

# Microwave Assisted Rapid, Efficient and Chemoselective Deoxygenation of Sulfoxides to Thioethers Using Zn/AcOH on Silica Gel

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**ABSTRACT:** *Zn/AcOH on silica gel converts a range of structurally different sulfoxides to their corresponding thioethers in excellent yields under microwave irradiation. It has been found that chemoselective deoxygenation of sulfoxides can be achieved in the presence of other reducible functional groups such as acetals, acids, amides, esters, ketones and nitriles.*

**KEY WORDS:** *Deoxygenation, Sulfoxide, Thioether, Silica gel, Microwave (MW).*

## INTRODUCTION

Sulfoxides are important intermediates in a variety of synthetic transformations, especially as chiral auxiliary in asymmetric synthesis [1-3]. This accordingly demands new techniques for removal of the residual sulfoxide moiety to generate the corresponding sulfide [4-7], which could be further reduced by treatment with raney nickel or with a reducing metal system such as lithium in liquid ammonia [1-3,8]. Deoxygenation of sulfoxides to corresponding thioethers are an active route in chemical research in recent years [9-12].

The uses of low valent oxophilic d-block metals have become important in deoxygenation of various types of organic substrates [13]. There are many available methods for the conversion of sulfoxides to sulfides by low valent metals as actual deoxygenating species. The examples are acetic anhydride or N,N-dimethyl carbamoyl chloride / DMAP / Zn [14], TiCl<sub>4</sub>/LiAlH<sub>4</sub> [15], TiCl<sub>4</sub>/Zn [16], TiCl<sub>4</sub>/NaI [17], CrCl<sub>2</sub> [18], K<sub>3</sub>W<sub>2</sub>Cl<sub>6</sub> in aqueous

methanol [19], MoOCl<sub>3</sub>/Zn, VCl<sub>2</sub> [20], SnCl<sub>2</sub> [21], WCl<sub>6</sub>-Zn and WCl<sub>6</sub>-NaI [12], Ph<sub>3</sub>P/ TiCl<sub>4</sub> [9], PMHS/MoO<sub>2</sub>Cl<sub>2</sub>(H<sub>2</sub>O)<sub>2</sub> [10], Woollins' reagent [11] and etc.

Although there are a good number of methods available for the deoxygenation of sulfoxides to thioethers, there still remain the important problems of reaction i.e. many of them need drastic conditions and / or long reaction time. Therefore, a search for new improved methods based on readily available reagents is still pursued. Many reactions proceed efficiently in the solid state [22]. Indeed, in many cases, solid-state organic reactions occur more efficiently and more selectively than do their solution counterparts, since molecules in a crystal are arranged tightly and regularly. Furthermore, the solid state reactions (or solvent-free reactions) have many advantages: simplicity in process, reduced pollution, low costs and handling. These factors are especially important in industry.

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Microwave (MW) activation as a non-conventional energy source has become a very popular and useful technology in organic chemistry [24]. The number of annual publications on microwave assisted organic chemistry is growing rapidly with more than one thousand publications in print since the first work was reported by Gedye [25] in 1986. Most of these publications describe important accelerations for a wide range of organic reactions especially when carried out under solvent-free conditions. The combination of solvent-free reaction conditions and microwave irradiation leads to large reductions in reaction times, enhancement in conversions and, sometimes [24, 26], in selectivity with several advantages of the eco-friendly approach, termed green chemistry.

## EXPERIMENTAL

All of the experiments are carried out in a domestic conventional microwave oven, in a high efficient hood cupboard. All yields refer to isolated pure products. Chemicals were either prepared in our laboratory or were purchased from Aldrich, Fluka, BDH and Merck chemical companies. In all the experiments Merck silica gel 60 F<sub>254</sub> (mesh, 63-200) was used as solid support. Most of products were purified by column chromatography or recrystallization and were identified by IR and NMR spectra. The melting points (uncorrected) were measured with an Electrothermal engineering LTD 9100 apparatus. IR spectra were measured on a Perkin-Elmer model 543, The <sup>1</sup>H NMR spectra run on Hitachi perkin 24RB 60 MHz instrument.

## RESULTS AND DISCUSSION

The use of Zn/AcOH reagent for deoxygenation of sulfoxides to thioethers was reported in literature [27]. In this article we have developed this reaction under microwave irradiation without solvent and in the presence of silica gel (SiO<sub>2</sub>, 60, mesh 63-200) as solid support.

This reaction was performed efficiently in good to excellent yields. The yields were higher and the time length for completion of the reactions were lower than that of reported procedures and the work up was simple. In this procedure the reactions were carried out without solvent as environment friendly procedures.

