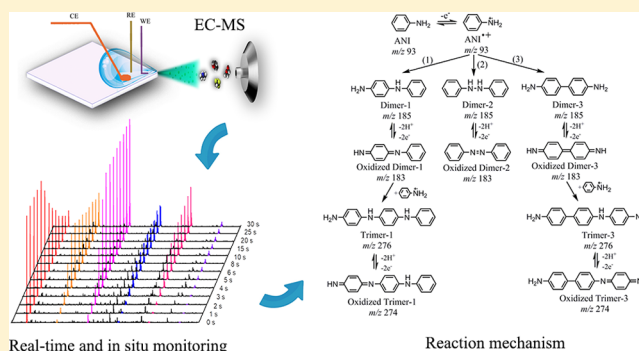


In Situ Mass Spectrometric Screening and Studying of the Fleeting Chain Propagation of Aniline

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Supporting Information

ABSTRACT: A simple and effective approach to studying the mechanism of electrooxidation of aniline (ANI) is reported in this paper. It was accomplished by an innovative electrochemistry (EC)-mass spectrometry (MS) coupling, which can sample directly from a droplet-scale reacting electrolyte for mass spectrometric analysis. With this setup, the polymer chain growth of ANI could be monitored in situ and in real-time. The short-lived radical cations ($\text{ANI}^{\bullet+}$, m/z 93.06) as well as the soluble dimer (m/z 183.09) and oligomers (m/z 274.13, 365.18, ...) were successfully captured. Using the EC-MS and tandem mass spectrometry, the dimers produced by head-to-tail (4-aminodiphenylamine), head-to-head (hydrazobenzene), and tail-to-tail (benzidine) coupling of radical cations were found in the same polymerization process. Moreover, the EC-MS method was also applicable for determining the propagation speed of ANI when applying different electrolyte salts and oxidizing potentials.



Bruckenstein and Gadde successfully detected the volatile electrode reaction intermediates and products by using a combined electrochemistry (EC)-mass spectrometry (MS) device in 1971.¹ Since then, EC-MS was established as an important auxiliary technique for the mechanism study of electrochemical reactions, and numerous ionization sources/setup have been established.^{2–11} However, many of these EC setups were assembled by connecting a flowing electrochemical cell (or a transferring capillary) to the inlet of MS. This might increase the response time from the reacting electrolyte to the inlet MS. Considering that the electrochemically generated intermediates commonly have a fleeting lifetime, the creation of an effective interface between the electrochemical electrolyte and the MS inlet poses an experimental challenge.

Recently, Zare and co-workers developed a rotating water-wheel setup combined with DESI. During the measurement, the rotating wheel functioned as both the working electrode and the sampler, which achieved a delay time at the scale of a millisecond.^{12–14} In another study by Qiu et al., a hybrid ultramicroelectrode was designed and performed as both a microelectrochemical cell and a nanospray emitter. An ultrasmall droplet of analyte on the tip of the micro-electrochemical cell can be sampled, ionized, and then analyzed

by MS immediately after triggering the piezoelectric pistol.¹⁵ However, the electrochemical setups in these two studies are too complicated to be assembled and/or utilized by others. Meanwhile, the studied samples have very simple or one electrochemical reaction procedure, and there was no evidence indicating whether they are applicable to the ones with complex reactions and multiple polymer chain growing steps.

Herein, a simple and effective electrochemical controlling system was introduced for the mechanistic studies of electrochemical reactions. The idea was based on our previous research, where a glass sheet ($18 \times 18 \times 0.15$ mm) was used for the spray ionization source for droplet-scale MS analysis.¹⁶ As depicted in Figure 1, the experimental design employed a typical electrochemistry three-electrode unit mounted on one corner (sample corner) of the glass sheet, which was positioned in front of the MS inlet. These three electrodes included a platinum-coil working electrode (WE), a platinum-plate counter electrode (CE), and a Ag/AgCl reference electrode (RE). Because the polymerization is mainly occurring

