Vanadium-Substituted Keggin Type Heteropolyacid are Used for the Selective Oxidation of Sulfides to Sulfoxides and Sulfones Using Hydrogen Peroxide

Gustavo P. Romanelli*,[1], Daniel O. Bennardi[1], Valeria Palermo[1], Patricia G. Vázquez[1] and Pietro Tundo[2,3]

[1]*Centro de Investigación y Desarrollo en Ciencias Aplicadas "Dr. Jorge J. Ronco" (CINDECA), Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, 47 Nº 257 (B1900AJK) La Plata, Argentina*

[2]*Dipartamento de Scienze Ambientali, Universitá Ca´Foscari, Venice, Italy*

[3]*Consorzio Interuniversitario Nazionale La Chimica per l'Ambiente (INCA), Venice, Italy*

Abstract: Various types of aromatic and aliphatic sulfides are selectively oxidized to sulfoxides and sulfones with good to excellent yields using H_2O_2 35% p/V in the presence of catalytic amounts of Keggin heteropolyacid ($H_5PMo_{11}Al_{0.5}V_{0.5}O_{40}$) using acetonitrile as solvent.

Keywords: Sulfides, sulfoxides, sulfones, hydrogen peroxide, keggin heteropolyacid, oxidation.

The oxidation of sulfides to sulfoxides has been the aim of considerable research due to the importance of sulfoxides as useful intermediates in various chemically and biologically significant molecules [1].

Sulfoxides are important in organic synthesis as an activating group, they have been utilized extensively in carbon bond-forming reactions [2], as building block, especially as chiral auxiliaries [3], and they play key roles in the activation of enzymes [4].

There are several reagents available for this key transformation; they are conventionally achieved using stoichiometric amounts of both organic and inorganic reagents, e.g., hydrogen peroxide, t-butyl hypochlorite, N-

imidazole have been used [6]. They have been developed to promote oxidation of organic substrates due to the effective oxygen content, low cost, and safety in storage and operation [7].

The use of sulfones in organic synthesis has become a classic strategy in the synthesis of many complex molecules. They are employed in the preparation and functionalization of a wide variety of products by stabilizing α-radicals, α-anions and acting as cationic synthons. Most of the methods include the same oxidant as that used for sulfoxides [8, 9]. Sulfides can be oxidized directly to the sulfone, e.g., treatment with H_2O_2 and iron catalyst [10], H_2O_2 and 10% Na_2WO_4 [11] and $H_2O_2/AcOH/MgSO_4$ [12].
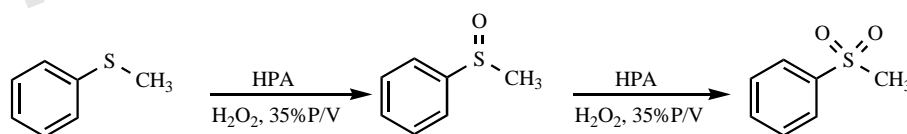
Scheme 1.

halosuccinimides, m-chloroperbenzoic acid, sodium metaperiodate, nitrogen tetroxide, CAN, tetrabutylammonium peroxydisulfate, 2,6-dicarboxypyridinium chlorochromate [5].

During the last years, very useful procedures involving catalysis and hydrogen peroxide as oxidant e.g. 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-

We have recently applied heteropolyacids with Keggin-type structure [13-15] for performing acidic catalysis and oxidation reactions e.g. the tetrahydropyranylation of phenols and alcohols [16-18], flavone preparation [19], phenol [20], and sulfide oxidations [6].

In the present work we study the influence of the Keggin-type heteropolyacids [HPA] on the selective oxidation, with hydrogen peroxide, of sulfides to sulfoxides or sulfones, at different temperatures, in a homogeneous medium.

The reaction conditions were optimized first using methylsulfanyl benzene (thioanisol) as substrate (Scheme **1**). The study of the oxidation reaction of thioanisol with H_2O_2 using different HPA is summarized in Table **1**. The reaction yields

*Address correspondence to this author at the Centro de Investigación y Desarrollo en Ciencias Aplicadas "Dr. Jorge J. Ronco" (CINDECA), Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, 47 Nº 257 (B1900AJK) La Plata, Argentina; E-mail: gpr@quimica.unlp.edu.ar

Table 1.   Catalytic Oxidation of Methylsulfanylbenzene, Using Different Catalysts

HPA	Time (h)	Conversion (%)	Selectivity Sulfoxide (%)	Selectivity Sulfone (%)
None	7	1	100	-
	20	10	100	-
$H_3PMo_{12}O_{40}$	0.33	28	100	-
	1	65	99	1
	2	95	95	5
	20	100	63	37
$H_4SiMo_{12}O_{40}$	0.33	25	100	-
	1	62	99	1
	2	92	95	5
	20	100	61	39
$H_6PMo_{11}AlO_{40}$	0.33	19	100	-
	1	47	100	-
	2	74	99	1
	20	100	97	3
$H_5PMo_{11}Al_{0.5}V_{0.5}O_{40}$	0.33	93	100	-
	1	100	99	1
	2	100	98	2
	20	100	98	2

2.8 mmol of H_2O_2 35% p/V was used, at 20°C.

