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Evaluation of the Catalytic Activity of H₃PW₁₂O₄₀ in the Selective Oxidation of Sulfides to the Corresponding Sulfoxides or Sulfones

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Abstract: $H_3PW_{12}O_{40}$ in bulk form presents suitable properties to be used as catalyst in the selective oxidation of sulfides with 35% aqueous hydrogen peroxide, and sulfoxides or sulfones were obtained as products in high to excellent yields and selectivity. We found that sulfides were oxidized to the corresponding sulfoxides, with near stoichiometric 35% w/V aqueous hydrogen peroxide, at room temperature (20°C) and with a catalytic amount of bulk $H_3PW_{12}O_{40}$. Similarly, sulfides were transformed to the corresponding sulfones using excess of 35% w/V aqueous hydrogen peroxide and a temperature of 70°C. In both cases acetonitrile was used as reaction solvent.

Keywords: Aqueous hydrogen peroxide, Keggin heteropolyacid, sulfide oxidation, sulfoxides, sulfones.

INTRODUCTION

There is a notable increasing interest in the area of heteropoly compound-induced organic transformations. In view of their remarkable catalytic properties, heteropoly compounds (HPCs) are applied in bulk or supported form, as homogeneous or heterogeneous catalysts. The HPCs with Keggin structure are polynuclear complexes mainly composed of molybdenum, tungsten or vanadium as polyatoms (M), and phosphorus, silicon or germanium as central atom or heteroatom (X). The Keggin structure is formed by a central tetrahedron XO_4 , surrounded by 12 octahedra MO_6 . They could be either multielectron oxidants or strong acids, with an acid strength higher than that of the classical acids [1-3]. Recently, our research group reported green catalytic acid and oxidation procedures using Keggin HPCs [4-8].

On the other hand, sulfoxides and sulfones are important intermediates in organic chemistry due to their application in fundamental research and other extended usage, specially because chiral sulfoxides are versatile intermediates for the preparation of biologically and medically important products [9-10]. Omeprazole and the pesticide Fipronil are two typical examples of the extensive application of these intermediates in pharmaceutical and fine chemical industries [11]. The most widely used method for the preparation of sulfoxides and sulfones is the selective oxidation of the corresponding sulfide. For this reason, sulfide oxidation to sulfoxides and sulfones has been the subject of many studies, and several methods for this transformation have been reported in the literature [12-20]. Some traditional oxidizing reagents used for this purpose include nitric acid, trifluoroperacetic acid, hydrogen peroxide, nitromethane solution in dilute

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NO₃H/H₂SO₄, iodic acid, other hypervalent iodine reagents, and CAN (cerium ammonium nitrate), among others [10, 12-20].

The aim of this paper is the study of the catalytic activity of $H_3PW_{12}O_{40}$ in the oxidation of sulfides to the corresponding sulfoxide and/or sulfone, with aqueous hydrogen peroxide, using $H_3PW_{12}O_{40}$ as catalyst (Scheme 1).

EXPERIMENTAL

General

All reagents were purchased from Merck and Aldrich and used without further purification. All yields refer to isolated products after purification. The products were characterized by mass spectrometry. The organic phase was dried on anhydrous Na_2SO_4 and filtered for its analysis by gas chromatography using Varian Scan 3400 cx equipment. The product distribution was quantified by a Shimadzu C-R34 instrument. Reactions were monitored by thin layer chromatography (TLC) analyses.

Optimization of reaction conditions by the selective oxidation of benzyl phenyl sulfide

The oxidation of benzyl phenyl sulfide was typically carried out by heating a solution of 1 mmol, 1 mmol % of $H_3PW_{12}O_{40}$ in 5 mL of acetonitrile at several temperatures (see Table 4). The oxidant used was aqueous H_2O_2 35% w/V. The sample was collected from the mixture at several times. About 20 µL of the reaction mixture was taken for each sample, which was then diluted in a mixture of waterdichloromethane (2 mL). The dichloromethane layer was shaken with anhydrous Na₂SO₄. GC/MS analyses were performed on an HP 5971 mass detector coupled to an HP gas chromatograph fitted with a 30 m x 0.25 mn DB5 capillary column. The percentages of each compound in the reaction mixture were directly estimated from the corresponding chromatographic peak areas.

