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Quantitative Online Analysis of Liquid-Phase Products of Methanol Oxidation in Aqueous Sulfuric Acid Solutions Using Electrospray Ionization Mass Spectrometry

W. Zhao, Z. Jusys, and R. J. Behm*

Institute of Surface Chemistry and Catalysis, Ulm University, D-89069 Ulm, Germany

We describe a novel method and setup for quantitative online analysis of the liquid-phase methanol oxidation products in acidic aqueous solutions by electrospray ionization mass spectrometry (ESI-MS). This includes a specially designed flow system, which allows continuous online mixing, derivatization, extraction, separation, and quantitative detection within ca. 3 min. For electrospray ionization of formaldehyde, it is first online-derivatized by 2,4-dinitrophenyl hydrazine to form the easily ionizable 2,4-dinitrophenyl hydrazone. Then, both formic acid and derivatized formaldehyde are online extracted into an immiscible organic phase, which, after separation from the aqueous phase, is piped to the ESI-MS for analysis. This strategy ensures complete removal of the highly corrosive sulfuric acid from the analyte and allows the liquid-phase methanol oxidation reaction (MOR) products (formaldehyde and formic acid) to be quantitatively detected by ESI-MS. Finally, the potential of this method for online analysis in electroanalysis and electrocatalysis is discussed.

The electrooxidation of small organic molecules often results in a variety of incomplete oxidation products, in addition to the stable product CO_2.[1−3] For a fundamental understanding of the reaction mechanism as well as for practical purposes, e.g., for minimizing the emissions of incomplete oxidation products such as formaldehyde or acetaldehyde in direct oxidation fuel cells by optimizing the selectivity of the catalyst and the reaction conditions, it would be highly desirable to identify and quantify the respective reaction products. During recent decades, various techniques such as in situ infrared spectroscopy (IR),[4−6] online differential electrochemical mass spectrometry (DEMS),[4,7−9] fluorescent spectroscopy,[10] gas chromatography (GC),[11] and high-performance liquid chromatography (HPLC)[12,13] have been employed to monitor and quantify the products of reactions such as the methanol oxidation reaction (MOR) in the gas phase, liquid phase, and on the electrode surface. Despite this variety of techniques, online detection of products has remained a problem for many cases. Chromatographic techniques, which allow us to separate and identify a wide range of products, lack the time resolution necessary for continuous online detection. IR spectroscopy, though fast enough, is often not able to distinguish between different products, and also the quantification is often problematic. Finally, DEMS is fast enough but, with the commonly used membrane interface, limited to volatile products and small molecules that can easily penetrate the membrane separating the electrochemical cell and the mass spectrometer chamber.[14−16] Therefore, there is a clear need for the development of analytic techniques that allow us to online monitor and quantify product molecules which are not detectable by a classic membrane-inlet DEMS setup.

One possible way to circumvent the problems confronted with when using a standard DEMS setup is to use electrospray ionization mass spectrometry (ESI-MS).[17] This technique, which is based on field-assisted evaporation and ionization of the analyte was already employed for the detection of organic molecules or direct analysis of electrochemical reaction products, mainly in organic electrolytes.[18−23] ESI-MS would be particularly suited for

* To whom correspondence should be addressed. E-mail: juergen.behm@uni-ulm.de.

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the direct detection of liquid-phase products of electrocatalytic reactions such as methanol oxidation, since, due to the membrane-inlet system in conventional online DEMS, the latter is limited to gaseous/volatile product analysis. In addition, since there is little or no fragmentation of the molecules during the soft ionization in ESI-MS, this could avoid the interference between the mass fragments occurring in electron impact ionization mass spectrometry.

On the other hand, a number of fundamental problems have to be solved to enable the application of ESI-MS for online monitoring the products of electrocatalytic reactions. This is the topic of the present paper, where we describe the design, operation, and performance of an ESI-MS setup for online quantitative ESI-MS detection of the liquid-phase MOR products formaldehyde and formic acid.

For this purpose, the following problems have to be solved. First, electrospray ionization does not allow ionizing carbonyl groups (aldehydes and ketones), since these functional groups can hardly add or lose a proton. Therefore, the detection of formaldehyde by ESI-MS requires an appropriate derivatization. 2,4-Dinitrophenyl hydrazine (2,4-DNPH) is commonly used for derivatizing aldehydes to form a hydrazone, which provides a lone electron pair at the nitrogen atom to add/lose a proton.[24] The online derivatization of analytes, however, is not widespread. The difficulties mainly concern the compatibility of the derivatization reagents and derivatized products with the mobile phase used for separation. For instance, Herráez-Hernández et al. reported about the online derivatization into precolumns for the determination of drugs by liquid chromatography, using both a precolumn and analytical column for the derivatization and separation of analytes, which required electrically controlled switching valves.[25] The latter can be avoided for the derivatization of formaldehyde, if the derivatized product does not have to be separated from the 2,4-DNPH for detection. In the present work, we tested the online derivatization reaction of 2,4-DNPH with the analyte (formaldehyde), both in 0.5 M sulfuric acid solution, in a first step.

