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Heterocyclic amine salts of Keggin heteropolyacids used as catalyst for the selective oxidation of sulfides to sulfoxides

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Abstract

A range of sulfides can be selectively oxidized to the corresponding sulfoxides in good yields using catalytic quantities of heterocyclic amine salts (quinoline, cinchonine, and cinchonidine) of Keggin heteropolyacids with different green oxidants. The cinchonine heteropolyacid catalyst is easily recoverable and reusable without loss of its catalytic activity, and an enantiomeric excess can be obtained.

Heteropolyacid compounds (HPAs) with Keggin-structure are polynuclear complexes principally constituted by molybdenum or tungsten as polyatoms, and phosphorus and silicon as central atoms or heteroatoms. They operate either as multielectron oxidants or strong acids, with an acid strength higher than that of classical acids. The list of liquid-phase reactions in which HPAs may be used to replace the conventional inorganic and organic acids is extensive. They are used as industrial catalysts for several liquid-phase reactions.[1–5]

We have recently reported a range of heteropolyacids with Keggin-type structure for performing acidic catalysis and oxidation reactions such as the tetrahydropyranylation of phenols and alcohols,[6–8] chromone and flavone preparation,[9] ethyl β-arylaminocrotonates,[10] and the phenol,[11] sulfide,[12] alcohol, and amine oxidations.[13] The pyridinium salts of Keggin-type molybdovanadophosphates are appropriate catalysts to perform the selective oxidation of sulfides to sulfoxides with hydrogen peroxide.[14]

On the other hand, the selective oxidation of sulfides to sulfoxides is of interest because of the importance of sulfoxides as synthetic intermediates in organic synthesis. Sulfoxides are important in organic synthesis as an activating group, they have been utilized extensively in carbon bond-forming reactions,[15] as building blocks, especially as chiral auxiliaries,[16] and they play key roles in the activation of enzymes.[17]

There are several reagents available for these key transformation; they are conventionally achieved using stoichiometric amounts of both organic and inorganic reagents, for example, nitric acid, chromic acid, manganese dioxide, ozone, sodium periodate, selenium dioxide, hypervalent iodine reagents, sodium perborate,[18] halogens, tetrabutylammonium peroxydisulfate,[19] binuclear manganese complex-periodic acid,[20] *N*-hydroxyphalimide-molecular oxygen,[21] and $FeBr_3$–nitric acid.[22]

During the last years, very useful procedures involving catalysis and hydrogen peroxide as oxidant, for example, H_2WO_4, $H_3PW_{12}O_{40} + [(C_8H_{17})_4N]Br$, rhenium(V) oxo phosphine complexes, methyltrioxorhenium, $Sc(OTf)_3$, (salen) Mn(III), and Ti(IV) complexes, tellurium dioxide and TPPFe(III)Cl-imidazole have been used.[21] They have been developed to promote the oxidation of organic substrates due to their effective oxygen content, low cost, and safety in storage and operation.[23,24] Other green oxidants such as urea–hydrogen peroxide complex,[25] sodium percarbonate,[26] and *tert*-butyl-hydroperoxide[23] have been

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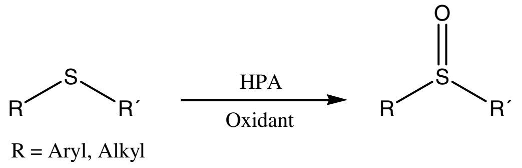


Scheme 1.

used for sulfide oxidation. More recent methods include gold(III)–hydrogen peroxide,[27] silica-immobilized vanadyl alkyl phosphonate–sodium bromate,[28] and silica sulfuric acid–hydrogen peroxide.[29]

In this Letter, we describe a procedure for the selective oxidation of sulfides to sulfoxides (Scheme 1) using Keggin-type structure catalysts, synthesized in our lab, by partial proton substitution of $H_3PMo_{12}O_{40}$ (PM_{12}) on different amines such as quinoline $QuiH_3PMo_{12}O_{40}$ ($PM_{12}Qui$), cinchonidine $CidH_3PMo_{12}O_{40}$ ($PM_{12}Cid$), and cinchonine $CinH_3PMo_{12}O_{40}$ ($PM_{12}Cin$). They were characterized by FT-IR, DRS, XRD, SBET, and in liquid phase by ^{13}C NMR.