Inspection of the data which are summarized in table 1, shows that the method of this study are well applicable to selective reduction of a variety of structurally

different sulfoxides to their corresponding thioethers in good to excellent yields. Efficient deoxygenation of sulfoxides in the presence of several functional groups (chemoselectivity) shows the usefulness of the presented method in organic synthesis (table 2). The mechanism of reduction process is shown in Fig. 1. It is noteworthy that the acetal group is not cleaved in the presence of other compounds containing sulfoxide group such as entry 6. The same result is obtained while the reduction of sulfoxide group is performed in the presence of other active functional groups such as -CO<sub>2</sub>H (entry 1), -CO<sub>2</sub>Me (entry 2), etc. In summary, we have demonstrated that Zn / AcOH / SiO<sub>2</sub> under microwave irradiation in the absence of solvent (Minimum of AcOH absorbed on the SiO<sub>2</sub>) is an inexpensive and excellent conditions for rapid deoxygenation of a variety of structurally diverse sulfoxides to their corresponding sulfides. This procedure shows good chemoselectivity and the reaction conditions, applications and handling are simple. Further applications of this reagent(s) are currently in progress in our laboratory.

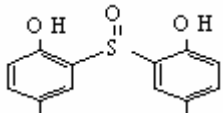
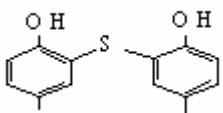
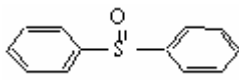
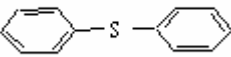
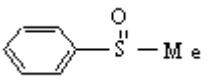
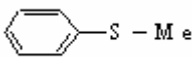
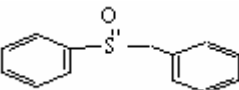
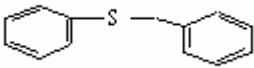
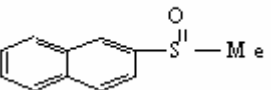
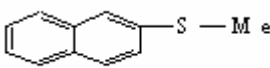
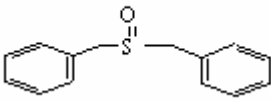
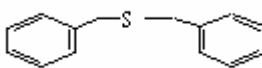
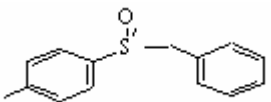
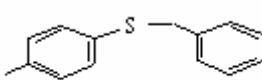
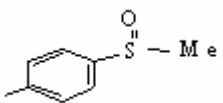
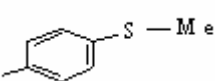
### *Microwave Assisted Deoxygenation of Sulfoxides to Thioethers Using Zn / AcOH / SiO<sub>2</sub>*

#### **Typical Procedure**

A mixture of SiO<sub>2</sub> (60, 0.3g) and 2,2'-sulfinyl-bis (4-methylphenol) [18-20] (0.262g, 1 mmol) (table 1, entry 1) and Zn powder (0.3g) were grinded and poured into a tube then AcOH (1ml) was added and the mixture was irradiated in microwave oven in 900 W for 10 sec. The progress of the reaction was monitored by TLC. The mixture was cooled to the room temperature and the irradiation was repeated. After cooling again to the room temperature, Zn powder (0.2 g) and AcOH (1ml) were added, after mixing, the new mixture was irradiated twice. Finally, after a rest time, the resulting solid was powdered and washed with 100ml (2×50 ml) of acetone. The combined acetone layers were dried (Na<sub>2</sub>SO<sub>4</sub>) evaporated and recrystallized from toluene/AcOH to afford corresponding sulfide in 91 % yield and melting point 114-115 °C. IR (KBr) 3200-3400, 2900-3100, 1800, 1480, 1200, 600 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz, Acetone-d<sub>6</sub>) δ 1.9 (s, 6H), 6.5-7 (m, 6H), 8.1 (s, 2H); X-ray [28].

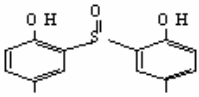
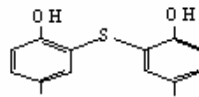


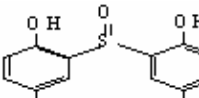
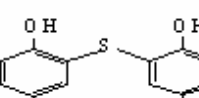


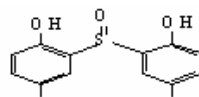
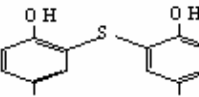


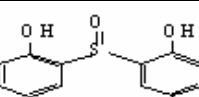
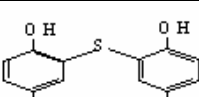


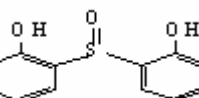
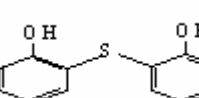


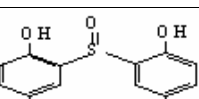
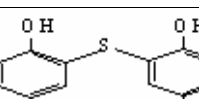


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Table 1: Microwave-assisted deoxygenation of sulfoxides to thioethers using Zn /AcOH /SiO<sub>2</sub>.

