

Silica functionalized sulfonic acid as a recyclable interphase catalyst for chemoselective thioacetalization of carbonyl compounds in water

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Abstract

Silica functionalized sulfonic acid which can be prepared by simple procedure using commercially available and relatively cheap starting materials, efficiently acts as highly active and reusable catalyst for thioacetalization of a variety of carbonyl compounds in water. The catalyst shows high thermal stability (up to 300 °C) and can be recovered and reused for at least five reaction cycles without loss of reactivity under the described reaction conditions.

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1. Introduction

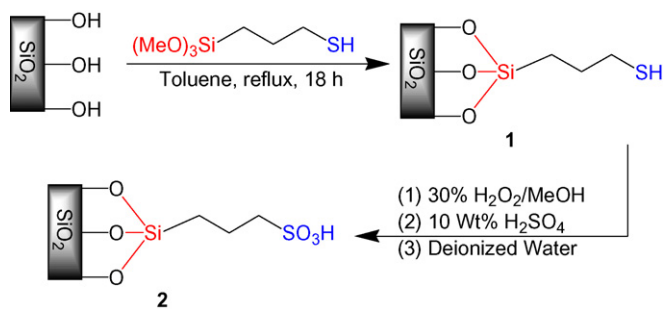
The protection of carbonyl groups as a dithioacetals is a common and popular practice in organic chemistry [1] as they are quite stable under basic or acidic conditions [2]. The dithioacetals in the form of 1,3-dithiolanes and 1,3-dithianes are also utilized as masked acyl anion [3] or masked methylene functions [4] in carbon–carbon bond forming reactions. In this view, there have been continued improvements in the methods of preparation of thioacetals. Generally, they are prepared by condensation of carbonyl compounds with thiols in the presence of strong acid catalysts such as AlCl_3 [5], LnCl_3 [6], ZnCl_2 [7], TiCl_4 [8], WCl_6 [9], InCl_3 [10], $\text{In}(\text{OTf})_3$ [11], $\text{Sc}(\text{OTf})_3$ [12], $\text{Bi}(\text{NO}_3)_3$ [13] and $\text{VO}(\text{OTf})_2$ [14]. A number of milder procedures employing lithium salts [15], NiCl_2 [16], CoCl_2 [17], NBS [18], and I_2 [19] have also been reported for this purpose. Unfortunately, many of these protocols suffer from the drawbacks such as a requirement for stoichiometric amounts of catalysts, the use of expensive reagents and/or chlorinated organic solvents, the requirement for harsh reac-

tion condition, and in some instances strong acidic reagents. Recently, a number of solid supported reagents have also been used for thioacetalization of various types of carbonyl compounds, e.g. $\text{ZrCl}_4\text{-SiO}_2$ [20], $\text{SOCl}_2\text{-SiO}_2$ [21], $\text{CoBr}_2\text{-SiO}_2$ [22], $\text{TaCl}_5\text{-SiO}_2$ [23], $\text{Cu}(\text{OTf})_2\text{-SiO}_2$ [24], $\text{NaHSO}_4\text{-SiO}_2$ [25] and $\text{I}_2/\text{natural phosphate}$ [26]. Although these methods also represent useful advantages in many synthetic transformations, the vast majority of them are carried out in organic solvents under strict anhydrous conditions, because Lewis acids used are hygroscopic and easily decompose in the presence of even small amount of water.

