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Mesoporous silica nanoparticles applied as a support for Pd and Au nanocatalysts in cycloisomerization reactions

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Ultra-small mesoporous silica nanoparticles (MSNs) have been synthesized at room temperature with particle sizes ranging from 28 to 45 nm. These MSNs have been employed as heterogeneous supports for palladium and gold nanocatalysts. The colloidal nature of the MSNs is highly useful for catalytic applications as it allows for better mass transfer properties and a more uniform distribution of the nanocatalysts in solution. The two nanocatalysts were evaluated in the cycloisomerization of alkynoic acids and demonstrated to produce the corresponding alkylidene lactones in good to excellent yield under mild conditions. In addition to their high activity, the catalysts exhibit low degree of metal leaching and straight-forward recycling, which highlight the practical utility of MSNs as supports for nanocatalysts.

I. INTRODUCTION

Transition metal-based catalysis has played a central role in advancing the field of organic synthesis, by allowing for the development of new types of reactions that have not been possible...
to achieve by classic chemistry.\textsuperscript{1} Moreover, transition metal catalysis has enabled protocols that display unprecedented efficiency and selectivity, which can often be performed under very mild reaction conditions. Recently, significant attention has been directed towards transition metal nanoparticles as they have shown to be promising catalysts for a wide range of organic transformations.\textsuperscript{2} The work in nanocatalysis has been greatly facilitated by the rapid progress in the field of nanotechnology during the past decades, which has provided a variety of size- and shape-selective methods for synthesizing metal nanoparticles.\textsuperscript{2e, 3} However, some challenges still remain in the synthesis of nanosized transition metal particles, where one of the most crucial issues concerns how to prevent the nanoparticles from aggregating during the catalytic conditions, which generally translates into reduced catalytic activity over time.

A simple and efficient way to avoid aggregation of nanoparticles is to immobilize them on a heterogeneous support, and this methodology also brings several practical advantages such as simpler separation of the catalyst from the reaction mixture and the possibility of catalyst recycling. To date, a wide range of porous solid supports has been developed for the immobilization of metal-based nanocatalysts, which includes carbon-based materials,\textsuperscript{4} metal-organic frameworks,\textsuperscript{5} metal oxides,\textsuperscript{6} polymers,\textsuperscript{7} and silica.\textsuperscript{8}

Inorganic porous materials have been used as supports because of their uniform porosity, size/shape selectivity, and significant thermal stability. However, the microporous system of traditional porous materials brings some drawbacks, such as slow diffusion of reactants and hindered access to and subsequent exit from the active sites located within the material. Consequently, a variety of novel mesoporous materials have been developed to overcome these drawbacks associated with microporous systems. The hierarchical porosity of these supports will increase the mass transfer rate, enlarge the external surface area and enhance the volume of the
reactors, which has significant advantages in organic reactions. Therefore, mesoporous silica has emerged as one of the most promising supports for transition metal nanoparticles owing to their good thermal stability, high surface area, tunable pore sizes, and straight-forward synthetic routes. In comparison to conventional mesoporous silica, mesoporous silica nanoparticles (MSNs) are expected to have better accessibility for reactants and a more uniform distribution in the reaction media (in liquid phase) because of their colloidal nature.

Herein, we present the preparation of ultra-small MSNs with the particle size between 28 to 45 nm and its application as a support for Au and Pd nanocatalysts. In this study, the cycloisomerization of alkynoic acids was chosen as the model reaction for the catalytic evaluation of synthesized catalysts.

II. RESULTS AND DISCUSSION

Preparation and functionalization of the MSN support

The MSN material was synthesized at room temperature using the two surfactants CTAB and F127 as structure directing agent and particle stabilization agent, respectively. The porosity of the MSNs was obtained by removing the surfactants from the pores of the MSNs under calcination. A pH adjustment protocol was applied to avoid aggregation of the MSNs, which could be thoroughly dispersed in aqueous solution, allowing them to be studied by DLS. The MSNs form spherical particles with a narrow size distribution in the range of 35 to 45 nm, as depicted by DLS (Figure 1a). HRSEM analysis, on the other hand, showed that these nanoparticles were in sizes ranging from 28 to 45 nm (Figure S1), which is slightly smaller than that given by DLS, because this technique presents the size of particles together with a thin electric dipole layer from the solvent which is not visible by HRSEM. From STEM, it was
demonstrated that the mesopores were uniformly distributed with the diameters ranging from 2 to 4 nm (Figure 1b). N₂ adsorption/desorption indicated a typical type IV isotherm of the MSNs with a specific surface area of 331 m² g⁻¹, a total pore volume of 1.83 cm³ g⁻¹ contributed by both mesopores and macropores (Figure S2). 3D electron tomography was performed on Pd loaded MSNs, and the reconstructed tomogram clearly showed that the mesopores are open to the external surface of the MSNs (Movie S1 and Figure S3).

