

Short communication

# Polymeric Ti(IV) glycolate: A heterogeneous catalyst for solvent-free sulfoxidation by *t*-butyl hydroperoxide

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## Abstract

The oxidation of sulfides to sulfoxides has been conveniently performed under heterogeneous and solvent-free conditions employing polymeric Ti(IV) glycolate as reusable catalyst and *t*-butyl hydroperoxide as oxygen donor. The catalyst can be very efficiently recovered and reused several times without any significant change in reactivity and selectivity.

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*Keywords:* Heterogeneous sulfoxidation; Solvent-free

## 1. Introduction

Sulfoxides are very important molecules in organic chemistry [1–4]. They can be extensively used as bioactive compounds [5–7], in carbon–carbon bond forming reactions [8,9] and as building blocks in organic synthesis [10–13]. For these reasons several procedures for the synthesis of sulfoxides have been developed [14–30]. Most of these methods are based on the oxidation of sulfides to sulfoxides and usually use toxic and/or expensive oxidizing systems or they need the employment of chlorinated solvents or complicated and resource-wasting work-up procedures are requested [14–31]. Therefore, an important aim is to develop simple catalytic methods with the possibility to recover and recycle the catalyst and in which the use of solvents is reduced or omitted.

Reactions under solvent-free conditions are receiving increasing attention in the recent years not only from a green chemistry point of view but also for a series of advantages mainly related to a greater selectivity and an enhanced reaction rate with respect to conventional reactions performed in solvents.

In the course of a previous investigation polymeric Ti(IV) glycolate,  $[\text{Ti}(\text{OCH}_2\text{CH}_2\text{O})_2]_n$ , proved to be a heterogeneous reusable catalyst in the chemo-, regio- and stereoselective epox-

idation of allylic alcohols by *t*-butyl hydroperoxide (*t*-BuOOH) [32]. It is noteworthy that polymeric Ti(IV) glycolate is easy to synthesize [33,34] to manipulate and highly stable in air; more interestingly, in the course of the above investigation it was found to be very poorly soluble both in halogenated and hydrocarbon solvents so that it could be efficiently recovered at the end of the epoxidation process (95% yield) by centrifugation or by filtration. Furthermore, the catalyst was reused several times without any change of reactivity and selectivity.

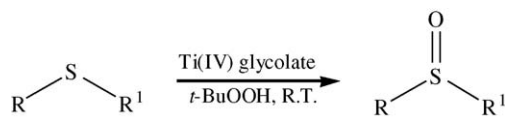
These results prompted us to verify the possibility of achievement of a new procedure for the oxidation of sulfides to sulfoxides by polymeric Ti(IV) glycolate/*t*-BuOOH system, combining the advantages of the heterogeneous catalysis and solvent-free reaction conditions.

## 2. Experimental

### 2.1. Materials

Starting materials and all other reagents, unless otherwise indicated, were purchased from Aldrich or Fluka and used without further purification. All the reactions were monitored by thin layer chromatography (TLC) on Merck silica gel plates (0.25 mm) and visualized by UV light or by  $\text{KMnO}_4$  spray test. The NMR spectra (Bruker DRX 400 ( $^1\text{H}$  NMR, 400 MHz;  $^{13}\text{C}$  NMR, 100 MHz)) were performed in  $\text{CDCl}_3$  solution.

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Scheme 1.

## 2.2. Polymeric Ti(IV) glycolate synthesis

Polymeric Ti(IV) glycolate was synthesized, according to reported procedures, heating a solution of Ti(OiPr)<sub>4</sub> (1.0 g, 3.5 mmol) in 10 mL of ethylene glycol for 5 h at 150 °C. At the end of the reaction, the obtained suspension was centrifuged and the white solid was washed with EtOH and with Et<sub>2</sub>O. Then the solid was dried under vacuum at 70 °C for 2 h.

## 2.3. Standard procedure for heterogeneous solvent-free sulfoxidation

In a typical experimental procedure 30 mg of Ti(IV) glycolate, 1.0 mmol of sulfide and 1 eq. of *t*-butyl hydroperoxide (5–6 M solution in decane) were allowed to react at room temperature under stirring. The reaction was monitored by TLC analysis and after the appropriate reaction time, 0.5 mL of AcOEt were added. Then the suspension was centrifuged and the solid was washed again with AcOEt (3 × 0.5 mL). The combined AcOEt solutions were concentrated under vacuum and purified by silica gel flash chromatography (eluent starting from petroleum ether/ethyl acetate mixture = 1/1 to ethyl acetate). The structure of the final products was confirmed by comparison of the physical and spectroscopic data (<sup>1</sup>H NMR and <sup>13</sup>C NMR) with the ones of authentic samples prepared according to a known procedure [35].

## 3. Results and discussion

In a preliminary phase methyl *p*-tolyl sulfide, chosen as model compound, was submitted to treatment with *t*-BuOOH in the presence of polymeric Ti(IV) glycolate under different experimental conditions (Table 1 and Scheme 1).

Table 1  
Oxidation of methyl *p*-tolyl sulfide under different reaction conditions

Entry	Time (h)	Solvent	Yield (%) <sup>a</sup>
1 <sup>b</sup>	36	CH <sub>2</sub> Cl <sub>2</sub>	65 (25)
2 <sup>b</sup>	36	<i>n</i> -Hexane	50 (25)
3 <sup>b</sup>	3	Solvent-free	75 (17)
4 <sup>c</sup>	3	Solvent-free	15 (0)
5 <sup>b,d</sup>	47	Solvent-free	32 (68)
6 <sup>b,e</sup>	24	Solvent-free	68 (7)

<sup>a</sup> Yields refer to chromatographically pure compounds. Values in parentheses refer to sulfone yields.

