

## Mn(III)-catalyzed oxidation of sulfides to sulfoxides with hydrogen peroxide

Farideh Hosseinpoor and Hamid Golchoubian\*

Department of Chemistry, University of Mazandaran, PO Box 453, Babolsar, Iran

Received 27 March 2006; revised 22 April 2006; accepted 4 May 2006

Available online 5 June 2006

**Abstract**—Sulfides were selectively oxidized to the corresponding sulfoxides in good yields with hydrogen peroxide using a manganese(III) Schiff-base complex as a catalyst in glacial acetic acid as solvent under mild conditions.

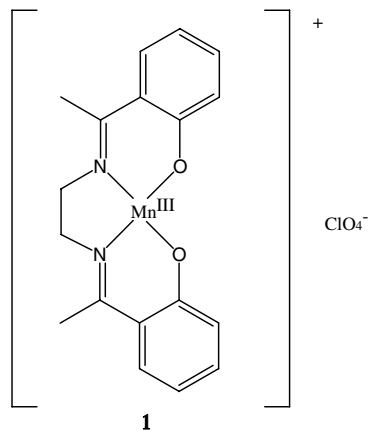
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The growing attention and applications of sulfoxides have encouraged research into new methods for their synthesis. Organic sulfoxides are valuable synthetic intermediates for the production of a range of chemically and biologically active molecules including therapeutic agents such as anti-ulcer (proton pump inhibitors),<sup>1</sup> antibacterial, antifungal, anti-atherosclerotic,<sup>2</sup> antihypertensive<sup>3</sup> and cardiotoxic agents<sup>4</sup> as well as psychotropics<sup>5</sup> and vasodilators.<sup>6</sup>

The oxidation of sulfides to sulfoxides is a straightforward synthetic method. There are several reagents and oxidative procedures available for this transformation. However, many result in over-oxidation to sulfones. Therefore, controlling the reaction conditions, that is, time, temperature and the relative amount of oxidants, plays an important role to avoid forming oxidative side products, however, these requirements are often hard to meet. Thus, there is still considerable interest in the development of selective oxidants for this transformation.<sup>7–12</sup>

Whilst the hydrogen peroxide oxidation of sulfides to sulfoxides catalyzed by several transition metal complexes has been reported,<sup>7,13,14</sup> oxidation catalyzed by Mn(III) has received less attention.<sup>15,16</sup> Hydrogen peroxide is considered as an ideal ‘green’ oxidant due to its strength and lack of toxic by-products.

In continuation of our work on the selective oxidation of hydrocarbons,<sup>17,18</sup> we report a very efficient and selective oxidation of sulfides to the corresponding sulfoxides using H<sub>2</sub>O<sub>2</sub> catalyzed by Mn(III) Schiff-base complex **1**, under mild conditions. The complex was prepared by a procedure similar to that used by Karmaker et al.<sup>19</sup> but 1,2-diaminoethane was used instead of 1,3-diaminopropane.

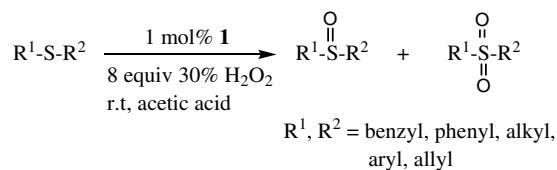


To the best of our knowledge, there is no literature report on the selective oxidation of sulfides to sulfoxides using a Mn(III) catalyst under these conditions. Oxidation of sulfides was performed at room temperature in the presence of a catalytic amount of the Mn(III) complex using 30% H<sub>2</sub>O<sub>2</sub> as the oxidant (Scheme 1) and glacial acetic acid as the solvent.<sup>20</sup>

Methyl phenyl sulfide was selected as a model substrate for optimization studies.

**Keywords:** Sulfide; Oxidation; Hydrogen peroxide; Catalyst; Selective oxidation; Mn(III) complex; Sulfoxide.

\* Corresponding author. Tel./fax: +98 1125242002; e-mail: [h.golchoubian@umz.ac.ir](mailto:h.golchoubian@umz.ac.ir)



Scheme 1.