![Figure 1](image.jpg)

**FIG. 1.** (a) DLS of MSNs in water solution and (b) STEM image of MSNs showing its morphology and uniformly distributed mesostructures.

After amino-functionalization, the specific surface area of AmP-MSN decreased to 234 m² g⁻¹ and total pore volume to 1.60 cm³ g⁻¹, as obtained from the N₂ adsorption/desorption isotherm of the AmP-MSN (Figure S2). Because the major decreases of the specific area and pore volume occurred in the range between 0.8 and 1.0 relative pressure, the decreases are mainly attributed by the incorporation of aminopropyl groups in the macropores between the MSNs. This indicates that the aminopropyl groups are mainly functionalized on the external surface of the MSN material, and not in the mesopores of the MSNs.
Characterization of the Pd and Au nanocatalysts by STEM

Both the Pd and Au loaded samples, denoted as Pd-AmP-MSN and Au-AmP-MSN respectively, kept the same morphology as that of the MSNs. The vast majority of the Pd nanoparticles were found to possess a narrow size distribution from 1 to 2 nm (Figure 2a). In order to locate the positions of the Pd nanoparticles, electron tomography was performed using STEM images, which shows that the Pd nanoparticles are dispersed homogeneously on the external surface of the MSNs (Figure S4, S5 and Movie S2). Both small Au nanoparticles (1 - 2 nm in size) and large Au nanoparticles (about 5 to 10 nm in size) were observed in the STEM image of the Au-AmP-MSN (Figure 2b). The larger nanoparticles are most likely a result of aggregation of smaller Au nanoparticles.

FIG. 2. STEM images of Pd-MSN (a) and Au-MSN (b). The Pd and Au nanoparticles are shown in white contrast.

Catalytic evaluation of the metal nanocatalysts

The cycloisomerization of alkynoic acids into their corresponding alkylidene lactones was chosen as the model transformation for the catalytic evaluation of the Pd-AmP-MSN. Previous
literature reports have shown that both homogeneous\(^9\) and heterogeneous\(^{10}\) Pd catalysts can effectively mediate this cycloisomerization reaction, making it an excellent choice for studying the activity and the robustness of the Pd-AmP-MSN. This transformation is also interesting from a practical perspective as it allows for straight-forward access to the \(\gamma\)-alkylidene lactone motif, which is a key fragment found in a variety of biologically active natural products.\(^{11}\)

The colloidal nature of the nanosized MSN support contributed to the improvement of the catalytic properties of the corresponding nanocatalyst. A study was conducted on the cycloisomerization of 4-pentynoic acid \(1\text{a}\) into \(\gamma\)-methylene-\(\gamma\)-butyrolactone \(1\text{b}\), where the activity of the Pd-AmP-MSN nanocatalyst was compared to that of Pd-AmP-MCF\(^{12}\) and commercially-available Pd/C (Figure 3). To our delight, the Pd-AmP-MSN nanocatalyst was found to be the most efficient catalyst in the comparison study, giving 93% conversion after only 60 min at 40 °C. We ascribe the high catalytic activity of the Pd-AmP-MSN to the colloidal nature of the AmP-MSN material, which allows for a better dispersion of the catalyst in the reaction medium and enables more expedient access of the reactants to the catalytic sites. The Pd-AmP-MCF that contains a similar Pd nanoparticle size distribution (1.5 - 3.0 nm) as the Pd-AmP-MSN also performed well in this study, although it gave a noticeably slower reaction. The lower activity of the Pd-AmP-MCF catalyst is ascribed to the larger size of the AmP-MCF particles, which resulted in worse dispersion properties compared to the AmP-MSN support. In the case of the commercial Pd/C, the larger mean size of the Pd nanoparticles was invoked as the main explanation for its poor performance. However, this heterogeneous Pd catalyst is also composed of micrometer-sized support particles, which might also contribute to the lower catalytic activity.
FIG. 3. Cycloisomerization of 4-pentynoic acid 1a at 40°C for 60 min. In a typical experiment, 4-pentynoic acid (0.40 mmol), a heterogeneous metal catalyst (1 mol% Pd, Pd-AmP-MSN (●), Pd-AmP-MCF (■), Pd/C (▲)) and triethylamine (0.10 mmol) were mixed in CH$_2$Cl$_2$ (1 mL). The progress of the reaction was periodically monitored by withdrawal of aliquots for $^1$H-NMR-analysis.