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Scheme (1). Oxidation of sulfides to the corresponding sulfoxide and/or sulfone.

General Procedure for the Selective Oxidation of Sulfides to Sulfoxides or Sulfones

To a stirred solution of sulfide (1 mmol) and $H_3PW_{12}O_{40}$ (1 mmol %) in acetonitrile (5 mL), H_2O_2 35% w/V (0.1 mL) was added at 20°C (sulfoxides) or 70°C (sulfones). The reaction was followed by TLC. The solvent was evaporated and the reaction mixture was extracted with toluene and dried with anhydrous Na₂SO₄; filtration and evaporation afforded the corresponding pure crude. The solid sulfoxides/sulfones were purified by recrystallization to afford the pure products. The structure of the products was confirmed by mass spectra.

Mass Spectra of Synthetized Sulfoxides

Dibutylsulfoxide

Colorless oil. EM, m/z (relative intensity): 162 (M⁺, 5%), 145 (11%), 106 (32%), 89 (45%), 57 (58%), 41 (98%), 29 (100%).

Dibenzylsulfoxide

Colorless solid. M.p.: $129-130^{\circ}$ C. EM, m/z (relative intensity): 230 (M⁺, 5%), 181 (2%), 180 (3%), 91 (100%), 65 (9%), 39 (3%).

Benzylphenylsulfoxide

Colorless solid. M.p.: 121-123°C. EM, m/z (relative intensity): 216 (M+, 10%), 182 (16%), 165 (2%), 125 (5%), 91 (100%), 77 (11%), 65 (18%).

Diphenylsulfoxide

Colorless solid. M.p.: 69-71 °C. EM, m/z (relative intensity): 202 (M+, 83%), 185 (18%), 154 (73%), 109 (90%), 97 (48%), 77 (78%), 65 (59%), 51 (100%), 39 (32%).

Mass Spectra of Synthetized Sulfones

Dibutylsulfone

Colorless solid. M.p.: 42-43°C EM, m/z (relative intensity): 178 (M+, 3%), 149 (2%), 123 (32%), 81 (4%), 57 (100%), 41 (52%), 29 (56%).

Dibenzylsulfone

Colorless solid. M.p.: 149-151 °C, EM, m/z (relative intensity): 182 (M+, 10%), 91 (100%), 65 (24%), 39 (11%).

Benzylphenylsulfone

Colorless solid. M.p.: 148-149 °C. EM, m/z (relative intensity): 232 (M+, 4%), 167 (2%), 165 (2 %), 152 (15%), 91 (100%), 77 (11%), 65 (17%), 51 (13%).

Diphenylsulfone

Colorless solid. M.p.: 127-129 °C. EM, m/z (relative intensity): 218 (M+, 36%), 153 (7%), 125 (100%), 97 (12%), 77 (37%), 51 (23%).

RESULTS AND DISCUSSION

First, we studied the influence of the Keggin heteropolyacid ($H_3PW_{12}O_{40}$) on the selective oxidation of sulfides, with 35% w/V aqueous hydrogen peroxide, at room temperature (20 °C), in acetonitrile. The reaction conditions were optimized using benzyl phenyl sulfide (BPS) as substrate and are summarized in Table 1. Very low conversion was detected in the absence of the catalyst (17% in 20 h, Table 1, entry 5), but when an HPC was added, the times were reduced considerably and the conversion increased to values close to 100%. When $H_3PW_{12}O_{40}$ was used, a conversion of 98% was observed at 5 h of reaction, with 90% of selectivity to sulfoxide (Table 1, entry 9).

The hydrogen peroxide concentration effect on the conversion of BPS and selectivity of reaction was studied using three different H_2O_2 amounts: 0.1, 0.3 and 1 mL, respectively (Table 2).