Furthermore, severe complications arise from the high acidity of the supporting aqueous electrolyte (sulfuric acid solution), which not only affects the ionization probability of organic molecules but also leads to severe corrosion of the instrument. Therefore, sulfuric acid must be fully removed before the analyte solution reaches the ESI-MS, while the aliquots of the molecules of interest should still be present in the analyte solution. Appropriate strategies need to be developed to achieve this goal. Here, we present an approach for the online extraction of organic molecules from a strongly acidic aqueous phase into an immiscible organic phase, which after phase separation is piped to the ESI-MS for quantitative analysis, while sulfuric acid solution remains in the aqueous phase waste. To achieve this objective, it is necessary to design an online extraction device, which can be operated continuously.

Online extraction has attracted considerable attention for various applications.[26,27] In general, online extraction devices are based on passing two or more phases through a capillary or through microfluidic systems (laminar flow). Alternatively, online extraction can be achieved via segmented flow of the immiscible phases.[28−30] In both cases, mass transfer between the phases occurs via diffusion, and the devices allow a high overall throughput. Recently, Kralj et al. reported an approach for continuous liquid−liquid extraction, which was based on a microfluidic device.[31] The complex setup, which includes three basic units, a mixer, an extractor, and a microporous membrane liquid−liquid separator, was applied for quantitative analysis of polar and chargeable compounds such as organic amines and acids in different matrixes.[32−34]

In the present work, a flow system for online liquid−liquid extraction was designed and constructed, which allowed for the effective removal of sulfuric acid from the analyte. The overall analytical procedure contained a sequence of mixing, derivatization, extraction, separation, and detection processes. Due to the low cross section of formaldehyde for ESI ionization, formaldehyde was first derivatized by 2,4-DNPH. After that, online extraction of formic acid and derivatized formaldehyde was performed in the second module. Then, the organic and aqueous phases were separated based on their specific weight, and only the organic phase eluent was admitted to the ESI-MS for detection. Following the mixing−reaction−extraction−separation sequence, quantitative online detection of formic acid and formaldehyde in 0.5 M sulfuric acid was achieved using ESI-MS. The method developed was tested for the quantitative analysis of the MOR products by ESI-MS.

EXPERIMENTAL SECTION

Equipment and Chemicals. For the mass spectrometric measurements, we used an electrospray ionization mass spectrometer model 1200 L (Varian Inc.). Since both analyte molecules, formic acid and the derivatized product of formaldehyde (2,4-Dinitrophenyl hydrazone), have functional groups that readily lose a proton, the negative ion ESI mode was used for the ionization. This also avoids possible oxidation of analyte during the electrospray process in the positive ion mode. The detector voltage was 1 kV, and the needle voltage was −4.5 kV. A Rheodyne LC switching six-port valve, located before the spray chamber of the ESI-MS, was used for the manual injection of the analyte from the sample loop (5 μL). The latter was filled with organic analyte in the load mode; subsequently its content was injected into the continuously flowing mobile phase (pure water) during the

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Table 1. Advantages and Disadvantages of Different Organic Phases for the Extraction

organic phases	advantage	disadvantage
dichloromethane	solubility in water: 20 g L^{-1}	low extraction efficiency
1-butanol	polarity: 3.7	solubility in water: 79 g L^{-1}
ethyl acetate	polarity: 4.3	easily hydrolyzed in sulfuric acid solubility in water: 85.3 g L^{-1}
diethyl ether	polarity: 2.9	highly volatile solubility in water: 69 g L^{-1}
isobutyl acetate	polarity: 4.0 solubility in water: 7 g L^{-1}	
isobutyl methyl ketone	polarity: 4.2 solubility in water: 18−20 g L^{-1}	
ethyl acetate/diethyl ether = 1:1 (v/v)	extraction efficiency for formic acid from water: 80%	highly volatile

"injection mode". For formic acid detection, the mass spectrometric $m/z = 45$ signal was monitored, and 2,4-Dinitrophenyl hydrazone was detected at the $m/z = 208.6$ signal. The presence of sulfuric acid in the organic phase was routinely checked at $m/z = 97$. The signals were quantified by integrating the areas of the corresponding mass spectrometric peaks using the software provided by Varian Inc.

Syringe pumps (single syringe, model 11Plus and multisyringe, model PHD 2000) and syringes (25 mL) were purchased from Harvard Apparatus. All connectors and capillaries were purchased from Upchurch Scientific. The chemicals, all of GC grade, were obtained from Merck (Germany) (formic acid, 2,4-dinitrophenyl hydrazine, dicloromethane, *n*-butanol, diethyl ether, ethyl acetate, isobutyl methyl ketone, isobutyl acetate) and from Alfa Aesar GmbH & Co. KG (methanol-free 16% aqueous paraformaldehyde solution). Millipore Milli Q water (18.2 MΩ cm) and suprapure sulfuric acid (Merck) were used to prepare the solutions.