After establishing that the Pd-AmP-MSN constituted the superior catalyst choice, we studied the scope of the catalytic protocol (Figure 4). As demonstrated above, the standard substrate 1a could be efficiently cycloisomerized by the Pd-AmP-MSN catalyst, leading to a quantitative yield of γ-methylene-γ-butyrolactone 1b within 1.5 h (Table I, Entry 1). Increasing the chain length of the alkynoic acid by one methylene group resulted in a significantly less efficient cycloisomerization reaction, which despite increased catalyst loading, longer reaction time and elevated temperature only produced the six-membered ring lactone 2b in 50% yield (Table I,
Entry 2). This finding is in line with the previous studies, which have shown that it is generally more challenging to form six-membered ring products in comparison to the corresponding five-membered ones. The Pd-AmP-MSN catalyst also proved capable of cyclizing the terminally substituted pentynoic acid 3a, which occurred by complete (Z)-selectivity (Table I, Entry 3). However, a longer reaction time (16 h) and a higher reaction temperature (50 °C) were needed to ensure high yields of the desired lactone product. Interestingly, the cycloisomerization of the Boc-protected amino acid derivative 4a proceeded remarkably well, and the corresponding product lactone 4b could be obtained in a good yield of 79%, when performing the reaction at 40 °C for 6 h (Table I, Entry 4).
TABLE I. Cycloisomerization of a condensed scope of acetylenic acids catalyzed by Pd(0)-AmP-MSN.\[a\]

![Chemical structure](image)

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<th>Temp (°C)</th>
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</table>

[a] Reaction conditions: alkynoic acid (0.40 mmol), triethylamine (0.10 mmol), Pd-AmP-MSN (see table), 1,3,5-trimetoxybenzene (internal standard, 0.10 mmol) and CH₂Cl₂ (1 mL) were added to a microwave vial, which was sealed and heated in an oil bath according to the temperatures and times given in the table. [b] The yields of the reactions were determined by \(^1\)H-NMR using the internal standard.
To establish the practical utility of the Pd-AmP-MSN catalyst, factors such as leaching and recyclability were examined. Gratifyingly, ICP-OES analysis of the reaction solution showed that the developed Pd nanocatalyst only exhibited a minor leaching of 1.1 ppm, demonstrating its high structural stability under the employed catalytic conditions. The recyclability of the Pd-AmP-MSN was assessed by subjecting the catalyst to four subsequent reaction cycles. In the first three cycles, each reaction was stirred for 120 min before it was stopped, and the conversion was determined by $^1$H-NMR. During the final cycle (the 4th cycle), the reaction was periodically sampled after 10, 30, 60 and 120 min, to allow for a kinetic comparison of the activity between unused and the recycled catalyst. The reactions involving the Pd nanocatalyst displayed gradually decreased efficiency over the four cycles, with 99 %, 80 %, 73 % and 59 % conversion after a full reaction time of 120 min, respectively. This decrease in efficiency was further demonstrated by comparing the kinetic profile of the reaction during the first and fourth cycles, which shows a clear decrease in the activity of approximately four times (Figure 4). There are two possible reasons that influence the decrease in catalytic activity over consecutive use, i.e. the agglomeration of the Pd nanoparticles and/or a passivation of the metal surface. The Pd nanoparticles were studied after the catalytic experiments by TEM, and these images showed that the recycled Pd-AmP-MSN exhibited comparable particle distribution and morphology as the fresh samples (in Figure 2a), suggesting that catalyst deactivation instead comes from passivation of the metal surface under the employed catalytic conditions.
To demonstrate the versatility of the developed AmP-MSN material, its possible use as a support for other transition metal nanoparticles was also investigated. A corresponding Au nanocatalyst was prepared by treating the AmP-MSN material with HAuCl₄ and subsequently reducing it with NaOH-activated NaBH₄ at 0 °C. This Au nanocatalyst also proved to be an efficient and stable catalyst for the cycloisomerization of 4-pentynoic acid 1a, by giving 83% yield of the desired lactone 1b after 2 h with a small leaching of 8.1 ppm (Scheme 1). However, the Au nanocatalyst exhibited a reduced activity over multiple re-uses in the cycloisomerization of 4-pentynoic acid 1a.

Scheme 1. Cycloisomerization of 4-pentynoic acid 1a into γ-methylene-γ-butyrolactone 1b catalyzed by Au-AmP-MSN.
III. CONCLUSIONS

In summary, mesoporous silica nanoparticles (MSNs) have been synthesized, characterized and applied as a support for heterogeneous catalysts. From this material, two metal nanocatalysts comprised of Pd and Au nanoparticles were prepared and used in the cycloisomerization of a small library of alkyne carboxylic acids into their corresponding alkylidene lactones in good to excellent yields. The colloidal nature of the MSNs led to better catalytic properties of the corresponding Pd nanocatalyst, which was ascribed to a more efficient transfer of reactant molecules to the catalytic sites and improved dispersion dynamics. Although the metal nanocatalysts were found to display low metal leaching, they exhibited a decreased activity upon recycling, which was attributed to a passivation of the metal surface under the catalytic conditions. Thus, this deactivation was not caused by the degradation of MSNs or aggregation of the metal nanoparticles. Motivated by these promising results, we will continue to look into further application of the MSNs as supports for other catalytic species and their potential use in organic synthesis.

IV. ACKNOWLEDGEMENTS

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V. REFERENCES


