

Heterogeneous Catalysis

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A Study of Heterogeneous Catalysis by Nanoparticle-Embedded Paper-Spray Ionization Mass Spectrometry

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Abstract: We have developed nanoparticle-embedded paper-spray mass spectrometry for studying three types of heterogeneously catalyzed reactions: 1) Palladium-nanoparticle-catalyzed Suzuki cross-coupling reactions, 2) palladium- or silver-nanoparticle-catalyzed 4-nitrophenol reduction, and 3) gold-nanoparticle-catalyzed glucose oxidation. These reactions were almost instantaneous on the nanocatalyst-embedded paper, which subsequently transferred the transient intermediates and products to a mass spectrometer for their detection. This *in situ* method of capturing transient intermediates and products from heterogeneous catalysis is highly promising for investigating the mechanism of catalysis and rapidly screening catalytic activity under ambient conditions.

Paper-spray ionization is a direct sampling ionization method in open air, recently introduced for the mass spectrometric analysis of complex chemical mixtures.^[1] By attaching nanoparticles (NPs) to the paper support, we are able to use paper spray as a chemical reactor for studying heterogeneous catalysis. The high surface-to-volume ratio and highly active surface atoms make NP catalysts capable of responding to mild reaction conditions with a high turnover number.^[2] Catalytically active NPs are being studied intensively in coupling reactions,^[3] reductions,^[4] oxidations,^[5] and electrochemical reactions in fuel cells.^[6] Herein, we investigated the feasibility of paper-spray mass spectrometry (PS-MS) to drive the reaction on the surface of solid NP catalysts embedded in the paper and thereby directly transfer the reactants, isolated intermediates (if any), and products to the mass spectrometer by paper spray, allowing their detection immediately after starting the reaction on the nanocatalyst-embedded paper support (Figure 1).

We apply this method to the study of three model reactions with different substrates and metal nanoparticle catalysts: 1) Two Suzuki cross-coupling reactions catalyzed by palladium nanoparticles (Pd-NPs), 2) the reduction of 4-nitrophenol catalyzed by Pd-NPs or silver nanoparticles (Ag-NPs), and 3) the oxidation of glucose catalyzed by gold

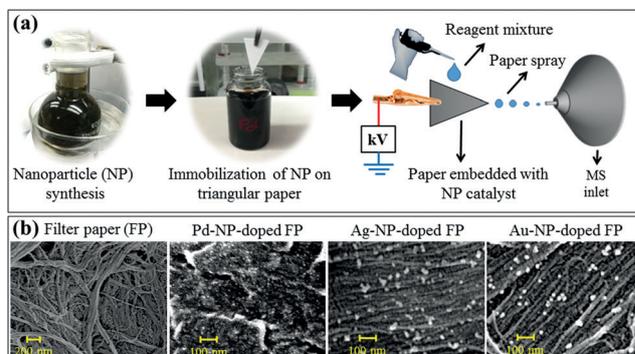


Figure 1. a) Workflow for studying heterogeneous catalysis using nanoparticle-embedded paper-spray mass spectrometry. b) SEM images of normal filter paper and the different metal-nanoparticle-doped filter papers used in the experiment.

nanoparticles (Au-NPs). Our results suggest that this rapid and convenient method of *in situ* observation of heterogeneous catalysis under microscale and ambient conditions (room temperature and atmospheric pressure) is highly promising for probing the reaction mechanism, evaluating the activity, and performing high throughput screening of nanocatalysts for characterizing new reactions.

The palladium-catalyzed carbon-carbon bond-forming Suzuki cross-coupling reaction is a popular gateway to the synthesis pharmaceuticals, molecular electronics, conjugated polymers, and natural products.^[7] Recently, the use of Pd-NPs in Suzuki cross-coupling reactions has been tailored to provide more efficient, environmentally benign, and ligand-free syntheses.^[3b,8] However, much controversy exists concerning the nature of the mechanism for this NP-catalyzed reaction. It has been debated whether the catalysis originates from metal leached out of the NP^[9] or from the surface activity of the NP.^[3b,10] To this end, we performed this reaction under the Pd-NP-embedded paper-spray condition.