Organic Phase Selection for the Extraction. For the extraction of formic acid and derivatized formaldehyde (2,4-Dinitrophenyl hydrazone) from sulfuric acid solution, the organic liquid phase should not only be polar but also immiscible with water. Six organic phases and their mixture were examined in preliminary experiments, involving off-line extraction of formic acid from 0.5 M sulfuric acid solution, followed by the ESI-MS analysis. The advantages and disadvantages of these organic phases are summarized in Table 1. On the basis of the extraction efficiencies for formic acid and derivatized formaldehyde, and the concentration of remaining of sulfuric acid in the organic phase, isobutyl acetate and the mixture of ethyl acetate and diethyl ether were selected as the optimum phases. For the extraction of formic acid from pure water, extraction efficiencies of about 80% were obtained, using either isobutyl acetate or the mixed organic phase. For extraction from 0.5 M sulfuric acid, the extraction efficiencies for formic acid using isobutyl acetate and the mixed organic phase were both 25%, as indicated by the intensities of the mass spectrometric signals. The extraction efficiency for derivatized formaldehyde in pure water cannot be determined, since there the derivatization reaction is too slow.[24] The remaining amount of sulfuric acid is less than 10 and 20 μM in isobutyl acetate and the mixed organic phase, respectively. This is tolerable for the ESI-MS measurements, since the ion suppression effect caused by sulfuric acid is negligible in this concentration range. However, during the online testing (see below) we found that the mixture of ethyl acetate and diethyl ether tends to form bubbles in the capillaries due to the evaporation, which caused an unstable mass spectrometric signal. Therefore, isobutyl acetate was selected as the organic phase for the extraction of formic acid and derivatized formaldehyde (see the Online Derivatization of Formaldehyde for the ESI-MS Detection section) from the aqueous phase.

Online Liquid−Liquid Extraction. The critical part of the device is the online extraction module, which is composed of three parts: a mixer, an extractor, and a separator. A three-port "T" connector (horizontally oriented) with an inner diameter of 0.5 mm was employed for mixing the aqueous and organic phases. The flow rate of the aqueous and organic solutions was controlled by a multisyringe pump (0.1 mL min^{-1}). The streams of aqueous and organic phases were flowing toward each other to meet in the "T" connector. Due to the immiscibility of the phases and their identical flow rates, the organic phase and aqueous phase formed small and rather regular separate segments, which were flowing through a following Teflon capillary (inner diameter 0.75 mm, length 20 cm) without intermixing. This allows an efficient extraction at the liquid−liquid phase interface due to the high ratio of the contact area between the phases and their volume. At the end of the extraction capillary, a second vertically oriented three-port "T" connector with an inner diameter of 2.0 mm served as a separator between the two phases, utilizing their different specific weights. To prevent trace residues of the acidic aqueous phase in the organic phase, only 30% of the organic phase was delivered from the upper separator outlet at a flow rate of 0.03 mL min^{-1} via the sample loop of the switching valve and then manually injected into the mobile phase continuously piped to the ESI-MS. The principle scheme of the online extraction device is shown in Figure 1. The performance of the combined derivatization/extraction modules was tested by standard solutions of formic acid with concentrations from 1.0 to 50.0 μM with 0.5 M sulfuric acid (see the Online Detection of Formic Acid section).

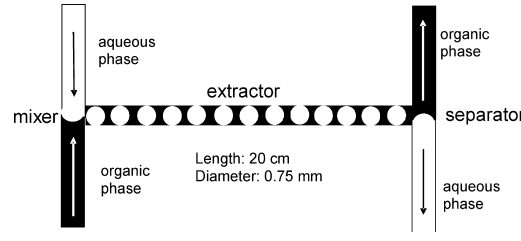


Figure 1. Schematic presentation of the online liquid−liquid extraction device.

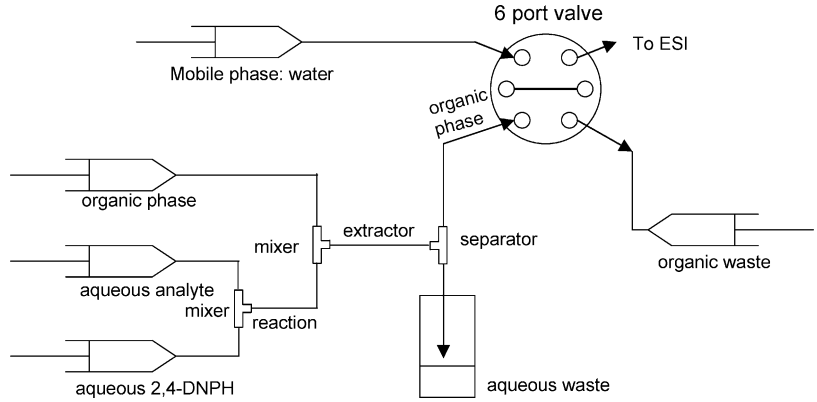
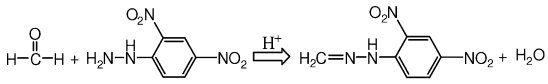


Figure 2. Principle scheme for online detection of formaldehyde.