Organic reactions in water without the use of harmful organic solvents are becoming of great interest in recent years, because water is an easily available, economical, and environmentally benign solvent [27]. Very recently, Kobayashi et al. showed that a hydrophobic emulsion system created by dodecylbenzenesulfonic acid (DBSA) as a surfactant-type Brønsted acid successfully catalyzes dehydrative esterification of carboxylic acids [28] and etherification of alcohols and thioacetalization of carbonyl compounds [29] in water. While these protocols demonstrate interesting advances in catalyzing organic reactions in water, owing to homogeneous reaction conditions, the catalyst is difficult to recover and reuse and to separate from the reaction mixture especially when the products are liquid. It is clear that green chemistry not only requires the use of environmentally benign reagents and solvents, but also it is very crucial to

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Scheme 1.

recover and reuse the catalyst. One way to overcome the problem of recyclability of the traditional acid catalysts is to chemically anchor their reactive center onto a large surface area inorganic solid carrier to create new organic–inorganic hybrid (interphase) catalyst [30]. In this type of solids, the reactive centers are highly mobile similar to homogeneous catalysts and at the same time it has the advantage of recyclability like heterogeneous catalysts. In this view, several types of solid sulfonic acid functionalized silica (both amorphous and ordered) have been synthesized and applied as an alternative to traditional sulfonic acid resins and homogeneous acids in catalyzing chemical transformations [31]. Despite the attractiveness of these reagents, to the best of our knowledge there is no report on the application of these catalyst either in thioacetalization of carbonyl compounds or in water as reaction media. Along the line of our studies in design and application of new solid catalysts in chemical transformations [32] herein, we wish to describe a new efficient method for highly chemoselective thioacetalization of a variety of carbonyl compounds using a dithiol in the presence of a catalytic amount of solid silica-based sulfonic acid in water. The preparation procedure to obtain catalyst 2 is demonstrated in Scheme 1 according to the known literature procedure with slight modification [29].

Quantitative determination of the organic functional group covalently anchored onto the surface in catalyst 2 was performed with thermogravimetric analysis (TGA) and ion-exchange pH analysis. Typically a loading at ca. 0.33 and 0.35 mmol/g for surface bound –SO₃H group and total surface bound organic group is obtained, respectively. This result shows that more than 94% of the surface bound thiol group are converted to the corresponding sulfonic acid group [32d].

2. Experimental

2.1. General remarks

Chemicals were either prepared in our laboratories or purchased from Merck, Fluka and Aldrich Chemical Companies. All yields refer to isolated products unless otherwise stated. The products were characterized by comparison of their physical data with those of known samples or by their spectral data. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker 500 MHz spectrometer in CDCl₃ as the solvent and TMS as internal standard. Gas liquid chromatography (GLC) was carried out on a Varian Star CP-3800 gas chromatograph, using nitrogen as car-

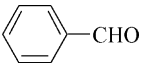
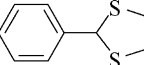
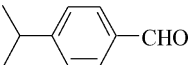
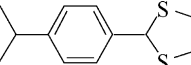
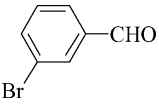
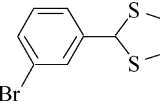
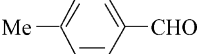
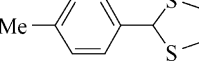
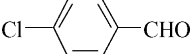
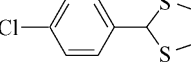
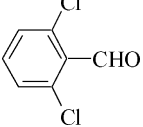
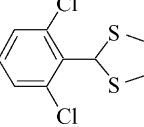
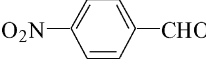
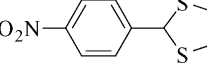
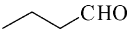
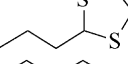
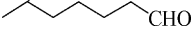


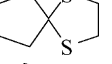
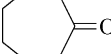
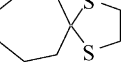
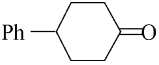
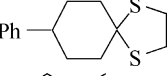
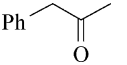
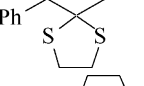
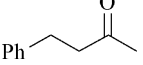
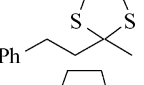
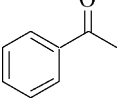
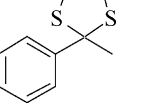
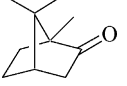
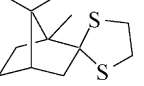
rier gas and capillary CP-SIL-8-CB (25 m, 0.25 mm, 0.25 μm). All of the products are known and the isolated products gave satisfactory IR and NMR spectra.

