

Silica Phenyl Sulfonic Acid as a Solid Acid Heterogeneous Catalyst for Chemoselective Thioacetalization of Carbonyl Compounds and Dethioacetalization under Mild Conditions

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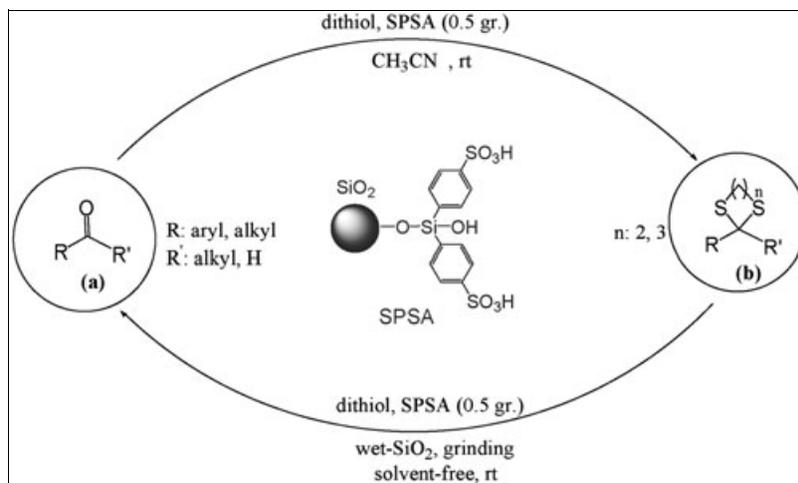
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Silica phenyl sulfonic acid (SPSA) is an effective catalyst for chemoselective thioacetalization of aldehydes in the presence of ketones under neutral conditions. In addition, a simple and an efficient procedure for deprotection of 1,3-dithianes and 1,3-dithiolanes of aromatic, aliphatic, and α,β -unsaturated aldehydes and ketones in the solvent-free to the corresponding parent carbonyl compounds was successfully carried out with SPSA in excellent yields.

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INTRODUCTION

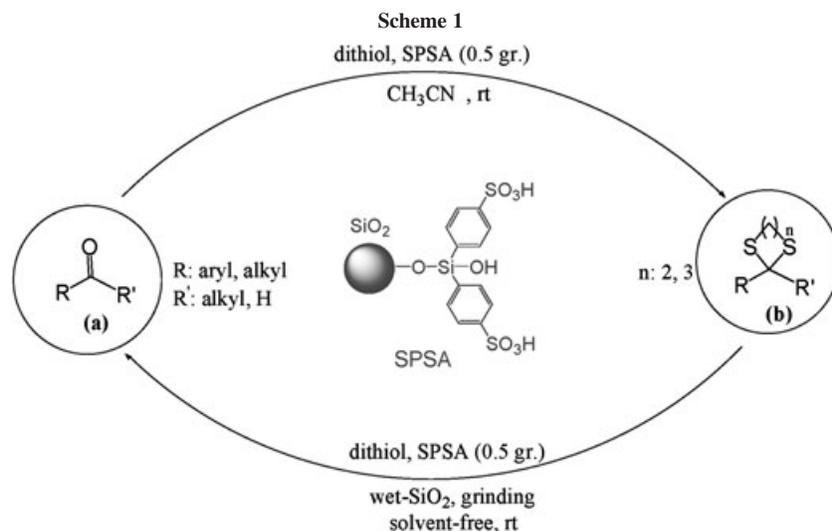
The protection of carbonyl functionality as a dithioacetal is important in the total synthesis of complex natural and non-natural products [1,2]. Thioacetals are relatively stable toward a wide variety of reagents and are also useful in organic synthesis as acyl carbanion equivalents in C–C bond-forming reaction [3,4]. They are usually prepared by the condensation of carbonyl compounds with thiols or dithiols using a strong protic acid such as HCl [5] or Lewis acids such as $\text{BF}_3 \cdot \text{OEt}_2$ [6] or ZnCl_2 [7] as catalysts. Other Lewis acids such as AlCl_3 [8], WCl_6 [3], InCl_3 [9], $\text{P}_2\text{O}_5/\text{SiO}_2$ [10], and $[\text{bmim}]\text{HSO}_4$ [11]. A number of milder procedures using lithium salts [12], NiCl_2 [13], trichloroisocyanuric acid [14], NBS [15], I_2 [16], microwave [17], $\text{HBF}_4 \cdot \text{SiO}_2$ [18], $\text{Y}(\text{OTf})_3$ [19], $\text{VO}(\text{OTf})_2$ [20], ScCl_3 [21], and silica functionalized sulfonic acid [22] have also been reported for this purpose. The regeneration of parent carbonyl compounds is not always a facile and straightforward process, and therefore, development of dethioacetalization protocols has engaged the attention of organic chemists over the years [23–26]. Unfortunately, many