The oxidation took place to afford methyl phenyl sulfoxide in 86% yield in the presence of **1** and 8 equiv of 30% H<sub>2</sub>O<sub>2</sub> in 25 min (Table 1, entry 1). The large excess of hydrogen peroxide required was a result of its decomposition in the presence of the Mn(III) catalyst. The oxygen released during decomposition played little role in the oxidation of the sulfides. The oxidation occurred, albeit in poor yield, by simply bubbling molecular oxygen through the reaction mixture under similar reaction conditions (Table 1, entry 2). The oxidation of methyl phenyl sulfide in various solvents was studied. Among the solvents examined, glacial acetic acid was the most effective (Table 1, entries 3–5).

Alternatively, the reaction was carried out at different temperatures under the same conditions. Although the

oxidation was complete after 25 min at elevated temperature, the selectivity decreased significantly (Table 1, entries 6–8). Further, when the oxidation of methyl phenyl sulfide was carried out using different concentrations of hydrogen peroxide, the reaction did not reach completion when using less than 8 mmol of H<sub>2</sub>O<sub>2</sub>. However, when a larger concentration was employed, neither the conversion nor selectivity of the reaction was improved (Table 1, entries 9–11). The oxidation occurred in poor yield when the reaction was carried out under similar reaction conditions, but in the absence of complex **1** (Table 1, entry 12) or when using other Mn(III) salts, such as Mn(III) acetate as the catalyst (Table 1, entry 13).

The oxidation of other sulfides such as dibenzyl, diphenyl, dialkyl, diallyl, phenyl alkyl, benzyl alkyl, benzyl phenyl, phenyl allyl and cyclic sulfides were then examined using the optimized reaction conditions (Table 2). In all cases, the reactions resulted in 100% conversion of the sulfides. In the case of benzyl sulfides (Table 2, entries 2 and 6), no oxidation was observed at the benzylic C–H bonds. Similarly, the carbon–carbon double bonds in allyl sulfides remained intact during the oxidation (Table 2, entries 5 and 9). This procedure can also be applied to the oxidation of a cyclic sulfide (Table 2, entry


Table 1. Oxidation of methyl phenyl sulfide

Entry	Complex <b>1</b> (mmol)	H <sub>2</sub> O <sub>2</sub> (mmol)	Solvent (2 mL)	Time (min)	Temp. (°C)	Conversion (%)	Sulfoxide selectivity (%) <sup>a</sup>
1	0.06	8	CH <sub>3</sub> COOH	25	25	100	86
2 <sup>b</sup>	0.06	—	CH <sub>3</sub> COOH	600	25	7	100
3	0.06	8	CH <sub>3</sub> CN	40	25	65	65
4	0.06	8	CH <sub>3</sub> NO <sub>2</sub>	30	25	100	62
5	0.06	8	CH <sub>3</sub> OH	240	25	90	79
6	0.06	8	CH <sub>3</sub> COOH	18	40	100	75
7	0.06	8	CH <sub>3</sub> COOH	7	60	100	60
8	0.06	8	CH <sub>3</sub> COOH	25	80	100	50
9	0.06	2	CH <sub>3</sub> COOH	25	25	<10	82
10	0.06	5	CH <sub>3</sub> COOH	25	25	52	75
11	0.06	10	CH <sub>3</sub> COOH	25	25	100	74
12	None	8	CH <sub>3</sub> COOH	25	25	45	100
13 <sup>b</sup>	Mn(OAc) <sub>3</sub>	8	CH <sub>3</sub> COOH	25	25	60	100

<sup>a</sup> Isolated yields.

<sup>b</sup> The reaction was carried out under an atmosphere of O<sub>2</sub> instead of in the presence of 30% H<sub>2</sub>O<sub>2</sub>.