- Preparation of 3-Mercaptopropylsilica 1 (MPS):** Mesoporous amorphous silica gel (average pore diameter 60 Å) was activated by refluxing in concentrated hydrochloric acid (6 M) for 24 h and then washed thoroughly with the deionized water and dried before undergoing chemical surface modification. Refluxing the activated silica gel (10 g) with 3-mercaptopropyltrimethoxysilane (MPTMS, 5 mmol) in dry toluene for 18 h. The solid materials were filtered off and washed with hot toluene for 12 h in a continuous extraction apparatus (Soxhlet) and then dried in an oven at 110 °C overnight to give the surface bound thiol 1 (MPS) group.
- Preparation of solid-based silica sulfonic acid 2:** The thiol groups of the modified silica (MPS, 5 g) were oxidized with a 30% H₂O₂ solution (50 mL) and concentrated H₂SO₄ (2 drop) in methanol (15 ml) for 12 h at room temperature and the solid was filtered off and washed three times with deionized water (50 mL). In order to ensure that all the sulfonic acid groups were protonated, the solid was suspended in 10 wt% H₂SO₄ solution (30 mL) for 4 h. The solid was then filtered off and washed thoroughly with deionized water and dried at 120 °C overnight. Quantitative determination of the organic functional group covalently anchored onto the surface in compound 1 was performed with thermogravimetric analysis (TGA). Typically a loading at ca. 0.35 mmol/g is obtained. On the other hand, when the washed sulfonated product 2 was placed in an aqueous NaCl solution, the solution pH dropped virtually instantaneously to pH ≈ 2, as ion exchange occurred between protons and sodium ions (proton exchange capacity: 0.33 mmol/g of sulfonic acid 2 which is in good agreement with the result obtained from TGA and titration).
- General procedure for thioacetalization of carbonyl compounds in water using 2:** The carbonyl compound (2 mmol), 1,2-ethanedithiol (2.2 mmol), and 2 (0.1 mmol, 0.3 g) were combined together in water (5 mL) and the mixture was stirred at 80 °C for time indicated in Table 1. The progress of the reaction was monitored by TLC or GC. After completion of the reaction, catalyst 2 was filtered off and washed with Et₂O (15 mL). The filtrate was then extracted with Et₂O (2 × 15), and the combined organic layers were washed with aqueous NaOH (5 mL, 5%) and dried (Na₂SO₄). Evaporation of the solvent under reduced pressure gave the almost pure thioacetal(s). Further purification of the products could be achieved by vacuum distillation or recrystallization to afford the corresponding pure thioacetals (Table 1).

3. Results and discussion

The scope and failure of the catalyst 2 as a heterogeneous catalyst in dithioacetalization of a variety of carbonyl compounds in water was examined. When a mixture of benzaldehyde (2 mmol), 1,2-ethanedithiol (2.1 mmol) and catalyst 2 (5 mol%, 300 mg) in H₂O (5 mL) was stirred at 80 °C for 100 min, 2-

Table 1
Efficient thioacetalization of carbonyl compounds in the presence of solid silica-based sulfonic acids in water

Entry	Substrate	Product	Time (min)/[h]	Yield (%) ^{a,b,c}
1			100	97
2			95	92
3			95	90
4			100	93
5			80	98
6			[6]	92
7			[8]	90
8			[3]	79
9			[5.5]	85
10			[9]	91
11			[12]	87
12			[14]	93
13			[14]	89
14			[11]	90
15			[18]	No reaction
16			[18]	No reaction