Online Derivatization of Formaldehyde for the ESI-MS Detection. Formaldehyde was derivatized by reaction with 2,4-DNPH to produce 2,4-Dinitrophenyl hydrazone as shown in eq 1.[24]



(1)

Since the reaction proceeds rapidly in acidic medium, the derivatization was performed in the 0.5 M sulfuric acid solution prior to the extraction. To increase the reaction rate and to optimize the reaction conditions, the reaction was first tested in preliminary off-line experiments at room temperature, 40, 60, and 80 °C, at three different formaldehyde concentrations (1.0, 5.0, and 20.0 μM), and 50.0 μM 2,4-DNPH in 0.5 M sulfuric acid. After the derivatization reaction and manual extraction into the organic phase and the phase separation, the amount of 2,4-Dinitrophenyl hydrazone in the organic phase was quantified by ESI-MS analysis. On the basis of the mass spectrometric signal of 2,4-Dinitrophenyl hydrazone ($m/z = 208.6$), we found that there were no significant differences in the reaction product yield within the 1−10 min reaction time and upon increasing the reaction temperature. In total, the derivatization proceeds at sufficient rates at room temperature and in acidic solution, making this suitable for online derivatization.

For online derivatization of formaldehyde, the derivatization reaction must proceed in a capillary before the organic extraction. Here, the formaldehyde solution (in 0.5 M sulfuric acid) and 50.0 μM 2,4-DNPH solution (in 0.5 M sulfuric acid) were filled into two separate 25 mL syringes and pumped at identical flow rate of 0.05 mL min^{-1} via the capillaries (inner diameter, 0.75 mm; length, 15 cm) into a horizontally oriented "T" connector (inner diameter, 0.5 mm), where they were mixed and fed into the following capillary (inner diameter, 0.75 mm; length, 20 cm) for the derivatization reaction. After passing through this capillary, the aqueous solution containing the derivatized formaldehyde was piped to the "T" connector for the online extraction process (see the Online Liquid−Liquid Extraction section). The general scheme of the derivatization/extraction modules, integrated into the whole mixing−reaction−extraction−separation system, is shown in Figure 2. In total, this sequence allowed direct quantitative ESI-MS analysis of the derivatized formaldehyde and formic acid, which were extracted from the strongly acidic aqueous phase. The performance of the combined derivatization/extraction modules was tested by standard solutions of formaldehyde with concentrations from 1.0 to 50.0 μM with 0.5 M sulfuric acid (see the Online Detection of Formaldehyde section).

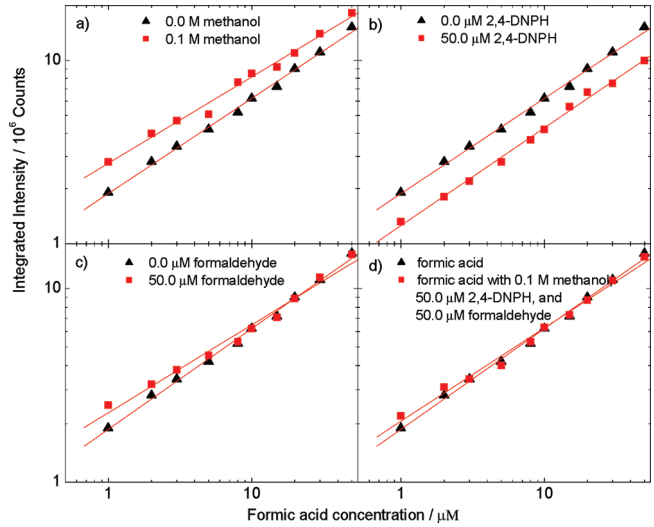


Figure 3. Calibration curves for formic acid in 0.5 M sulfuric acid solution showing the correlation between formic acid concentration and mass spectrometric intensity in the presence/absence of (a) 0.1 M methanol, (b) 50 μM 2,4-DNPH, (c) 50 μM formaldehyde, and (d) a 0.1 M methanol + 50 μM 2,4-DNPH + 50 μM formaldehyde.

RESULTS AND PERFORMANCE

In the following, we present results of measurements evaluating the performance of the system in detecting and separating the different components.

Online Detection of Formic Acid. The organic phase (isobutyl acetate) and standard formic acid solutions of different concentrations (1.0−50.0 μM) in 0.5 M sulfuric acid were filled into two separate 25 mL syringes, respectively, and pumped by a multisyringe pump at equal flow rates of 0.1 mL min^{-1} into the extraction device (see Figure 1). After passing the extraction capillary, the organic phase was separated from the aqueous phase and delivered to the ESI-MS for the analysis. The signal intensities (m/z = 45) of formic acid extracted from 0.5 M sulfuric acid solution were recorded; the corresponding calibration curve is shown in Figure 3 (linear regression, see Table 2). Quantitative analysis of formic acid solution of different concentrations after extraction and separation using ESI-MS was achieved, with a detection limit of around 0.5 μM.

