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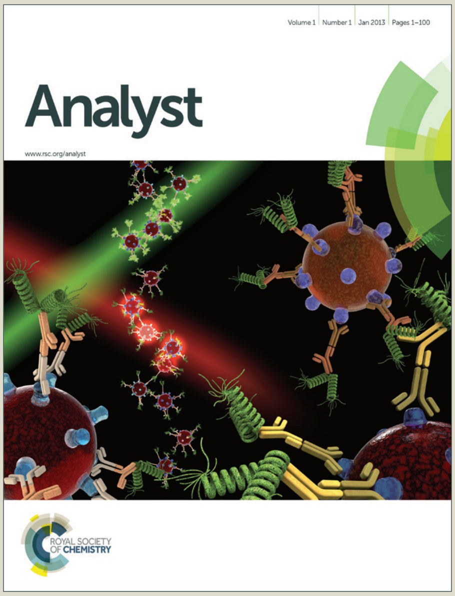

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Analysis of Diarylmethylamine Compounds Using Electrospray Mass Spectrometry: Formation Mechanisms of Radical Ions and Dehydro Cations†

Tian Cai [a,b,c], Xiao-Ying Xu[b], Zhi-Jun Wu [a*]

Correspondence to: Zhi-Jun Wu, Chengdu Institute of Biology, University of Chinese Academy of Sciences, Chengdu 610041, China. E-mail: wuzj@cib.ac.cn

a Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu 610041, China

b Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences, Chengdu 610041, China

c University of Chinese Academy of Sciences Beijing 100039, China.

Abstract

A series of diarylmethylamine compounds were analyzed using electrospray ionization quadrupole time-of-flight mass spectrometry (ESI-QTOF-MS). $[M]^{+\cdot}$ and $[M\text{-}H]^{+}$ were both observed, but shown different abundances. A possible mechanism forming $[M]^{+\cdot}$ and $[M\text{-}H]^{+}$ was proposed to explicate the change rule of the ratio of $I_{[M]+\cdot}/I_{[M\text{-}H]+}$. The $[M]^{+\cdot}$ has two structures, which can interconvert into each other in gas phase. The substituted groups on the benzene rings play a crucial role in the transfer of the two structures. Electron withdrawing groups can prevent the formation of carbocation, thus nitro-containing diarylmethylamines remain mainly structure I and were detected as $[M]^{+\cdot}$. On the contrary, electron donating groups help to stabilize carbocation. This makes structure I transfer to structure II, and structure II prefers to further generate $[M\text{-}H]^{+}$ by loss of an H radical. Nuclear magnetic resonance and D-labelled MS experiments indicate that 1-C-H bond has strong activity.

Key words: diarylmethylamine, electrospray, $[M]^{+\cdot}$, $[M\text{-}H]^{+}$, Electron withdrawing group, electron donating groups

Introduction

Electrospray ionization (ESI) is one of atmospheric pressure ionization (API) methods, which produce charged ions under atmospheric pressure. ESI technique transfers the ions from solution to gas phase in a soft way, and it is an useful tool to analyze a majority of polar molecules even unstable compounds.[1] In ESI source, analyte molecules are charged through several pathways, mainly including ionization through charge separation, adduct formation, gas-phase reactions, and electrochemical oxidation or reduction.[2] In positive-ion mode of ESI-MS, even-electron ions are observed always, such as $[M+H]^+$, $[M+Na]^+$, $[M+K]^+$ and so on. However, in a few cases, some special ions can be detected as $[M-H]^+$ [3-4], $M^{+\cdot}$ [5-7], $[M+Na-H]^{+\cdot}$ [8] and $[M+H]^-$ [9] ions. In our previous study, $M^{+\cdot}$ radical ions of two diarylmethylamine compounds were detected.[7] Radical ion resulting from iodine-containing diarylmethylamines during ESI is reasonable. However, why can the nitro-containing diarylmethylamines produce the radical ions? And what is the role of nitro group in the formation of radical ions? Why did the radical ion generate from 1-C-H instead of 4-methoxyaniline group? To gain insights into these queries, a series of diarylmethylamine compounds were analyzed by ESI-MS. The formation mechanisms of $[M]^{+\cdot}$ and $[M-H]^+$ were proposed.

