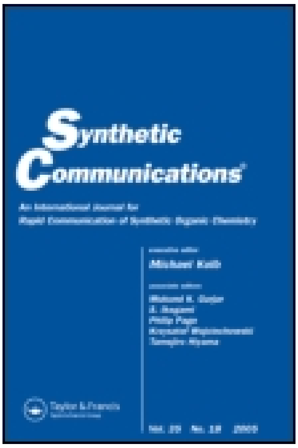

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Synthesis and Catalytic Applications of Sulfonic Acid Group-Functionalized Nano- and Microsilica Structures

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SYNTHESIS AND CATALYTIC APPLICATIONS OF SULFONIC ACID GROUP–FUNCTIONALIZED NANO- AND MICROSILICA STRUCTURES

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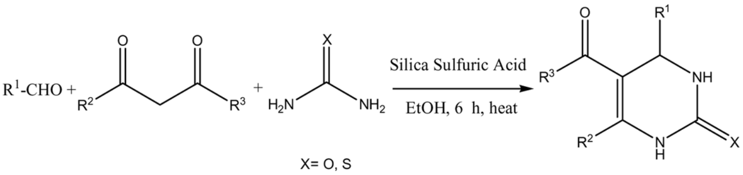
GRAPHICAL ABSTRACT



Abstract *Sulfonic acid group–functionalized nano- and microsilica with different sizes and shapes were synthesized. Silica nanospheres with an average size of 225 nm, silica microtubes, and fine silica gel were prepared and functionalized by sulfonic acid. Their catalytic activity was investigated in the three-component Biginelli reaction for the synthesis of dihydropyrimidinones.*

Keywords Biginelli reaction; silica microtubes; silica nanospheres; silica sulfuric acid; supported catalyst

INTRODUCTION

Acidic catalysts are widely used, in various industries, for producing a huge amount of valuable products every year.[1] Immobilization of an acid or base on silica via covalent bonding has many advantages over homogeneous

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catalysts. Heterogeneous catalysts can be recovered and reused, whereas homogeneous catalysts are less stable and contaminate reaction mixtures.[2] Heterogeneous systems are of great interest and importance because of their applications in industry and developing technologies.[3] The use of solid acids has many advantages over liquid acids such as ease of handling, decreasing reactor and plant corrosion problems, and environmentally safe disposal.[1,4] Also, wastes and by-products can be minimized or avoided by developing cleaner synthetic routes.[5]

The immobilization of the reagents on the surface of porous solid supports has advantages over the conventional solution-phase reactions because of the good dispersion of active reagent sites, associated selectivity, and easier workup.[6] High surface area of porous solids makes them good candidates for reagent support in heterogeneous reactions since the catalytic reactions take place on or near the catalyst's surface. Mesoporous structures of silica have, so far, been very popular as catalyst supports.[7] The functionalization of silica surface, by using required reagents and/or linkers, results in the production of solid catalysts.[8] The silica surface consists of two types of functional groups, namely siloxane (Si–O–Si) and silanol (Si–OH),[9–11] which provide functionalization with different functional groups. Thus, silica modification can occur via the reaction of particular molecules with either the siloxane or the silanol.[12] Zolfigol et al. have synthesized and applied silica sulfuric acid (SSA),[13,14] silica chloride (SC),[15] and silica phosphoric acid (SPA)[16] as reagents or as catalysts under heterogeneous conditions for different organic functional group transformations.

3,4-Dihydropyrimidin-2-(1*H*)-one (DHPM) was first synthesized by the three-component Biginelli reaction[17] in 1893, and its derivatives show a diverse range of therapeutical properties and pharmacological activities[18] such as antimitotic,[19] analgesic,[20] antiviral,[21] and antihypertensive agents.[22] The simple and direct method for the synthesis of DHPMs involves the one-pot condensation of an aldehyde, an β-ketoester, and urea under acidic conditions.

Here, we report the synthesis of sulfonic acid group–functionalized particles of silica, with different sizes and shapes, and catalytic performance of these reagents as reusable catalysts for the one-pot synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones in good yields.[23]

EXPERIMENTAL

Techniques and Materials

The infrared (IR) spectrum was obtained in the 400–4000 cm^{-1} range by a Fourier transform (FT)–IR 10MB BOMEM spectrometer. KBr pellets were used for solid samples. Scanning electron microscopy (SEM) of the particles was carried out using a Philips XLO SEM instrument. Samples were prepared by dispensing drops of an aqueous suspension of particles onto a glass plate. This was allowed to dry at room temperature and was then coated with a thin Au film. All commercially available chemicals were obtained from Merck and Fluka companies and used without further purifications.

