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Copper catalyzed oxidation of sulfides to sulfoxides with aqueous hydrogen peroxide

Subbarayan Velusamy, Akkilagunta V. Kumar, Rakesh Saini and T. Punniyamurthy*

Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati 781039, India

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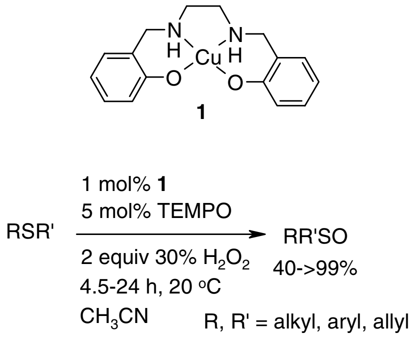
Abstract—Copper(II) complex **1** catalyzes the oxidation of sulfides to sulfoxides with 30% H_2O_2 in high yields. Addition of a catalytic amount of TEMPO to the reaction mixture enhances the conversion and selectivity. Complex **1** can be recycled without loss of activity.

Synthetic building blocks containing sulfoxide functional groups are particularly useful for the construction of various important compounds.[1] These derivatives are usually prepared by oxidation of sulfides and several oxidative procedures are applicable for this transformation.[2–4] Generally, it is important to stop the oxidation at the sulfoxide stage by controlling the electrophilic character of the oxidant, but this requirement is often hard to meet and failure results in over oxidation to sulfones. Thus, there is still considerable interest in the development of selective oxidants for this important transformation.[5] We have recently reported that copper(II) complex **1** catalyzes the oxidation of alkanes and alcohols to the corresponding carbonyl compounds in the presence of 30% H_2O_2.[6] Complex **1** is water soluble and catalyzes oxidations without additives generating water as the only by-product, and does not require halogenated solvents.[7] In continuation of our studies on the oxidation of organic compounds,[8] we report herein the oxidation of sulfides to sulfoxides using complex **1** in the presence of 30% H_2O_2 in high yields (Scheme 1). The addition of TEMPO to the reaction mixture increases the selectivity and conversion. To the best of our knowledge, this is the first report on the oxidation of sulfides with a copper catalyst which is recyclable without loss of activity.



Scheme 1.

The oxidation of methyl phenyl sulfide, as a standard substrate, was first studied in the presence of copper(II) complex **1** and 30% aqueous H_2O_2 at ambient temperature (Table 1, entries 1, 3, and 4). We were pleased to find that the oxidation occurred to afford a 8:1 mixture of sulfoxide and sulfone in 70% yield in the presence of 1 mol % of the complex **1** and 2 equiv of 30% H_2O_2 in acetonitrile. Addition of 3 mol % TEMPO to the reaction mixture led the oxidation to a 17:1 mixture of sulfoxide and sulfone in 90% yield. The selectivity and conversion of the sulfoxide were further increased to >99% when the amount of TEMPO was increased to 5 mol %. A control experiment without complex **1** provided the sulfoxides in only 5% yields and no sulfone was observed (entry 2). These studies suggest that complex **1** together with TEMPO catalyzed the oxidation of sulfide to the sulfoxide in the presence of 30% H_2O_2.

Keywords: Oxidation; Sulfide; Hydrogen peroxide; CuSalenH_4; TEMPO.

* Corresponding author. Tel.: +91 361 2691083; fax: +91 361 2690762; e-mail: tpunni@iitg.ernet.in

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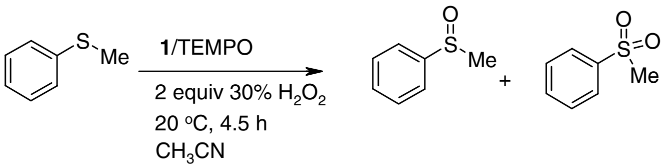
Table 1. Oxidation of methyl phenyl sulfide[a]



Entry	Complex **1**	TEMPO	Conversion (%)[b]	Sulfoxide (%)[b]	Sulfone (%)[b]
1	1 mol %	None	70	89	11
2	None	5 mol %	5	>99	—
3	1 mol %	3 mol %	90	94	6
4	1 mol %	5 mol %	>99	>99	—
5[c]	Recovered	5 mol %	>99	>99	—

[a] Substrate (5 mmol), complex **1** (1 mol %), TEMPO (5 mol %) and 30% H_2O_2 (10 mmol) were stirred for 4.5 h at 20 °C in CH_3CN (2 mL).
[b] Determined from 400 MHz ^1H NMR of the crude product.
[c] Recovered copper(II) complex was used.

