

# Tungstophosphoric acid supported on silica gel ( $\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{SiO}_2$ ) as an eco-friendly, reusable and heterogeneous catalyst for chemoselective oxathioacetalization of carbonyl compounds in solution or under solvent-free conditions

Habib Firouzabadi\*, Nasser Iranpoor\*, Abbas Ali Jafari, Mohammad Reza Jafari

Department of Chemistry, College of Sciences, Shiraz University, Shiraz 71454, Iran

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## Abstract

Solid heteropoly acid supported on silica gel ( $\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{SiO}_2$ ) is easily used as a heterogenous, reusable and efficient catalyst for conversion of aromatic and aliphatic aldehydes and ketones to their corresponding 1,3-oxathiolanes at room temperature in solution or under solvent-free conditions. The catalyst can be easily recovered and reused for several times without loss of its activity.

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**Keywords:** Protection;  $\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{SiO}_2$ ; 1,3-Oxathiolanes; Solvent-free; Aldehyde

## 1. Introduction

The protection of carbonyl group is a very important sequence in multi-step syntheses of man-made complex organic molecules or natural products [1–3]. The electrophilic properties of carbonyl group in aldehydes and ketones can be a good choice to be aimed by a nucleophilic attack at the site. One of the most popular method is to convert carbonyl groups to their *S/S*-acetals [2]. *S/S*-acetals are quite stable in different acidic conditions and their removal as protecting groups is not a straightforward task that needs harsh reaction conditions. For this purpose, using toxic heavy metals such as  $\text{Hg}^{2+}$  is one of the most popular procedure. *S/S*-acetals derived from aldehydes are good precursors for the formation of C–C bond under basic conditions. In contrast, *O/O*-acetals are very sensitive towards acids and their manipulation in acidic media requires strict precautions. In addition, *O/O*-acetals derived from aldehydes are not suitable precursors for C–C bond formation.

Conversion of carbonyl groups to their *O/S*-acetals is very important from different aspects. They can be used as either acyl anion equivalents for C–C bond formation [1,2] or carbonyl protecting group [2]. Moreover, their considerable stability in acidic conditions rather than *O/O*-acetals and their ease of removal in comparison with *S–S* acetals, make them good choices to be used as protecting tools in organic synthesis. Eliel et al. [3], however, have established the use of 1,3-oxathiolanes as chiral starting materials for enantioselective synthesis of tertiary  $\alpha$ -hydroxy aldehydes,  $\alpha$ -hydroxy acids and glycols. Many of the reagents and catalysts used for the preparation of *S/S*-acetals from carbonyl compounds do not work successfully for the preparation of *O/S*-acetals [2]. Among the available methods applied for the preparation of *O/S*-acetals [4,5], sometimes harsh reaction conditions, long reaction times [4a,b], low yields of the products and using stoichiometric or expensive reagents [4b–d], limit their uses for this purpose. In addition, some of the reagents or catalysts, are not eco-friendly and are not recoverable or reusable materials. Furthermore, lanthanide triflates [6] applied for this purpose shows attractions. However, they are rather expensive, thus their uses especially for the large-scale synthetic operations, may not be recommended from economical point of view. For these reasons, cheaper commercially available catalysts that secure catalytic activity, low toxicity, high stability

\* Corresponding authors. Fax: +98 711 2280926.

E-mail addresses: [firouzabadi@chem.susc.ac.ir](mailto:firouzabadi@chem.susc.ac.ir) (H. Firouzabadi), [iranpoor@chem.susc.ac.ir](mailto:iranpoor@chem.susc.ac.ir) (N. Iranpoor).

towards humidity, and air tolerance are of high demands from academic and industrial chemists.

In recent decades, uses of heteropoly acids (HPAs) as catalysts for fine organic synthetic processes have been developed and are important for industries related with fine chemicals [7], including flavors, pharmaceuticals and food industries [8]. Heteropoly acids are more active catalysts than conventional inorganic and organic acids for various reactions in solutions [9]. They are used as industrial catalysts for several liquid-phase reactions [10–13]. Among heteropoly acids, polytungstic acids are the most widely used catalysts owing to their high acid strengths, thermal stabilities, and low reducibilities. Catalysts based on heteropoly acids as Bronsted acids have many advantages over liquid acid catalysts. They are non-corrosive and environmentally benign, presenting fewer disposal problems. Solid heteropoly acids have attracted much attention in organic synthesis owing to easy work-up procedures, easy filtration, and minimization of cost and waste generation due to reuse and recycling of the catalysts [14]. Supported heteropoly acid on silica gel has been used as effective catalyst for Diels Alder [15a] and Fries rearrangement [15b], Friedel Crafts reactions [15c,d].

