Selective oxidation of sulfides to sulfoxides and sulfones using 30% aqueous hydrogen peroxide and silica-vanadia catalyst

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A B S T R A C T

A green, efficient and selective approach for the oxidation of sulfides to sulfoxides and sulfones with stoichiometric amount of 30% aq. H_2O_2 is reported. The reaction is performed in methanol with silica-vanadia as heterogeneous and reusable catalyst.

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1. Introduction

The chemoselective preparation of chiral/achiral sulfoxides and sulfones represents an extremely important synthetic process in organic chemistry. Infact, sulfoxides and sulfones are valuable intermediates utilized since long time for the synthesis of fine chemicals and biologically active compounds [1].

To date, the most important method for the preparation of those compounds involves the oxidation of thioethers. The sulfur atom can be easily oxidized by different electrophilic oxidants, but special conditions must be set up to chemoselectively obtain sulfoxides or sulfones. Moreover, if additional oxidizable functional groups are present, such as C–C double bond and alcohol, a further problem arises from the need to save them during the oxidation process.

Due to the great interest of these compounds, different synthetic methods have been developed for chemoselective oxidation of sulfides. However, many of these procedures utilize environmentally unfavorable reagents, solvents and catalysts that bring out the matter of ecoefficiency in our environmentally conscious times. These include, for example, use of $FeBr_3$-nitric acid [2], mercury

(II) oxide-iodine [3], oxodiperoxo molybdenum complexes [4], *o*-iodoxybenzoic acid [5], chromium(VI) oxide [6], periodic acid or molecular bromine [7], potassium permanganate [8], sodium perchlorate [9], *m*-chloroperbenzoic acid [10] and benzeneseleninic peracid [11].

Aqueous hydrogen peroxide was also utilized as terminal oxidant [12] due to the effective oxygen content, low cost and environmentally friendly character. However, being H_2O_2 a relatively weak electrophile, the sulfide oxidation requires a catalyst such as Mo, V, W and Se acid metal oxides [13].

In agreement with the ever increasing environmental awareness, new oxidative processes based on the activation of H_2O_2 by robust, efficient and recyclable heterogeneous catalysts were developed [14]. Despite these recent improvements the thioether oxidation reaction requires further studies with particular focus on the chemoselectivity of the reaction as well as the effective oxygen utilization avoiding unproductive H_2O_2 decomposition.

Here we report the efficient and selective oxidation of sulfides to sulfoxides or sulfones with 30% aqueous H_2O_2 in a 1:1 or 1:2 molar ratio in the presence of silica-vanadia gel as the reusable solid catalyst.

2. Experimental

All commercial chemicals were of analytical grade and were used as received.

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Metal elemental analyses were performed by ICP-AES on Ultima 2 Jobin Yvon HORIBA instrument. FT-IR spectra of all the catalysts (KBr pellets) were recorded on a Nicolet FT-IR Nexus spectrophotometer (resolution 4 cm^{-1}) in the range of 4000–400 cm^{-1}. X-ray diffraction analyses were performed on Philips PW1710 instrument. Gas-chromatographic analyses were accomplished on a TraceGC ThermoFinnigan instrument with a fused silica capillary column SPB-20 from Supelco (30 m × 0.25 mm).

2.1. Preparation and characterisation of silica-vanadia (Si-V10-2) catalyst

A simple sol–gel synthesis procedure was used during which vanadyl acetylacetonate [VO(acac)$_2$] (0.53 g, 2 mmol) and tetraethoxysilane (TEOS) (2.23 ml, 10 mmol) were mixed in ethanol (1.16 ml). The solution was refluxed for 15 min and cooled to room temperature. Nitric acid (0.20 ml, 2 mmol) and deionized water (2.70 ml) were added. The mixture was refluxed under stirring for 15 min. The colloidal solution was transferred into a dessicator and aged for 30 days. The ochre-yellow gel was crushed in a mortar giving a fine powder. The powder was heated at 200 °C for 4 h and washed with deionized water (10 ml) and methanol (10 ml). The parent silica sample (for IR studies) was prepared by the same procedure without addition of VO(acac)$_2$.

The fresh "Si-V10-2" material appears as an homogeneous powder with mean grain dimension of about 250 μm. The content of vanadium is 11.6 wt%. Its X-ray diffraction pattern exhibits a very large band, centered at 2θ 23° (Cu Kα radiation), typical of an amorphous material. The material contains trace amounts of the orthorhombic V$_2$O$_5$ phase as suggested by the presence of very weak peaks at 2θ values of 20.31°, 26.15° and 31.05°, hardly detectable among the background noise.

