Facile Synthesis of Spatially-Functionalized Core-Shell Nanocatalysts with 3-D Mesopore Structure

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Hollow mesoporous silica particles (HMSPs) have recently drawn much attention as nanocatalysts, owing to their benefits and potential for greener chemical processes. Here, improved synthesis of HMSPs exhibiting a shell with a 3-D pore structure is proposed to overcome previous synthetic issues, such as reproducibility, particle size distribution, precise tailoring of size/shell thickness, low yield, etc. Additionally, precisely controlled and selective functionalization with amine groups is achieved owing to careful protection and sequential extraction protocols. To overcome time-consuming and complex multistep extraction procedures, different methods were optimized towards the most efficient protocol. The obtained materials are characterized in terms of structure, porosity and functions, and the confined catalytic activity was tested in a Knoevenagel reaction. The nanocatalysts were compared before and after the core template was removed to confirm that the only catalytic species are free amines located on the inner external surface of the shell (i.e., the surface exposed towards the hollow core).

The main advantages of using hollow core-porous shell (nano) particles in catalysis are that (a) the active sites confined in the core cavity are well-protected from the environment, ultimately acting in a separated phase, and (b) the channels in the shell may serve as gate allowing for size- and shape-selective transport of molecules, which can diffuse in and out of the inner void.[11] These nanoreactors demonstrate great selectivity and due to the specific composition of the shell material, may offer other attractive properties (e.g., optical, magnetic, etc.), which make these hollow structures suitable candidates for a variety of applications.[2] Hollow mesoporous silica particles (HMSPs) combine a macroporous core and mesoporous shell characteristics in one single unit.[3] The large cavity can act as a reservoir or nanoreactor, while the mesoporous shell may enable a controlled in-and-out transfer based on size exclusion. The internal surface of the mesopores can also carry different charges that could enable charge-selective processes, which may be interesting as well, for separation, electro/photocatalytic reactions and many more applications.[4]

Various approaches for the synthesis of such particles have already been reported, including soft and hard templating approaches.[2] As a core template, polystyrene latex beads (PS) were found very useful to generate well-defined and tunable particle size distributions. To obtain ordered mesopore channels in the shell, synthesis parameters such as the concentration of aqueous ammonia solution used,[5] the reagent ratio,[6] and the concentration of the latex (e.g., use of high amounts)[7] have been varied. However, a 3-D mesopore shell structure similar to that of MCM-48 silica[8] has not been reported. Yet, such open and interconnected 3-D pore structures can provide substantial advantages in catalysis, sorption, bioimaging and drug delivery applications. When compared to 2-D mesoporous materials, materials with 3-D pore structure are believed to possess more favorable characteristics due to potentially improved diffusion of guest species (facilitated by highly interconnected pores) and higher capacity as adsorbent for liquid and gaseous reactants.[9]

Catalytic reactions using HMSPs have been realized by introducing organic groups, metal oxides, metal nanoparticles, enzymes and other functionalities in the core void. For instance, incorporation of noble metals was utilized for reduction reactions,[10] oxidation of carbon monoxide,[11] photodegradation,[12] and various other coupling and degrada-

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such as system, the outer external surface of the HMSPs is exposed to the extra-particle space, the internal surface of the shell is that of the mesopores, and the inner external surface is the one exposed towards the hollow core.

This contribution shows the synthesis of MCM-48-type HMSPs in a simple way. Furthermore, the necessary template removal sequences were optimized to preserve the functionalities while opening successively the multipore structure. Owing to the template extraction sequence, selective confinement could be realized, and the catalytic activity of free amine groups placed in the inner void space was tested, as illustrated in Scheme 1.

HMSPs were synthesized by hard templating and deposition on the sphere surface using a weakly basic ethanol/water solution of the precursors, such as previously reported for an MCM-41-type system. To achieve an MCM-48-type HMSP system exhibiting a 3-D cubic $Ia3d$ interconnected mesopore structure, Pluronic F127 was added to the reaction mixture. The detailed synthetic procedures can be found in the Supporting Information. All the materials were characterized by the typical methods, including $N_2$ physysisorption, transmission electron microscopy (TEM), solid-state nuclear magnetic resonance spectroscopy (ssNMR), low-angle powder X-ray diffraction (PXRD), dynamic light scattering (DLS), elemental analysis (EA) and thermogravimetric analysis (TGA).

Note that changing various synthesis parameters, such as (a) the stirring time after the addition of TEOS, (b) the reaction time (24 vs. 48 h), and (c) the addition method of TEOS (dropwise vs. at once), did not show any significant influence on the final material properties (see Figure S1). This clearly demonstrates the robustness of this synthesis protocol (see Figure S1–S3 for details). Additionally, several batches were prepared, demonstrating negligible changes in the porosity of the materials (see Figure S4 and S5).