In the last few years, we have paid attention to explore new catalytic activities of  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  [16], and its salts [17], for basic chemical transformations. Along this line of our interest, we have also successfully applied  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  as an effective catalyst for protection of carbonyl groups as their *S/S*-acetals [16b].

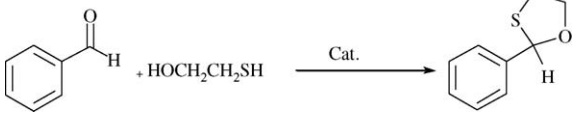
In this article we report that  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  supported on silica gel could be used as a highly efficient catalyst for protection of carbonyl compounds as their important 1,3-oxathiolanes in solution or under solvent-free conditions.

## 2. Result and discussion

At first, for optimization of the reaction conditions, the reaction of benzaldehyde (1 mmol) with 2-mercaptoethanol (1.2 mmol) in  $\text{CH}_2\text{Cl}_2$  or EtOAc at room temperature in the presence of a catalytic amount of  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  (3 mol%) was studied. The analysis of the reaction mixture showed that the desired product; 2-phenyl-1,3-oxathiolane was produced in only 50% after 1 h plus unreacted starting materials (Table 1, entries 2 and 3). We have also observed that even the elongation of the reaction time to 24 h did not affect the yield of the product. Then, we decided to study the catalytic ability of supported  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  on silica gel. We observed that the reaction of benzaldehyde (1 mmol) with 2-mercaptoethanol (1.2 mmol) in  $\text{CH}_2\text{Cl}_2$  in the presence of the supported catalyst (0.2 g, 3 mol%) was performed smoothly and the desired product; 2-phenyl-1,3-oxathiolane was obtained in 90% yield after 20 min. We have also studied the similar reaction in the presence of silica gel. The reaction did not proceed at all and the starting materials were remained intact after 24 h (Table 1). These results show the strong synergistic effect of silica gel upon the catalytic activity of  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  in the reaction of benzaldehyde with 2-mercaptoethanol (Table 1). In addition, due to the current challenges for developing solvent-free and environmentally benign

Table 1

Protection of benzaldehyde with 2-mercaptoethanol at different conditions



Entry	Catalysis	Solvent	Time (min)	Yield (%)
1	$\text{SiO}_2$ (0.2 g)	$\text{CH}_2\text{Cl}_2$	120	N.R.
2	$\text{H}_3\text{PW}_{12}\text{O}_{40}$ (0.1 g, 3 mol%)	$\text{CH}_2\text{Cl}_2$	60	50
3	$\text{H}_3\text{PW}_{12}\text{O}_{40}$ (0.1 g, 3 mol%)	EtOAc	60	40
4	$\text{AlPW}_{12}\text{O}_{40}$ (0.1 g, 3 mol%)	$\text{CH}_2\text{Cl}_2$	60	55
5	$\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{SiO}_2$ (0.2 g, 3 mol%)	$\text{CNCH}_3\text{CN}$	20	85
6	$\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{SiO}_2$ (0.2 g, 3 mol%)	$\text{CH}_2\text{Cl}_2$	20	90
7	$\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{SiO}_2$ (0.06 g, 1 mol%)	Solvent-free	15	90

1 mmol of benzaldehyde with 2-mercaptoethanol (1.2 mmol) was used.  $\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{SiO}_2$  (50% W/W).

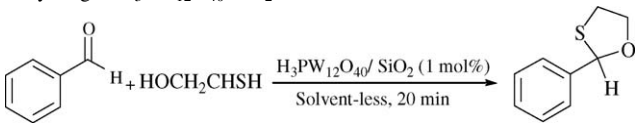
protocols [17], we have studied the reaction of benzaldehyde (1 mmol) with 2-mercaptoethanol (1.2 mmol) under solvent-free conditions in the presence of this catalyst. We have found that solvent-free condition was more suitable and efficient in which a lesser amount of  $\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{SiO}_2$  (0.06 g, 1 mol%) was sufficient to complete the reaction within 15 min. The results of this study are tabulated in Table 1.

We have noticed that after the addition of  $\text{CH}_2\text{Cl}_2$  to the reaction mixture, the catalyst ( $\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{SiO}_2$ ) can be easily recovered quantitatively by simple filtration. The recovered catalyst has been charged to the reaction mixture for 5 runs without any observable loss of its catalytic activity (Table 2).