Table 2. Linear Regression Equations of the Calibration Curves for the Detection of Formic Acid and Formaldehyde (*y*, MS Signal Intensity; *x*, Concentration of Formic Acid; Double-Logarithmic Plot) and Formaldehyde (*y*, MS Signal Intensity; *x*, Concentration of Formaldehyde; Linear Plot)

contents in the analyte solution	linear regression equation
Detection of Formic Acid	
formic acid	$y = (0.27 \pm 0.012) + (0.52 \pm 0.012)x$
formic acid + 0.1 M methanol	$y = (0.43 \pm 0.018) + (0.47 \pm 0.018)x$
formic acid + 50 μM 2,4-DNPH	$y = (0.10 \pm 0.013) + (0.53 \pm 0.012)x$
formic acid + 50 μM formaldehyde	$y = (0.36 \pm 0.022) + (0.45 \pm 0.021)x$
formic acid + 0.1 M methanol + 50 μM 2,4-DNPH + 50 μM formaldehyde	$y = (0.31 \pm 0.018) + (0.48 \pm 0.018)x$
Detection of Formaldehyde	
formaldehyde + 50 μM 2,4-DNPH	$y = (0.67 \pm 0.093) + (0.16 \pm 0.004)x$
formaldehyde + 50 μM 2,4-DNPH + 0.1 M methanol	$y = (1.03 \pm 0.093) + (0.19 \pm 0.005)x$
formaldehyde + 50 μM 2,4-DNPH + 50 μM formic acid	$y = (0.71 \pm 0.047) + (0.15 \pm 0.002)x$
formaldehyde + 50 μM 2,4-DNPH + 0.1 M methanol + 50 μM formic acid	$y = (0.99 \pm 0.13) + (0.18 \pm 0.006)x$

In model studies of methanol electrooxidation, the solution will contain additional components, including unreacted methanol and the incomplete oxidation products formic acid and formaldehyde in supporting electrolyte (0.5 M sulfuric acid). Therefore, the quantitative ESI-MS detection of a single product must be possible without interference with other components present in the solution. Accordingly, the influence of methanol, formaldehyde, and of the derivative reagent, 2,4-DNPH on the detection of formic acid have to be investigated. From this reason, measurements using pure formic acid solutions were followed by analogous measurements, where the additional components were added in different combinations to the standard formic acid solution. The resulting data are presented in Figure 3. As shown in Figure 3a, the addition of 0.1 M methanol increased the intensity of the formic acid response, in this case mainly the offset of the double-logarithmic intensity−concentration profile (linear regression, see Table 2). The purity of the methanol solution was tested separately by ESI-MS, yielding formic acid concentrations of 1.0−2.0 μM in pure methanol. Accordingly, the concentration of formic acid in 0.1 M methanol aqueous solution was below 1.0 nM prior to the reaction, which could hardly influence the formic acid signal. Therefore, the presence of methanol seems to enhance the ESI-MS signal of formic acid, in agreement with the findings reported in refs 35 and 36. The increased signal in the presence of methanol could result from two effects: a possible enhancement of the extraction efficiency for formic acid and a slightly increased needle current in the presence of methanol (−17.21 μA in the presence of 0.1 M methanol in aqueous mobile phase vs −17.05 μA in pure water at identical needle voltages). Figure 3b demonstrates that, in the presence of 50.0 μM 2,4-DNPH, the mass spectrometric signal of formic acid decreased. Since 2,4-DNPH can also easily be ionized, it may affect formic acid ionization and vice versa ("ion suppression") and thus influence the signal intensity of formic acid (linear regression, see Table 2). The addition of formaldehyde (nonderivatized) was found to hardly influence the response of formic acid (Figure 3c) (linear regression, see Table 2). The addition of methanol, formaldehyde, and 2,4-DNPH results in counteracting effects of methanol and 2,4-DNPH, and thus in total the signal intensities of formic acid were barely influenced. The results are shown in Figure 3d (linear regression, see Table 2). Quantitative ESI-MS analysis of formic acid in the range of 1.0−50.0 μM in 0.5 M sulfuric acid solution is possible. The concentration of formic acid in a sample of unknown formic acid concentrations can be determined from the calibration curve, as will be shown for the analysis of formic acid from the real MOR product sample in the section on Quantitative ESI-MS Analysis of Liquid-Phase Methanol Oxidation Products.

Online Detection of Formaldehyde. The performance of the system for detecting and quantifying formaldehyde in the acidic analyte solution was tested in a similar way as described above for the online detection of formic acid. Formaldehyde solution (in 0.5 M sulfuric acid) and 50.0 μM 2,4-DNPH solution (in 0.5 M sulfuric acid) were filled in two 25 mL syringes, respectively, and pumped at a flow rate of 0.05 mL min^{-1}, through the "T" connector ("mixer") for the online derivatization reaction in the following capillary. Afterward, the aqueous phase containing the derivatized formaldehyde and the organic phase (isobutyl acetate) were pumped through the capillary to proceed to the online extraction device (see Figure 1). Finally, the organic phase was separated from the aqueous phase and delivered to the ESI-MS for analysis (see the schematic description in Figure