The FT-IR spectrum of the fresh material in the range 1200–500 cm^{-1} appears reminiscent of that of amorphous silica obtained from TEOS by the same sol–gel procedure and in particular shows three broad absorption peaks at 1048(vs), 936(s) and 787(s) cm^{-1}.

It is interesting to note that the second peak at 936 cm^{-1} moves to higher frequencies during the utilization of the gel material. In fact, it shifts to 948 cm^{-1} after the first oxidation reaction and definitively to 955 cm^{-1} after the catalytic cycles. Taking into account that a similar peak at 960 cm^{-1} was attributed to SiO$_4$ units bonded to V in vanadium silicates [15a] (indicating the possible presence of Si-O-V bridges) and that a peak at 933 cm^{-1} was recently reported as Si-O-V absorption in a silica-vanadia catalyst [15b], the observed shift should be related to changements in the bonding state of the vanadium atoms owing to the oxidative conditions of the catalytic process (see Fig. 2).

2.2. Oxidation experiments

Thioether oxidation studies were performed with thioanisole as the model reagent and with 30% aq. H$_2$O$_2$ as the oxidant in the selected solvent and with the selected amount of catalyst in a batch reactor under magnetic stirring at room temperature. The reaction products were analysed by gas chromathography.

2.3. Synthesis of sulfoxides and sulfones

To a stirred suspension of the selected sulphide (10 mmol) and the heterogeneous catalyst Si-V10-2 (0.019 g, 0.043 mmol vanadium) in methanol (10 ml), 30% aq. H$_2$O$_2$ (1.13 ml, 10 mmol) was added in one portion. The slurry was stirred at room temperature for 20 min. The catalyst was filtered off and washed with methanol (10 ml). Ethyl acetate (10 ml) was added and the resulting solu-
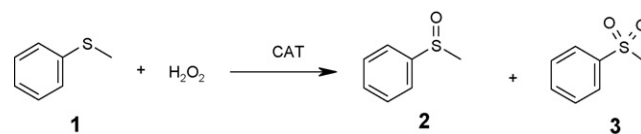
Scheme 1. Model reaction between thioanisole and 30% aq. H$_2$O$_2$.

tion was dried with anhydrous sodium sulphate and evaporated in vacuo to afford the crude product which was purified by column chromatography on silica gel (10% EtOAc in hexane) to afford the pure sulfoxide.

Similar method was utilized to produce sulfones. In this case 2.3 ml of 30% aq. H$_2$O$_2$ (20 mmol) were utilized.

3. Results and discussion

The influence of different reaction parameters on the efficiency of the oxidation process was evaluated in the model reaction depicted in Scheme 1.

All experiments were carried out with the silica-vanadia catalyst Si-V10-2 described in the experimental part since in preliminary studies this material showed the best activity in comparison with gels produced by different TEOS/VO(acac)$_2$ ratios.

The reaction time was first analysed by carrying out experiments using thioanisole (1.24 g, 10 mmol), catalyst Si-V10-2 (0.037 g, 0.086 mmol V), 30% aq. H$_2$O$_2$ (1.13 ml, 10 mmol) in acetone (10 ml) at room temperature.

The reaction is fast giving 70% yield of product **2** after 5 min; increasing the reaction time from 5 to 20 min the sulfoxide yield reached the maximum value (86%) with 95% selectivity.

By further increasing the reaction time to 40 min a small lowering of the sulfoxide **2** yield to 80% was observed due to the expected subsequent oxidation to sulfone. Therefore, we decided to stop the reaction after 20 min.

The effect of catalyst amount was then evaluated. Results are reported in Fig. 1.

Without any catalyst the reaction occurs under the conditions reported in Fig. 1 giving the product **2** in 9% yield. The yield was significantly increased by adding the catalyst and reached the best value (84%) with 1.5 wt% of catalyst with respect the thioanisole, namely 0.019 g of Si-V10-2, corresponding to 0.043 mmol of vanadium. In all experiments the selectivity was high (∼95%). Further increasing of the catalyst amount caused a decrease of selectivity due to overoxidation. The effect of the reaction medium was then examined by comparing the activity of the catalyst in some
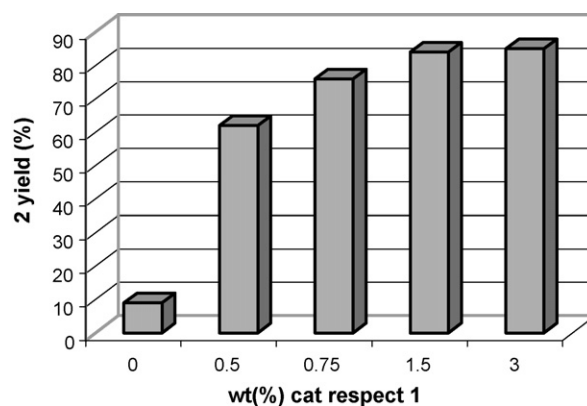

