# Green, Reusable and Highly Efficient Solid Acid Catalyst for Oxidation of Thiols under Microwave Irradiation

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**Abstract:** $H_5[PV_2Mo_{10}O_{40}]$ catalyzed oxidation of thiols to related disulfides under microwave irradiation(MW). Hydrogen Peroxide as an oxidizing reagent under mild conditions carried out this reaction. This system provides an efficient convenient and practical method for the syntheses of symmetrical disulfides. In this work, the comparisons among the Keggin and Dawson type polyoxometalates are addressed in term of relative stability hardness and acidity.

**Key words:** Heteropolyacids · Thiols · Disulfides · Hydrogen Peroxide · Keggin type · Polyoxometalate · Dawson

## INTRODUCTION

The catalytic function of heteropolyacids (HPAs) and related polyoxometalate compounds have attracted much attention, particularly over the last two decades [1]. In this context, heteropoly acids (HPAs) are promising catalysts. A common and important class of these acids and those used in the majority of catalytic applications is the Keggin compounds, with the general formula $H_nXM_{12}O_{40}$ (X = P, Si, As, Ge, B; M = Mo, W) [2-9]. These solid acids are usually insoluble in non-polar solvents but highly soluble in polar ones. They can be used in bulk or supported forms in both homogeneous and heterogeneous systems. Furthermore, these HPAs have several advantages, including high flexibility in modification of the acid strength, ease of handling, environmental compatibility, non-toxicity and experimental simplicity [10-11]. Keggin type polyoxoanions have widely been studied as homogeneous and heterogeneous catalyst for the oxidation of organic compounds [12].

Further catalytically important subclasses of the Keggin compounds are the mixed-addenda vanadium (V) substituted HPAs with the general formula of $H_{3+n}PM_{12-n}V_nO_{40}$ (M = Mo and W; n = 1–6). These compounds exhibit high activity in acid- base type catalytic reactions; hence they are used in many catalytic areas as homogeneous and heterogeneous catalysts. The most well-known of these HPAs is the 10-molybdo-2-vanadophosphoric acid $H_5PV_2Mo_{10}O_{40}$.

Previously reported procedures for large ring disulfides synthesis from thiols produced poor to moderate yield. We wish to report a very efficient and simple method for oxidative coupling of thiols into the disulfides using Potassium permanganate as an oxidizing reagent catalyzed by the mixed-addenda vanadium (V) substituted HPAs under mild conditions. Disulfide plays an important role in biology and synthetic organic chemistry [13-14]. In order to control cellular redox potential in biological systems; thiols are oxidized to prevent oxidative damage [15]. Disulfide is used as a protecting group under oxidative conditions for thiol and can be regenerated by S-S bond cleavage. Disulfides have also found industrial applications as vulcanizing agent and is important synthetic intermediates in organic synthesis [16]. Thiol can also be over-oxidized to sulphoxide and sulphone, therefore controlled and selective studies were carried out for their oxidation. Various reagents and oxidants have been employed for conversion of thiols to disulfides [17]. Some of these methods suffer from obvious disadvantages such as long reaction times, limited availability of the oxidant, toxicity of reagents and difficult isolation of products. Consequently, the introduction of readily available, safe and stable reagents for the oxidation of thiols to disulfide is still a necessity. We wish to report a very efficient and simple method for oxidative of thiols into the corresponding disulfides using hydrogen

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peroxide as an oxidizing reagent catalyzed by the mixed-addenda vanadium (V) substituted HPAs under mild conditions.

**Experimental:** All reagents and solvents used in this work are available commercially and used as received, unless otherwise indicated. Previously reported methods were used to purify the thiols [16]. Preparation of $H_5[PMo_{10}V_2O_{40}]$ catalyst and other mixed-addenda heteropolyacids and salts were based on a literature procedure with following modifications [9]. The acids of $[NaP_5W_{30}O_{110}]^{14-}$, $[P_2W\ O\ ]^{6-}$ and $[P\ Mo\ O\ ]^{6-}$ were prepared according to published methods and were identified by infrared spectroscopy [8]. All chemicals were purchased from Merck and used without purification. A LG-804 microwave was used for all experiments. $^1$HNMR spectra were recorded on a FT – NMR Brucker 100 MHz Aspect 3000. IR spectra were recorded on a Buck 500 Scientific Spectrometer (KBr Pellets).