Received: June 4, 2018

Accepted: June 6, 2018

Published: June 6, 2018



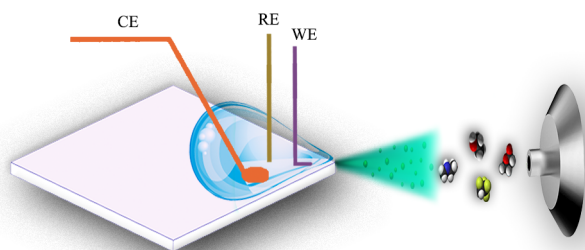


Figure 1. EC-MS apparatus for studying the electrooxidation of ANI; the ionization source is composed by a three-electrode system (working, counter, and reference electrode) mounted on a glass sheet.

surrounding the WE, it was placed in front of the MS inlet at a distance of 5.3 mm. The glass sheet was the reservoir of electrolyte as well as the spray ionization source, and the distance from the sample corner to the MS inlet was 2.2 mm. Electrooxidation of the studied samples was performed by the potentiostatic method. Compared with the traditional way, two high voltages were separately applied to the WE and CE in order to achieve the electrochemical reaction and meanwhile to generate the electric field for spraying out the reacting electrolyte from the sample corner. During the experiment, the applied voltages were 4.5 kV + ΔE and 4.5 kV for WE and CE, respectively. ΔE could be regarded as the electrooxidation potential of aniline (ANI) and 4.5 kV is the droplet spray voltage. Hence, the electrodes functioned as both the electrooxidation controller and the high-voltage input, which could be competent for real-time, in situ monitoring of the whole reaction process.

As a proof-of-concept analyte in this research, 5 mM aniline (ANI) solution (pH = 6.3) was prepared in 99:1 MeOH/H₂O with 100 μ M lithium trifluoromethanesulfonate. To achieve a good electrooxidation and meanwhile a steady spray, approximately 80 μ L of the solution was added to the sample corner. When the analyte solution was sprayed at voltages of 4.5 kV + 0 V (WE) and 4.5 kV (CE), a cation at m/z 94.07 attributed to the protonated ANI monomer ([ANI + H]⁺) was observed (Figure 2a). Electrooxidation of ANI was started by applying an additional potential of 10 V to the WE (the total was 4.5 kV + 10 V), and the results are shown in Figure 2b. As can be seen, the major peaks are ascribed to a series of oxidized ANI oligomers in the singly charged protonated state. The base peak at m/z 274.13 in this spectrum is from the most abundant ions of the trimer.^{17,18} Other oligomers including dimer, tetramer, pentamer, hexamer, heptamer, and octamer were found at m/z 183.09, 363.16/365.18, 454.20, 545.24, 634.27, and 725.31.^{19,20} Appearance of the peak cluster on the basis of m/z value, e.g., m/z 363.16 and 365.18, implies that at least two different tetramers were formed. More importantly, the nature of the electrochemically generated mass spectrum in Figure 2b suggests that the oxidative process would not be influenced substantially by the high spray voltage (4.5 kV).

Also in Figure 2b, a peak at m/z 93.06 is observed (inset window, marked with blue), which is assigned to the ANI radical cation (ANI^{•+}). It is the first ambient ionization MS evidence for the electrochemical generation and isolation of ANI^{•+}. Figure 2c shows the extracted ion chromatogram (EIC) of the m/z 93.06 peak during the electrooxidation of ANI. Obviously, the signal intensity of the radical cation ANI^{•+} increased greatly when an oxidation potential ($\Delta E = 10$ V) was