Figure 1d–h shows TEM images of the different types of HMSPs as prepared herein, illustrating well the core-shell/hollow mesoporous particle morphologies. In terms of porosity, $N_2$ physisorption analysis revealed a sharp and reversible pore condensation/evaporation step at a relative pressure below 0.4, which is characteristic for mesoporous materials. In addition, a wide hysteresis loop (H2-type) at $P/P_0$ above 0.4 (Figure 1a and b, black line) was observed. The origin of the hysteresis loop is attributed to the presence of the large inner void, whereby the void access is controlled by the smaller pores in the mesoporous shell. In this situation, desorption is induced via cavitation effects (leading to the wide H2(a) hysteresis loop). This is usually observed for large cavities with small aperture (or neck) diameters. With a decreased amount of polystyrene in the reaction mixture, the shell thickness increased (Figure 1e–h). This was found in agreement with the hysteresis loop in the physisorption isotherms, which became smaller (Figure 1a) in line with a smaller contribution of the inner void volume. Nevertheless, the pore size, the total pore volume and the specific surface area were similar for all samples tested (see Table S1). PXRD revealed the typical cubic $Ia3d$ symmetry of the mesopore network for the thick shell samples (Figure 1c, violet and red). For the other two cases, the shell is rather thin (10 nm and 50 nm), leading to much broader reflections (arising from smaller coherent scattering domain sizes) and the cubic symmetry could not be fully corroborated by PXRD. Similar behavior was reported for MCM-48-type nanoparticles having a particle size below 150 nm. Furthermore, a smaller particle size (i.e., 120 vs 84 nm) was achieved by simply changing the size of the polystyrene core (see Figure S6). The exact synthesis descriptions for the polystyrene beads can be found in the Supporting Information.

With increased shell thickness, the mean particle diameter increased (see Table 1). However, for synthesis mixtures with very low amounts of polystyrene (with respect to the standard HMSP synthesis conditions) the shell became non-uniform (Figure 1g and h). These non-uniform particles reflect the importance of the correct synthesis conditions and TEOS/PS ratio. However, using different stirring rates in the synthesis after the addition of TEOS might result in more uniform particles.

To generate functional particles, amino and thiol groups were introduced during the synthesis via co-condensation using 3-aminopropyltriethoxysilane (APTS) and a delayed co-condensation (selective functionalization of the outer surface due to delayed addition time of the silane) of 3-mercaptopropyltriethoxysilane (MPTS), respectively. In this

Scheme 1. Schematic illustration of the preparation of the base nanocatalyst.
synthesis, in addition to APTS, the introduction of MPTS is required in order to avoid the loss of the 3-D pore symmetry of the mesoporous silica nanoparticles.\(^{19}\) The successful integration of the functional silanes into the silica network was confirmed by \(^{13}\)C and \(^{29}\)Si ssNMR (see Figure S7).

Since the organic functionalities have to remain within the material, no simple calcination could be implemented to remove the templates and a sequence of template extraction steps is required. The optimization of the extraction procedure was performed on non-functionalyzed HMSPs to monitor the extraction process using TGA. First, the well-documented but
time-consuming acidic ethanol procedure for extraction of the pore template from MCM-48-type silica was optimized. As it can be seen in Figure S8, simple sonification for 30 min appeared to be sufficient for the complete removal of the surfactant. This was further verified by ssNMR, where the dominant and very sharp peaks of the surfactant template are absent after the extraction process (see Figure S7). Nitrogen physisorption analysis indicates the presence of open mesopores after this extraction step (Figure S9). Thus, instead of several refluxing steps, the optimized extraction was always performed by sonification for 1 h.

Then, the extraction of the polystyrene hard template using several solvents or solvent mixtures was performed. Unfortunately, simple immersion in toluene, DMF, DCM, acetone etc., as often reported in the literature[26], did only lead to a small decrease in mass loss attributed to PS in the TGA (see Table S2 and Figure S10 for more details). Therefore, an optimized multistep extraction sequence using different solvents (THF, toluene and DCM) was required (see Figure S11 for more details about the extraction).

With the optimized extraction protocols in hand, the APTS- and MPTS-modified HMSPs were first extracted using EtOH/HCl to remove the mesopore template (2). Then, the free amine groups which are located on the external surface of the particles and inside the mesopores of the shell were protected in order to confine the base reactive sites to the inner hollow core surface of the particles and allow to perform size-exclusive catalysis (i.e., amine groups are only available in the inner cavity which access is controlled by the mesoporous shell). The protection was carried out using acetic anhydride in pyridine and dimethylaminopyridine (DMAP), and the corresponding signals in the $^{13}$C (CP/MAS) ssNMR (Figure S7) were visible. Furthermore, zeta-potential measurements confirmed the successful capping of the amino groups due to a shift towards more negative values (before +26 mV; after −30 mV).