Figure 1 illustrates our workflow. We synthesized Pd-NPs and immobilized them onto filter paper cut in the form of an isosceles triangle with the apex pointing toward the inlet of a mass spectrometer (see the Supporting Information, Figure S1a and the experimental section). Scanning electron microscopy (SEM) images showed that the Pd-NPs are densely packed on the paper, and the average size of the Pd-NPs is around 10 nm (Figure 1 and the Supporting Information, Figure S2). This NP-doped dry paper was clipped to a high-voltage power supply (typically -7 kV) in front of a high-resolution mass spectrometer. A microscale reaction was initiated by dispensing $7 \mu\text{L}$ of the reagent mixture onto the catalyst-doped paper. Within few seconds of

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the initiation of the reaction, paper-spray ionization occurred, followed by mass spectrometric detection of the species formed in the reaction.

Two Suzuki cross-coupling reactions involving phenylboronic acid (**1**) and 4-bromophenylacetic acid (**2a**) or 4-bromophenol (**2b**) (Figure 2a) were studied under the

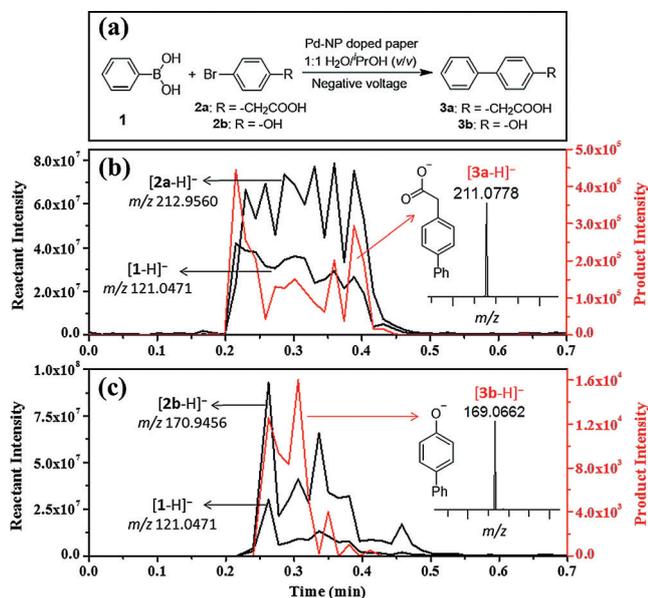


Figure 2. Pd-NP-catalyzed Suzuki cross-coupling reaction of phenylboronic acid (**1**) and 4-bromophenol (**2a**) or 4-bromophenylacetic acid (**2b**) under paper-spray conditions. a) General reaction scheme. The abundances of reactants and products with time (extracted ion chromatogram) after starting the reaction are shown for the reaction between b) **1** and **2a** and c) **1** and **2b**. Insets of (b) and (c) show the detected product ion signals with high mass accuracy (see the Supporting Information, Table S1). The full average spectra are given in the Supporting Information, Figure S3.

present conditions. We monitored the formation of the products over time using extracted ion chromatograms as shown in Figure 2b,c. The results suggest that the reaction is nearly instantaneous as there is no detectable time delay between the appearances of reactants and the product ion signals, although it took nearly 12 s for the spray to start after dispensing the reagent onto the paper. It should be noted that we have not used any base (for example, NaOH) in the reagent mixture, although a basic environment is generally required in the Suzuki cross-coupling reaction^[11] (Supporting Information, Scheme S1). We have detected the formation of trihydroxy(phenyl)borate (**1'**; Supporting information, Figure S4), a precursor of the transmetalation step in the catalytic cycle (Supporting Information, Scheme S1), which indicates the formation of OH⁻ ions from the solvent reduction of water on the paper under the high negative voltage (−7 kV).^[12] We have also inspected the mass spectra for the isolated Pd-containing intermediates, for example, Ar-Pd-Br and Ar-Pd-Ph (see the Supporting Information, Scheme S1), if formed by the metal leaching process in the reaction. However, we have not detected any of these

intermediates in the corresponding mass spectra (Supporting Information, Figures S5 and S6) of either of the reactions (Figure 2), which suggests that metal leaching is not necessary to drive the catalytic cycle under these relatively gentle conditions. We conclude that these reactions are catalyzed by the chemisorption of substrates onto the surface of the heterogeneous catalyst (Pd-NPs) under the present conditions.