**Preparation of $H_5[PMo_{10}V_2O_{40}]$ [7]:** Sodium metavanadate (12.2 g, 100 mmol) was dissolved by boiling in 50 mL of water and then mixed with (3.55 g, 25 mmol) of $Na_2HPO_4$ in 50 mL of water. After the solution was cooled, (5 mL, 17 M, 85 mmol) of concentrated sulfuric acid was added and the solution developed a red color. An addition of (60.5 g, 250 mmol) of $Na_2MoO_4.2H_2O$ dissolved in 100 mL of water and then was added to the red solution with vigorous stirring, followed by slow addition of concentrated sulfuric acid (42 mL, 17 m, 714 mmol). The hot solution was allowed to cool to room temperature. The 10-molybdo-2-vanadophosphoric acid was then extracted with 500 mL of ethyl ether. Air was passed through the heteropoly etherate (bottom layer) to free it of ether. The solid remaining behind was dissolved in water, concentrated to first crystal formation, as already described and then allowed to crystallize further. The large red crystals that formed were filtered, washed with water and air-dried.

**Preparation of $H_4[PMO_{11}VO_{40}]$:** $Na_2HPO_4$ (3.55 g, 25 mmol) was dissolved in 50 mL of water and mixed with (3.05 g, 25 mmol) of sodium metavanadate that had been dissolved by boiling in 50 mL of water. The mixture was cooled and acidified to a red color with (2.5 mL, 17 M, 42.5 mmol) of concentrated sulfuric acid. To this mixture was added a solution of (66.5 g, 274.8 mmol) of $Na_2MoO_4.2H_2O$ dissolved in 100 mL of water. Finally, 42.5 mL of concentrated sulfuric acid was added slowly with

vigorous stirring of the solution. With this addition the dark red color changed to a lighter red. The heteropoly acid was then extracted with 200 mL of ethyl ether after the water solution was cooled. In this extraction, the heteropoly etherate was resent as a middle layer; the bottom layer (water) was yellow and probably contained vanadyl species. After separation, a stream of air was passed through the heteropoly etherate layer to free it of ether. The orange solid that remained was dissolved in 50 mL of water, concentrated to the first appearance of crystals in vacuum desiccators over concentrated sulfuric acid and then allowed to crystallize further. The orange crystals that formed were filtered, washed with water and air-dried.

## General Procedure for the Oxidation of Thiols to Disulfides

**Method(A):** Thiol, heteropoly compound and $H_2O_2$ are mixed thoroughly in a small beaker. The mixture was placed in microwave oven and irradiated for 3min. at 25-100% power (full power 1000 watts). The solvent was then removed and the resulting residue was then washed with $CH_2Cl_2$. A simple filtration followed by removal of the solvent from the filtrate give the product of acceptable purity. The products were characterized by comparison of their spectroscopic (IR, $^1$H-NMR, Mass) data and melting points with those of authentic samples. *(Microwave irradiation condition)*

**Method (B):** $H_5[PMo_{10}V\ O\ ]_0$ (0.5 g, 0.2 mmol) was dissolved in the mixture of 25 mL of ethanol and 5 mL of $H_2O$. The substrate thiol (4mmol) and 1.5 mL $H_2O_2$ were added to solution. The reaction mixture was stirred at 25°C until TLC indicated the reaction was complete. The solvent was then removed and the resulting residue was then washed with $CH_2Cl_2$. A simple filtration followed by removal of the solvent from the filtrate give the product of acceptable purity. The reactions were monitored by TLC. The products were isolated and identified by comparison of their physical and spectral data with authentic samples prepared according to a previous method (Table 3). *(Reflux condition)*.

$$2RSH \xrightarrow[H_2O_2, Solvent]{H_5Mo_{10}V_2O_{40}} RSSH$$
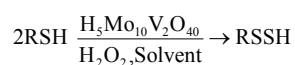
Scheme 1: General reaction for the oxidation of thiols catalyzed by $H_5[PMo_{10}V_2O_{40}]$ under microwave irradiation.

