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Silica sulfuric acid: A versatile reagent for oxathioacetalyzation of carbonyl compounds and deprotection of 1,3-oxathiolanes

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Abstract

Oxathioacetalyzation of carbonyl compounds with 2-mercaptoethanol and deprotection of the obtained 1,3-oxathiolanes is easily performed in the presence of silica sulfuric acid (SSA). All reactions were performed under mild and completely heterogeneous reaction conditions in good to high yields.

Keywords: Silica sulfuric acid; Oxathioacetalyzation; 1,3-Oxathiolane; Heterogeneous reaction conditions; Carbonyl compounds

Because of the reactivity of carbonyl group against different types of nucleophiles, introduction of efficient methods for the protection of this group in aldehydes and ketones, is a major challenging problem during a multi-step synthesis. Different methods are available for this purpose, which of them oxathioacetalization is attracted the considerable attention of many organic chemists. The main reasons for the attention to 1,3-oxathiolanes, are their considerable stability under a variety of reaction conditions, ease of formation and removal, equality to acyl carbanions in C–C bond forming reactions [1], and use in enantioselective synthesis of tertiary α-hydroxy acids and glycols [2]. Generally 1,3-oxathiolanes are obtained from carbonyl compounds and 2-mercaptoethanol using catalysts such as HCl [3], *p*-TsOH [4], $BF_3{\cdot}Et_2O$ [5], $ZrCl_4$ [6], TMSOTf [7], Amberlyst®-15 [8], I_2 [9], $Y(OTf)_3$ [10], $Fe(CF_3CO_2)_3$ and $Fe(CF_3SO_3)_3$ [11], novel catalyst [12], $HClO_4$ [13], PPS/SiO_2 [14], $H_3PW_{12}O_{40}/SiO_2$ [15], $MoO_2(acac)_2$ [16], $TaCl_5/SiO_2$ [17], $Sn(HPO_4)_2{\cdot}H_2O$ [18], [bmim]BF_4 [19], $Pr(OTf)_3$ [20] and Me_2S/Br_2 [21]. However, most of the reported methods suffer from one or more of the following disadvantages: long reaction times, low yields, harsh reaction conditions, use of halogenated solvents, use of expensive and moisture sensitive catalyst and tedious work-up procedure. Thus, the development of new, mild and efficient methodology involving a reusable catalyst for this important transformation is desirable.

1. Experimental

All of the products were characterized by comparison of their spectral and physical data with those of authentic samples. Yields refer to isolated products. The purity determination of the substrate and reaction monitoring were accompanied by TLC on silica-gel polygram SILG/UV 254 plates.

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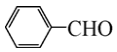
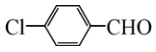
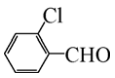
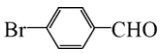
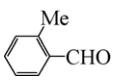
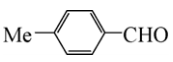
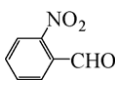
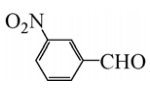
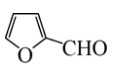
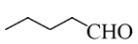
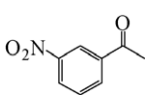
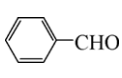
Table 1
Oxathioacetalyzation of carbonyl compounds and deprotection of 1,3-oxathiolanes[a].

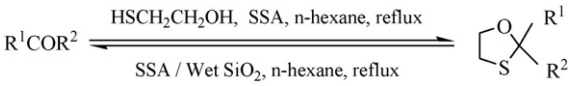
Entry	Substrate	Oxathioacetalyzation		Deprotection of 1,3-oxathiolanes	
		Time (min)	Yield (%)	Time (min)	Yield (%)
1		5	95	35	95
2		10	92	50	85
3		3	90	25	90
4		7	95	25	95
5		10	92	20	90
6		10	93	35	95
7		5	90	60	85
8		3	95	60	70
9		5	92	35	90
10		25	90	120	60
11		15	85	40	92
12		10	95	30	90
13		60	0[b]	–	–

[a] Products were characterized by their physical constants, comparison with authentic samples, and IR and NMR spectroscopy.
[b] Isolated yields.

Preparation of silica sulfuric acid [22]: A 500 mL suction flask was used. It was equipped with a constant-pressure dropping funnel containing chlorosulfonic acid (23.3 g) and gas inlet tube for conducting HCl gas over an adsorbing solution i.e. water. Into it were charged 60.0 g of silica gel. Chlorosulfonic acid was added dropwise over a period of 30 min at room temperature. HCl gas evolved from the reaction vessel immediately.

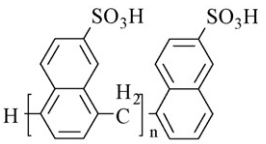
After the addition was complete the mixture was shaken for 30 min. A white solid (silica sulfuric acid) of 76.0 g was obtained.