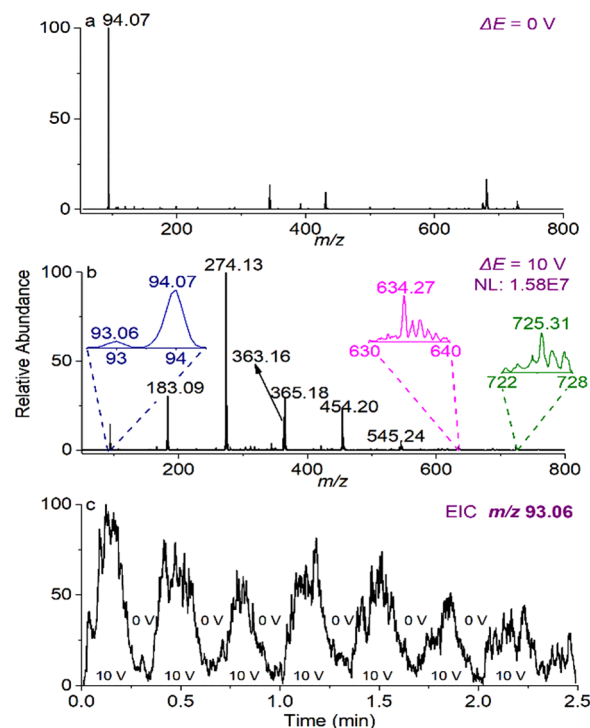


Figure 2. EC-MS mass spectra of electrooxidation of ANI obtained at positive-ion mode: (a) the additional potential (ΔE) applied on WE is 0 V, (b) $\Delta E = 10$ V, and (c) EIC for the m/z 93.06 peak as the ΔE is turned on and off.

applied to the WE compared to that of no oxidation potential ($\Delta E = 0$ V). In addition, when 10 V was applied, the signal intensity decreased as the test proceeded, suggesting that the ANI monomers were consumed by the formation of oligomers. It demonstrates that electrooxidation of ANI is originating from the oxidation of ANI monomers.

By means of the EC setup, the electrooxidation can be continuously performed in a droplet, allowing the monitoring of the polymer chain growth in real-time. Figure 3 shows the mass spectra of electrooxidation of ANI recorded at different reaction times. As the reaction proceeded, a dramatic decrease in the signal intensity of ANI monomer (m/z 94.07) and increase in those associated with the oligomeric products (from

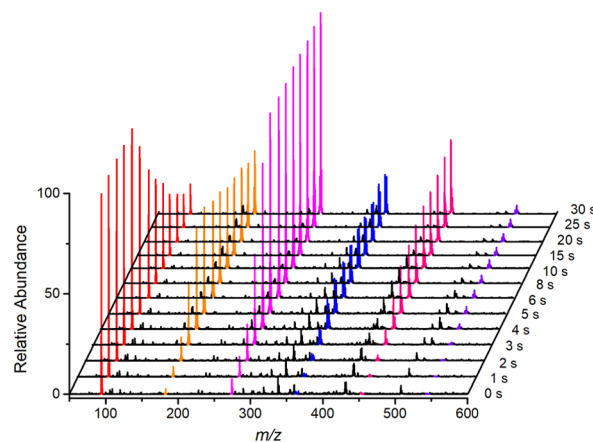


Figure 3. Real-time, in situ monitoring of electrooxidation of ANI by using EC-MS coupling. The mass spectra were obtained at different reaction times.

dimer to hexamer) occurred. This observation strongly proves the mechanism of electrooxidation of ANI; i.e., the large oligomer is formed by oxidation of small oligomer and following addition of radical cations or other oligomers.²¹ In addition, the base peak of the spectrum was shifted to the trimer (m/z 274.13) after five seconds, indicating the most abundant ions of this oligomer were generated during the reaction. Hence, the polymer chain growth might be dominated by coupling of one radical cation with one oxidized dimer to form the trimer.

As discussed, the peak clusters appearing at the m/z values revealed that such oligomers contain different molecular structures. This might be caused by various dimer species including 4-aminodiphenylamine (head-to-tail structure), hydrazobenzene (head-to-head structure), and benzidine (tail-to-tail structure).²² Using the EC-MS setup and tandem mass spectrometry (MS^2), we are able to characterize the category of the ANI dimers. All the three standard dimer samples with molecular weight of 184.24 are commercially available. A 5 μ M standard dimer solution was prepared in MeOH. Approximately 50 μ L of the solution was dropped to the sample corner and ionized at a spray voltage of 4.5 kV. To achieve the MS^2 spectrum, the collision-induced dissociation (CID) voltage was adjusted to 30 V and the ion maximum injection time was 100 ms.

