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Detection of the Short-Lived Radical Cation Intermediate in the Electrooxidation of *N*,*N*-Dimethylaniline by Mass Spectrometry

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Abstract: *The N,N-dimethylaniline (DMA) radical cation DMA$^{\bullet+}$, a long-sought transient intermediate, was detected by mass spectrometry (MS) during the electrochemical oxidation of DMA. This was accomplished by coupling desorption electrospray ionization (DESI) MS with a waterwheel working electrode setup to sample the surface of the working electrode during electrochemical analysis. This study clearly shows that DESI-based electrochemical MS is capable of capturing electrochemically generated intermediates with half-lives on the order of microseconds, which is 4–5 orders of magnitude faster than previously reported electrochemical mass spectrometry techniques.*

Determining the first step in electrooxidation poses an experimental challenge. Often, a one-electron loss occurs, but the resulting radical cation escapes detection because it reacts so rapidly. One such example that has been extensively studied is the radical cations of aromatic amines.[1–9] Efforts to identify the radical cation species of aromatic amines with MS have been successful for some of the more stable radical cations.[2,3,8] However, identification of the radical cation of *N*,*N*-dimethylaniline (DMA) has not been achieved by thermospray MS,[10] spectroelectrochemistry, and electron paramagnetic resonance,[11] or fast scanning cyclic voltammetry.[12–14] By using fast scanning cyclic voltammetry, the second-order rate constant for the dimerization of DMA$^{\bullet+}$, as well as other aromatic amines, was determined to be on the order of $10^5\,\text{M}^{-1}\,\text{s}^{-1}$.[12,14] In 2014, however, Cao, Kim, and Bard succeeded in observing what is proposed to be DMA$^{\bullet+}$ by using scanning electrochemical microscopy (SECM) with ultramicroelectrodes.[1] DMA$^{\bullet+}$ is generated at the tip of a Pt wire (ca. 500 nm radius) and is collected on a Pt substrate (5 μm radius) separated from the Pt tip by a few hundred nanometers. By varying the separation, the dimerization process was shown to follow second-order kinetics with a rate constant of $2.5\times10^8\,\text{M}^{-1}\,\text{s}^{-1}$. SECM experiments could be performed at DMA concentrations as high as 0.4 mM in acetonitrile, under which conditions the half-life is 10 μs. At greater concentrations, the dimerization is reported to be too fast to obtain good collection efficiency.[1] We report herein MS detection of the electrochemical formation of DMA$^{\bullet+}$ at a concentration of 4.7 mM DMA in acetonitrile by using an ambient ionization platform described recently[6]. Using the measured rate constant of $2.5\times10^8\,\text{M}^{-1}\,\text{s}^{-1}$,[1] the calculated half-life of DMA$^{\bullet+}$ is less than 1 μs. Our approach is general, easy to implement, and is compatible with a wider range of operational concentrations relative to SECM.[1] This study suggests that many other short-lived electrochemical intermediates could be identified and studied by this means since MS is a general detector with high chemical specificity, unlike electrochemical detectors.

The experimental design in Figure 1 greatly resembles the waterwheel setup previously reported,[6] which employs a round rotating platinum working electrode immersed in an acetonitrile solution containing 1 mM lithium triflate as the electrolyte. The distance between the MS inlet and the working electrode surface is approximately 2 mm. As the working electrode rotates, a thin layer of liquid film develops on the electrode surface (approximately 1 mm in thickness). A plain carbon cloth counter electrode and an Ag/AgCl reference electrode are immersed in the reservoir of electrolyte solution. A metal contact (not shown) rests against the platinum working electrode to complete the three-electrode system. A potentiostat (WaveNow, Pine Research Instrumentation, Durham, NC) is used to apply a potential across the three electrodes. The typical current is on the order of milliamperes and the typical resistance between the working

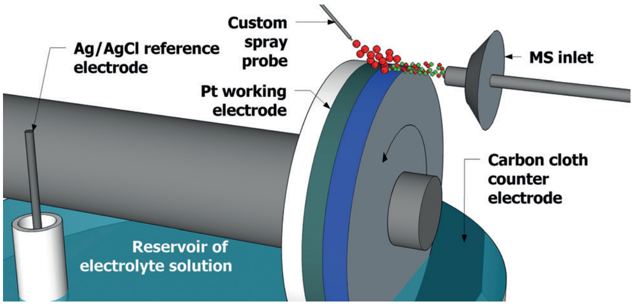

Figure 1. The apparatus used for the detection of electrochemical reaction intermediates employs a rotating waterwheel electrode. The enlarged red droplets are the sample microdroplets formed from the spray. The smaller red and green secondary microdroplets represent the electrolyzed solution that is bound for the mass spectrometer. Direction of rotation is indicated by the curved arrow.

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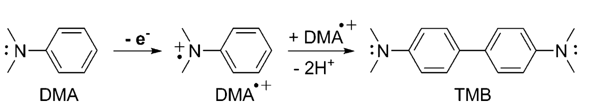
electrode and the counter electrode is on the order of kiloohms.