Preparation of Silica Nanospheres

Monodispersed silica spheres were prepared by the modified Stöber process.[24] A mixture of 2.79 ml tetraethyl orthosilicate (TEOS) and 22.2 ml ethanol was added to the mixture of 0.638 ml 28 wt% ammonia, 6.8 ml deionized water, and 17.6 ml ethanol, under stirring, at room temperature. The reaction was allowed to continue for 3.5 h with stirring. The particles were then separated by centrifugation and washed with doubly distilled water. The size, as well as the size distribution for these particles, was calculated from SEM images.

Preparation of Silica Microtubes

Silica microtubes were synthesized by hydrolyzing TEOS in a mixture of ethanol, ammonia, water, and *dl*-tartaric acid, following the procedure reported by Nakamura et al.[25] Thus, 7.8 ml of TEOS was dissolved in 50 ml of ethanol containing 0.2 g of *dl*-tartaric acid and 0.6 ml of water. The solution was permitted to stand for 30 min to form SiO_2 solution, and finally 20 ml of ammonium hydroxide solution (28% NH_3 solution) was added. After 15–20 min, the reaction was observed to be completed. The precipitate was separated and washed several times after filtering, redispersing in water, and centrifugating.

Preparation of Silica Sulfuric Acid

Silica powder (2.0 g, fine silica gel, silica nanosphere, or silica microtube) was dispersed in 10 ml of dry dichloromethane and stirred in a round-bottomed flask. Chlorosulfonic acid (6.3×10^{-3} mmol for fine silica gel, 6×10^{-3} mmol for silica microtube, and 4.5×10^{-3} mmol for silica nanosphere) was added dropwise at room temperature. HCl gas evolved from the reaction vessel immediately. After the addition was complete, the mixture was stirred for 30 min. Evaporation of the solvent on a rotary evaporator resulted in formation of silica sulfuric acid (SSA) as a white solid.

General Procedure for the Synthesis of DHPMs

A mixture of the aldehyde (2 mmol), the β-dicarbonyl compound (2 mmol), urea or thiourea (3 mmol), and the catalyst (equal to 0.6 mmol H^+) in ethanol (10 ml) was refluxed for 6 h. Then, the solvent was evaporated under reduced pressure. The solid mixture was washed with cold water (20 ml) to remove the excess of urea or thiourea and filtered. The remaining solid material was washed with hot ethyl acetate (30 ml). The filtrate was concentrated, and the solid product was recrystallized from ethyl acetate/*n*-hexane or ethanol.

RESULTS AND DISCUSSION

Two types of nanosilica structures were synthesized. The size and shape of the synthesized silica particles were confirmed by using scanning electron microscopy

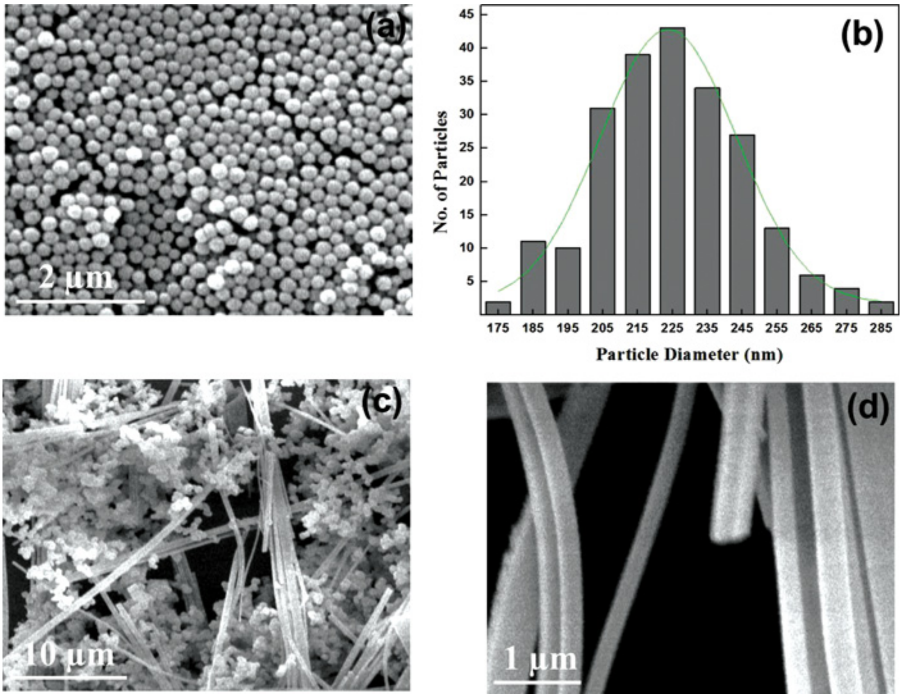


Figure 1. SEM micrographs of the silica nanospheres (a) and their size distribution (b) and silica microtubes (c) and (d).

