

# Preyssler-type heteropoly acid: A new, mild and efficient catalyst for protection of carbonyl compounds

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## Abstract

Preyssler-type heteropoly acid is introduced as a new, mild and efficient catalyst for protection of a variety of carbonyl compounds with 1,3-propane dithiol.

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The protection of carbonyl compounds as dithioacetals is an important sequence in multi-step preparation of many important organic compounds including multifunctional complex molecules [1,2]. Moreover, the electrophilic properties of carbonyl group in aldehydes and ketones can be a good choice to be attacked by a nucleophile at the site. Thus, one of the most popular methods for protection of carbonyl groups is to convert them into their corresponding dithioacetals [3].

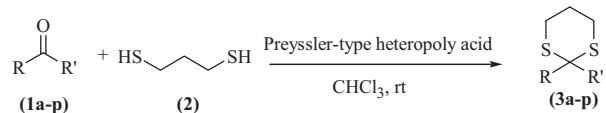
There are many methods in the literature for the protection of carbonyl compounds as dithioacetals using various catalysts or stoichiometric reagents [3]. However, most of these procedures have some restrictions such as low yields of the products, long reaction times, harsh reaction conditions, difficulties in work-up and the requirement for an inert atmosphere. Therefore, the search for alternative methods that can overcome these drawbacks is desirable.

In the past three decades, the broad utility of heteropoly acids (HPAs) as solid acids and multi-electron oxidation catalysts in solution as well as in the solid state for a wide variety of synthetic and industrial organic useful transformations like alcohol dehydration, alkylation, and esterification has been demonstrated [4–10].

On the other hand, precise control of the acidity in a small-scale reaction with usual corrosive any strong acid is extremely difficult. Considering the reversible nature of some processes in organic syntheses, low yield in reaction with previous usual strong liquid acid is expected. So Preyssler-type heteropoly acid ( $H_{14}NaP_5W_{30}O_{110}$ ) has been introduced as an efficient alternative. The advantages of Preyssler acid as a solid acid catalyst may include large number of balanced protons, strong acidity, high hydrothermal stability, and wide pH range stability in solution [10,11]. A few of researchers have investigated the catalytic performances of Preyssler-type heteropoly acid in a number of organic synthesis processes [12–15].

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Scheme 1.

Within our ongoing research program to develop new synthetic methodologies [16–20], we proposed that Preyssler-type heteropoly acid might be a useful catalyst for thioacetalization of carbonyl compounds. In this paper, we wish to report a simple and easy method for chemoselective thioacetalization of various aromatic and aliphatic aldehydes and ketones using Preyssler-type heteropoly acid as a new and efficient catalyst, depicted in Scheme 1.

The Preyssler-type heteropoly acid was prepared and characterized according to the previously published method [21] and then the reaction of 1,3-propanedithiol (2) with benzaldehyde (**1a**) as a model reaction was performed in different solvents and different catalytic amount of Preyssler acid. On the basis of the reaction times and yields,  $\text{CHCl}_3$  and 0.1 mol% of the catalyst was selected as the most suitable reaction conditions.

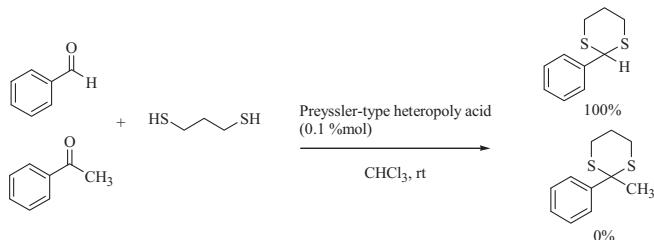
Various aldehydes and ketones (**1a–1p**) used as substrates to react with 1,3-propanedithiol (2). The results in Table 1 clearly demonstrate that protecting of carbonyl compounds using 1,3-propanedithiol as protection reagent in

**Table 1**  
Protection of different aldehydes and ketones as their corresponding 1,3-dithianes by reaction with 1,3-propanedithiol.<sup>a</sup>

Entry	Substrate	Time (min)	Product	Yield <sup>b</sup> (%)	Entry	Substrate	Time (min)	Product	Yield <sup>b</sup> (%)
<b>1a</b>		5		96	<b>1i</b>		5		90
<b>1b</b>		10		92	<b>1j</b>		15		87
<b>1c</b>		10		90	<b>1k</b>		15		80
<b>1d</b>		5		95	<b>1l</b>		25		92
<b>1e</b>		2		96	<b>1m</b>		40		83
<b>1f</b>		2		95	<b>1n</b>		45		87
<b>1g</b>		10		85	<b>1o</b>		30		90
<b>1h</b>		20		80	<b>1p</b>		20		90

<sup>a</sup> Reaction conditions as explained in the experimental procedure and the products are characterized from their spectral data.

<sup>b</sup> Isolated yields.