Figure 4a–c shows the MS^2 spectra of the three standard dimers. The peaks at m/z 185.11 represented the protonated molecules of standard 4-aminodiphenylamine, hydrazobenzene, and benzidine. A parallel experiment has been done corresponding to the dimeric products generated from the electrooxidation of ANI. The peak of m/z 185.11 attributed to [dimers + H]⁺ was also observed on the spectrum of electrooxidation of ANI (see the inset window in Figure 4d, marked with pink). However, owing to the rapid deprotonation of this dimer and following formation of large oligomers, the signal intensity of this peak was very low. Hence, the MS^2 spectrum of m/z 185.11 was determined, and the result is shown in Figure 4d. There are mainly four fragment ions observed on this spectrum, and two of them at m/z 93.06 and 168.09 can be also found in the spectra of the three standard samples. However, the one at m/z 153.13 only appeared on the spectrum of standard hydrazobenzene with much higher signal intensity, indicating the formation of head-to-head dimer during polymerization. Because the relative signal intensity of the fragment ions at m/z 108.00 and 153.13 in Figure 4d is dissimilar to that of in Figure 4b, there should be other dimer species existing in this dimeric product. Considering that the ion of m/z 108.00 appears in the spectra of standard 4-aminodiphenylamine and hydrazobenzene, the dimeric product might contain both head-to-tail and head-to-head dimers.

Thus, the initial stages of electrochemical polymerization of ANI obtained in this research are concluded in Scheme 1. Obviously, all of the ANI oligomers are formed via a series of oxidation and/or addition reactions. Polymer chain grows via (a) dimerization reaction where two radical cations (ANI^{•+}) form a dimer; (b) oxidation of the dimer which gives an oligomeric radical; (c) combination of this oligomeric radical with a radical cation to form a trimer or combination of this oligomeric radical with another oligomeric radical to form a tetramer (e.g., m/z 363.16 in Scheme 1). A large oligomer is formed by oxidation of small oligomer and following addition of radical cations or other oligomers.²³ On the basis of our knowledge, it is not possible to obtain a large oligomer by