**Recycling of the Catalyst:** We investigated the reusability of the catalyst. At the end of the oxidation of thiols to disulfides, the catalyst was filtered, washed with dichloromethane, In order to know whether the catalyst would succumb to poisoning and lose its catalytic activity during the reaction, we investigated the reusability of the catalyst. For this purpose we first carried out the reaction in the presence of the catalyst. For this purpose after completion of the model reaction (Scheme 1), dichloromethane was added to the solid reaction mixture. All products are soluble in dichloromethane but the catalyst is not. So it could be separated by a simple filtration and washed with dichloromethane and dried at 90°C for 1 h and reused in another reaction with the same substrate. Even after five runs for the reaction, the catalytic activity of $H_5PV_2Mo_{10}O_{40}$ was almost the same as that freshly used catalyst. The results are summarized in table 1. IR spectra of the resulting solids indicate that the catalyst can be recovered without structural degradation.

## RESULTS AND DISCUSSION

**Effect of the Solvent:** 4-Chlorothiophenol was taken as a model compound and the reaction conditions were optimized by varying the solvent. The reaction was carried out in different solvents such as methanol, dichloromethane and ethanol (Table 2). In (EtOH + $H_2O$), the reaction was completed within 20 minutes. Other solvents provide moderate yields with longer reaction times, while in $H_2O$ there were a few yields even after 50 minutes.

**Effect of the Catalyst Structure:** Table 3 shows catalyst structure effect on oxidation of thiols by $H_2O_2$ under reflux condition. 4-Chlorothiophenol was taken as a model compound. Also, the amount of each catalyst is used the same. In the Keggin type polyoxometalates series $H_5[PMo_{10}V_2O_{40}]$ shows the highest catalytic activity. In general, the heteropoly salt type catalysts were less efficient than heteropolyacids. The keggin-type polyoxometalates lead to effective reaction in comparison with wells-Dawson type polyoxometalates.

Table1: Reuse of the catalyst for oxidation of 4- Chlorothiophenol (Table 4, Entry 4)

| Entry | Isolated yield (%) |
|---|---|
| 1 | 94 |
| 2 | 92 |
| 3 | 91 |
| 4 | 90 |
| 5 | 92 |

Table 2: Oxidation of thiols by $H_5[PMo_{10}V_2O_{40}]$ in different solvents under microwave irradiation

| Entry | Solvent | Time (min) | Power (Watt) | Yield (%) [a] |
|---|---|---|---|---|
| 1 | EtOH + $H_2O$ | 20 | 500 | 92 |
| 2 | EtOH + $H_2O$ | 20 | 1000 | 88 |
| 3 | EtOH + $H_2O$ | 20 | 300 | 61 |
| 4[b] | EtOH + $H_2O$ | 20 | 500 | 92 |
| 5[c] | EtOH + $H_2O$ | 20 | 500 | 92 |
| 6 | MeOH + $H_2O$ | 30 | 500 | 80 |
| 7 | MeOH + $H_2O$ | 30 | 1000 | 79 |
| 8 | EtOH | 30 | 500 | 63 |
| 9 | MeOH | 30 | 500 | 58 |
| 10 | $H_2O$ | 50 | 1000 | 25 |
| 11 | $CH_3NO_2$ | 50 | 500 | 38 |
| 12 | $CH_3CN$ | 50 | 500 | 34 |
| 13 | $CH_2Cl_2$ | 20 | 500 | 44 |
| 14 | DMF | 20 | 500 | 43 |

[a]Isolated yield on the basis of the weight of the pure product obtained.

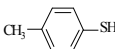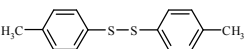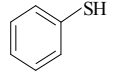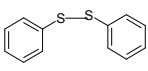[b]The reaction was carried out with the first recycled catalyst.
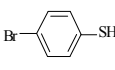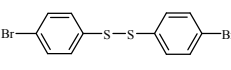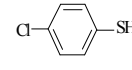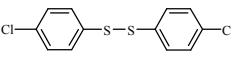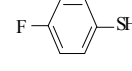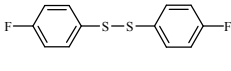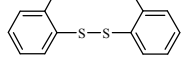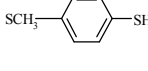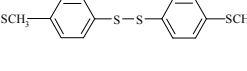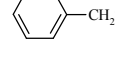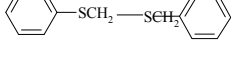
[c]The reaction was carried out with the second recycled catalyst.