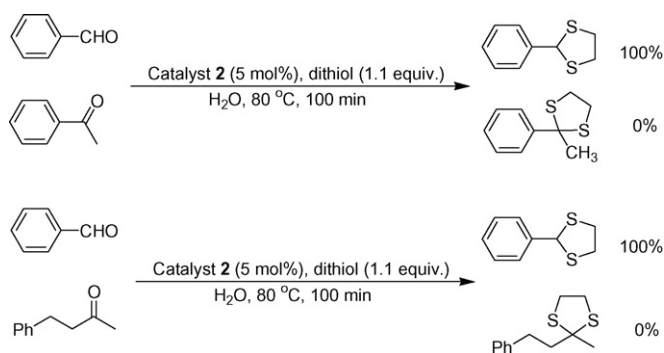
^a Yields refer to isolated pure product unless otherwise stated.

^b All products were known and gave satisfactory IR spectra.

^c The substrate:1,2-ethanedithiol:catalyst **2** ratios were 1:1.1:0.05.

phenyl-1,3-dithiolane was produced and isolated in 92% yields after workup (Table 1, entry 1). This interesting result prompted us to investigate the possibility of developing a new general catalytic system for thioacetalization of carbonyl compounds in water in the presence of **2**. Along this line, we have found that several types of substituted benzaldehydes with electron-

donating and electron-withdrawing groups as well as aliphatic aldehydes can be also protected in a similar manner in good to excellent yields (Table 1, entries 2–9). It is also worth nothing that with **2** as catalyst in water thioacetalization of both saturated cyclic and acyclic ketones proceeded well to produce the corresponding 1,3-dithioacetals in good to excellent yields (Table 1



Scheme 2.

entries 10, 14). These results clearly demonstrate the high reactivity of silica-functionalized sulfonic acid under the described reaction conditions. However, It is observed that under similar reaction conditions, other carbonyl compounds such as aromatic and sterically hindered ketones remained intact in refluxing water ($\sim 94^{\circ}\text{C}$) even after several hours (Table 1, entries 15, 16). Inspection of the data in Table 1 shows that ketones need more time to be converted into their thioacetals. Based on this observation, we conducted a set of competitive protection reactions between aldehydes and ketones that the results of which are shown in Scheme 2.

These observations show that the presented method is potentially applicable for chemoselective conversion of aldehydes to corresponding thioacetals in the presence of ketone functions in multi-functional molecules.

When using a supported catalyst one of the most important issue is the possibility of leaching of the reactive center into the reaction mixture. To rule out the role of homogeneous catalysis in the results shown in Table 1, the catalyst allowed to react with distilled water for 10 min under operated temperature and filtered off. We observed that the filtrate showed no catalytic activity in thioacetalization of benzaldehydes under the operated reaction condition, confirming the heterogeneous catalysis of **2**. It is also worth mentioning the catalyst **2** could be recovered and reused for at least five run when the recycling experiments were examined for thioacetalization of benzaldehyde. The average GC yields for 5 consecutive runs was 90%, which clearly demonstrates the practical recyclability of this catalyst. This reusability demonstrates the high stability and turn over of solid silica-based sulfonic acid under operating condition. After using the catalyst **2**, the solid was simply filtered off, washed with EtOH, and ether and reused.

In conclusion, this work shows that silica-based sulfonic acid, which can be prepared by simple operation from commercially available and relative cheap starting materials, efficiently catalyzes the dithioacetalizations of a variety of carbonyl compounds in water. To the best of our knowledge this protocol is the first example of utilizing silica-based sulfonic acids in water as reaction media. The catalyst shows high thermal stability (up to 300°C). It could also be recovered and reused for at least five reaction cycles without noticeable loss of reactivity. Mild reaction condition, the use of water as reaction media, simplicity of the procedure, and chemical selectivity offer improvement

over many existing methods. Work on other applications of the catalyst **2** to other types of functional group transformations is ongoing in our laboratories.

Acknowledgments

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