Scheme 2.

the presence of catalytic amounts of Preyssler-type heteropoly acid is efficient, with almost quantitative conversion and exclusive selectivity in most cases.

Aromatic aldehydes, with electron donating or electron withdrawing substituents such as 4-chlorobenzaldehyde (**1b**), 4-bromobenzaldehyde (**1c**), 4-methoxybenzaldehyde (**1e**), 4-hydroxybenzaldehyde (**1f**) and 4-nitrobenzaldehyde (**1h**) could be protected to afford the corresponding 1,3-dithianes with high conversions in the same conditions. This method is also applicable for aldehydes bearing double bond like cinnamaldehyde. It was converted to the corresponding protected product without any reaction on the double bond (entry **1i**).

The thioacetalization and thioketalization reactions were also examined over the Preyssler acid system. The linear chain aldehydes such as hexanal and octanal can also be converted to the corresponding thioacetals in relatively good yields (entries **1j** and **1k**). Cyclopentanone and cyclohexanone are also worked well, but the reactivity of cyclopentanone seems to be slightly lower than that of cyclohexanone (entries **1o** and **1p**). This method is also applicable for protecting of relatively unreactive and steric-hindered ketones such as benzophenone and diisopropylketone (entries **1m** and **1n**).

It is noteworthy that the method can also be extended for the chemoselective protection of an aldehyde in the presence of a ketone. For instance, when an equimolar mixture of benzaldehyde and acetophenone was allowed to react with 1,3-propanedithiol in the presence of a catalytic amount of Preyssler acid, only the corresponding aldehyde was protected (Scheme 2). This indicates that the presented protocol is potentially applicable for the chemoselective protection of aldehydes to the corresponding thioacetals in the presence of ketones in multi-functional compounds. In this condition, the aldehyde functionality of a keto-aldehyde compound was protected chemoselectively under identical condition.

These reactions which proceeded in CHCl<sub>3</sub> were performed heterogeneously and the isolation of the catalyst from the reaction mixture was easy and not a time consuming process. Thus, the reusability of the catalyst was checked. After each run, Preyssler acid was filtered and washed with CHCl<sub>3</sub> and dried at 70 °C for 1 h. This catalyst was reused for the protection reaction four times without significant loss of activity.

The comparison of Preyssler-type heteropoly acid with previous published catalysts for the dithioacetalization of a typical carbonyl compound like benzaldehyde with 1,3-propanedithiol was studied. As it is shown in Table 2, the Preyssler-type heteropoly acid is a good catalyst for the dithioacetalization of carbonyl compounds.

Table 2  
The comparison of some other catalyst with Preyssler acid.

Entry	Catalyst	mol% catalyst	Time (min)	Yield (%)	Literature
1	Y(OTf) <sub>3</sub>	5	45	89	[22]
2	NiCl <sub>2</sub> <sup>a</sup>	10	170	94	[23]
3	DBH <sup>b</sup>	10	35	90	[24]
4	MoO <sub>2</sub> (acac) <sub>2</sub> <sup>c</sup>	10	180	94	[25]
5	I <sub>2</sub> <sup>d</sup>	10	10	95	[26]
6	Preyssler acid <sup>e</sup>	0.1	5	96	—

<sup>a</sup> The reactions were conducted in a solution of CH<sub>2</sub>Cl<sub>2</sub>:MeOH (5:1) and also the ketones could not be protected.

<sup>b</sup> 1,3-Dibromo-5,5-dimethylhydantoin.

<sup>c</sup> The reactions were conducted under an atmosphere of argon.

<sup>d</sup> The reactions eventually were quenched with aqueous solutions of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and the catalyst could not be recovered.

<sup>e</sup> Reaction conditions as exemplified in the experimental procedure.

In conclusion, a very simple and benign method for the protection of various aldehydes and ketones as dithioacetals using a catalytic amount of Preyssler-type heteropoly acid has been demonstrated. Further, the catalyst can be readily recovered and reused, thus making this method profitable and environmentally acceptable. A high degree of chemoselectivity, easy work-up, low reaction times and high product yields are the main advantages of this new method, which will make it a useful and important addition to the present methodologies.

## 1. Experimental

### 1.1. General procedure for thioacetalization of aldehydes and ketones (**1a–1p**)

To a magnetically stirred solution of aldehyde or ketone (**1a–1p**) (2 mmol) and 1,3-propane dithiol (**2**) (2.1 mmol, 0.23 g) in CHCl<sub>3</sub> (10 mL), Preyssler acid (0.1 mol%) was added. The mixture was stirred at room temperature and the progress of the reaction was monitored by TLC using petroleum ether:EtOAc (7:3). After the completion of the reaction, Preyssler acid was filtered and the mother liquor was washed with 10% NaOH solution (10 mL) and water (10 mL) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, respectively. The solvent was removed under reduced pressure to obtain the corresponding product (**3a–3p**).

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