Table 3 displays the effect of the amount of catalyst on the conversion and selectivity in the oxidation of BPS. The experimental reaction conditions were BPS, 1 mmol; 35% w/V, H₂O₂ 0.1 mL; acetonitrile, 5 mL, 20°C and a variable amount of catalyst (0.5, 1, 2 and 5 mmol %). It can be seen that the conversion increased from 80% to 95% when the amount of H₃PW₁₂O₄₀ increased from 0.5% to 1% in 5 h. No relevant changes of reaction conversion and selectivity were observed with further increase in the amount of H₃PW₁₂O₄₀ (5 mmol %). Thus 1% of H₃PW₁₂O₄₀ is a suitable amount in this reaction.

In order to continue with the study of the reaction optimization, the temperature effect on the conversion rate and selectivity was studied keeping the H_2O_2 /substrate ratio constant (Table 4). The experimental reaction conditions were BPS, 1 mmol; 35% w/V H_2O_2 , 1 mL; acetonitrile, 5 mL; $H_3PW_{12}O_{40}$, 1 mmol % and variable temperature: 20°C, 40°C and 70°C. As can be observed, at 20°C the reaction is selective to sulfoxide with 100% conversion and 90% of selectivity in a reaction time of 2 h. On increasing the reaction temperature, the conversion rate increases and higher selectivity to sulfone results. For example, at 70°C and 1 h, a selectivity of 100% to sulfone is achieved.

Encouraged by the remarkable results obtained with the above reaction and in order to show the generality and scope of this catalytic method, the selective oxidation of four sulfides to sulfoxides or sulfones was studied under similar conditions. The results are summarized in Table **5**. All the reactions were run within a very short time and the sulfoxides

Entry	Catalyst	Time (h)	Conversion (%)	Sulfoxide Selectivity (%)	Sulfone Selectivity (%)
1	None	0.33	-	-	-
2		1	-	-	-
3		2	2	100	-
4		5	4	100	-
5		20	17	100	-
6	$H_{3}PW_{12}O_{40}$	0.33	30	100	-
7		1	68	98	2
8		2	90	93	7
9		5	98	90	10
10		20	100	60	40

Reaction conditions: benzylphenylsulfide: 1 mmol; 35% w/V H2O2: 0.1 mL; solvent: acetonitrile: 5 mL; catalyst: H3PW12O40: 1 mmol %; temperature: 20°C.

Table 2.	Catalytic oxidation	of benzylphenylsulfide.	H ₂ O ₂	amount influence.
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Amount Oxidant (mL)	Time (h)	Conversion (%)	Sulfoxide Selectivity (%)	Sulfone Selectivity (%)
0.1	0.33	30	100	-
	1	68	98	2
	2	90	93	7
	5	95	90	10
	20	100	60	40
0.3	0.33	42	100	-
	1	78	95	5
	2	98	93	7
	5	100	89	11
	20	100	60	40
1	0.33	60	95	5
	1	95	92	8
	2	100	90	10
	5	100	87	13
	20	100	40	60

Reaction conditions: benzylphenylsulfide: 1 mmol; solvent: acetonitrile: 5 mL; catalyst: H₃PW₁₂O₄₀: 1 mmol %; temperature: 20°C.

Table 3. Catalytic oxidation of benzylphenylsulfide. Catalyst amount influence.

Catalyst Amount (mmol %)	Time (h.)	Conversion (%)	Selectivity (%) Sulfoxide	Selectivity (%) Sulfone
0.5	0.33	20	100	-
	1	51	98	2
	2	75	93	7
	5	80	92	8
	20	89	93	7
1	0.33	30	100	-
	1	68	98	2
	2	90	93	7
	5	95	90	10
	20	100	60	40
2	0.33	32	100	-
	1	80	95	5
	2	92	93	7
	5	95	91	9
	20	100	60	40
5	0.33	35	95	5
	1	82	90	10
	2	94	85	15
	5	97	80	20
	20	100	45	55

Reaction conditions: benzylphenylsulfide: 1 mmol; 35% w/V H2O2: 0.1 mL; solvent: acetonitrile: 5 mL; catalyst: H3PW12O40; temperature: 20°C.