<sup>b</sup> 30 mg of Ti(IV) glycolate/1 mmol of sulfide were used. In entries 1 and 2, 4.0 mL of solvent were used.

<sup>c</sup> Reaction was performed in the absence of Ti(IV) glycolate.

<sup>d</sup> 2.4 eq. of *t*-BuOOH were used.

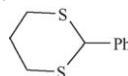
<sup>e</sup> Reaction temperature = 0 °C.

It is noteworthy that the reaction performed under solvent-free conditions (entry 3) afforded the corresponding sulfoxide with better chemoselectivity and in shorter reaction time with respect to the same reaction performed both in CH<sub>2</sub>Cl<sub>2</sub> and *n*-hexane (entries 1 and 2). In a control experiment the reaction, carried out in the absence of Ti(IV) glycolate under solvent-free conditions (entry 4), gave the sulfoxide in rather low yield (15%). The employment of an excess of oxidant and more prolonged reaction times showed to favour the over-oxidation process to sulfone, although significant amounts of sulfoxide intermediate could be usually recovered (entry 5). On the contrary, a better chemoselectivity was obtained by performing the oxidation at 0 °C, although a notable enhancement of reaction time was required to achieve satisfactory yields (entry 6).

In all the experiments reported in Table 1 *t*-BuOOH was used as 5–6 M decane solution; in order to exclude the possibility that leaching of Ti(IV) species in hydrocarbon solution could be responsible of the sulfoxidation reaction (and consequently to assess the really heterogeneous nature of the process), polymeric Ti(IV) glycolate (30 mg) was suspended in a mixture of *n*-hexane (0.5 mL) and *t*-BuOOH decane solution (0.180 mL). After stirring for 30 min at room temperature the suspension was centrifuged at 4000 rpm for 10 min; the clear liquid phase was then separated and used in a control experiment under the conditions of entry 4 (Table 1). After the usual work-up and purification procedure methyl *p*-tolyl sulfoxide was obtained in comparable yield (10%) to the one observed in the absence of catalyst (entry 4).

The oxidation of several representative linear alkyl aryl, dialkyl and cyclic thioacetals (Table 2) in the presence of Ti(IV) glycolate and *t*-BuOOH under solvent-free conditions was performed to test the generality of the method. In all entries 1–8 good yields and an acceptable chemoselectivity were usually observed and, as regards aryl alkyl sulfides, the procedure proved to be compatible with the presence of different functional groups on the aromatic ring. Only in the oxidation of *p*-nitrophenyl methyl sulfide (entry 3), a more prolonged reaction time was required to isolate the corresponding sulfoxide in yield similar to the ones observed with the other examined sulfides. In this

Table 2  
Oxidation of several sulfides in the presence of Ti(IV) glycolate and *t*-BuOOH under solvent-free conditions

Entry	R	R <sup>1</sup>	Time (h)	Yield (%) <sup>a</sup>
1	<i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	Me	3	75 (17)
2	C <sub>6</sub> H <sub>5</sub>	Me	2	71 (14)
3	<i>p</i> -OMeC <sub>6</sub> H <sub>4</sub>	Me	3	75 (19)
4	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	Me	6	72 (13)
5	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	Me	2	72 (16)
6	<i>n</i> -Octyl	Me	2	72 (17)
7	C <sub>6</sub> H <sub>5</sub>	Et	2	70 (14)
8			3	67 (>99/1) <sup>b</sup>

<sup>a</sup> Yields refer to chromatographically pure compounds. Values in parentheses refer to sulfone yields.

<sup>b</sup> In parenthesis is reported the diastereoselectivity ratio *trans/cis*.

case, a deep influence on the reaction rate was probably exerted by the very poor solubility of the solid sulfide in the liquid phase constituted by the highly concentrated hydroperoxide decane solution. Very interestingly, in the case of a cyclic substituted thioacetal, 1-Ph-2,3-dithiane (entry 8), the mono-sulfoxidation was the only detectable process and showed to proceed with high level of diastereoselectivity (>99/1 *trans/cis* ratio).

From a preparative point of view it is noteworthy that, once the reactions were completed, the catalyst could be very efficiently recovered (>95% yield) by centrifugation of the reaction mixture (previously diluted with ethyl acetate) and reused without any significant change in reactivity and selectivity. For example, the same recovered catalyst was used in four subsequent oxidations of methyl *p*-tolyl sulfide and the yields of both the corresponding sulfoxide and sulfone were always found to vary in  $\pm 2\%$  range with respect to entry 3 (Table 1).

The resource saving feature of the procedure has been confirmed by repeating the set of experiments reported in Table 2 in the presence of the same batch of catalyst and we were pleased to observe no significant variation both of efficiency and reaction rate in all entries 1–8.

#### 4. Conclusion

In conclusion this new procedure for the oxidation of sulfides has shown to summarise many of the main requirements of a green process: (a) high operationally simplicity of set-up and work-up (because of the heterogeneous conditions only a filtration was required for the isolation of the products), (b) solvent-free conditions allowed rather short reaction times and, furthermore, avoiding the use of volatile, often flammable, expensive and toxic solvents strongly reduced the waste production and (c) no energy consumption (the oxidation took satisfactorily place at room temperature), no resource consumption (the polymeric catalyst could be readily recovered and reused several times).

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