Table 3: Oxidation of thiols by $H_2O_2$ was examined in the presence of a variety of heteropolyacids under reflux condition
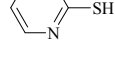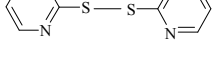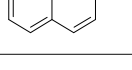
| Entry | Catalyst | Time( h ) | Temperature(°C) | Yield ( %)[a] |
|---|---|---|---|---|
| 1 | $H_5PMo_{10}V_2O_{40}$ | 2 | 25 | 97 |
| 2 | $H_4PMo_{11}VO_{40}$ | 2 | 25 | 95 |
| 3 | $H_6PMo_9V_3O_{40}$ | 2 | 25 | 96 |
| 4 | $H_3PMo_{12}O_{40}$ | 4 | 45 | 92 |
| 5 | $H_3PW_{12}O_{40}$ | 4 | 52 | 90 |
| 6 | $H_4SiW_{12}O_{40}$ | 4 | 50 | 89 |
| 7 | $H_{14}[NaP_5W_{30}O_{110}]$ | 5 | 70 | 75 |
| 8 | $Na_3PMo_{12}O_{40}$ | 5 | 80 | 68 |
| 9 | $Na_3PW_{12}O_{40}$ | 5 | 90 | 63 |
| 10 | $(NH_4)_3H[PMo_{11}VO_{40}]$ | 5 | 120 | 56 |
| 11 | $H_6P_2Mo_{18}O_{62}$ | 4 | 90 | 79 |
| 12 | $H_6P_2W_{18}O_{62}$ | 4 | 90 | 72 |
| 13 | None | 4 | 90 | 28 |

[a]Isolated product

Table 4: Oxidation of thiols with different substituents

| Entry | Thiol | Disulfide | Time (h) | Yield % | M.P(ºC) found | M.P(ºC) literature |
|---|---|---|---|---|---|---|
| 1 |  |  | 2 | 97 | 43-44 | 44-45 |
| 2 |  |  | 2 | 96 | 60-61 | 61 |
| 3 |  |  | 2 | 95 | 90-92 | 91-93 |
| 4 |  |  | 2 | 97 | 72-73 | 70-71 |
| 5 |  |  | 3 | 79 | liquid | -- |
| 6 |  |  | 3 | 89 | liquid | -- |
| 7 |  |  | 3 | 82 | 40-43 | 40-43 |
| 8 |  |  | 3 | 78 | 69-71 | 69-70 |
| 9 |  |  | 3 | 77 | 55-56 | 55-57 |
| 10 |  |  | 4 | 78 | 144-146 | 142-145 |

But $H_6[P_2Mo_{18}O_{62}]$ is more effective than $H_6[P_2W_{18}O_{62}]$ in oxidation of thiols. It may be difference in tungsten and molybdenum reduction potentials. However, the results indicate that the highest yield of disulfides is obtained when the oxidation of substrates is carried out with $H_5[PMo_{10}V_2O_{40}]$ as catalyst. This behavior is found to be quite general. The high activity of $H_5[PMo_{10}V_2O_{40}]$ in comparison of other HPAs (Table 3) confirms that in addition to $H^+$, the $V^{5+}$ ions probably play a catalytic role in the reaction.

**Effect of the Substituent:** The effects of various substituents on the yields of produced disulfides have been examined in the presence of $H_5[PMo_{10}V_2O_{40}]$ catalyst under reflux condition. As shown in table 4, not only the nature of the substituent is important, but so is its position. As examples of electron-withdrawing groups, bromo, chloro and nitro substituted thiophen were chosen and were converted to their corresponding disulfides. Methyl and hydroxy groups were chosen as electron-donating groups. Thiols with electron-donation substituents were oxidized easily respect to thiols with electron-drawing substituents. We think, in such cases this catalytic system in our conditions runs the selective oxidation of the SH-position of the thiols only to corresponding disulfides.

## CONCLUSION

The $H_5[PMo_{10}V_2O_{40}]$ heteropolyacid was the most successful heteropolyacids under microwave irradiation. Although it is difficult to offer an explanation for the different activity between these HPAs, certainly there is a complex relationship between the activity and structure of polyanion. By changing the constituent elements of polyanion (both hetero and addenda atoms), the acid strength of HPAs as well as its catalytic activity is able to vary in a wide range. For the first time, by an inexpensive solid acid catalyst and an easily prepared $H_5[PMo_{10}V_2O_{40}]$ oxidation of thiols with electron-withdrawing and electron-donating groups to the corresponding disulfides have been studied. The results show that the catalyst type, the nature and positions of substituents and temperature are important factors. The keggin-type polyoxometalates lead to effective reaction in comparison with Well-dawson type polyoxometalates.

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