of these protocols suffer from the drawbacks such as a requirement for stoichiometric amounts of catalysts, long reaction times, the use of expensive reagents and/or chlorinated organic solvents, harsh reaction conditions, difficulties in work-up, and in some instances strong acidic reagents.

RESULTS AND DISCUSSION

Silica phenyl sulfonic acid (SPSA) [27] is easily prepared from the silanization of activated silica gel with diphenyldichlorosilane followed by adding chlorosulfonic acid at room temperature and washed with water.

In continuation of the authors ongoing research on the development of more efficient and environmentally friendly procedures for some important transformations in organic synthesis [28], herein, they wish to report a mild and highly chemoselective procedure for the conversion of aldehydes in presence of ketones into 1,3-dithiolanes and 1,3-dithianes using SPSA as a solid acid heterogeneous catalyst under almost neutral reaction conditions (Scheme 1).



First the reaction of benzaldehyde, with 1,2-ethanedithiol in the presence of SPSA (0.5 g) at room temperature using different solvents such as CH₂Cl₂, CHCl₃, CCl₄, CH₃CN, and EtOH were carried out. The results show that CH₃CN is a better solvent.

To test the generality and versatility of this procedure in the thioacetalization, the authors have examined a number of aromatic, aliphatic, and α,β -unsaturated aldehydes and ketones using the optimized conditions (Table 1). As shown in Table 1, various types of aromatic aldehydes with electron-donating and -withdrawing groups were cleanly

and rapidly converted to the corresponding dithianes and dithiolanes in the presence of catalysts. However, aromatic and aliphatic ketones were slowly converted to their corresponding S,S-acetals (Table 1, entries 19–22).

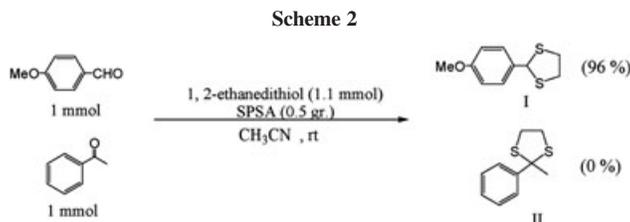
The difference in reactivity of the SPSA toward aldehydes and ketones gave them the impetus to study chemoselective reactions (Scheme 2).

In continuation of their work, the authors decided to study the role of SPSA in the deprotection of thioacetals and thioketals under various conditions (Scheme 2). The authors found that the deprotection of acetophenone

Table 1
Thioacetalization and dethioacetalization of carbonyl compounds catalyzed by SPSA at ambient conditions.