Finally, the polystyrene core was removed following the above described protocol (see Figure S12 for detailed characterization). As it can be seen in the TEM images (Figure 2b), the hollow interior was clearly visible after these steps. The same was true for $N_2$ physisorption analysis, where a dominant hysteresis loop at a $P/P_0$ above 0.4 could be observed (Figure S12a). Preservation of the protecting groups throughout the extraction steps is expected since acetamides are known to be very stable vs. hydrolysis and only cleavable using very harsh reaction conditions.[21]

To validate site accessibility and the desired catalytic activity of the amino groups located only in the internal surface (internal void) of the final material, a base-catalyzed Knoevenagel condensation between benzaldehyde and ethyl cyanoacetate was carried out as a model reaction (Figure 2a) in batch conditions. The reaction progress was followed by quantitative $^1$H NMR spectroscopy with $1,3,5$-trimethoxybenzene as internal standard. Note that amino-modified mesoporous silica materials are usually quite stable and their regeneration/recycling over several cycles in the base-catalyzed Knoevenagel condensation has been validated many times before,[22] and therefore these aspects will not be discussed in detail herein. Instead, we focus on simple tests which unambiguously demonstrate site accessibility only. To compare the different materials with or without templates, the product yield was normalized to the amount of nitrogen present in the catalysts, as obtained from elemental analysis data (see Table S3 for exact values). As it can be seen in Figure 2a, no conversion of the product was observed for the sample with the polystyrene beads still within the inner particle core (catalyst 3, illustrated in purple in Figure 2a; please note an overlap of the purple and black curves). This absence of activity can be attributed to the fact the amine groups are not accessible for the substrates due to blockage of the inner void by PS and complete acetylation of the amines located on the external particle surface and inside the shell mesopores. On the other hand, after removal of the polystyrene hard template, the same weight amount of final catalyst (catalyst 4, illustrated in red in Figure 2a) exhibited good conversion in the condensation reaction. This clearly indicates that the substrates were small enough to diffuse...
through the mesopores and react only inside the void of the hollow particles.

To obtain a synthetically meaningful yield, the amount of catalyst was increased by 50% (red dotted line, Figure 2a) and after 6 h, almost full conversion to the product could be obtained. For a comparison, a similar behavior was reported for aminated SBA-15 material (88% conversion after 8 h).22a However, when the Extr.-HMSP-APTS-MPTMS was used directly as the catalyst (i.e., before the amine protection step), a much faster conversion could be observed (see Figure S13) under the same testing conditions, underlining the impact of the in-and-out diffusion of substrates/products on the reaction time when the catalysts have only active sites deep on the inner core surface (i.e., slower reaction). As such, the nanocatalysts truly act as a nanoreactor with confined reaction sites within the inner external surface of the hollow particles.

Obviously, as the shell is mesoporous (pore size ≈ 3–4 nm), it cannot act as a true sievel for molecular size exclusion reactions. However, we were eager to explore the potential of such a catalyst design and expand its use to macromolecular and solid substrates. To do so, the same reaction was carried out using a resin bearing an aldehyde moiety. This may further be exploited to allow interfacial reactions on solids/resins, which is of interest for the conjugation of biomolecules, materials functionalization or preparation of chromatographic materials, for instance. The catalytic test was performed by mixing a stock suspension (in toluene) with the catalyst at 80 °C while stirring vigorously. After 6 h, the resin was collected by centrifugation and washed several times to remove unreacted reagents (see Experimental in SI). As it can be seen in the ssNMR spectra (Figure S14), the resin showed full conversion of the aldehyde units after 6 h, when the core-shell nanocatalyst bearing reactive sites on the outside shell (catalyst 1) was used. This indicates that the reaction was allowed to take place at the interface of the solids in suspension in toluene. On the contrary, when particles with the reactive sites inside the internal cavity only (catalyst 4) were used, no conversion of this aldehyde function could be obtained. This proves that the bulky resin aldehyde species cannot interact with the active sites within the hollow particles which are accessible only when diffusion through the mesoporous shell is possible. Hence, shielding of the basic functionalities was very efficient which indicates absence of major defects and leaching issues.

In summary, the synthesis of a 3-D mesoporous shell (MCM-48-type) HMSPs was successfully conducted and improved. The sole presence of catalytically active amine groups in the inner void of the particles was effectively demonstrated by Knoevenagel condensation reactions carried out before and after the polystyrene template extraction. With this type of active catalyst in hand, the next steps would be to investigate further acid- or base catalysis processes and diversify functionalities (e.g., include Lewis acids, redox capabilities), and this, not only in liquid but also in gaseous phase reactions to explore the full potential of these materials. Additionally, integrating such catalysts in small flow-through/
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