Fig. 1. Effect of the amount of catalyst on the product **2** yield. Reaction conditions: thioanisole (1.24 g, 10 mmol), 30% aq. H$_2$O$_2$ (1.13 ml, 10 mmol), acetone (10 ml), r.t., 20 min.

Table 1
Effect of the solvent (10 ml) on the product **2** yield. Reaction conditions: thioanisole (1.24 g, 10 mmol), catalyst (0.019 g, 0.043 mmol V), 30% aq. H_2O_2 (1.13 ml, 10 mmol), r.t. 20 min

Solvent	**2** Yield (%)	Selectivity (%)
–	66	85
Water	90	96
Methanol	94	97
Ethyl acetate	65	65
Acetone	86	95

Table 2
Reusability of the catalyst in the model reaction for the production of sulfoxide **2** and sulfone **3**
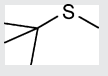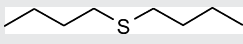
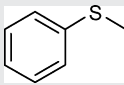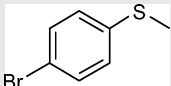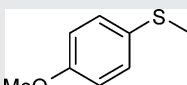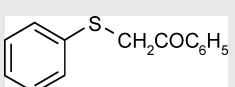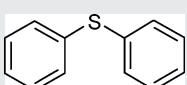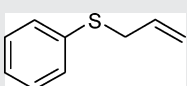| Run	**2** Yield (selec.) (%)	Cat. recovered (%)	**3** Yield (selec.) (%)	Cat. recovered (%)
1	94 (97)	88	99 (99)	91
2	92 (95)	98	98 (99)	97
3	93 (95)	97	96 (97)	98
4	92 (94)	98	98 (99)	98

halogen-free solvents commonly utilized in the oxidation with H_2O_2. Results are reported in Table 1.

As clearly shown in Table 1 and in agreement with studies previously reported in the literature, solvents of high hydrogen bonding capacity, such as methanol and water, favour the formation of sulfoxide with high chemoselectivity [14b,16,17]. Methanol was consequently the solvent of choice.

In previous mechanistic studies on the oxidation with H_2O_2 over vanadium-based heterogeneous catalysts it was shown that vanadium can exist in two species, V^{4+} and V^{5+}, undergoing different peroxo complexes upon chem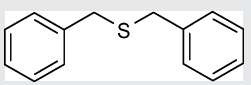isorption of H_2O_2 [15,18]. The initial formation of such active peroxo complexes was related to the frequently observed induction period in the oxidation reactions [19]. On the basis of this information we investigated the possible positive effect of the previous treatment of the catalyst with H_2O_2. We

found that the catalyst showed a remarkable growing of the initial activity upon activation by treatment with 30% aq. H_2O_2 at 80 °C under stirring for 30 min as clearly shown in Fig. 2.

By now it is impossible to give a complete rationale for these results; however, the possible production of surface active vanadium (V) peroxocomplexes by interaction with H_2O_2 could be responsible for the higher activity. This fact could also be related to the shift observed in the FT-IR spectrum of the peak attributed to SiO_4 units bonded to V from 936 to 955 cm^{-1} before and after treatment with H_2O_2 [20] as well as upon use in the present reaction.

The possible effect of active vanadium leaching was examined by removing the catalyst from the reaction mixture through filtration after 3 min, when the yield of **2** was 66%. The filtrate was then stirred at room temperature for an additional 20 min and analysed. Product **2** was present in 73% (66 + 7%) yield being the difference ascribable

Table 3
Selective oxidation of sulfides to sulfoxides and to sulfones with 30% aq. H_2O_2 using Si-V10-2 gel as catalyst

Entry	Substrate	Yield (select.) (%) Sulfoxide[a]	Sulfone[b]
1		94 (97)	99 (99)
2		93 (97)	95 (97)
3		95 (98)	96 (97)
4		95 (97)	99 (99)
5		70 (95)	90 (96)
6		75 (94)	95 (97)
7		95 (98)	99 (99)
8		80 (96)	97 (98)
9		89 (97)	92 (98)
10		80 (98)	95 (97)

[a] Reaction conditions: thioether (10 mmol), 30% aq. H_2O_2 (1.13 ml, 10 mmol), catalyst (0.019 g, 0.043 mmol of vanadium) methanol (10 ml), r.t., 20 min.