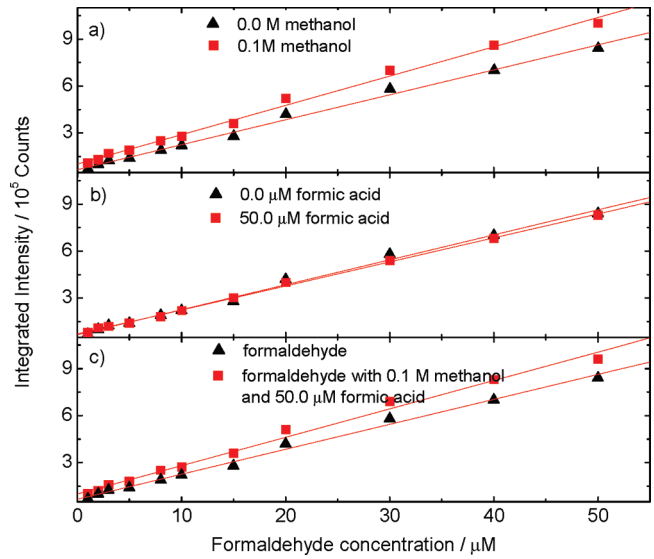


Figure 4. Calibration curves for derivatized formaldehyde in 0.5 M sulfuric acid solution showing the correlation between derivatized formaldehyde concentration and mass spectrometric intensity in the presence/absence of (a) 0.1 M methanol, (b) 50 formic acid, and (c) 0.1 M methanol + 50 μM formic acid.

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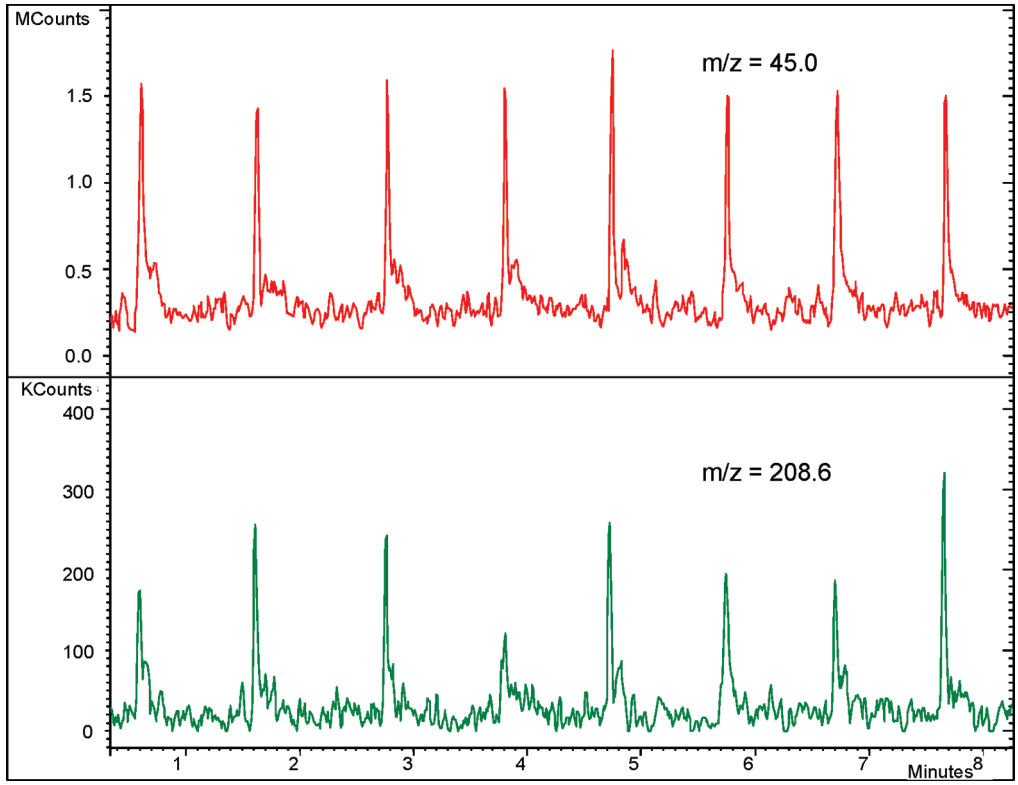

Figure 5. Mass spectrometric signals for the online detection of formic acid ($m/z = 45$) and formaldehyde ($m/z = 208.6$) in 0.5 M sulfuric acid solution after electrooxidation of a 0.01 M methanol sample over Pt/C catalyst at 0.6 V (RHE) sampled at the outlet of a thin-layer flow cell.

2). Standard solutions of formaldehyde with concentrations from 1.0 to 50.0 μM in 0.5 M sulfuric acid were prepared and tested. The concentration of formaldehyde in 0.5 M sulfuric acid solution was quantified via the signal intensities of 2,4-Dinitrophenyl hydrazone ($m/z = 208.6$), with a detection limit for formaldehyde of ~0.5 μM. The calibration curve is shown in Figure 4 (linear regression, see Table 2).

Also in this case, we tested the influence of the other molecules present in the analyte, methanol and formic acid, on the detection efficiency of formaldehyde. As shown in Figure 4a, the addition of 0.1 M methanol increases the signal of derivatized formaldehyde, mainly by providing an additional background contribution (increase of the intercept of the calibration curve, linear regression, see Table 2). Since the concentration of formaldehyde in 0.1 M methanol solution was found to be in the picomolar range, as tested in separate measurements of pure methanol, this increase is attributed to an enhanced signal intensity, induced by the presence of methanol.[35,36] On the other hand, the addition of formic acid barely influences the signal of the derivatized formaldehyde (Figure 4b). Both the slope and intercept of the regression equation are hardly changed in this case (linear regression, see Table 2). Finally, the combined influence of 0.1 M methanol and 50 μM formic acid on the derivatized formaldehyde signal (Figure 4c) is essentially identical to that found for methanol containing formaldehyde solution (Figure 4a). The signal intensities in Figure 4c, which cover the range from 1.0 to 50.0 μM formaldehyde concentration (linear regression, see Table 2), can serve as calibration curve for the quantification of formaldehyde in realistic MOR product samples (Quantitative ESI-MS Analysis of Liquid-Phase Methanol Oxidation Products section).