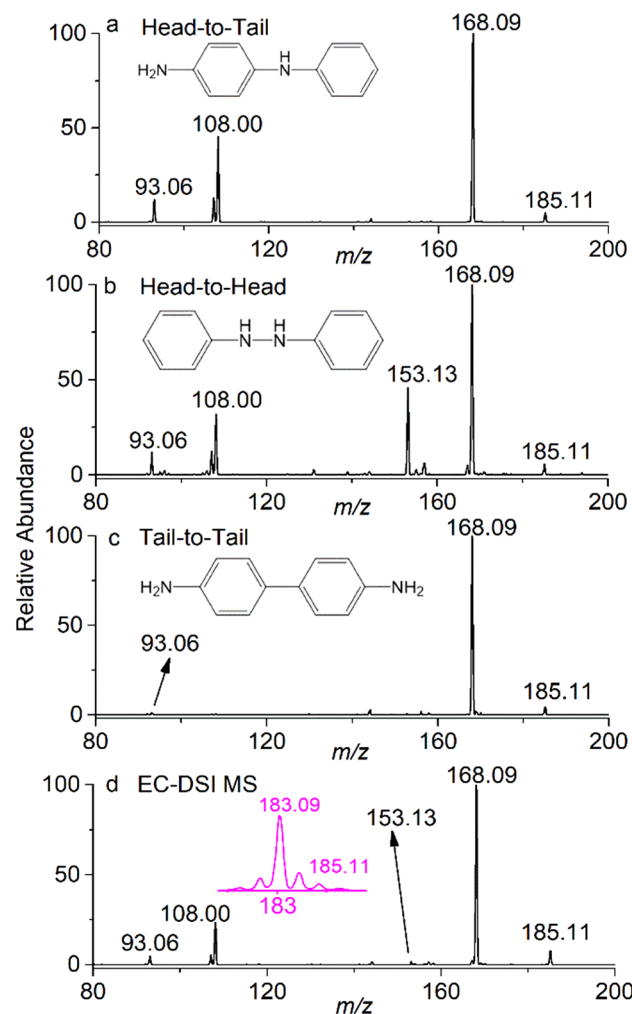


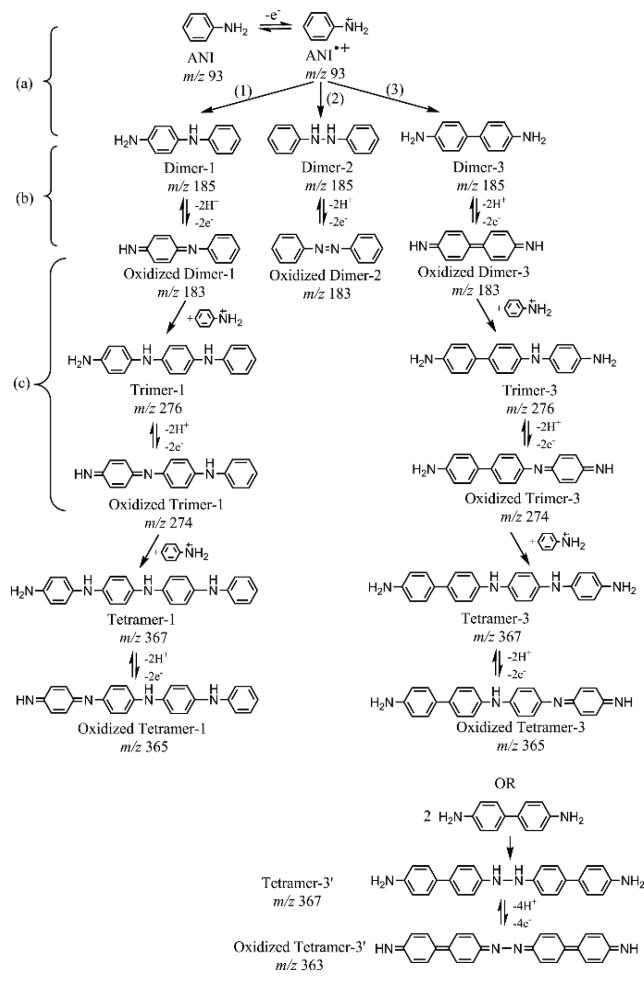
Figure 4. MS^2 spectra of the standard dimers and experiment generated ANI dimers (m/z 185.11): (a) 4-aminodiphenylamine, head-to-tail type, (b) hydrazobenzene, head-to-head type, (c) benzidine, tail-to-tail type, and (d) experiment generated ANI dimers.

coupling the head-to-head radical with other radical cations or oligomeric products.

Electrooxidation of ANI with different electrolyte salts was also studied by the EC-MS coupling. Figure S2 presents the spectra when the analyte solutions were spraying for ten seconds. By comparing the signal intensities of the dimer and oligomer peaks on the spectra, it can be concluded that the polymerization rate was influenced by the electrolyte salts and decreased in the order of $\nu_{KH_2PO_4} \geq \nu_{NH_4Ac} > \nu_{LiCF_3SO_3} > \nu_{KCl}$. This observation is the first ambient ionization MS evidence that the polymerization rate is affected by electrolyte salts. In another experiment, the ANI was polymerized by using various oxidizing potentials for ten seconds (Figure S3). As expected, a high potential would enhance the polymerization rate, which was directly reflected by the signal intensities of the dimer and oligomer peaks in these spectra. The oligomer species influenced by the various synthetic potentials and electrolyte salts will be reported in the future.

The EC-MS coupling developed in this research successfully monitored the complex polymer chain growing steps of ANI. The existence of radical cation ANI^{•+} and other transient intermediates from dimer to octamer were confirmed. Because the electrooxidation was performed in a droplet, the polymer-

Scheme 1. Initial Stages of Electrooxidation of ANI



ization rate of ANI with different salts and oxidizing potentials can be identified. This EC setup combined with MS has the advantages of high sensitivity, easy assembly, and convenient utilization and could be carried out in real-time and in situ monitoring, making itself a promising technique for mechanistic studies of electrochemical reactions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.analchem.8b02498.

Mass spectra and text giving the experimental details (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research is supported by the National Key R&D Program of China (grant numbers 2016YFF0100302, 2016YFF0103801), National Natural Science Foundation of China (grant number 21705030), and Natural Science Foundation of Shandong (grant number ZR2018PB016). R.N.Z. thanks the US Air Force Office of Scientific Research through the Basic Research Initiative Grant (AFOSR FA9550-16-1-0113).

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