of aromatic amines. Thus, acetone could be another choice of the spray solvent when DESI-MS is used for quantitative analysis.

### 3.5. Direct observation and identification for the intermediates of the Schiff-base reaction

Along with the proton-transfer reaction for detecting aromatic amines, the Schiff-base reaction also occurs when acetone is sprayed. For aniline, the peaks at  $m/z$  152 and  $m/z$  134 in the full-scan spectrum (Fig. 2 (a)) correspond to the protonated intermediate and the



**Fig. 3.** Linear responses of 6 aromatic amines in the reactive DESI experiments: I, aniline,  $y = 12236x + 5076.4$ ,  $R^2 = 0.992$ ; II, 4-chloroaniline,  $y = 10170x + 4950.1$ ,  $R^2 = 0.992$ ; III, 2-aminonaphthalene,  $y = 5147.4x + 2727.7$ ,  $R^2 = 0.998$ ; IV, 2,4,5-trimethylaniline,  $y = 3081.5x + 2164.7$ ,  $R^2 = 0.990$ ; V, 2-nitroaniline,  $y = 1379.5x + 1035.9$ ,  $R^2 = 0.992$ ; VI, 4-chloro-2-methylaniline,  $y = 942.17x + 1232.6$ ,  $R^2 = 0.994$ . Each data point performs six measurements; the range of RSD values for the data points are 1.5–5.3% ( $S/N=3$ ).



**Table 2**  
RSDs (%) for 6 aromatic amines on filter paper measured by DESI-MS ( $n = 6$ ).

Compounds	Concentration of aromatic amines (pg/mm <sup>2</sup> )				
	1	10	100	1000	10,000
Aniline	2.1	5.3	3.6	3.2	3.1
2-Aminonaphthalene	2.6	1.4	3.9	4.9	4.8
2-Nitroaniline	3.8	2.1	2.2	1.5	1.9
2,4,5-Trimethylaniline	4.1	2.1	1.4	5.2	4.7
4-Chloroaniline	2.3	3.2	2.6	3.3	2.4
4-Chloro-2-methylaniline	4.2	3.0	1.6	3.3	2.2

product of Schiff-base reaction, respectively. The two ions are identified by the CID experiments in Fig. 4. Upon CID, the ions of  $m/z$  134 break into the ionic fragments of  $m/z$  117, 119, 106 and 93 by the loss of  $\text{NH}_3$ ,  $\cdot\text{CH}_3$ ,  $\text{CH}_2\text{CH}_2$ , and  $\text{CH}_3\text{CN}$  (Fig. 4 (a)), respectively. These fragments were consistent with those observed in the reference experiment using acetone *N*-phenylimine standard (SI Appendix, Fig. S1). To obtain the intermediate structural information, the ions of  $m/z$  152 were isolated for CID experiments. Under the experimental conditions, the ions of  $m/z$  152 produced peaks at  $m/z$  134, 137, 135, 124, 120, 110, and 94 by the loss of water,  $\cdot\text{CH}_3$ ,  $\cdot\text{OH}$ ,  $\text{CH}_2\text{CH}_2$ ,  $\text{CH}_3\text{OH}$ ,  $\text{CH}_2\text{CO}$  and  $\text{CH}_3\text{COCH}_3$  (Fig. 4 (b)), respectively. In Fig. 4 (b), the peak at  $m/z$  134 dominates the MS/MS spectrum showing that the elimination of water rather than acetone from the intermediate ions was favored under the conditions. These neutral losses demonstrate that the precursor ions of  $m/z$  152 were the intermediates rather than the noncovalently bound acetone-aniline complexes (see Fig 2 (a)). More interestingly, as shown in the inset of Fig. 4(b), the ionic fragments ( $m/z$  134) from the MS/MS experiment gave the same fragments as those observed using either the acetone *N*-phenylimine (SI Appendix, Figure S1) or the ions ( $m/z$  134) observed in the full-scan MS spectrum (see Fig 2(a)). These data further confirmed that the ions of  $m/z$  152 were the carbinolamine. Similar results were also obtained using 2-aminonaphthalene, 2-nitroaniline 2,4,5-trimethylaniline, 4-chloroaniline and 4-chloro-2-methylaniline (SI Appendix, Table S1).

The Schiff-base reaction occurred on the surfaces in these experiments are heterogeneous reactions at a solution/solid interface. They are different from the traditional, liquid-phase reaction that the intermediates cannot be detected by ESI-MS. The data indicate that reactive DESI-MS is a valid tool for identifying transient intermediates of this type reaction.

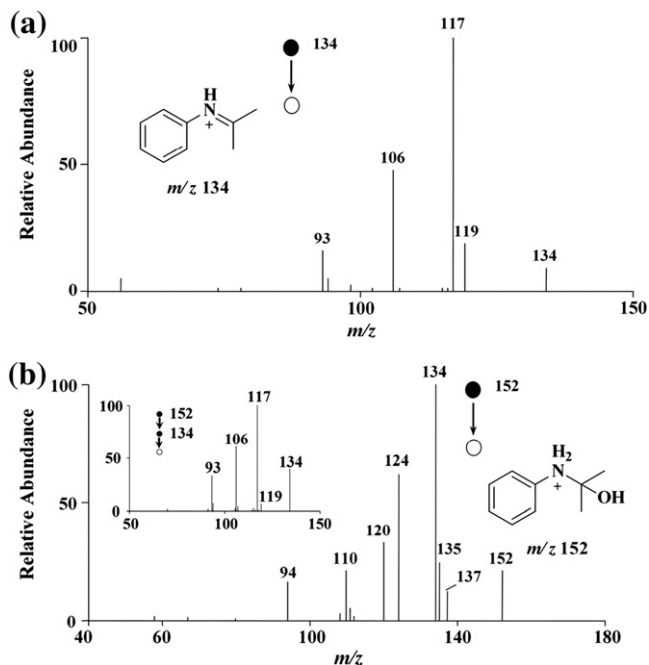
#### 4. Conclusions

As a demonstration, without tedious sample pretreatments, six aromatic amines on the surface were detected directly by DESI-MS. The linear signal responses with a dynamic range of 5 orders of magnitude were obtained. The RSD (1.5–5.3%) and LOD (0.03–0.2 pg/mm<sup>2</sup>) for these amines are notable. These data indicated that using acetone as the spray solvent can give quantitative results for aromatic amines, and provided an alternative spray solvent for DESI-MS.

In this study, the Schiff-base reactions between six aromatic amines and acetone that occurred on filter paper were observed and were verified. The successful detection for intermediates of 6 Schiff-base reactions

**Table 3**  
LOD values for detection of 6 aromatic amines on the filter paper by DESI-MS.

Aromatic amines	LOD (pg/mm <sup>2</sup> )
Aniline	0.03
2-Aminonaphthalene	0.08
2-Nitroaniline	0.18
2,4,5-Trimethylaniline	0.08
4-Chloroaniline	0.06
4-Chloro-2-methylaniline	0.20



**Fig. 4.** The mass spectra obtained by DESI-MS<sup>n</sup> for the Schiff-base reaction between aniline and acetone: (a) the product, (b) the intermediate, the inset shows the MS<sup>3</sup> spectrum of the ionic fragment ( $m/z$  134) produced from protonated intermediate ( $m/z$  152).

showed that reactive DESI-MS is a valid tool for studying heterogeneous organic reactions and that DESI-MS is also a valuable method to detect transient intermediates on the milliseconds timescale. In conclusion, the results show that reactive DESI-MS is a promising platform for the detection of analytes and the study of organic reaction at the same time.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.microc.2012.10.021>.

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