Quantitative ESI-MS Analysis of Liquid-Phase Methanol Oxidation Products. Quantitative ESI-MS analysis of samples with unknown concentrations of methanol electrochemical oxidation products was performed using the data for formic acid (Figure 3d) and derivatized formaldehyde (Figure 4c), which were obtained in the presence of both products and of methanol in the analyte, as calibration curves for the methanol oxidation product analysis.

Figure 5 shows ESI-MS signals of formic acid and derivatized formaldehyde using the setup for online derivatization/extraction/separation developed in this work. The samples were collected at the outlet of a thin-layer flow cell during continuous methanol oxidation over a 40 wt % Pt/C catalyst (10 mM methanol in 0.5 M sulfuric acid, E-TEK catalyst, 0.6 V vs that of the reversible hydrogen electrode (RHE), electrolyte flow rate 20 μL s^{-1}), performed in a separate experiment (for details see ref 5). The signal of formic acid ($m/z = 45$) is quite stable. Using the calibration curve from Figure 3d, we can derive a concentration of ~10.0 μM. The formaldehyde signal was rather weak and not very stable. The concentration of formaldehyde was estimated in the range of 1.0−3.0 μM, not much above the detection limit of ~0.5 μM. These results are consistent with results of a quantitative analysis of MOR products obtained over a high-loading Pt/C catalysts.[10,37] Under these conditions, readsorption and further oxidation of the incomplete methanol oxidation products formaldehyde and formic acid shift the product distribution toward the stable product CO_2. Overall, these results underline the suitability of the proposed approach for the quantitative analysis of liquid-phase products of methanol electrooxidation.[8]

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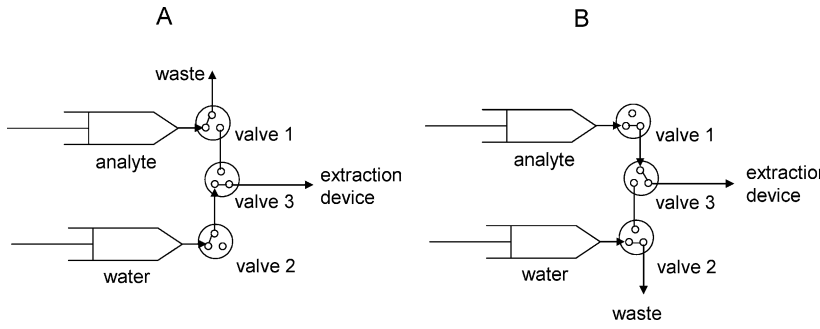

Figure 6. Principle scheme of the setup for the time response experiments.

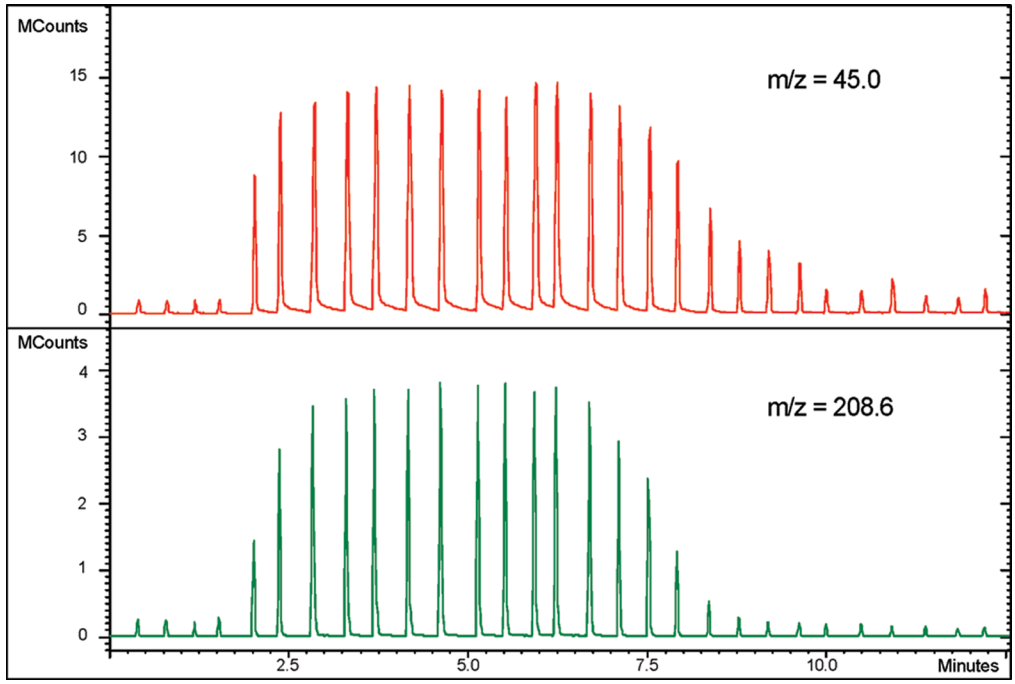

Figure 7. Time response of the mass spectrometric signals for formic acid (m/z = 45) and 2,4-dinitrophenyl hydrazone (m/z = 208.6) after switching from pure water to the analyte (100.0 μM formic acid, 100.0 μM formaldehyde, and 2,4-DNPH in 0.5 M sulfuric acid) at t = 0 and back to pure water (after 5 min).