We initially screened the oxidation of the methyl *p*-tolyl sulfide using different HPAs, oxidants, solvents, and reaction conditions (Table 1).

The reaction yields very low conversions in the absence of a catalyst (10% for 20 h), at 20 °C using a stoichiometric amount of 35% p/v hydrogen peroxide and acetonitrile as solvent of the reaction (Table 1, entry 1) but when an HPA is added, the times are reduced considerably and the conversion increases to values close to 100%. When commercial HPA such as $H_3PMo_{12}O_{40}$ is used (Table 1, entry 2), a conversion of 100% is observed at 3.5 h of reaction, with 99% selectivity to sulfoxide. The hydrogen peroxide concentration effect on the selectivity of reaction was studied. As can be observed, on increasing the hydrogen peroxide/sulfide molar ratio, the selectivity to sulfone increases (Table 1, entry 3), and on increasing the temperature, the conversion rate increases and a higher selectivity to sulfone results. For example, at 50 °C and for 3 h, a 99% selectivity to sulfone is achieved (Table 1, entry 4).

The catalytic activity of some amine salts of Keggin-type heteropolyacids in the selective oxidation of sulfides to sulfoxides with hydrogen peroxide is reported in Table 1, entries 5–7. When $PM_{12}Cin$ was used, the catalytic activity decreased, but these catalysts have the advantage on being insoluble in the mixture reaction. When $PM_{12}Cin$ is used as catalyst, a conversion of 100% is observed at 15 h of reaction, with 95% selectivity to sulfoxide (Table 1, entry 7).

The replacement of acetonitrile by a green solvent such as ethanol increases the catalytic activity of $PM_{12}Cin$. A conversion of 100% is observed at 8 h, with 90% selectivity to sulfoxide (Table 1, entry 8). Water is also a good solvent to perform this reaction, conversion of 100% and selectivity of 95% was obtained in 3 h (Table 1, entry 11).

Other oxidants such as urea–hydrogen peroxide 1:1 complex, sodium percarbonate and *t*-butyl-hydroperoxide were used (Table 1, entries 9–14). Table 1, entry 9 shows that the urea–hydrogen peroxide was the most active oxidant. A conversion of 100% is observed at 20 °C and for 2 h with a 100% of the selectivity in the sulfoxide. On increasing the reaction temperature, the conversion rate increases and a higher selectivity to sulfone results. For example, at 50 °C and for 3 h, a 100% selectivity to sulfone is achieved (Table 1, entry 11).

The cinchonine and cinchonidine catalysts represent an alternative for the enantioselective oxidation of sulfides to sulfoxides. For example, entry 9 in Table 1, the sulfoxide was obtained with a ratio of *R*:*S* 70:30, estimated by polarimetry.

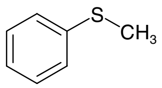
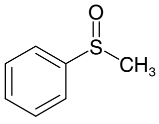
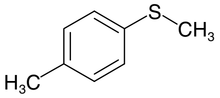
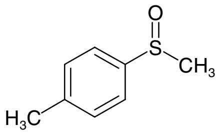
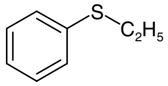
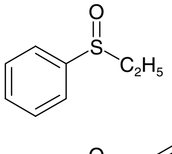
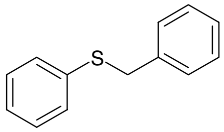
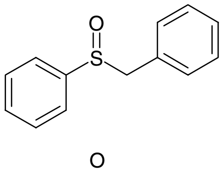
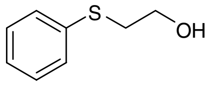
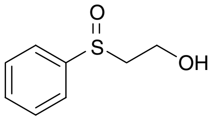
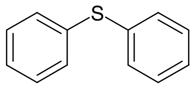
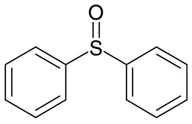
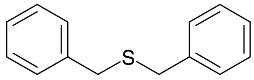
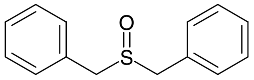
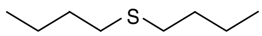
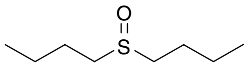
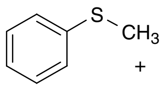
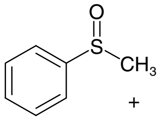
Once the reaction conditions for the selective oxidation of sulfides to sulfoxides and sulfones had been optimized, the reaction was extended to other starting substrates. Table 2 shows the results for the selective oxidation of different sulfides to sulfoxides.[30] All the reactions were run within a very short time and the sulfoxides were obtained in excellent yields, as practically the only oxidation product. For