We have analyzed the substrate-specific catalytic activity of the Pd-NPs by estimating reaction yields (Figure 2). From standard calibration plots (Supporting Information, Figure S7) we find an approximately 7% yield from the reaction of **1** and **2a** and an approximately 3% yield from the reaction of **1** and **2b** within 30 s of the reactions (Figure 2) on paper. Indeed, an electron releasing group (for example, −OH) present on the aryl halide substrate (for example, **2b**) is known to suppress the yield of the Suzuki cross-coupling reaction.^[13] Therefore, this method could also be used to screen the activity of the nanocatalyst on a given set of substrates. These results also suggest marked acceleration of these reactions on the Pd-NP-doped paper when compared with conventional bulk-phase methods, which typically take several minutes to hours to yield a significant amount of product even at elevated temperatures.^[3a]

The catalytic reduction of 4-nitrophenol by sodium borohydride is one of the popular model reactions for evaluating the performance of metal nanocatalysts.^[4b,c] Nitro-aromatic pollutants are stable against chemical and biological degradation.^[14] Much attention has been paid to converting 4-nitrophenol to the less toxic 4-aminophenol, which can be used as the precursor for the synthesis of pharmaceuticals and dyestuffs.^[14] Based on absorption spectroscopy studies,^[15] the NP-catalyzed reduction of 4-nitrophenol (**4**) to 4-amino phenol (**8**) was proposed previously to proceed through the stepwise formation of a number of intermediates including the nitroso compound **6** and hydroxylamine compound **7** (Figure 3a). To our knowledge, no in situ approach was previously used to capture and detect individual intermediates (**5–7**).

We have successfully detected three intermediates (deprotonated **5–7**), along with the reactant (deprotonated **4**) and product (deprotonated **8**), using Pd-NP-embedded PS-MS (Figure 3). The experimental details are given in the Supporting Information. The time-dependent abundances of those species are given as extracted ion chromatograms in Figure 3b–f. These results unambiguously demonstrate that the reduction of **4** occurs in a number of steps, in which intermediates (**5–7**) are able to leave the nanoparticle surface after each reduction step. The mobility of the desorbed product in the paper is likely to be faster than that of the intermediates, some of which might be reabsorbed by the surface of the nanocatalyst for further reaction. Therefore, intermediate ion signals are abundant during the late stage of the paper spray (Figures 3c–e). Furthermore, the differential ion current profiles of the intermediates might also be attributed to their different kinetic stability and retention time on paper during the reaction. It should be noted that the presence of the isolated intermediate **5** was never confirmed before, although spectroscopic signatures provided evidence

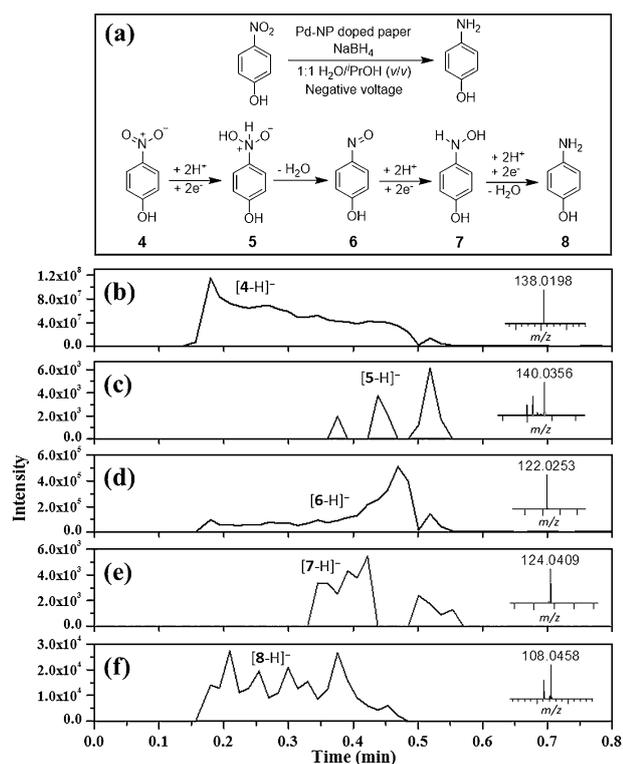


Figure 3. Pd-NP-catalyzed reduction of 4-nitrophenol (**4**) under the paper-spray conditions. a) General reaction scheme in which details of the mechanism are supported by the ion signals of the individual species (**4–8**). The extracted ion chromatogram of b) $[4-H]^-$, c) $[5-H]^-$, d) $[6-H]^-$, e) $[7-H]^-$, and f) $[8-H]^-$. Insets in (b)–(f) show the detected ion signals of the corresponding species (reactant/intermediate/product) with high mass accuracy (see the Supporting Information, Table S1). The full average spectrum is given in the Supporting Information, Figure S8.

of other intermediates (**6** and **7**).^[15] Herein, we confirm the presence of **5**, from the ion signal at m/z 140.0356 (Figure 3 c).

