## One-pot reaction cascades catalyzed by base- and acid-functionalized mesoporous silica nanoparticles<sup>†</sup>

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Received (in Montpellier, France) 18th April 2008, Accepted 10th June 2008 First published as an Advance Article on the web 23rd June 2008 DOI: 10.1039/b806664g

Mesoporous silica nanoparticles (MSNs) containing base (primary amine) and sulfonic acid inside the MCM-41 type porous channels were successfully used as compatible catalysts for one-pot reaction cascades.

Nature's strategy of employing multistep reaction cascades for the synthesis of complex and bioactive organic molecules in living systems has long been a goal for designing artificial catalysts. While recent advancements in supramolecular chemistry, nanomaterial synthesis, and catalyst design have significantly improved our ability in mimicking this ingenious strategy of biocatalysis, the progress in constructing a compatible multifunctional catalytic system that can operate synergistically in one-pot sequential reactions is still relatively limited. Nonetheless, the recently developed "site isolation" concept for synthesizing surface-supported catalysts with multiple functionalities has led to many efficient biomimetic catalysts. In these systems, the different and often incompatible catalytic functionalities, such as acidic and basic groups, are separately isolated within the supporting matrices. The spatial separation of these chemical species that react avidly with each other in solution prevents the undesired self destruction of the catalytic capability. A few recent literature reports have highlighted the success of this approach. For example, Cohen and co-workers first developed a "wolf and lamb" twostage reaction system, where a soluble reagent reacts first with one polymeric reagent and the product with the second polymeric reagent.<sup>1</sup> Blum, Avnir et al. further developed "wolf and lamb" type one-pot reactions by encapsulating opposing catalysts in a sol-gel.<sup>2-6</sup> More recent investigations on using soluble star polymers<sup>7</sup> and other polymers<sup>8</sup> as site-isolating matrices also led to effective catalytic systems for one-pot reaction cascades.

Ever since the discovery of MCM-41 mesoporous silica,<sup>9</sup> these structurally ordered materials have been regarded as the ideal solid support for various catalysts due to their high surface areas (>800 m<sup>2</sup> g<sup>-1</sup>) and tunable pore sizes (2–20 nm). Several recent reports on the multifunctionalization of

mesoporous silica materials have rendered several interesting systems for cooperative catalysis.<sup>10–13</sup> Given that Blum, Avnir et al. have pioneeringly demonstrated that sol-gel silica can serve as an effective matrix for entrapping opposing catalysts for one-pot reaction cascades,<sup>2-6</sup> we are interested in taking advantage of the unique properties, i.e., homogeneous mesoporous structure and tunable particle size and pore diameter, of the MCM-type of mesoporous silicas for the site isolation of opposing catalytic reagents as well as the pore size discrimination that can regulate the mass-transport properties of a given reaction. By "hiding" one kind of functional group inside the mesopores of a mesoporous silica particle, while ensuring the other opposing reagent is situated inside another mesoporous silica material with different particle and pore sizes, the reaction kinetics could foreseeably be further manipulated. To achieve this goal, a key prerequisite is to functionalize the interior mesoporous surface with homogeneously distributed, high concentrations of functional groups, along with precise morphology control. We have recently developed an interfacial designed co-condensation method under low surfactant concentration condition for the synthesis of a series of organically functionalized mesoporous silica nanoparticle (MSN) materials.<sup>13–18</sup> Herein, we report on the synthesis and characterization of two MCM-41 type MSN materials that are functionalized with a 4-ethylphenylsulfonic acid (SAMSN) and an aminopropyl functionality (APMSN) as depicted in Fig. 1. We demonstrated that SAMSN and APMSN could serve as acid and base catalysts, respectively, for the wolf-andlamb type of one-pot reaction cascades. As a proof of principle, we examined the catalytic conversion of 4-nitrobenzaldehyde dimethyl acetal (Compound A) to (E)-1-nitro-4-(2nitrovinyl)benzene (Compound C), which involved two separate reactions, *i.e.*, an acid-catalyzed deprotection to yield the 4-nitrobenzaldehyde denoted as Compound B, followed by a base-catalyzed Henry reaction in nitromethane to generate the final product (E)-1-nitro-4-(2-nitrovinyl)benzene (Table 1).

The SAMSN and APMSN materials were synthesized *via* the previously described co-condensation of tetraethyl orthosilicate (TEOS) and 4-chlorosulfonophneylethylene-trimethoxysilane (CSTMOS) (or 3-aminopropyl-trimethoxysilane (APTMOS)) in the presence of cetyltrimethylammonium bromide (CTAB) as template under basic conditions as detailed in the ESI.† The CTAB-removed SAMSN and APMSN materials were characterized with nitrogen sorption analysis, powder X-ray diffraction (XRD), scanning electron microscopy (SEM), transimission electron microscopy (TEM), and the <sup>13</sup>C and <sup>29</sup>Si solid-state NMR. The TEM (Fig. 1a and b) and SEM

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<sup>†</sup> Electronic supplementary information (ESI) available: Syntheses of APMSN and SAMSN, nitrogen adsorption/desorption isotherms and pore size distributions, powder small angle XRD, SEM images, <sup>29</sup>Si solid state NMR spectra of APMSN and SAMSN. See DOI: 10.1039/ b806664g



Fig. 1 Mesoporous silica nanoparticles functionalized with an ethylphenylsulfonic acid (SAMSN) and an aminopropyl group (APMSN). The transmission electron micrographs (TEM) of SAMSN (a) and APMSN (b). Scale bar = 50 nm.