Table 2   Catalytic Oxidation of Methylsulfanylbenzene Using $H_5PMo_{11}Al0._5V_{0.5}O_{40}$. Hydrogen Peroxide Concentration Influence

Entry	H_2O_2 (mmol)	Time (h)	Conversion (%)	Selectivity Sulfoxide (%)	Selectivity Sulfone (%)
1	1	0.33	90	99	1
2		1	91	98	2
3		2	91	98	2
4		20	91	98	2
5	2.8	0.33	93	100	-
6		1	99	99	1
7		2	100	98	2
8		20	100	98	2
9	28	0.33	99	99	1
10		1	100	99	1
11		2	100	97	3
12		20	100	96	4

very low conversions in the absence of a catalyst (10% for 20 h), 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 $H_3PMo_{12}O_{40}$ and $H_4SiMo_{12}O_{40}$ are used (Table **1**), a conversion of 95 and 92%, respectively, is observed at 2 h of reaction, with 95% selectivity to sulfoxide in both cases. Although $H_6PMo_{11}AlO_{40}$ is noticeably less active than commercial HPA, it is more selective. When vanadium is incorporated to the $H_6PMo_{11}AlO_{40}$ structure, a marked increase in activity is observed, which produces a 93% conversion of sulfide at 20 min of reaction, with 100% selectivity to sulfoxide. The H_2O_2 concentration effect on selectivity of reaction was studied and three different H_2O_2/substrate molar ratios were used: 1, 2.8 and 28 (Table **2**). No significant effect on con-

Table 3.   Catalytic Oxidation of Methylsulfanylbenzene Using $H_5PMo_{11}Al_{0.5}V_{0.5}O_{40}$. Reaction Temperature Influence.

Entry	Temperature (°C)	Time (h)	Conversion (%)	Selectivity Sulfoxide (%)	Selectivity Sulfone (%)
1	20	0.33	99	99	1
2		1	100	99	1
3		2	100	97	3
4		20	100	96	4
5	40	0.33	100	70	30
6		1	100	42	58
7		3	100	-	100
8	70	0.33	100	43	37
9		1	100	11	88
10		2	100	-	100

28 mmoles of H_2O_2 35 % p/V was used.

version was observed, but the selectivity to sulfoxide is excellent.

In order to continue with the study of the optimization of reaction, the effect of temperature on the conversion rate and selectivity was analyzed keeping the H_2O_2/substrate ratio constant (Table **3**). As can be observed, at 20°C the reaction is selective to sulfoxide with 100% conversion and 99% selectivity. On increasing the temperature, the conversion rate increases and a higher selectivity to sulfone results. For example, at 40°C and for 3 h, a 100% selectivity to sulfone is achieved (Table **3**, Entry 7).

Once the reaction conditions for the selective oxidation of sulfides to sulfoxides and to sulfones had been optimized, the reaction was extended to other starting substrates. Table **4** shows the results for the selective oxidation of different sulfides to sulfoxides. 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 example, in Entry 9, the benzaldehyde group was not affected by the reaction conditions.

Table **5** gives the results for the selective oxidation of different sulfides to sulfones. The reaction was performed at 40°C and, as in the case of sulfoxides, the yields were very good.

In conclusion, in this research we have found a new, convenient and selective procedure for oxidizing sulfides to sulfoxides, with 35% aqueous H_2O_2 and a catalytic amount of $H_5PMo_{11}Al_{0.5}V_{0.5}O_{40}$. The yields were excellent. All reagents are cheap and the catalyst has an easy preparation. The reaction for the preparation of sulfoxides was carried out at room temperature and short reaction time. The oxidation to sulfones proceeded at 40°C in also excellent yields. Further studies on the oxidations of other organic substrates and other heteropolyacids are currently in progress.

EXPERIMENTAL

Catalyst Preparation

$H_6PMo_{11}AlO_{40}$

The following procedure was used for the preparation of the molybdenum-substituted heteropolyacid: a stoichiometric mixture of 85% H_3PO_4 (0.58 g (0.01 mol)), $AlCl_3.6H_2O$ (1.21 g (0.005 mol)) and MoO_3 (14.4 g (0.11 mol)) was suspended in 150 ml of distilled water. The mixture was stirred for 6 h at 80°C. After cooling down to room temperature and removal of insoluble polymolybdates, the heteropolyacid solution was evaporated and dried at 85°C for 24 h. After that, yellow crystals of $H_6PMo_{11}AlO_{40}$ were obtained.