Entry	Substrate	Dithiol	Protection ^a Time (min; h) yield (%)	Deprotection ^a Time (min) yield (%)	Ref.
1	Benzaldehyde	HSCH ₂ CH ₂ SH	(45) 98	(3) 98	[13]
2	Benzaldehyde	HSCH ₂ H ₂ CH ₂ SH	(45) 90	(3) 98	[13]
3	<i>p</i> -Me-benzaldehyde	HSCH ₂ CH ₂ SH	(50) 92	(3) 96	[16]
4	<i>p</i> -Me-benzaldehyde	HSCH ₂ H ₂ CH ₂ SH	(55) 89	(3) 92	[16]
5	<i>p</i> -MeO-benzaldehyde	HSCH ₂ CH ₂ SH	(15) 96	(2) 98	[13]
6	<i>p</i> -MeO-benzaldehyde	HSCH ₂ H ₂ CH ₂ SH	(20) 90	(2.5) 97	[13]
7	<i>p</i> -Cl-benzaldehyde	HSCH ₂ CH ₂ SH	(30) 98	(3) 95	[16]
8	<i>p</i> -Cl-benzaldehyde	HSCH ₂ H ₂ CH ₂ SH	(35) 98	(3.5) 90	[11]
9	<i>p</i> -OH-benzaldehyde	HSCH ₂ CH ₂ SH	(40) 92	(3) 90	[13]
10	<i>p</i> -OH-benzaldehyde	HSCH ₂ H ₂ CH ₂ SH	(50) 90	(3.5) 92	[13]
11	3-NO ₂ -benzaldehyde	HSCH ₂ CH ₂ SH	(120) 85	(2) 98	[16]
12	3-NO ₂ -benzaldehyde	HSCH ₂ H ₂ CH ₂ SH	(120) 80	(2) 95	[16]
13	4-NMe ₂ -benzaldehyde	HSCH ₂ CH ₂ SH	(75) 90	(4) 92	[18]
14	4-NMe ₂ -benzaldehyde	HSCH ₂ H ₂ CH ₂ SH	(90) 90	(3.5) 90	[18]
15	Heptanal	HSCH ₂ CH ₂ SH	[2] 85	(5) 93	[13]
16	Heptanal	HSCH ₂ H ₂ CH ₂ SH	[3] 80	(4) 96	[13]
17	Cinamaldehyde	HSCH ₂ CH ₂ SH	[1.5] 90	(3) 92	[16]
18	Cinamaldehyde	HSCH ₂ H ₂ CH ₂ SH	[1.5] 85	(3) 90	[16]
19	2-Butanone	HSCH ₂ CH ₂ SH	[4] 75	(4) 90	[18]
20	2-Butanone	HSCH ₂ H ₂ CH ₂ SH	[5] 70	(4) 90	[18]
21	Acetophenone	HSCH ₂ CH ₂ SH	[5] 70	(5) 98	[16]
22	Acetophenone	HSCH ₂ H ₂ CH ₂ SH	[6] 60	(6) 90	[16]

^aProducts were characterized from their physical properties when compared with the authentic samples and by spectroscopic methods.



dithioacetal was rapid and gave excellent yields of the products, when catalyzed by SPSA in the presence of wet-SiO₂ (5 min, 98%, entry 21, Table 1). As shown in Table 1, various types of 1,3-dithianes and 1,3-dithiolanes (aromatic, aliphatic, and α,β -unsaturated) with electron-donating and -withdrawing groups were cleanly and rapidly converted to the corresponding parent carbonyl compounds in the solvent-free conditions using SPSA at room temperature.

CONCLUSION

In conclusion, in this study, the authors have introduced a new and useful solvent-free application of SPSA as an efficient solid acid heterogeneous catalyst for the thioacetalization of aldehydes and ketones and dethioacetalization under mild reaction conditions at room temperature. The method is highly chemoselective for protection of aldehydes in the presence of ketones. Moreover, the method has advantages in terms of high yields of products, short reaction times, operational simplicity, and easy work up of products.

EXPERIMENTAL

All commercially available chemicals were obtained from Merck and Fluka companies and used without further purifications unless otherwise stated. ¹H NMR spectra were recorded on a Jeol 90-MHz FT NMR spectrometer using TMS as internal standard and chemical shift are in δ (ppm). Infrared (IR) was conducted on a Perkin Elmer GX FT-IR spectrometer. All yields refer to isolated products.

General procedure for thioacetalization catalyzed silica phenyl sulfonic acid in CH₃CN. To a stirred solution of substrate (1 mmol) and SPSA (0.5 g) in CH₃CN (3 mL) was added 1,2-ethanedithiol or 1,3-propanedithiole (1.1 mmol) at room temperature. The mixture was stirred for an appropriate time (Table 1). After completion of reaction as indicated by TLC, the organic solvent was filtrated and the catalyst was removed. The filtrate was evaporated under reduced pressure to achieve crude products. The crude products were purified by recrystallization from ethanol or column chromatography using *n*-hexane/acetone (10:1) as the eluent system.

General procedure for deprotection of 1,3-dithianes and 1,3-dithiolanes using silica phenyl sulfonic acid in solvent-free condition. Substrate (1 mmol), SPSA (0.5 g) and 0.5 g wet-SiO₂ were added to a mortar and the mixture was pulverized with a pestle. A spontaneous reaction took place [2–5 min, Table 1, monitored by TLC (9:1, hexane/acetone)]. After completion of

the reaction, EtOH (10 mL) was added and insoluble catalyst was removed by filtration. The filtrate was evaporated under reduced pressure and the resulting crude material was purified by chromatography column (eluent: CH₂Cl₂) to give pure carbonyl compounds.

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