We have also measured the NP-specific catalytic efficiency of 4-nitrophenol reduction by changing the nanocatalyst from palladium to silver. When Ag-NP-doped paper (Supporting Information, Figure S9) was used to study this reaction, we observed similar mass spectral features, which allowed us to identify the intermediates as shown in the Supporting Information, Figure S10. The yields of both these reactions were measured by using standard calibration plots (Supporting Information, Figure S11 a). Yields from the Pd-NP and the Ag-NP catalysis were circa 42% and circa 10%, respectively. The higher yield from the Pd-NPs is attributed to their smaller size (10 nm; Supporting Information, Figure S2) compared to that of the Ag-NPs (20 nm; Supporting Information, Figure S9), which provides more effective surface area for the reaction to occur. Thus, this method for studying heterogeneous catalysis could be used to rapidly screen the activity of different nanocatalysts for a given reaction. Once again, the approximately 42% yield within 30 s (Figure 3 f) represents a significantly faster rate of reduction of 4-nitrophenol on the Pd-NP-doped paper when compared with conventional bulk-phase methods, which require minutes to hours.^[16]

Oxidation of organic molecules by an eco-friendly catalytic method is of growing interest for developing sustainable chemical processes.^[17] Particularly, the oxidation of glucose is important in biosensor development.^[18] The use of gold catalysts in chemical oxidation is important owing to their resistance to deactivation by oxygen.^[17b] We have also studied the aerobic oxidation of glucose (**9**) to gluconic acid (**11**) by using Au-NP-doped PS-MS (Figure 4). The average size of

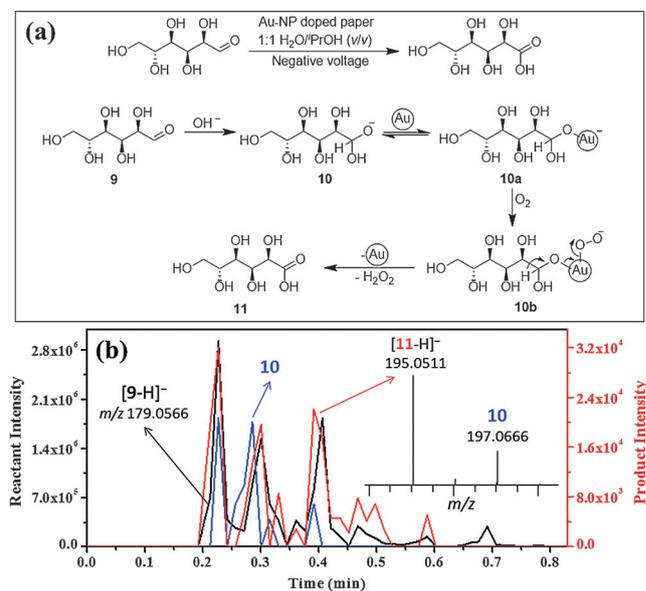


Figure 4. Aerobic oxidation of D-glucose (**9**) catalyzed by gold nanoparticles (Au-NPs) under paper-spray conditions. a) Reaction scheme with details of the mechanism, which is also supported by the ion signals of the intermediate **10** and product **11**. b) The extracted ion chromatograms of $[9-H]^-$ (black), **10** (blue), and $[11-H]^-$ (red). Inset of (b) shows the detected ion signals of species **10** and **11** with high mass accuracy (see Table S1, in the Supporting Information). The intensity of **9** is associated with the left y-axis and that of **10** and $[11-H]^-$ with the right y-axis. The full average spectrum is given in the Supporting Information, Figure S13.