[b] Reaction conditions: similar to (a) by using 30% aq. H_2O_2 (2.26 ml, 20 mmol).
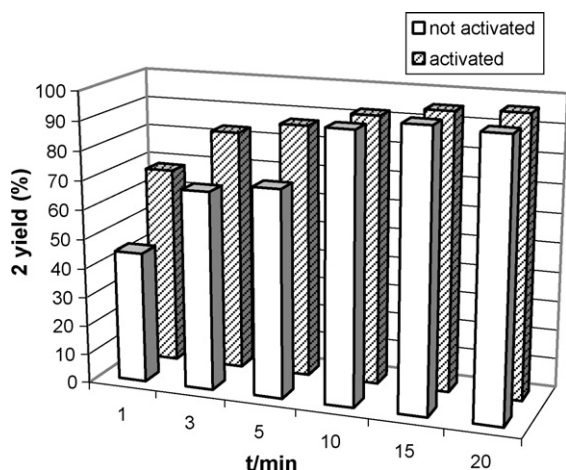
Fig. 2. Effect of catalyst preactivation on the product **2** yield by treatment with aq. H_2O_2. Reaction conditions: thioanisole (1.24 g, 10 mmol), 30% aq. H_2O_2 (1.13 ml, 10 mmol), catalyst (0.019 g, 0.043 mmol V), methanol (10 ml), r.t., 20 min.

to the modest reactivity of the system even in the absence of the catalyst (see Fig. 1). This result allows us to exclude the leaching of the active vanadium species into solution.

Easy reciclability and the prolonged retention of catalytic activity are very important features for practical and efficient applications of catalytic processes. In order to check the reusability of the catalyst, it was employed in both the model reactions under the optimum conditions. In the first cycle 94% of product **2** was obtained. Addition of an equimolecular amount of H_2O_2 gave product **3** in 99% yield. The catalyst powder was recovered by filtration, washed with methanol and immediately reused for both oxidation processes, taking into account the partial loss of catalyst during the recovery. The larger loss after the first run is due to the initial presence of very fine powder in the catalyst. The second cycle was performed with the recovered catalyst and the process was repeated through three cycles without significant loss of productivity (Table 2).

To evaluate the applicability of the reaction also to the selective sulfone synthesis, the effect of the increasing amount of hydrogen peroxide was examined.

The reaction is a typical two-step process. Being H_2O_2 an electrophilic oxidant, the initial oxidation of the highly nucleophilic sulphide to sulfoxide is an easier process than the second oxidation of the resulting much less nucleophilic sulfoxide to sulfone [21].

However, exceptions to this general rule were frequently reported in the literature and the chemoselectivity of the process was shown to be strongly dependent on the nature of the catalyst.

The reaction proceeds smoothly with a 1:1 thioanisole/H_2O_2 ratio giving the sulfoxide in 94% yield (97% selectivity) in 15 min. The sulfoxide was then quantitatively converted into sulfone by further adding a stoichiometric amount of H_2O_2 (under ratio thioanisole/H_2O_2 = 1:2). It is also noteworthy that the reaction shows very high level of the effective oxygen utilization being a 1:1 and 1:2 thioanisole/H_2O_2 molar ratio utilized for the synthesis of sulfoxides or sulfones, respectively. Under these conditions, unproductive decomposition of H_2O_2 via homolytic pathways was completely avoided (or, at least, minimized).

A series of sulfides was then subjected to oxidation under the specific conditions required for sulfoxide and sulfone production. Some synthetic results are presented in Table 3.

The reaction shows satisfactory general applicability for the production of both sulfoxides and sulfones. The reaction with diphenyl sulphide and phenyl allyl sulphide affords the sulfoxides in moderate yield (entries 5 and 6) whereas the corresponding sulfones are obtained in high yields. In these cases an increase of reaction time or temperature gave a lower selectivity due to the overoxidation to the sulfone.

4. Conclusions

An economic, facile and eco-efficient process for the synthesis of sulfoxides and sulfones by oxidation of sulfides with 30% aq. H_2O_2 over silica-vanadia heterogeneous catalyst was developed.

The reaction was performed in methanol at room temperature with 1.5 wt% of the ready available catalyst with respect the sulphide. The methodology offers the advantage of the catalyst recyclability without significant loss of catalytic activity avoiding the unproductive H_2O_2 decomposition.

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