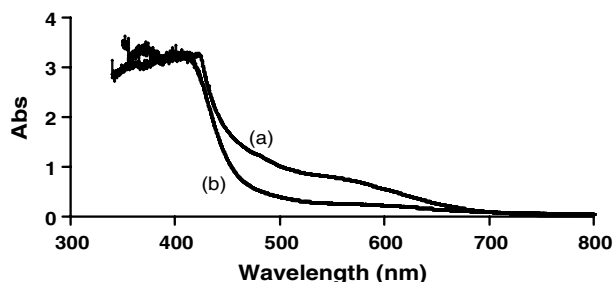
Table 2. Oxidation of sulfides to sulfoxides with hydrogen peroxide catalyzed by Mn(III) complex **1** at room temperature<sup>a</sup>

Entry	Substrate	Time (min)	Conversion (%)	Sulfoxide (%) <sup>b,c</sup>
1	Ph–S–Me	25	100	86
2	(Ph–CH <sub>2</sub> ) <sub>2</sub> S	100	100	95
3	Ph–S–Ph	35	100	91
4	Ph–CH <sub>2</sub> –S–CH <sub>3</sub>	9	100	100
5	(CH <sub>2</sub> =CH–CH <sub>2</sub> ) <sub>2</sub> S	4	100	100
6	Ph–CH <sub>2</sub> –S–Ph	19	100	84
7	(CH <sub>3</sub> –CH <sub>2</sub> –CH <sub>2</sub> ) <sub>2</sub> S	4	100	100
8	(CH <sub>3</sub> –CH <sub>2</sub> –CH <sub>2</sub> –CH <sub>2</sub> ) <sub>2</sub> S	25	100	100
9	CH <sub>2</sub> =CH–CH <sub>2</sub> –S–Ph	22	100	92
10		9	100	92
11	CH <sub>3</sub> –S–CH <sub>2</sub> –CH <sub>2</sub> –CHO	7	100	100

<sup>a</sup> 2 mmol of substrate at room temperature with 0.06 mmol of Mn(III) catalyst **1**, and 8 mmol of 30% aqueous H<sub>2</sub>O<sub>2</sub>, in glacial acetic acid (2 mL).

<sup>b</sup> Isolated yields.

<sup>c</sup> The products were identified by comparison of physical and spectroscopic properties with authentic compounds.



**Figure 1.** Spectral changes associated with the formation of a possible oxomagnesium(V) species: (a) absorption spectrum of LMn<sup>III</sup> in acetic acid; (b) spectrum of the resulting solution obtained after addition of 30% H<sub>2</sub>O<sub>2</sub> at room temperature.

10). Furthermore, the aldehyde group tolerated oxidation of methyl aldehyde sulfide (Table 2, entry 11).

The spectral changes observed (as shown typically in Fig. 1) upon addition of H<sub>2</sub>O<sub>2</sub> to the solution of catalyst complex LMn<sup>III</sup> in acetic acid, is attributed to the formation of a reactive LMn<sup>V</sup>-oxo intermediate. The spectral features noted earlier for Mn(V)-oxo complexes are comparable to those observed in the present case (Fig. 1).<sup>21–23</sup>

Large scale oxidation of methyl phenyl sulfide (10 mmol) was also investigated and the results demonstrated that oxidation took place in good yield (typically 5–10% yield was lost).

In summary, the results indicate that complex **1** is an efficient catalyst for the oxidation of sulfides to the corresponding sulfoxides with hydrogen peroxide. Although the exact mechanism of this transformation is still unclear, the catalytic system probably involves the formation of an intermediate oxo-Mn(V) complex. Moreover, this catalytic oxidation system is clean, safe and operationally simple and the yields of the products are high.

### Acknowledgements

We are grateful for the financial support of Mazandaran University of the Islamic Republic of Iran.

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- A typical experimental procedure is as follows: to the Mn(III) complex **1** (0.06 mmol) in glacial acetic acid was added the sulfide (2 mmol), then hydrogen peroxide (8 mmol, 30%) was slowly added. The reaction mixture was stirred at room temperature until TLC indicated the reaction was complete. The resulting solution was neutralized with aqueous NaOH (6 M) and the product was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and then concentrated under reduced pressure to yield a residue, which was passed through a short pad of silica gel using ethyl acetate and hexane (1:1) as eluent to provide analytically pure product.
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