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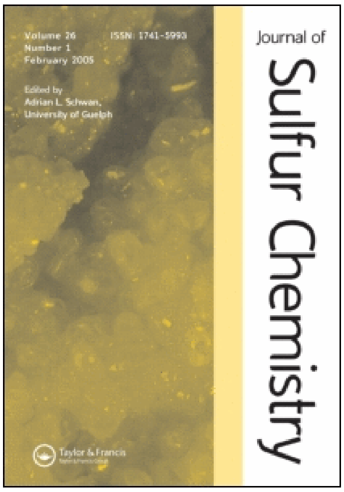

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# Silica sulfuric acid as a mild and chemoselective catalyst for dithioacetalization under solvent-free conditions

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RESEARCH ARTICLE

# Silica sulfuric acid as a mild and chemoselective catalyst for dithioacetalization under solvent-free conditions

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(*Received 4 August 2004; in final form 25 September 2004*)

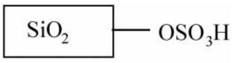
Various carbonyl compounds have been protected as dithioacetals in very good yields using silica sulfuric acid as a mild, chemoselective catalyst under solvent-free conditions.

*Keywords*: Silica sulfuric acid; Dithioacetalization; Protection; Carbonyl compounds

## 1. Introduction

Dithioacetals are efficient protecting groups [1] and excellent acyl carbanion equivalents in organic synthesis [2]. Of the various dithioacetals, diethyldithioacetal has been commonly used as a protecting group for the preparation of acyclic derivatives of monosaccharides in carbohydrate chemistry [3]. Although many methods have been reported for the conversion of dithioacetals and diethyldithioacetals into their corresponding carbonyl derivatives [4, 5], there is still a great demand in this area of chemistry for the introduction of mild, efficient and selective practical methods.

In continuation of our studies on the application of solid acids we found that silica gel reacts with chorosulfonic acid to give silica sulfuric acid (**I**). Interestingly, the reaction is straightforward, clean and does not need further purification, because HCl gas is evolved from the reaction vessel. We also found that silica sulfuric acid (**I**) is an excellent candidate for sulfuric acid replacement in organic reactions [6].



**I**

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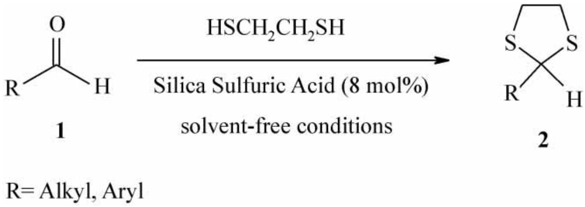
In continuation of our ongoing program to develop environmentally benign methods under solvent-free conditions [7], we report here an extremely convenient, mild and highly chemoselective procedure for the conversion of aldehydes and ketones into 1,3-dithiolanes using a catalytic amount of silica sulfuric acid under solvent-free conditions [7].

## 2. Results and discussion

The protection of various aldehydes and ketones containing electron-withdrawing and electron-donating substituents, heteroaromatic and $\alpha,\beta$-unsaturated aldehydes and various ketones with ethane 1,2-dithiol in the presence of a catalytic amount of silica sulfuric acid was examined under solvent-free condition at room temperature (scheme 1). The results are summarized in table 1. In each case dithioacetal was obtained in good to excellent yields after a short time.



SCHEME 1

Table 1. Dithioacetalization of aldehydes and ketones in the presence of silica sulfuric acid.[a,b]

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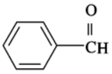
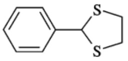
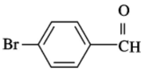
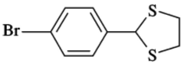
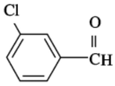
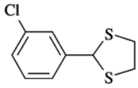
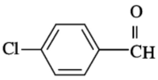
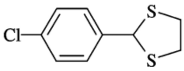
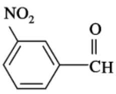
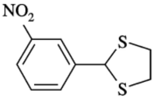
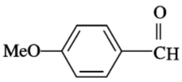
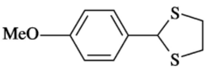
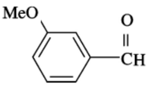
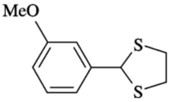
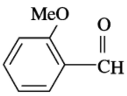
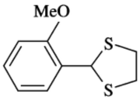
| 1 |  |  | 2 | 95 |
| 2 |  |  | 2 | 98 |
| 3 |  |  | 2 | 97 |
| 4 |  |  | 2 | 98 |
| 5 |  |  | 2 | 95 |
| 6 |  |  | 2 | 97 |
| 7 |  |  | 2 | 96 |
| 8 |  |  | 2 | 95 |

(*continued*)