Table 1
Selective oxidation of methyl *p*-tolyl sulfide to sulfoxide employing different HPAs as catalyst

Entry	Catalyst	Solvent	Oxidant (mmol)	Time (h)	Temp (°C)	Convn.[a] (%)	$SO:SO_2$[a] (%)
1	None	CH_3CN	H_2O_2 (2)	20	20	10	100:0
2	PM_{12}	CH_3CN	H_2O_2 (2)	3.5	20	100	99:1
3	PM_{12}	CH_3CN	H_2O_2 (20)	15	20	100	2:98
4	PM_{12}	CH_3CN	H_2O_2 (2)	3	50	100	1:99
5	$PM_{12}Qui$	CH_3CN	H_2O_2 (2)	3	20	100	95:5
6	$PM_{12}Cid$	CH_3CN	H_2O_2 (2)	15	20	100	93:7
7	$PM_{12}Cin$	CH_3CN	H_2O_2 (2)	15	20	100	95:5
8	$PM_{12}Cin$	CH_3CH_2OH	H_2O_2 (2)	8	20	100	90:10
9	$PM_{12}Cin$	CH_3CH_2OH	1:1 H_2O_2/urea (2)	2	20	100	100:0
10	$PM_{12}Cin$	CH_3CH_2OH/H_2O 4:1	1:1 H_2O_2/urea (2)	2.5	20	100	100:0
11	$PM_{12}Cin$	H_2O[c]	1:1 H_2O_2/urea (2)	3	20	100	95:5
12	$PM_{12}Cin$	CH_3CH_2OH	1:1 H_2O_2/urea (20)	3	50	100[b]	0:100
13	$PM_{12}Cin$	CH_3CH_2OH	$Na_2CO_3{\cdot}1.5H_2O_2$ (2)	7	20	100	100:0
14	$PM_{12}Cin$	CH_3CH_2OH	*t*-Butyl-hydroperoxide (2)	21	20	100	100:2

[a] Determined by GC analysis.
[b] Ratio *R*:*S* 70:30. Estimated by polarimetry.
[c] Methyl *p*-tolyl sulfide is insoluble in water.

Table 2
Oxidation of sulfides to sulfoxides with 1:1 H_2O_2–urea catalyzed by $PM_{12}Cin$[a]

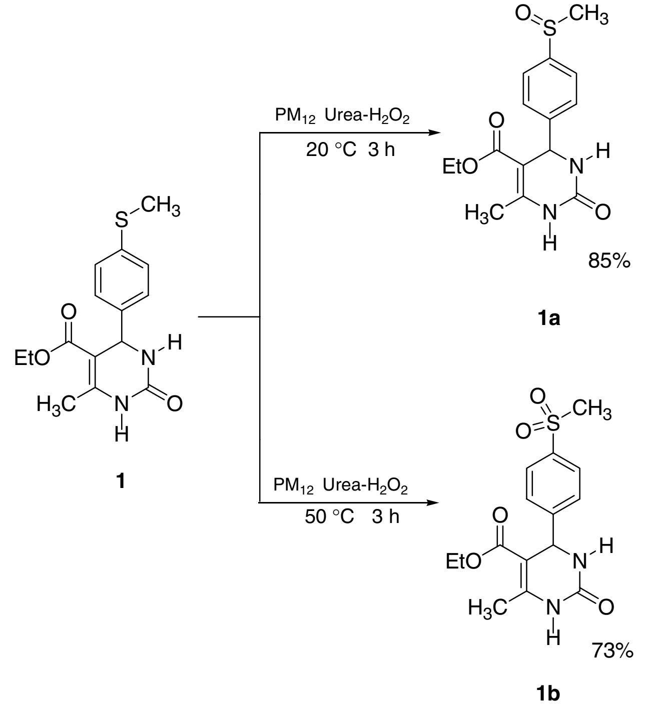
Entry	Substrate	Product	Yield[b] (%)
1			95[c]
2			100
3			82
4			80
5			96
6			88
7			97
8			93
9	 + PhCHO	 + PhCHO	100