FT-IR

The spectrum of bulk $H_6PMo_{11}AlO_{40}$ showed bands at 1064 (P-Oa), 962 (Mo=Od), 869 (Mo-Ob-Mo), 787 (Mo-Oc-Mo), 378 and 342 (bending) cm^{-1}.

$H_5PMo_{11}Al_{0.5}V_{0.5}O_{40}$

According to the synthesis of $H_6PMo_{11}AlO_{40}$, a stoichiometric mixture of 0.58 g (0.01 mol) of H_3PO_4 85%, 0.6 g (0.0025 mol) of $AlCl_3.6H_2O$, 0.22 g (0.0012 mol) of V_2O_5 and 14.4 g (0.11 mol) of MoO_3 was suspended in 150 ml of distilled water. The mixture was stirred for 6 h at 80°C. After cooling down to room temperature and removal of insoluble molybdates and vanadates, the heteropolyacid solution was evaporated and dried at 85°C for 24 h. After that, yellow orange crystals of $H_5PMo_{11}Al_{0.5}V_{0.5}O_{40}$ were obtained.
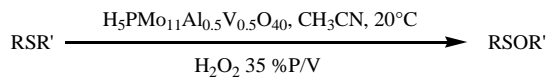
FT-IR

The spectrum of bulk $H_5PMo_{11}Al_{0.5}V_{0.5}O_{40}$ showed bands at 1059 (P-Oa), 960 (Mo=Od), 871 (Mo-Ob-Mo), 786 (Mo-Oc-Mo), 377 and 343 (bending) cm^{-1}.

Optimization of Reaction Conditions by Selective Oxidation of Sulfides, with Hydrogen Peroxide, to Sulfoxides or Sulfones
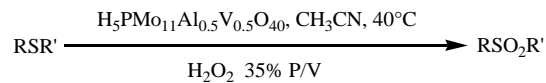
The oxidation of methylsulfanylbencene was typically carried out by heating a solution of 0.7 mmol of the substrate and 0.007 mmol of the catalyst in 5 ml of acetonitrile, at 20°C. The oxidant used was aqueous H_2O_2 35% p/V. The sample was collected from the reaction mixture during the reaction at time intervals. About 20 µl of the reaction mixture was taken for each sample, which was then diluted in a mixture of water-dichloromethane (2 ml). The dichloro-

Table 4.   Selective Oxidation of Different Sulfides to Sulfoxides

$$RSR' \xrightarrow[\text{H}_2\text{O}_2\ 35\ \%\text{P/V}]{\text{H}_5\text{PMo}_{11}\text{Al}_{0.5}\text{V}_{0.5}\text{O}_{40},\ \text{CH}_3\text{CN},\ 20°\text{C}} RSOR'$$

Entry	Substrate	Product	Time (h)	Yield (%)
1			1	94
2			1	86
3			1	92
4			1	91
5			1	93
6			2	100
7			1	95
8			0.5	89
9			0.5	90
10			0.5	96
11			1	95
12	+ PhCHO	+ PhCHO	1	92

Table 5. **Selective Oxidation of Different Sulfides to Sulfones**

$$RSR' \xrightarrow[\text{H}_2\text{O}_2 \ 35\% \ \text{P/V}]{\text{H}_5\text{PMo}_{11}\text{Al}_{0.5}\text{V}_{0.5}\text{O}_{40}, \text{ CH}_3\text{CN, } 40°\text{C}} RSO_2R'$$

Entry	Substrate	Product	Time (h)	Yield (%)
1			3	98
2			3	96
3			3	96
4			4	93
5			3	91
6			4	95
7			4	93
8			3	93
9			3	90
10			3	92
11			3	91

methane layer was shaken with anhydrous Na_2SO_4. 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.

General Procedure for Oxidation of Sulfides to Sulfoxides

A stirred solution of sulfide (0.7 mmol) and $H_5PMo_{11}Al_{0.5}V_{0.5}O_{40}$ (0.01 mmol), in acetonitrile (5 ml), was added to H_2O_2 35% p/V (2 mmol), at 20°C. The mixture was

stirred at 20°C between 30 min and 2 h and the reaction time depended on the substrate. The solvent was evaporated and the substrate was extracted with dichloromethane 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 structure of the products was confirmed by ^{1}H-NMR and ^{13}C-NMR analyses.

General Procedure for the Oxidation of Sulfides to Sulfones

A stirred solution of sulfide (0.7 mmol) and $H_5PMo_{11}VO_{.5}A_{l0.5}O_{40}$ (0.01 mmol), in acetonitrile (5 ml), was added to H_2O_2 (20 mmol) at 20°C. The mixture was stirred at 40°C between 3 and 4 h and the reaction time depended on the substrate. The solvent was evaporated and the substrate was extracted with dichloromethane and dried with anhydrous Na_2SO_4; filtration and evaporation afforded the corresponding pure crude sulfone. The solid sulfone was purified by recrystallization to afford the pure products. The structure of the products was confirmed by ^{1}H-NMR and ^{13}C-NMR analyses.

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