(SEM). Figure 1 shows the SEM micrographs of the silica nanospheres (a), their size distribution (b), and silica microtubes (c) and (d).

The silica nanospheres, as seen in the SEM images, have an average size of 225 nm with a narrow size distribution of 1%. SEM micrographs of silica tubes confirm the formation of hollow tubes with a submicrometer diameter. However, large agglomerates of silica spherical particles can also be observed. Figure 1(d) shows the magnified view of a bunch of tubes, where the color contrast confirms the hollow nature of the structures.

The IR spectroscopy presents a useful tool to initially detect the success of the immobilization process. This proposal can be clarified by comparing the precursor and modified surfaces. IR spectroscopy was applied to find the surface groups on all samples. The presence of a silanol (Si–OH) group on the SiO_2 surface results in the appearance of an absorption band around 950 cm^{-1}. This can be used as a reference to qualitatively investigate the replacement of OH group with sulfonic acid, on the surface of the particles. Figure 2 shows the Fourier transform (FT)–IR spectra of all samples, before and after sulfonic acid functionalization. As it could be observed, the intensity of the peak around 950 cm^{-1} was reduced, as compared to other peaks [viz., 1100 cm^{-1} (Si–O–Si),] in all samples. The other evidence is the appearance of signature bands of the SO_3 group (1070 cm^{-1}) on the surface, after functionalization.

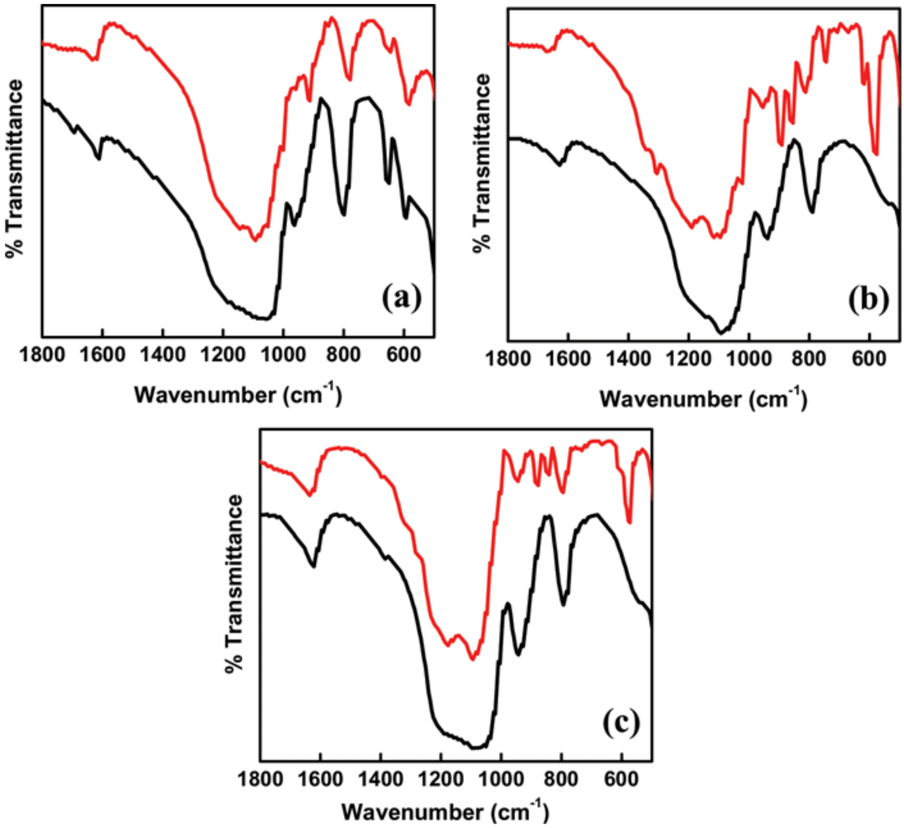
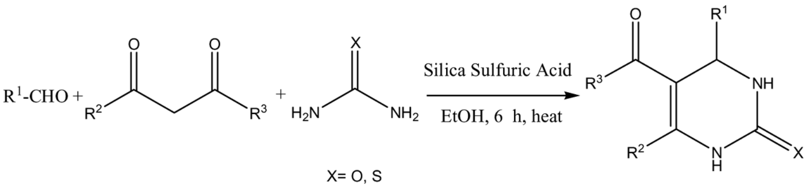