[a] Reactions were carried out at 20 °C for 2 h.
[b] Pure product yields.
[c] Ratio *R*:*S* 60:40. Estimated by polarimetry.

Table 3
Oxidation of methyl *p*-tolyl sulfide with 1:1 hydrogen peroxide–urea catalyzed by reused $PMo_{12}Cin$[a]

Entry	Catalyst	Yields[b] (%)
1	1st use	90
2	2nd use	88
3	3rd use	89
4	4th use	89

[a] The reactions were carried out with 1:2 substrate and 1:1 hydrogen peroxide–urea at 20 °C.
[b] Yields % of pure sulfoxide. Conversions were >99% by proton NMR; only trace amounts of residual sulfide were observed, and oxidation was generally selective with only trace amounts of sulfone seen in most cases. Run time was 2 h.



Scheme 2.

example, entry 9 in Table 2, the benzaldehyde group was not affected by the reaction conditions.

Due to the need to obtain catalysts for green processes, the use of recycled catalysts is required for reducing the catalytic cost. When the reaction was completed, the catalyst (insoluble) was filtered, dried under vacuum (20 °C), and reused. The catalyst was used and reused for four cycles with similar activity (Table 3).

This protocol also represents a clean alternative to prepare more sophisticated molecules.[31] For example, Biginelli derivatives can be oxidized selectively to new sulfoxides or sulfones using these catalysts (Scheme 2). The sulfone derivatives compounds are promising agents with potential plant fungicides activity.

As conclusions, we developed a procedure for the selective oxidation of sulfides to sulfoxide using Keggin-structure catalysts, synthesized in our lab, by partial proton substitution on different amines such as quinoline ($PM_{12}Qui$), cinchonidine ($PM_{12}Cid$), and cinchonine ($PM_{12}Cin$). First, methyl *p*-tolyl sulfide was used as substrate, commercial PM_{12} as catalyst, and hydrogen peroxide (35% (p/v)) and acetonitrile as solvent to optimize homogeneous reaction conditions. The sulfoxides were obtained at 20 °C, using a stoichiometric amount of hydrogen peroxide, in 3–4 h. Under this condition, sulfoxides were obtained with a yield higher than 95%. Also, the sulfones were obtained at 50 °C and with excess of hydrogen peroxide with similar yields. The PM$_{12}$Cin was an appropriate catalyst for carrying out this transformation in heterogeneous medium. The *p*-tolyl sulfide oxidation at 20 °C, with 1:1 hydrogen peroxide–urea and ethanol (96%) as solvent, gives 90% of the corresponding sulfoxide. The catalyst was recovered and reused without loss of its catalytic activity. The main advantages of this procedure are the operational simplicity, the use of a noncorrosive, reusable catalyst in mild, clean oxidation, and the very good yields attained. The use of an insoluble catalyst instead of soluble inorganic acids contributes to waste reduction. Further investigations about the use of this heterogeneous catalyst for enantioselective oxidations of sulfides in sulfoxides are in progress.