(Fig. S1 of the ESI†) images of SAMSN and APMSN showed that both materials have the typical MCM-41 type, highly ordered parallel channel-like porous structure packed in a hexagonal symmetry. The XRD diffraction patterns (Fig. S2†) further confirmed the MCM-41 type mesoporous structure with the  $d_{100} = 42.5$  Å and 40.9 Å (SAMSN and APMSN, respectively). As illustrated in Fig. S3,† the N<sub>2</sub> surface sorption analysis showed very high total surface areas (SAMSN: 827.9 m<sup>2</sup> g<sup>-1</sup>; APMSN: 789.0 m<sup>2</sup> g<sup>-1</sup>) and narrow pore diameter distributions (SAMSN: 25.4 Å; APMSN: 22.3 Å).

The <sup>29</sup>Si solid-state crossed polarization magic angle spining (CP-MAS) NMR (Fig. S4 and S5†) of these materials confirmed the covalent linkage between the organic functional groups to the silica surfaces as indicated by the T<sup>2</sup> and T<sup>3</sup> peaks, which are derived from ( $\equiv$ SiO)<sub>2</sub>Si(OH)R and ( $\equiv$ SiO)<sub>3</sub>SiR, respectively.<sup>19–21</sup> Furthermore, the presence



**Fig. 2** <sup>13</sup>C CP-MAS spectra of SAMSN (above) and APMSN (bottom).

and chemcial structures of the desired organic acid and base functionalities were quantatively verified by the <sup>13</sup>C solid-state CP-MAS NMR spectra (Fig. 2). The loading of sulfonic acid was determined to be 0.32 mmol  $g^{-1}$  of SAMSN, whereas the loading of amine was 0.40 mmol  $g^{-1}$  of APMSN.

In order to test the compatibility of these mesoporeconfined acid and base solids in catalyzing the one-pot reaction cascade, different molar ratios of SAMSN : APMSN were applied to the chemical transformation of 4-nitrobenzaldehyde dimethyl acetal (Compound A) to (E)-1-nitro-4-(2-nitrovinyl)benzene (Compound C). Reactions without any catalysts, with either free acid or free base, and with nonfunctionalized MSN were also performed as control experiments (Table 1).

As shown in entries 1–4 in Table 1, the acid-catalyzed deprotection of **A**, which is the first step of this two-step cascade reaction, was completed within 24 h in the presence of SAMSN (1.0 mol%) and APMSN (1.0–6.0 mol%). The result suggested that the sulfonic acid functionality of SAMSN was not affected by the presence of APMSN. Interestingly, the conversion of **B** to the final product **C** of the second Henry

Table 1 One-pot reaction cascade catalyzed by SAMSN and APMSN

D <sub>2</sub> N CCH <sub>3</sub>	Acid H <sub>2</sub> O O <sub>2</sub> N	Dense NO2
Α	В	С

Entry	SAMSN (mol%)	APMSN (mol%)	Conversion of A (%)	Yield of B (%)	Yield of C (%)
1	1.0	1.0	99.9	56.4	43.5
2	1.0	2.0	100	22.0	78.0
3	1.0	4.0	100	5.0	95.0
4	1.0	6.0	100	2.3	97.7
5	1.0	0	98.1	98.1	0
6	0	1.0	0	0	0
7	1.0	1.0 (tert-butylamine)	0	0	0
8	1.0 (para-toluenesulfonic acid)	1.0	0	0	0
9	1.0 ( <i>para</i> -toluenesulfonic acid)	1.0 (tert-butylamine)	0	0	0
10	Pure MSN	Pure MSN	0	0	0

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reaction was significantly enhanced from 43.5 to 97.7% as the amount of base-catalyst (APMSN) increased from 1.0 to 6.0 mol%. Also, different amounts of compound **B** (56.4–2.3%) were isolated at the end of 24 h in these reactions (entries 1–4) of various quantities of APMSN. Apparently, the more APMSN introduced to the reaction mixture, the faster the kinetics that could be achieved in the Henry reaction.

Furthermore, the desired Henry adduct C did not form in entries 5–6, where only one of the two MSN catalysts was present in the reaction. In entries 7 and 8, a molecular base (*tert*-butylamine) and an acid (*para*-toluenesulfonic acid) that are structurally similar to the corresponding organic groups immobilized in APMSN and SAMSN, respectively, were used to replace the solid catalysts. As predicted, these molecular substitutes could freely diffuse into the mesopores of APMSN (or SAMSN) and reacted to the surface-anchored acidic/basic functional groups. The deactivated solids could no longer catalyze the reaction cascade. This homogeneous acid–base neutralization-induced destruction was confirmed by mixing both *tert*-butylamine and *para*-toluenesulfonic in the reaction solution (entry 9).

In conclusion, we have demonstrated that by confining an organic acid and base inside mesoporous silica nanoparticles, these opposing reagents can be isolated and can serve as effective catalysts for a one-pot reaction cascade that requires incompatible catalysts. We envision that this approach can be further developed into a general design principle for mimicking biological systems, in which a series of reactions are catalyzed by different enzymes in a precise sequence.

The authors thank the Office of Basic Energy Sciences of the U.S. Department of Energy (DOE) under Contract No. DE-AC02-07CH11358 for providing financial support of this research.

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