$R_1 - \overset{\text{O}}{\parallel} S - R_2 \xrightarrow[\text{SiO}_2 / \text{MW}]{\text{Zn} / \text{AcOH}} R_1 - S - R_2$ <p style="text-align: center;">40 Sec.</p>			
Entry	Substrate	Product	Yield <sup>a</sup> (%)
1			91 <sup>28-32</sup>
2			92 <sup>33-36</sup>
3			89 <sup>34-36</sup>
4			91 <sup>34-36</sup>
5			93 <sup>37-39</sup>
6			94 <sup>33-36</sup>
7			87 <sup>36</sup>
8			89 <sup>33-36</sup>
9	$n\text{-Bu} - \overset{\text{O}}{\parallel} S - n\text{-Bu}$	$n\text{-Bu} - S - n\text{-Bu}$	97 <sup>33-36</sup>

a) Isolated yields.

Table 2: Chemoselective deoxygenation of sulfoxides to thioethers.

Entry	Substrate	Product	Yield <sup>a</sup> (%)
1			91
			0
2			90
			0
3			93
			0
4			89
			0
5			94
			0
6			91
			0

a) Isolated yields.

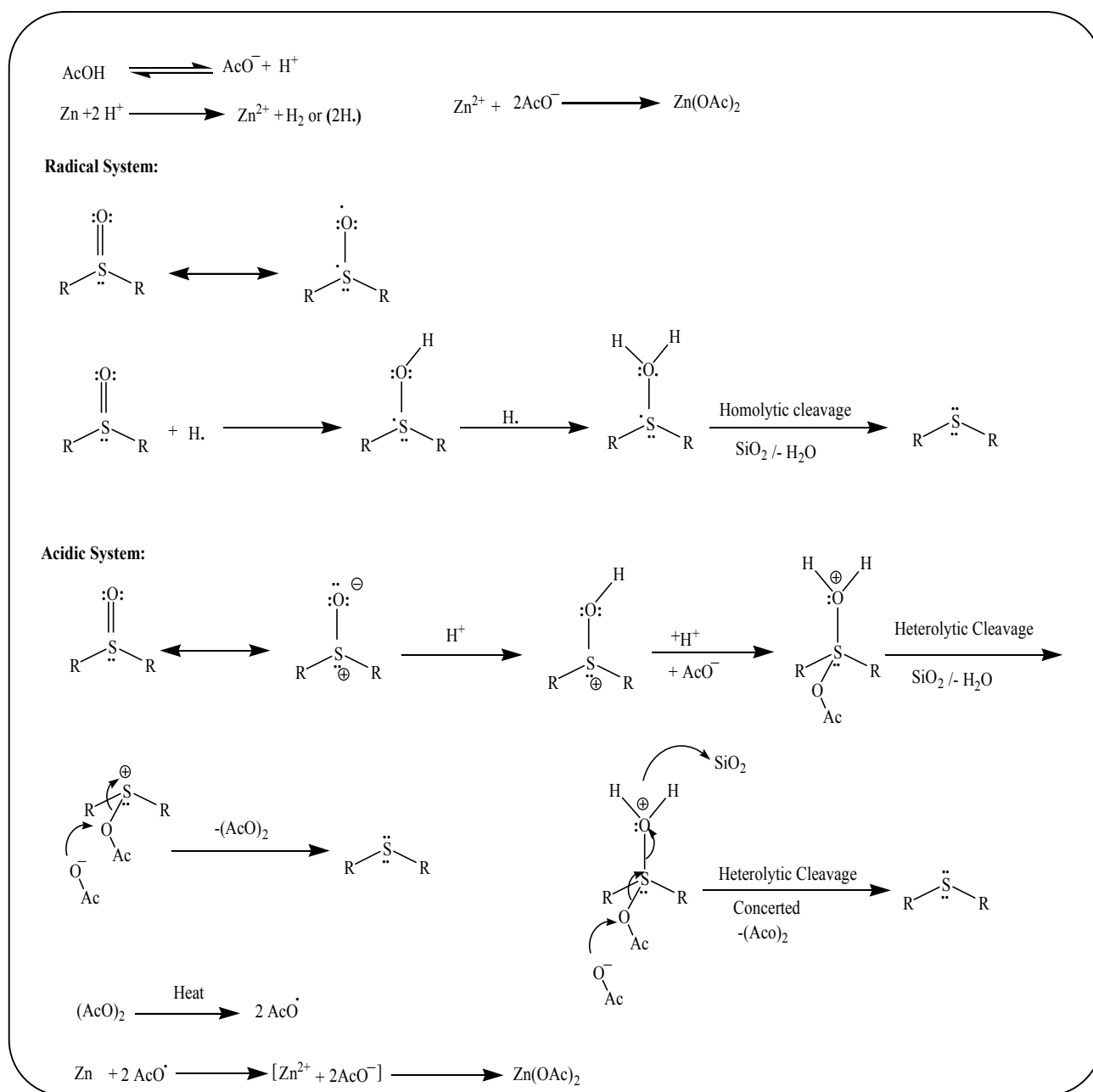


Fig. 1: Mechanism of the deoxygenation reaction.

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