Experiment setup

High-performance liquid chromatography-grade methanol and acetonitrile were procured from Fisher Scientific (Pittsburgh, PA, USA). Formic acid, sodium hydroxide, and methanol-D4 were purchased from Fluka (Switzerland), Alfa Aesar

(Ward Hill, MA, USA) and Cambridge Isotope Laboratories (Andover, MA, USA), respectively. The diarylmethylamine compounds were obtained from Zhang's laboratory.[10] Mass experiments were accomplished on a Bruker micrOTOF-Q mass spectrometer (Bremen, Germany). The mass resolution was 10,000 FWHM (full width at half maximum) at 922 u. Helium was used as the collision gas and high-purity nitrogen gas as the nebulizer and dry gas at flowing rate of 4.0 L/min and the pressure of 0.3 bar. The ESI source conditions were as follows: capillary V, -4500 V; end plate voltage, -4000 V; capillary exit voltage, 120 V and dry gas temperature, 180 ^{o}C. The isolation window was set as 1.0 Da for CID. The concentrations of the samples were 1×10^{-6} mol/L. The injection rate was set as 180 μL/h. The mass data were processed by Bruker Compass DataAnalysis 4.0. Nuclear magnetic resonance (NMR) experiments were completed on a Bruker Avance 600 (Bremen, Germany) NMR spectrometer.

Result and discussion

A series of diarylmethylamine compounds (compounds **1-7**, Fig. 1) were dissolved in methanol and analyzed by ESI-MS in positive-ion mode. For compounds **1-4** **c**ontaining nitro group, both $[M]^{+\cdot}$ and $[M\text{-}H]^{+}$ with high relative abundance were observed, while for compounds **5-7**, only $[M\text{-}H]^{+}$ show high relative abundance (Fig. 2). The relative abundance of $[M]^{+\cdot}$ and for compounds **1-7** were shown in supporting information.† Obviously, although the structures of these compounds are very similar, the relative intensities of $[M]^{+\cdot}$ and $[M\text{-}H]^{+}$ vary greatly.

Herein, a possible mechanism (Scheme 1) forming $[M]^{+\cdot}$ ion and $[M\text{-}H]^{+}$ was proposed to explicate the differences of their relative intensities. The $[M]^{+\cdot}$ are formed by loss of an electron and have two structures, structure I and structure II. The two structures can interconvert into each other in gas phase. Structure I is detected as $[M]^{+\cdot}$ and structure II prefers to further generate $[M\text{-}H]^{+}$ by loss of an H radical. The substituted groups on the benzene rings affect greatly the transfer of the two structures. Electron withdrawing group can prevent the formation of 1-carbocation (Scheme 1), thus nitro-containing diarylmethylamines remain mainly structure I during ESI. On the contrary, the electron donating groups contribute to stabilizing carbocation. This makes structure I transfer to structure II, and structure II further generate $[M\text{-}H]^{+}$ ions. The ratio of $I_{[M]+\cdot}/I_{[M\text{-}H]+}$ for compounds **1**-**7** were shown in Fig. 3. For compound **1**, there is a nitro-group in benzene ring A. Thus, the $[M]^{+\cdot}$ was detected as primary peak. When benzene ring B is substituted by thiophene ring for compound **2**, the relative abundance of $[M\text{-}H]^{+}$ increases. The reason is that sulfur atom of thiophene contributes two π electrons and the $\Pi56$ conjugation system is electron richer than benzene ring.[11] There is a methoxyl group linked to benzene ring B for compound **3**, the relative abundance of $[M\text{-}H]^{+}$ is higher than that of $[M\text{-}H]^{+}$. When benzene ring B is linked to two methyl groups in compound **4**, the relative abundance of $[M\text{-}H]^{+}$ further increases. For compound **5**-**7**, only the electron donating groups are linked to benzene ring A or B, therefore, the $[M\text{-}H]^{+}$ become dominant. Interestingly, iodine can stabilize radical, and structure I is primary. Therefore, iodine-containing diarylmethylamines is detected as a $[M]^{+\cdot}$.[7] Incidentally, when trace acid or alkali were added into solution, the ratio of $I_{[M]+\cdot}/I_{[M\text{-}H]+}$ were not affected. This implies that these ions are formed in the gas phase.