Table 1. Continued

| Entry | Substrate | Product | Time (min) | Yield (%) |
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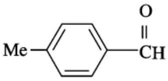
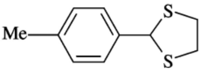
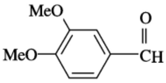
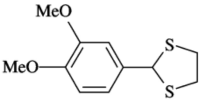
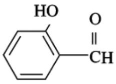
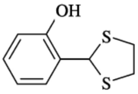
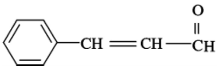
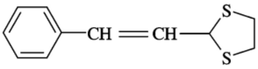
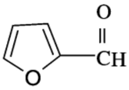
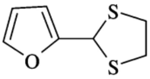
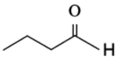
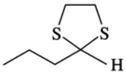
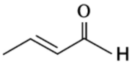
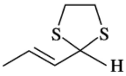
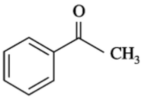
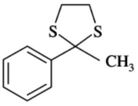
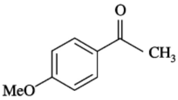
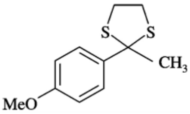
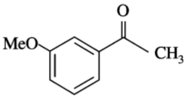
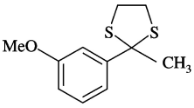
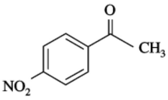
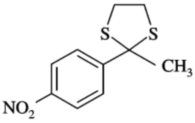
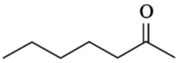
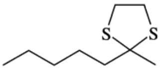
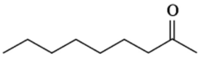
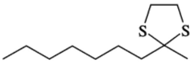
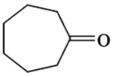
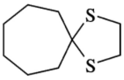
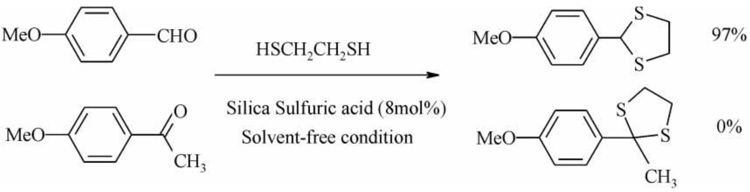
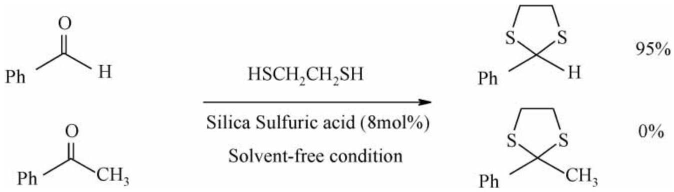
| 9 |  |  | 2 | 95 |
| 10 |  |  | 2 | 93 |
| 11 |  |  | 2 | 94 |
| 12 |  |  | 2 | 95 |
| 13 |  |  | 2 | 98 |
| 14 |  |  | 2 | 95 |
| 15 |  |  | 2 | 92 |
| 16 |  |  | 10 | 70 |
| 17 |  |  | 10 | 50 |
| 18 |  |  | 10 | 55 |
| 19 |  |  | 10 | 51 |
| 20 |  |  | 4 | 96 |
| 21 |  |  | 4 | 98 |
| 22 |  |  | 4 | 96 |

[a]Yields refer to the isolated products after purification. [b]All products characterized from their spectral data (IR, $^1$H NMR, TLC and GC) and by comparison with authentic samples [5a,b, 8].

Products were purified by column chromatography and their purity determined by GC analysis. Moreover, this procedure is highly chemoselective, providing selective protection of aldehydes in the presence of ketones. In representative examples, an equimolar mixture of *p*-methoxybenzaldehyde and *p*-methoxyacetophenone or an equimolar mixture of benzaldehyde and acetophenone were allowed to react with ethane-1,2-dithiol in the presence of a catalytic amount of silica sulfuric acid. Schemes 2 and 3 show the results.



SCHEME 2



SCHEME 3

In conclusion, both aromatic and aliphatic aldehydes and ketones were converted into their corresponding dithioacetals, employing silica sulfuric acid as a catalyst under extremely mild conditions. Moreover, the high chemoselectivity, good to excellent yields, short reaction times and availability of reagent makes this method a practical protocol for dithioacetalization of carbonyl compounds.

## 3. Experimental procedure

### 3.1 *Preparation of silica sulfuric acid (I)*

A 500 mL suction flask was equipped with a constant-pressure dropping funnel containing chlorosulfonic acid (46.6 g, 0.4 mol) and a gas outlet tube for conducting HCl gas over an adsorbing solution, i.e., water. Into the flask was charged 60.0 g of silica gel. Chlorosulfonic acid was added dropwise over 40 min at room temperature. HCl gas evolved from the reaction vessel immediately after the addition. The mixture was then shaken for 30 min at room temperature. A white solid (silica sulfuric acid) (92.0 g) was obtained.

### 3.2 *Thioacetalization of p-methoxybenzaldehyde with ethane-1,2-dithiol using silica sulfuric acid. Typical procedure*

In a mortar, a mixture of *p*-methoxybenzaldehyde (0.12 mL, 1 mmol), ethane-1,2-dithiol (0.11 mL, 1.3 mmol) and silica sulfuric acid (0.02 g, 8 mol%) was ground with a pestle for 2 min. The progress of the reaction was followed by TLC or GC. Product was isolated with diethyl ether (2 × 10 mL), and after vigorously stirring the reaction mixture the solid was filtered off through a sintered glass funnel and the solvent was evaporated under vacuum. The crude product was purified through a short silica column. The GC retention time was identical with that of an authentic sample.

## Acknowledgments

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