Table 2. Copper(II) complex **1** and TEMPO catalyzed selective oxidation of sulfides to sulfoxides with 30% H_2O_2[a]

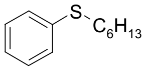
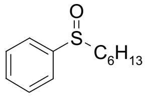
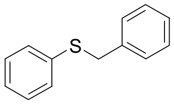
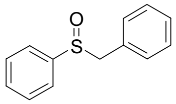
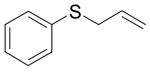
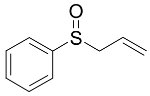
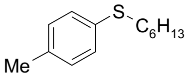
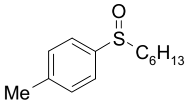
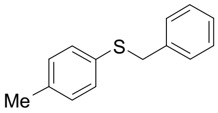
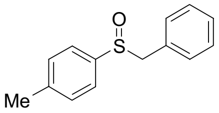
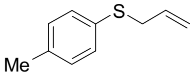
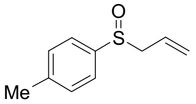
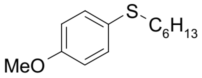
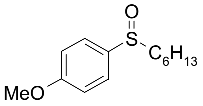
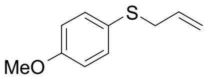
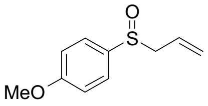
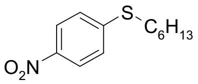
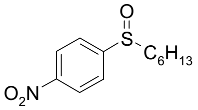
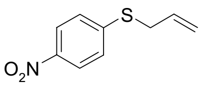
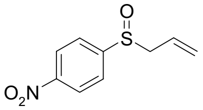
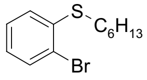
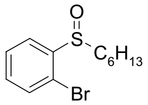
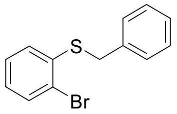
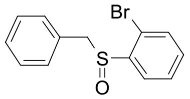
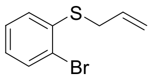
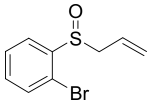
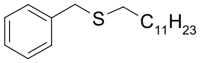
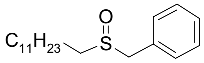
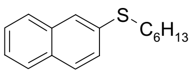
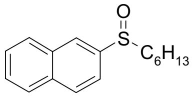
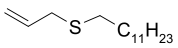
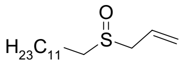
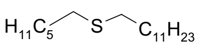
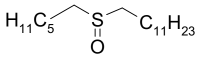
Entry	Substrate	Time (h)	Sulfoxide	Yield (%)[b,c]
1		15		83
2		20		52
3		11		92
4		16		89
5		21		57
6		14		96
7		15		87
8		11		94
9		23		51
10		22		71
11		23		51

Table 2 (*continued*)

Entry	Substrate	Time (h)	Sulfoxide	Yield (%)[b,c]
12		22		48
13		23		69
14		21		54
15		24		40
16		23		62
17		24		48[d]

[a] Substrate (5 mmol), complex **1** (1 mol %), TEMPO (5 mol %) and 30% H_2O_2 (10 mmol) were stirred in acetonitrile (2 mL) at 20 °C. The identity of the products was ascertained by ^{1}H and ^{13}C NMR, mass, IR and elemental analysis.

[b] Isolated yield.

[c] No sulfone was observed.

[d] Accompanied by sulfone <2%.

To study the scope of this procedure, the oxidation of other sulfides was studied (Table 2).[9] A series of substrates, aryl alkyl, aryl allyl and dialkyl sulfides, could be oxidized to the corresponding sulfoxides. The reactivity and conversion were dependent on the nature of the substituents. In the case of allyl sulfides, no oxidation was observed at the carbon–carbon double bond. Similarly, benzylic sulfides could be oxidized to the corresponding sulfoxides without affecting the benzylic C–H bond. Dialkyl sulfides were moderately reactive providing the corresponding sulfoxide. These oxidations could usually be stopped at the sulfoxide stage without over oxidation to the sulfone.

To study the recyclability of complex **1**, the oxidation of methyl phenyl sulfide was examined. After completion of the reaction, acetonitrile was evaporated under reduced pressure to provide an aqueous residue which was treated with ethyl acetate and water (3:1). The organic layer, after drying (Na_2SO_4) and HPLC analysis (>99% conversion), was evaporated under reduced pressure to provide a residue which was passed through a short pad of silica gel using ethyl acetate and hexane to give analytically pure sulfoxide. Evaporation of the aqueous layer afforded the copper salt, which was reused for the oxidation of methyl phenyl sulfide in the presence of 5 mol % of fresh TEMPO and 2 equiv of 30% H_2O_2 in acetonitrile (Table 1, entry 5). As above, the oxidation occurred to provide methyl phenyl sulfoxide suggesting that complex **1** is recyclable without loss of activity.

In conclusion, the oxidation of sulfides to sulfoxides is described using copper(II) complex **1** and TEMPO in the presence of 30% aqueous H_2O_2 at ambient temperature. The addition of TEMPO enhances the sulfoxide selectivity and yield. From an environmental and economic standpoint, this procedure provides a simple method for the formation of sulfoxides from sulfides.

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9. To a stirred solution of sulfide (5 mmol), complex **1** (1 mol %) and TEMPO (5 mol %) in acetonitrile (2 mL) at ambient temperature (20 °C), 30% aqueous H_2O_2 (10 mmol) were added. The progress of the reaction was monitored by TLC. After completion, the aqueous acetonitrile was removed on a rotary evaporator under reduced pressure and the residue was partitioned between ethyl acetate and water (3:1). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to yield a residue which was passed through a short pad of silica gel using ethyl acetate and hexane as eluent to provide analytically pure sulfoxide. Evaporation of the aqueous layer provided the copper(II) complex which could be recycled without loss of activity.