Why does the loss of electron occur in 1-C-H bond? In addition to the reported experiment,[7] nuclear magnetic resonance (NMR) experiment indicated that 1-C-H bond exhibit strong activity. When oxidant was added into D-$CHCl_3$ solvent of compound **1**, the ratio of hydrogen atom in 1-C-H (5.5 ppm) and N-H (4.0 ppm) in ^1H NMR spectrum (supporting information†) decreased. This indicates that part of compound **1** transferred into imide soon after. Obviously, 1-C-H bond is easily oxidized. In addition, when CD_3OD was selected as solvent, the *m/z* 317 was detected instead of *m/z* 316 for compound **5** (supporting information†). This implies that active D atom remains in *m/z* 317 and the loss of H result from 1-C-H. Contrast MS/MS experiments of *m/z* 316 and 317 (supporting information†) further supported the result.

Conclusions

In this study, several diarylmethylamine compounds were analyzed using ESI-QTOF-MS, and the unexpected ions, $M^{+\cdot}$ and $[M\text{-}H]^+$, were detected. A mechanism forming $[M]^{+\cdot}$ and $[M\text{-}H]^+$ was proposed at the first time to explicate the change rule of the ratio of $I_{[M]+\cdot}/I_{[M\text{-}H]+}$. It was found that substituent effect plays a crucial role in contributing to the formation of $[M]^{+\cdot}$ and $[M\text{-}H]^+$. Solution acidity cannot affect the the ratio of $I_{[M]+\cdot}/I_{[M\text{-}H]+,}$ which implies that these ions are formed in the gas phase. In summary, this finding indicates that the diversity of ionization modes in ESI source resulted in the generation of abnormal ions. What's more, the study can help to understand the nature of chemical bond breaking.

Acknowledgments

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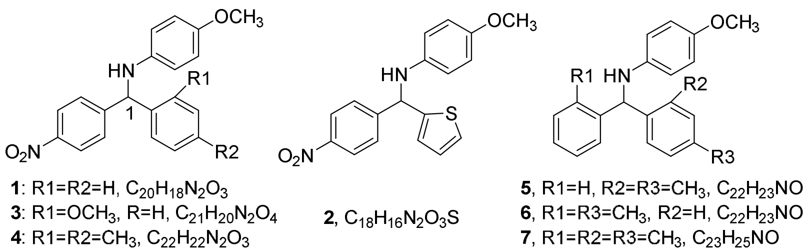


Figure 1. Diarylmethylamine compounds: (**1**) ***Mr*** 334.1317; (**2**) ***Mr*** 340.0882; (**3**) ***Mr*** 364.1423; (**4**) ***Mr*** 362.1630; (**5**) ***Mr*** 317.1780; (**6**) ***Mr*** 317.1780; (**7**) ***Mr*** 331.1936.