the Au-NPs was approximately 25 nm (Supporting Information, Figure S12). The experimental details are given in the Supporting Information. Figure 4a shows the proposed mechanism of glucose oxidation,^[5a] in which glucose is first hydrated for its adsorption onto the gold surface and then oxidized by molecular oxygen. The hydration of glucose under Au-NP-doped paper spray is directly evident by the formation of ions at m/z 197.0666 corresponding to the species **10** (Figure 4). The time-dependent abundances of the reactant (**9**), isolated intermediate (**10**), and product (**11**) are shown in their extracted ion chromatograms (Figure 4b). This study confirms the presence of the crucial intermediate **10**, which was previously postulated.^[5a,19] Furthermore, we have not detected gold-atom-bound species corresponding to **10a** and **10b** (Supporting Information, Figure S14), which suggests that the reaction is not conducted by the gold leaching process. From the standard calibration plot (Supporting Information, Figure S11 b), the estimated yield within 30 s of the reaction was found to be less than 0.1%. This low yield

is attributed to the requirement of molecular oxygen for this oxidation process. However, the reaction on the paper was assisted by the oxygen from the air, and no additional oxygen source was used to drive the reaction.

For the above three reactions (Figures 2, 3, and 4), we performed control studies with normal filter paper without the embedded nanocatalysts. None of the control studies (data not shown) was able to catalyze any of the above reactions in the absence of catalytic nanoparticles. We also performed a voltage-dependent study of those reaction (Figures 2, 3, and 4). On changing the paper spray voltages from 0 to -7 kV, the reaction efficiencies (formation of intermediates and products) increased (Supporting Information, Figures S15 and S16), which indicates the requirement of a basic environment for these reactions, which is provided by the abundant solvent (water) reduction at elevated negative voltages. It should be noted that the increased negative spray voltage can also improve the ionization efficiency and ion detection sensitivity in mass spectrometry, which can also contribute to modifying the product-to-reactant ratios^[20] (Supporting Information, Figures S15 and S16). We also investigated the addition of base to the reaction mixture (pH \approx 11) but found no increase in the reaction yield. This suggests that water electrolysis is sufficient for providing a basic environment.

We have evaluated the catalytic response of the nanocatalysts (Pd-NP, Ag-NP, and Au-NP) for their corresponding reactions (Figures 2, 3, and 4) from several cycles of paper-spray ionization. In each cycle (ca. 4-minute interval), 7 μ L of reactant mixture was dispensed onto the NP-doped paper, which was maintained at a constant voltage (-7 kV) throughout the experiment, and the corresponding product formation was monitored by the extracted ion chromatogram of the product. Figure 5 shows representative data obtained from

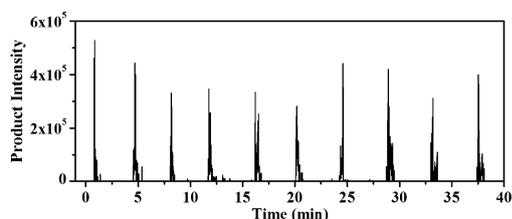


Figure 5. Catalytic response of Pd-NPs for the Suzuki cross-coupling reaction of **1** and **2a** (see Figure 2a) from ten cycles of paper-spray ionization. In each cycle (ca. 4-min interval), 7 μ L of a mixture of **1** and **2a** was dispensed onto the Pd-NP-doped paper, which was held at -7 kV throughout the experiment, and the corresponding product (**3a**) formation was monitored over time.

the Suzuki cross-coupling reaction of **1** and **2a**. The formation of nearly constant amounts of product throughout the cycles indicates the recovery of active nanocatalyst after each cycle, that is, the NP-doped paper remains active for multiple uses.

In summary, we present a convenient in situ method of analyzing nanocatalysis reactions by means of a NP-embedded paper-spray mass spectrometric technique. Three model reactions, Pd-NP catalyzed Suzuki cross-coupling reactions, Pd-NP/Ag-NP catalyzed 4-nitrophenol reduction, and Au-NP

catalyzed glucose oxidation were studied as a proof of concept of this method. These reactions were almost instantaneous, transferring the transient isolated intermediates and products to the mass spectrometer for their subsequent detection. The data provide compelling evidence that a metal leaching process is not important to drive these reactions on the paper; rather, the reactions occurred on the surface of the nanocatalysts. Direct detection of transient isolated intermediates provides valuable information on the mechanistic details of these reactions, as some of the intermediates had been postulated but not directly observed. Furthermore, estimates of the reaction yields suggest that the reactions are many fold faster (typically by a factor of one thousand or more) on nanoparticle-embedded paper under the spray conditions, when compared to conventional reactions in the bulk phase. This technique can serve as a lab-on-paper for engineering new heterogeneous catalysis reactions, for mechanistic studies, and for high throughput screening of nanocatalyst performance, especially because of the simplicity of this method for conducting reactions under ambient conditions.

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