In order to show the general applicability of the protocol, we have applied this catalytic system for the preparation of structurally diverse 1,3-oxathiolanes from different carbonyl compounds in  $\text{CH}_2\text{Cl}_2$  and also in the absence of solvent. However, various types of aromatic and aliphatic carbonyl compounds were reacted with 2-mercaptoethanol in the presence of  $\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{SiO}_2$  in  $\text{CH}_2\text{Cl}_2$  or in the absence of solvent (Table 3). Activated aromatic aldehydes were efficiently and rapidly converted to their corresponding 1,3-oxathiolanes in excellent yields (Table 3, entries 1–9). Reaction of 4-nitrobenzaldehyde with 2-mercaptoethanol (Table 3, entry 5) in solution or in the absence of solvent is of interest which shows

Table 2

Recycling of  $\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{SiO}_2$



Run	Yield (%)
1	95
2	94
3	93
4	92
5	94

Table 3  
 Protection of carbonyl compounds with 2-mercaptoethanol (1.2 mmol) to produce corresponding 1,3-oxathiolane catalyzed by  $\text{H}_3\text{PW}_{12}\text{O}_{40}/\text{SiO}_2^a$

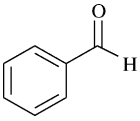
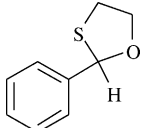
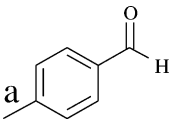
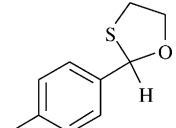
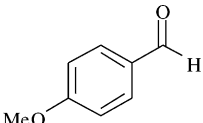
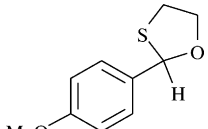
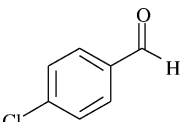
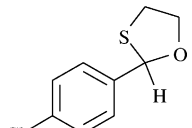
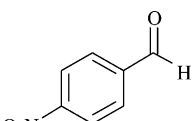
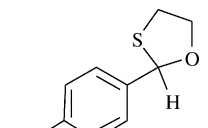
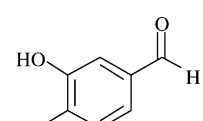
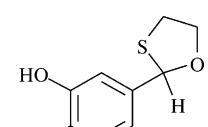
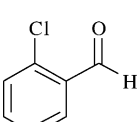
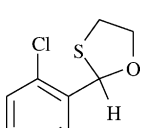
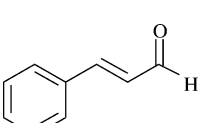
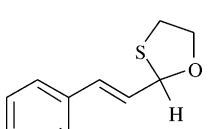
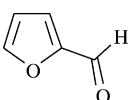
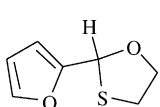
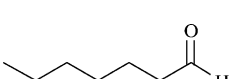
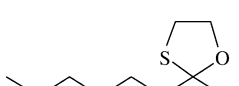
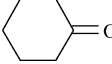
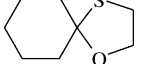
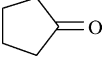
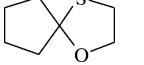
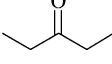
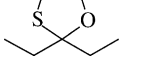
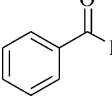
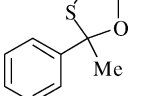
Entry	Substrate	Product	In solution (3 mol% of catalysis)		Solvent-free (1 mol% of catalysis)	
			Time (min)	Yield (%)	Time (min)	Yield (%)
1			20	95	15	95
2			20	93	15	97
3			30	90	20	92
4			90	85	30	89
5			10h	40	40	90
6			20	75	20	91
7			20	93	15	93
8			20	80	15	94
9			20	90	15	91
10			30	95	15	94

Table 3 (Continued)

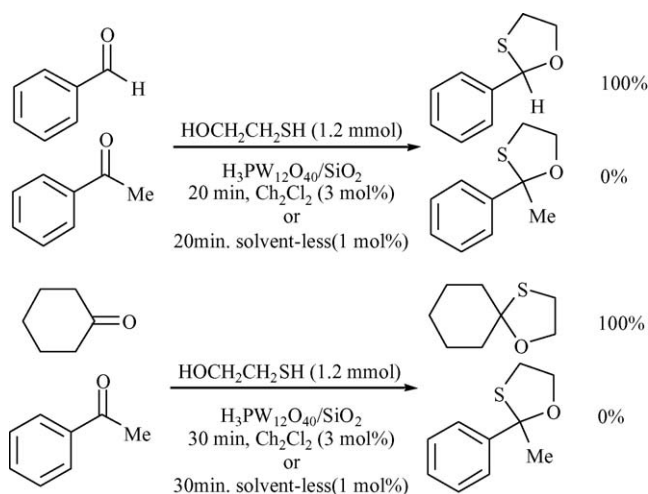
Entry	Substrate	Product	In solution (3 mol% of catalysis)		Solvent-free (1 mol% of catalysis)	
			Time (min)	Yield (%)	Time (min)	Yield (%)
11			20	94	15	96
12			20	75	15	93
13			30	85	20	89
14			24 h	55 <sup>b</sup>	24	50 <sup>b</sup>

<sup>a</sup> All products were characterized by NMR, IR and mass spectroscopy.