Time-Resolved Response of the Online Extraction Process. For the online detection of the MOR products, the analyte pretreatment procedure should be as fast as possible. Therefore, it is necessary to estimate the time response for the online derivatization and extraction process. For that purpose, the online system was modified by introducing three three-way valves for switching from blank water to the analyte under continuous analyte flow (for a schematic description see Figure 6). Initially, the valves were positioned such that the water flow is led into the extraction device (Figure 6A). Then, at a certain time, the valves were switched to lead the analyte flow through the extraction device (Figure 6B). The time delay between switching the valves to analyte and approaching a stable mass spectrometric signal was defined as the time response of the system.

For these time response measurements, we used a mixture of 100.0 μM formic acid, 100.0 μM formaldehyde, and 100.0 μM 2,4-DNPH in 0.5 M sulfuric acid solution as analyte. The flow rate was set to 0.1 mL min^{-1}. At first, the valves were positioned to feed water into the extraction line. Subsequently, the valves were switched to the analyte flow and simultaneously we started to record the mass spectra. Figure 7 shows the time development of the mass spectrometric signals for formic acid (m/z = 45.0) and derivatized formaldehyde (m/z = 208.6). Initially, only weak signals were determined, which may be due to residues of remaining analyte in the sample loop and in the connections. After about 2 min, the signals increased significantly and became stable within ~1 min. The valves were switched back after 5 min. Again, the decay of signals started about 2 min after switching back to water. After additional 4 or 5 min, both mass spectrometric signals had returned to their background levels. It should be noted that the time resolution, which is defined by the decay time of the signal and does not include the time delay between switching the valve and the onset of signal increase/decay, is on the order of 1 min at a flow rate of 0.1 mL min^{-1} and the present length of the capillaries.

Overall, the device clearly fulfills the time resolution requirements for online analysis, accounting for the corresponding time delay. The response time is determined by the flow rate and the length of the capillary. However, increasing the flow rate or decreasing the length of the capillary was found to result in a significant decrease of the extraction efficiency. Therefore, the

present delay times seem to represent the lower limit for the current setup and separation/detection procedure.

CONCLUSIONS AND OUTLOOK

We have developed a novel setup and procedure for the quantitative online ESI-MS analysis of the liquid-phase methanol oxidation products in strongly acidic aqueous solutions. Formaldehyde can be converted online into an easily detectable form, by derivatization with 2,4-DNPH. Subsequent online extraction allows us to effectively remove sulfuric acid from the organic phase analyte, which is necessary to avoid the "ion suppression" from sulfuric acid and severe corrosion of the ESI-MS instrument. The sensitivities for formaldehyde and formic acid and the effects induced by the presence of other reactant and products species were determined in calibration measurements. The performance of the system was tested using a realistic sample from continuous methanol oxidation in a thin-layer flow cell, which was analyzed by the online derivatization/extraction system. Reliable quantitative results were found based on the calibration curves for formic acid and formaldehyde. The relatively short response time (about 2−3 min) at the applied conditions (analyte flow rate and the length of the extraction capillary) make this scheme and setup suitable for continuous online analysis.

The experimental protocol developed in this work can easily be modified and adopted for the quantitative analysis of liquid-phase products resulting from other electrocatalytic reactions, e.g., ethanol oxidation, where acetaldehyde and acetic formation are formed as incomplete oxidation products. Hence, this approach has a high potential for more general application of ESI-MS analysis of organic molecules in corrosive aqueous solutions and in particular for online studies of electrocatalytic reactions such as the electrooxidation of small organic molecules, where conventional DEMS is not applicable because of principle experimental problems. This would open up new possibilities for the understanding of these reactions, in particular of their dynamic behavior.

The successful proof-of-concept demonstration provided in the present study allows us to integrate the flow system for online reaction/extraction/separation into a single unit, following a lab-on-a-chip design. The approach presented here allows us to further extend a recently developed combination of membrane-inlet mass spectrometry (online analysis of gaseous/volatile products) and infrared spectroscopy in an attenuated total reflection configuration (in situ detection of adsorbed species/intermediates) with a dual thin-layer flow cell interface.[38,39] After electrical decoupling,[19] the flow cell can be incorporated between the supply syringe and the microfluidic device for online analysis of the out-flowing acidic electrolyte, with derivatization/extraction/separation and quantitative ESI-MS analysis (liquid-phase product detection) occurring simultaneously with the electrochemical measurement.

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