General procedure for oxatioacetalyzation of carbonyl compounds: A mixture of the substrate (1 mmol), 2-mercaptoethanol (1 mmol, 157 mg) and SSA (10 mg) in n-hexane (3 mL) was stirred at reflux temperature. The



Scheme 1.

Table 2
Comparison of the efficiency of SSA in the oxathioacetalyzation of benzaldehyde, with other reported methods.

Entry	Reagent, catalyst load	Catalyst load (mg)	Time (min)	Yield (%)	Reference
1	$MoO_2(acac)_2$	22	240	86	[16]
2	PPA/SiO_2	500	30	99	[14]
3	$[bmim]BF_4$	2 mL	150	92	[19]
4	Amberlyst®-15	220	60	84	[8]
5	$Fe(CF_3CO_2)_3$	20	20	90	[11]
6	 (Novel catalyst)	60	25	96	[12]
7	$Sn(HPO_4)_2{\cdot}H_2O$	17	30	96	[18]
8	SSA	10	5	95	Present method

progress of the reaction was monitored by TLC. After completion of the reaction, the solvent was evaporated under reduced pressure. CH_3CN (5 mL) was added and the catalyst was recovered by filtration and washed with CH_3CN. The solvent was evaporated from the filtrate, H_2O (5 mL) was added and the product was extracted with Et_2O (3× 5 mL). The organic layer was dried over $MgSO_4$. Evaporation of the solvent followed by column chromatography on neutral silica gel gave the corresponding 1,3-oxathiolanes in excellent yields. Representative data are presented from Table 1:

Entry 1: IR ($CHCl_3$, cm^{-1}): 1065, 680; ^1H NMR ($CDCl_3$, δ ppm): 3.0–3.25 (m, 2H), 3.78–3.91 (m, 1H), 4.25–4.58 (m, 1H), 6.04 (s, 1H), 7.30–7.42 (m, 3H), 7.45–7.50 (m, 2H).
Entry 9: IR ($CHCl_3$, cm^{-1}): 3055, 2964, 1687, 1578, 1505, 1456, 1280, 1128, 1018, 775, 674; ^1H NMR ($CDCl_3$, δ ppm): 3.05–3.12 (m, 2H). 4.10 (m, 1H), 4.21 (m, 1H), 6.02 (s, 1H), 6.25 (dd, 1H), 6.40 (d, 1H), 7.40 (d, 1H).

General procedure for deprotection of 1,3-oxathiolanes: A mixture of the substrate (1 mmol), SSA (0.25 g) and wet SiO_2 [(SiO_2/H_2O: 50% w/w), 0.3 g] in n-hexane (5 mL) was stirred at reflux temperature of the time indicated in Table 1. After completion, the reaction (monitored by TLC), the solvent was evaporated under reduced pressure, CH_3CN (5 mL) was added and the mixture was filtered. The solvent was evaporated from the filtrate, H_2O (5 mL) was added and the product was extracted with Et_2O (3× 5 mL). The organic layer was dried over $MgSO_4$. Evaporation of the solvent followed by column chromatography on neutral silica gel gave the corresponding 1,3-oxathiolanes in excellent yields.

2. Results and discussion

Recently, silica sulfuric acid has been prepared and used as an efficient catalyst in many important organic reactions [22–25]. In continuation of our ongoing research program on the development of the applications of this reagent in organic chemistry [23,26], herein, we wish to report the applicability of SSA in the promotion of the oxathioacetalization of aldehydes and ketones with 2-mercaptoethanol. All reactions were performed in n-hexane at reflux temperature and under completely heterogeneous reaction conditions in excellent yields (Scheme 1, Table 1).

As shown in Table 1, different types of aldehydes and ketones are efficiently converted to their corresponding 1,3-oxathiolanes under the selected conditions. It is important to point out that the progress of the reaction is so depends to

the presence of SSA in the reaction mixture, that the reaction did not proceed in the absence of this reagent even after prolonged heating (Table 1, entry 13).

We have found that SSA is a reusable catalyst and even after three runs for the oxathioacetalization of aldehydes and ketones with 2-mercaptoethanol, the catalytic activity of SSA was almost the same as that of the freshly used catalyst.

Our investigations clarified that deprotection of 1,3-oxathiolanes can also be performed using SSA in the presence of wet SiO_2. The reaction is fast and the corresponding carbonyl compounds are separated in high yields (Table 1).

In order to show the efficiency of the present method, Table 2 compares the results obtained from the oxathioacetalyzation of benzaldehyde in the presence of SSA and some of the other catalysts.

Mildness of the reaction conditions, availability and reusability of the reagent, high efficiency, short reaction times, reasonable yields of products, simple and clean work-up and heterogeneous reaction conditions are among the outstanding advantages of this new method. We believe that the present method could be an important addition to the existing methodologies.

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