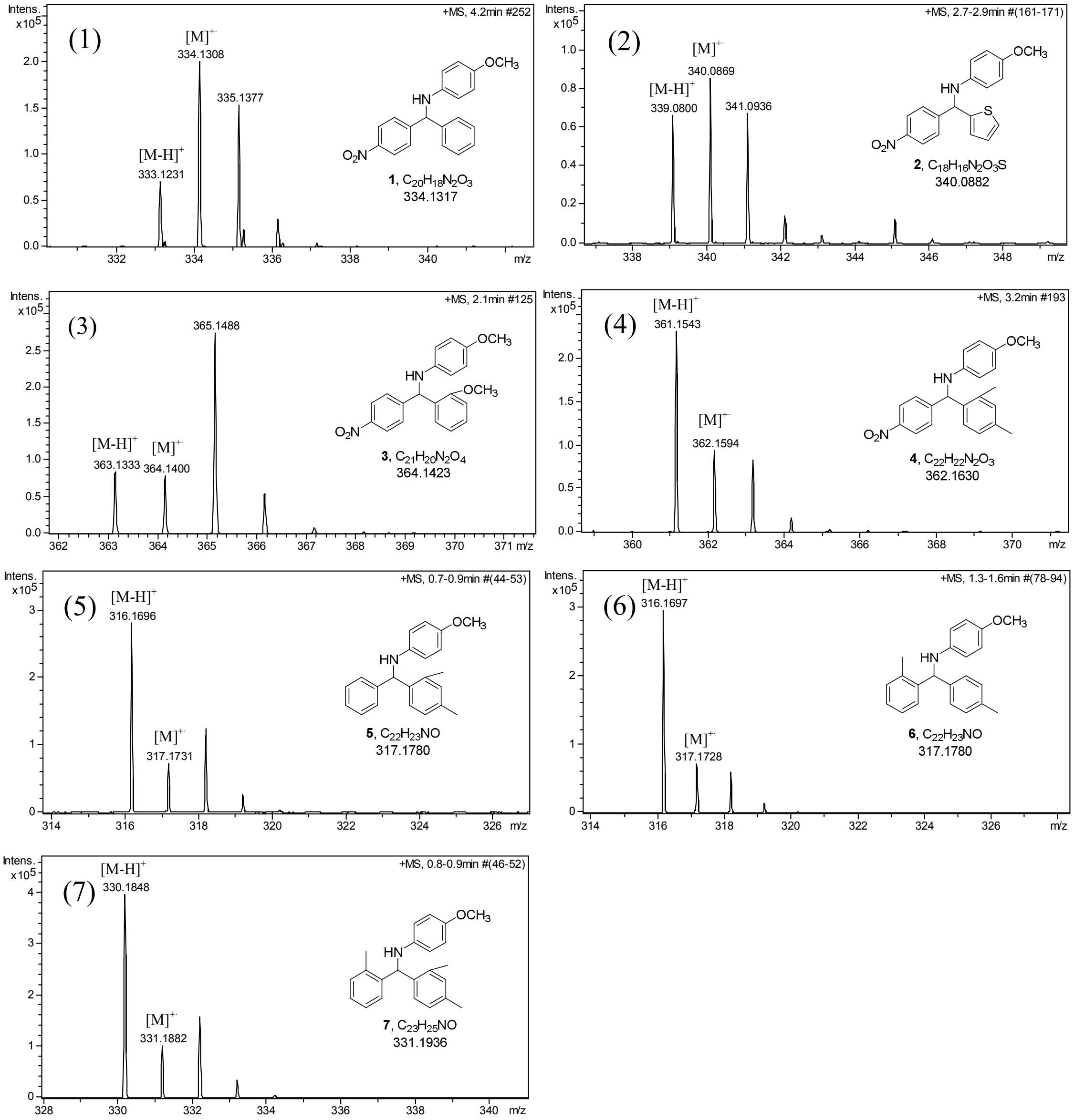


Figure 2. (1)-(7) were the mass spectra of compounds **1-7**, respectively.

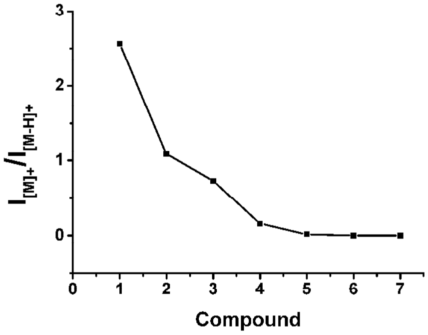
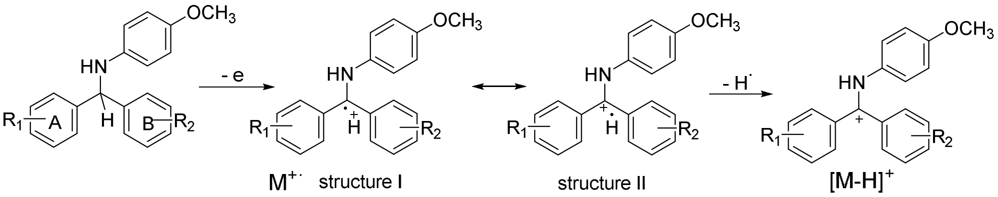


Figure 3. The ratio of $I_{[M]+\cdot}$%/$I_{[M-H]+}$ % for compounds **1**-**7**. $I_{[M]+\cdot}$% = $I^{*}_{[M]+\cdot}$% (observed) - $I_{[M-H]+}$% (observed)× Isotope $Ratio_{(m+1)}$% (theory).



Scheme 1. The possible forming process of $[M]^{+\cdot}$ and $[M-H]^{+}$ ions of Diarylmethylamines.