Acknowledgments

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30. The commercial catalyst $H_3PMo_{12}O_{40}$ (PM$_{12}$) was provided by Aldrich. All the other catalysts were synthesized in our lab, by partial proton substitution on different amines such as quinoline (PM$_{12}$Qui), cinchonidine (PM$_{12}$Cid), and cinchonine (PM$_{12}$Cin). Another ethanolic solution of the corresponding amine was added to an ethanolic solution of $H_3PMo_{12}O_{40}$. The mixture was stirred at 75 °C for 1.5 h and concentrated. The precipitate was filtered, washed with more ethanol and dried at 20 °C under vacuum. Catalysts were characterized by FT-IR, DRS, DRX, BET, and liquid ^{13}C NMR.
    General procedure of oxidation of sulfides to sulfoxide in homogeneous conditions. A stirred solution of sulfide (1 mmol) and catalyst (0.01 mmol), in acetonitrile or ethanol (5 ml), was added to H_2O_2 35% p/v (2 mmol) at 20 °C. The mixture was stirred at 20 °C for a time period (see Table 1). The solvent was evaporated and then H_2O (5 ml) was added. The substrate was extracted with toluene (2 × 5 ml) and dried with anhydrous Na_2SO_4; filtration and evaporation afforded the corresponding pure crude sulfoxides. The solid sulfoxides were purified by recrystallization to afford the pure products. The products were confirmed by ^{1}H NMR and ^{13}C NMR analyses.
    General procedure of oxidation of sulfides to sulfoxide in heterogeneous conditions. A stirred solution of sulfide (1 mmol) and catalyst (0.01 mmol), in acetonitrile or ethanol (5 ml), was added to 1:1 hydrogen peroxide–urea (2 mmol), at 20 °C. The mixture was stirred at 20 °C for a time period (see Table 1). The catalyst was filtered and reused. The solvent was evaporated and then H_2O (5 ml) was added. The substrate was extracted with toluene (2 × 5 ml) and dried with anhydrous Na_2SO_4; filtration and evaporation afforded the corresponding pure crude sulfoxides. The solid sulfoxides were purified by recrystallization to afford the pure products. The products were confirmed by ^{1}H NMR and ^{13}C NMR analyses.
    Sample analysis. Samples were withdrawn from the organic phase at 15 minute intervals. Each volume sample was approximately 20 µl and it was diluted with 1–2 ml of acetonitrile or ethanol, the concentrations of which were calculated with internal standard method. Conversions were obtained with CG analysis performed with a Varian GC 3400 instrument. The capillary column was a 30 m Chromopack CP Sil 8 CB, whose diameter was 0.32 mm in diameter. The identification of products was performed with GC–MS (detector HP 5971) for comparison with GC–MS authentic samples.
31. Compound **1a**: mp 183–184 °C. ^{1}H NMR (DMSO-d_6, 200 MHz): $\delta = 1.10$ (t, $J = 7$ Hz, 3H), 2.27 (s, 3H), 2.72 (s, 3H), 3.99 (q, $J = 7$ Hz, 2H), 5.21 (d, $J = 3.2$ Hz, 1H), 7.41–7.67 (m, 4H), 7.82 (s, 1H), 9.28 (s, 1H). ^{13}C NMR (DMSO-d_6, 50 MHz): $\delta = 14.55$, 18.32, 43.64, 54.21, 59.77, 99.24, 124.37, 127.63, 140.22, 149.68, 150.75, 152.46, 165.69. Anal. Calcd for $C_{15}H_{18}N_2O_4S$: C, 55.88; H, 5.63; N, 8.69. Found: C, 55.83; H, 5.65; N, 8.72.
    Compound **1b**: mp 200–202 °C. ^{1}H NMR (DMSO-d_6, 200 MHz): $\delta = 1.10$ (t, $J = 7$ Hz, 3H), 2.27 (s, 3H), 3.19 (s, 3H), 3.99 (q, 2H), 5.25 (d, $J = 3.2$ Hz, 2H), 7.48–7.88 (m, 4H), 7.92 (s, 1H), 9.32 (s, 1H). ^{13}C NMR (DMSO-d_6, 50 MHz): $\delta = 14.75$, 18.55, 44.21, 54.40, 60.05, 99.09, 127.91, 128.03, 140.42, 149.90, 150.95, 152.53, 165.82. Anal. Calcd for $C_{15}H_{18}N_2O_5S$: C, 53.24; H, 5.36; N, 8.28. Found: C, 53.26; H, 5.37; N, 8.25.