Figure 2. FT-IR spectra of the silica gelfine (a), silica nanospheres (b), and silica microtubes (c) before (black) and after (light gray) functionalization with chlorosulfonic acid.

Next, we studied the three-component Biginelli condensation catalyzed by sulfonic acid group–functionalized particles of silica, with different sizes and shapes, to afford the DHPM (Scheme 1).

A summary of the results obtained is provided in Table 1. The reactions proceeded smoothly in refluxing ethanol and were completed within 6 h. Table 1 shows the generality of the present protocol, which is equally effective for urea and thiourea in the presence of a variety of aldehydes and β-dicarbonyl compound.



Scheme 1. Three-component Biginelli reaction.

Table 1. Synthesis of dihydropyrimidin-ones and -thiones (DHPMs) by the condensation of aldehydes, dicarbonyls, and urea or thiourea catalyzed by silica sulfuric acid in ethanol

Entry	R^1	R^2	R^3	X	Yield (%)[a]	Yield (%)[b]	Yield (%)[c]
1	4-Cl-C_6H_4	Me	OEt	O	89	88	85
2	2,4-$(Cl)_2$-C_6H_3	Me	OEt	O	90	88	86
3	2-O_2N-C_6H_4	Me	OEt	O	87	85	82
4	4-F-C_6H_4	Me	OEt	O	88	87	84
5	4-CH_3O-C_6H_4	Me	OEt	O	93	93	90
6	4-CH_3O-C_6H_4	Me	OMe	O	95	94	92
7	4-CH_3O-C_6H_4	Me	OEt	S	85	84	80
8	4-O_2N-C_6H_4	Me	OEt	S	94	92	89
9	4-F-C_6H_4	Me	OEt	S	90	86	85
10	4-O_2N-C_6H_4	Me	OMe	S	90	88	87

[a] Silica microtubes.
[b] Silica nanospheres.
[c] Fine silica gel.

According to the type of the used silica structures, the maximum amount of chlorosulfonic acid was loaded on the surface of the silica powder in the functionalization reactions (0.209, 0.199, and 0.15 ml per gram of fine silica gel, silica microtube and silica nanosphere, respectively). Great amounts of chlorosulfonic acid changed the color of the catalyst to pale yellow or light brown. To compare the activity of the catalysts, the reactions were carried out with equal amounts of H^+ for different catalysts (i.e., 0.3 g SSA based on fine silica gel, 0.33 g SSA based on silica microtubes, and 0.44 g SSA based on silica nanospheres).

The results in Table 1 show that all of the catalysts were effective for progress of the reaction in a similar way, although the amounts of silica used were in the order of nanosphere > microtube > fine. This can be attributed to the amount of the silanol (Si–OH) groups, which are functionalized by chlorosulfonic acid.

The reusability of the catalyst is an important factor from economical and environmental points of view. Therefore, the reusability of SSA was examined in the reaction of 4-chlorobenzaldehyde, urea, and ethyl acetoacetate under optimized reaction conditions. The product was isolated by filtration, and after washing the solid residues with ethyl acetate, the remaining catalyst was reloaded with fresh reagents for further runs. The results showed that the catalyst can be used four times without loss of its activity (Table 2).

Table 2. Reusability of SSA in the reaction of ethyl acetoacetate, 4-chlorobenzaldehyde, and urea

Run	Yield (%)[a]	Yield (%)[b]	Yield (%)[c]
1	89	88	85
2	90	89	86
3	89	88	84
4	88	87	84

[a] Silica microtubes.
[b] Silica nanospheres.
[c] Fine silica gel.

CONCLUSIONS

Different types of silica structures were synthesized and functionalized by sulfonic acid. The loading of $-SO_3H$ functional group per gram of the silica was dependent on the amount of available silanol groups, which were in the order of fine > microtube > nanosphere. All of the catalysts were effective for the synthesis of DHPMs in the three-component Biginelli reaction.

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