<sup>b</sup> 2 mmol of 2-mercaptoethanol, and 0.4 g of H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>/SiO<sub>2</sub> (6 mol%) were used.

the advantage of the solvent-less condition. This reaction in solution proceeded very slowly (10 h) in a low yield (40%) whereas, in the absence of solvent, the reaction proceeded within 40 min in 90% yield. Aliphatic aldehydes and ketones were also reacted rapidly to produce the corresponding 1,3-oxathiolanes in good to high yields (Table 3, entries 10–13). Acetophenone as an aryl ketone, reacted rather slowly with 2-mercaptoethanol in the presence of this catalyst (Table 3, entry 14).

Selectivity of the catalyst in solution and in the absence of solvent has been also studied. For this purpose, a mixture of equimolar amounts of benzaldehyde and acetophenone were reacted with 2-mercaptoethanol. The results show that this reaction proceeded with absolute chemoselectivity. This absolute chemoselectivity has been also observed by the reaction of 2-mercaptoethanol with acetophenone and cyclohexanone in solution or in the absence of solvent (Scheme 1).



Scheme 1. Chemoselective reactions of carbonyl groups with 2-mercaptoethanol.

In order to show the merit of the presented protocol, we have compared some of the results obtained by the other catalysts such as ZrCl<sub>4</sub>, Sc(OTf)<sub>3</sub>, Yb(OTf)<sub>3</sub>, PPA/SiO<sub>2</sub>, Montmorillonite K 10, HClO<sub>4</sub>, which have been reported recently for the reaction of benzaldehyde with 2-mercaptoethanol in Table 4.

In summary H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>/SiO<sub>2</sub> has been employed as an effective catalyst for the preparation of structurally diverse *O/S*-acetals in high yields in solution or under solvent-free conditions. The catalyst is recyclable and has been used in several runs without losing its catalytic activities. Absolute chemoselectivity, easy recycling, and reusability are worth of mentioning for the presented protocol.

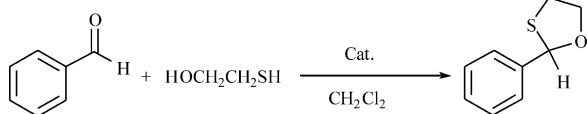
### 3. Experimental

All solvents and reagents were purchased from Fluka or Merck chemical Companies. The products were purified by column or thick layer chromatography techniques. FT-IR spectra were recorded on a Shimadzu DR-8001 spectrometer. NMR spectra were recorded on a Bruker Avance DPX 250 MHz instrument. Mass spectra were recorded on a Shimadzu GC-MS-QP 1000PX. Melting points are not corrected.

#### 3.1. Typical procedure oxathioacetalization of benzaldehyde

To a mixture of benzaldehyde (2 mmol, 0.21 g) and 2-mercaptoethanol (6 mmol, 0.16 g) was added H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>/SiO<sub>2</sub> (0.12 g, 1 mol%), and the resulting mixture was shaken at room temperature for 15 min. Completion of the reaction was monitored by GC. After completion of the reaction, CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added to the reaction mixture and the precipitated catalyst was filtered off. The resulting organic solution was washed with H<sub>2</sub>O, and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed in vacuo to produce pure 2-phenyl-1,3-oxathiolane.

Table 4  
Comparison of the effect of catalysts in oxathioacetalization of benzaldehyde



Entry	Catalysis	Solvent	Time (min)	Yield (%)	Reference
1	H <sub>3</sub> PW <sub>12</sub> O <sub>40</sub> /SiO <sub>2</sub> (0.2 g, 3 mol%)	CH <sub>2</sub> Cl <sub>2</sub>	20	95	–
2	H <sub>3</sub> PW <sub>12</sub> O <sub>40</sub> /SiO <sub>2</sub> (0.06 g, 1 mol%)	Solvent-free	15	95	–
3	ZrCl <sub>4</sub> (4 mol%)	CH <sub>2</sub> Cl <sub>2</sub>	30	91	5f
4	Sc(OTf) <sub>3</sub> (1 mol%)	CH <sub>2</sub> Cl <sub>2</sub>	10	90	6b
5	Yb(OTf) <sub>3</sub> (1 mol%)	[bmim][PF <sub>6</sub> ]	60	95	5c
6	PPA/SiO <sub>2</sub> (0.5 g)	CH <sub>2</sub> Cl <sub>2</sub>	30	99	5c
7	Montmorillonite K 10 (0.2 g)	CH <sub>2</sub> Cl <sub>2</sub>	30	86	5d
8	HClO <sub>4</sub> (10 mol%)	CH <sub>2</sub> Cl <sub>2</sub>	20	68	5e

in 95% yield (0.80 g). No further purification was required (GC).

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