Table 4. Catalytic oxidation of benzylphenylsulfide. Temperature influence.

Temperature (°C)	Time (h)	Conversion (%)	Selectivity (%) Sulfoxide	Selectivity (%) Sulfone
20	0.33	60	95	5
	1	95	92	8
	2	100	90	10
	5	100	87	13
	20	100	40	60
40	0.33	90	70	30
	1	99	40	70
	2	100	0	100
	5	100	0	100

Table 4. contd....

Temperature (°C)	Time (h)	Conversion (%)	Selectivity (%) Sulfoxide	Selectivity (%) Sulfone
	20	100	0	100
70	0.33	100	41	59
	1	100	0	100
	2	100	0	100
	5	100	0	100
	20	100	0	100

 $Reaction \ conditions: \ benzylphenylsulfide: \ 1 \ mmol; \ 35\% \ w/V \ H_2O_2: \ 1 \ mL; \ solvent: \ acetonitrile: \ 5 \ mL; \ catalyst: \ H_3PW_{12}O_{40}: \ 1 \ mmol \ \%.$

Table 5. Selective oxidation of different sulfides to sulfoxides or sulfones.

Entry	Substrate	Product	Time/Temperature (h/°C)	Yields (%)
1	S	O S S	2/20	85
2		O, O S	1/70	89
3	S.S.	O S S	3/20	88
4			1/70	94
5	S.	O S S	3/20	89 (89,88) ^a
6		O O O S	1/70	95
7	S C	O S S	12/20	91
8		O O O	1/70	97

Reaction conditions (sulfoxides): sulfide: 1 mmol; 35% w/V H₂O₂: 0.1 mL; solvent: acetonitrile: 5 mL; catalyst: H₃PW₁₂O₄₀: 1 mmol %; temperature: 20°C. Reaction conditions (sulfone): sulfide: 1 mmol; 35% w/V H₂O₂: 1 mL; solvent: acetonitrile: 5 mL; catalyst: H₃PW₁₂O₄₀: 1 mmol %; temperature: 70°C. ^aFirst and second reuse



Scheme (2). Plausible mechanism of the oxidation of sulfide to sulfoxide.



Scheme (3). Plausible mechanism of the oxidation of sulfoxide to sulfone.

were obtained in excellent yields (greater than 85 in all cases) at room temperature (20°C). Similarly, sulfones were also obtained with excellent yields at 70° C using 35% w/V aqueous hydrogen peroxide in excess (1 mL).

We also investigated the reuse of the catalyst (Table 5, entry 5). For this purpose, after completion of the reaction the solvent was evaporated and dichloromethane (5 mL) was added at 20°C. The catalyst could be separated by simple filtration. The catalyst was dried under vacuum (20°C). The catalyst was recycled and the product yields for the first and second reuse were 89% and 88%, respectively.

A plausible mechanism for the oxidation of sulfide to sulfoxide is shown in Scheme 2; hydrogen peroxide in the presence of HPA generates an electrophilic intermediate, which undergoes nucleophilic attack by the sulfur atom, and the peroxo species transfer oxygen generating sulfoxide as shown in Scheme 2. Meanwhile, the oxidation of sulfoxide to sulfone is a nucleophilic attack by a SN_2 mechanism as shown in Scheme 3 [21-23].

CONCLUSION

In this research we have found a simple, convenient and selective procedure for the oxidation of sulfides to sulfoxides or sulfones, with 35% aqueous hydrogen peroxide and a catalytic amount of commercial $H_3PWo_{12}O_{40}$ heteropolyacid. The oxidation of sulfides to sulfoxides was carried out at 20°C and with a near stoichiometric amount of hydrogen peroxide, and the direct conversion of sulfides to sulfones at 70°C using hydrogen peroxide in excess. In both cases the yields are excellent. The oxidation of sulfides using $H_3PW_{12}O_{40}$ included in a superadsorbent polymer is currently in progress in our laboratory.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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