Above the rotating waterwheel system, a custom spray probe directs a stream of sample microdroplets to the surface of the working electrode. No high voltage is applied to the sample spray to minimize in-source oxidation. The spray droplets hit the surface of the thin film of electrolyte solution, now thinner than 1 mm owing to the N_2 nebulizing gas pressure, on the surface of the working electrode. Much like in desorption electrospray ionization DESI-MS[15,16] and easy ambient supersonic spray MS[17–19], tinier secondary microdroplets are directed into the mass spectrometer[20,21] and are analyzed with an LTQ Orbitrap XL hybrid mass spectrometer (Thermo Fisher Scientific, San Jose, CA), where the *m*/*z* ratio is determined by utilizing the high mass accuracy and high resolving power of the Orbitrap mass analyzer.[22]

DMA is proposed to electrochemically dimerize (Scheme 1) through electrooxidation to first form DMA$^{\bullet+}$. Two DMA$^{\bullet+}$ units react to form the dimer, *N*,*N*,*N*′,*N*′-tetramethylbenzidine (TMB). TMB can be subsequently electrooxidized to form TMB$^{\bullet+}$ and TMB^{2+}.[1,12]



Scheme 1. Proposed DMA electrochemical oxidation leading to the formation of TMB.

Solutions of DMA were prepared in 1 mM lithium triflate at concentrations ranging from 24 μM to 4.7 mM. When the sample solution is sprayed onto the working electrode rotating at 1 rev/s, the protonated DMA cation is observed at *m*/*z* 122.0962 (Figure 2a, theoretical *m*/*z* 122.0964, error −0.8 ppm). When an oxidation potential is applied across the rotating working electrode, a peak at *m*/*z* 121.0885 is observed, which is ascribed to the DMA radical cation intermediate (Figure 2b, theoretical *m*/*z* 121.0886, error −0.8 ppm). The MS signal of this species increases greatly when an oxidizing potential is applied to the working electrode, as is observed in the extracted ion chromatogram (EIC) in Figure 2c.

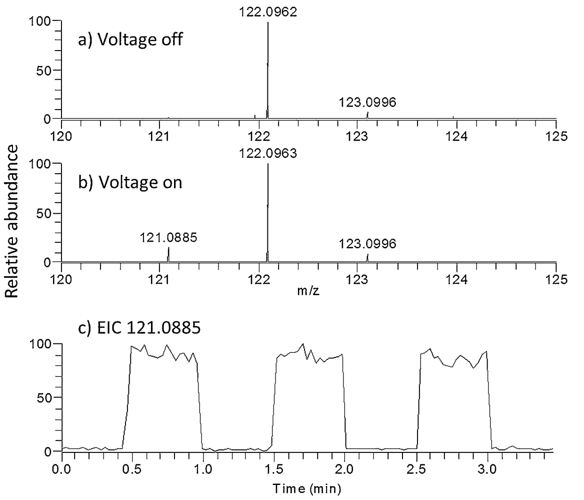


Figure 2. Positive-ion-mode mass spectra of 4.7 mM dimethylaniline. a) 0.0 V applied to the working electrode; b) 2.0 V applied to the working electrode; and c) the EIC for the 121.0885 peak as a function of the applied potential, which is varied between 0.0 V and 2.0 V in 30 s intervals.

This observation indicates that the 121.0885 peak originates from the electrochemical oxidation of DMA. Peaks were also observed at *m*/*z* 241.1698, attributed to the protonated TMB (theoretical *m*/*z* 241.1699, error −0.4 ppm), and *m*/*z* 240.1624, attributed to the radical cation of TMB (theoretical *m/z* 240.1621, error +1.2 ppm; see the Supporting Information). The MS signal intensity for each of these species increases greatly with the applied potential, thus indicating that they originate from the electrochemical oxidation of DMA. This mass information emphasizes the fact that the dimerization reaction proceeds via initial electrochemical oxidation. Coupled with the measured second-order rate constant of $2.5\times10^{8}\,\text{M}^{-1}\,\text{s}^{-1}$ from Cao et al.,[1] and assuming full electrochemical conversion of DMA to DMA$^{\bullet+}$, the half-life of the observed DMA$^{\bullet+}$ is calculated to be 0.85–170 μs, dependent on the initial concentration of DMA. While complete conversion of DMA into DMA$^{\bullet+}$ is not expected, peak intensities for the protonated TMB and TMB$^{\bullet+}$ are both on the same order of magnitude, sometimes higher, than that of protonated DMA, thus indicating a significant conversion of DMA into DMA$^{\bullet+}$. In light of the fact that the transmission of microdroplets from the DESI surface (i.e., the ring working electrode surface in this case) to the MS inlet would take a number of half-lives, it might at first seem surprising that DMA$^{\bullet+}$ with a half-life on the order of microseconds was still detected by MS in this study. However, this behavior can be accounted for by the high sensitivity of MS and the fact that the concentration of DMA$^{\bullet+}$ after *n* half-lives is the initial concentration of DMA$^{\bullet+}$ divided by $(n+1)$, based on second-order reaction kinetics. It is also possible that the droplet flight time is shortened somewhat by the pneumatic effect of instrument pumping.

This study shows the first ambient ionization mass spectrometry evidence for the electrochemical generation and isolation of DMA$^{\bullet+}$. This result confirms the previous work of Cao, Kim, and Bard,[1] who found evidence for this species by using scanning electrochemical microscopy. The significance of this finding, however, is that the coupling of a waterwheel working electrode setup and DESI-MS can lead to the isolation of fleeting electrochemical intermediates and products on the order of microseconds, which is 4–5 orders of magnitude faster than for previously reported electrochemical mass spectrometry techniques.[6,23,24]

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