

# A Solvent Free Route to the Synthesis of Diaryl Sulfoxides

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**ABSTRACT:** *The solvent free route for the synthesis of diaryl sulfoxides from arenes and thionyl chloride in the presence of Lewis acids such as aluminum chloride and ferric chloride on silica gel are described.*

**KEY WORDS:** *Diaryl sulfoxide, Solvent-free, Synthesis, Friedel-Crafts, Green chemistry.*

## INTRODUCTION

Sulfoxides and sulfones have fascinated organic chemists for a long time owing to their varied reactivity as a functional group for transformation into a variety of organo sulfur compounds. These transformations are useful for the synthesis of drugs and sulfur-substituted natural products[1].

Optically active [2] sulfoxides continue to deserve much attention as important chiral auxiliaries in asymmetric synthesis [3] and in C-C bond forming reactions [4]. The synthesis of diaryl sulfoxides also provide a convenient route to triarylsulfonium salts [5] which are used as photoactive cationic initiators [6] and for the photogeneration of protonic acids in the lithographic resist field [7].

Methodologies for the direct synthesis of sulfoxides are rarely observed in the literature [8,19]. Oxidation of the sulfides is a very useful route for preparation of the sulfoxides. Several methods are available for conversion of sulfides to sulfoxides [9]. However, some of the existing methods use sophisticated reagents, complex catalysts, toxic metallic compounds, or rare oxidizing reagents that are difficult to prepare [9a-n]. Otherwise

overoxidation of sulfides resulting in sulfone formation and undesired reactions of other functional groups are common problems, particularly when preparing biologically relevant sulfoxides [9r].

Other routes for the synthesis of sulfoxides are indirect reduction of sulfones [10] and by the reaction of organometallic reagents with sulfinic acid esters, mixed anhydrides or sulfines. A direct method for the synthesis of diaryl sulfoxides is the Friedel-Crafts sulfonylation of arenes using a catalysts such as AlCl<sub>3</sub> [11] or trifluoromethane sulfonic acid [12]. Sulfoxide synthesis is also achieved by dehydration of arenes and SO<sub>2</sub> mediated by magic acid (FSO<sub>3</sub>H / SbF<sub>5</sub>) [13]. Several recent reports on sulfoxide synthesis include their formation from thionyl chloride and arenes employing trifluoromethane sulfonic acid [14] or scandium triflate [15] as the catalyst. The direct preparation of sulfoxides often suffers from the formation of mixtures of products containing sulfonium salts and chlorinated by-products along with the desired sulfoxides [16]. Therefore, there is a need for a simple, less expensive, and safer method for the synthesis of sulfoxides.

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*1021-9986/05/3/47*

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Many reactions proceed efficiently in the solid state [17]. Indeed, in many cases, solid-state organic reaction occurs more efficiently and more selectively than does its solution counterpart, since molecules in a crystal are arranged tightly and regularly.

Furthermore, the solid state reaction (or solvent - free reaction) has many advantages: reduced pollution, low costs and simplicity in process and handling. These factors are especially important in industry.

## EXPERIMENTAL

All of the experiments were carried out in a high efficient hood cupboard. All yields refer to the isolated pure products. Chemicals were purchased from Aldrich, Fluka, BDH and Merck chemical companies and applied without further purification. In all the experiments silica gel 60 F<sub>254</sub> (mesh 63-200), Merck was used as solid support. Products were purified by column chromatography or recrystallization and were identified by IR and <sup>1</sup>H NMR spectra, and melting point. GC-MS analysis (Table 2) were performed with Shimadzu GC-MS-QP 1100 EX model. Melting points were recorded on Electro-thermal Engineering LTD 9100 apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 543 spectrophotometer. The <sup>1</sup>H NMR spectra run on Hitachi-perkin 24RB 60 MHz instrument.

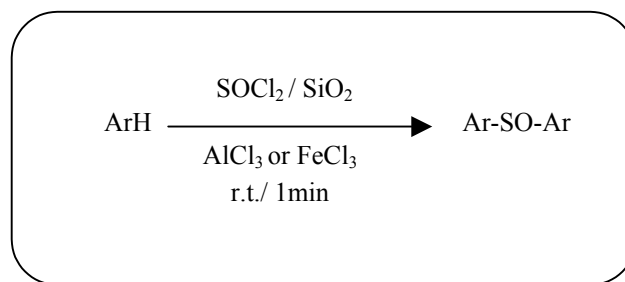
### Solvent-Free Synthesis of Diaryl Sulfoxides

#### Typical Procedure

To a homogenized mixture of p-cresol (0.22 g, 2 mmol), silica gel (60, 0.20 g) and AlCl<sub>3</sub> (0.28 g, 2 mmol) was added thionyl chloride (0.16 ml, 1 mmol). After mixing and grinding for one minute (the progress and completion of the reaction was monitored by TLC), HCl 10% (30 ml) was added (decomposition of complex between Lewis acid and arene) and the resulting precipitate was filtered off. The crude product was recrystallized from ethanol to afford sulfoxide in 85 % yield and melting point 194 -195 °C (Lit.[8a,b] 191-192 °C). IR (KBr) 3200, 1600, 1520, 1250, 1050 cm<sup>-1</sup>; <sup>1</sup>H NMR (60 MHz, acetone - d<sub>6</sub>, ppm) δ 1.8 (s, 6H), 6.35 (d, j = 6 Hz, 2H), 6.7 (d, j = 6 Hz, 2H), 7.0 (s, 2H), 9.3 (s, 1H).

## RESULTS AND DISCUSSION

In continuation of our research to explore new reactions in the solvent-free conditions, we thought it



**Scheme 1:** Synthesis of diaryl sulfoxides from arenes and thionyl chloride in the solid-state.

would be worthwhile to investigate the direct synthesis of diaryl sulfoxides in these conditions. We report herein, for the first time, the synthesis of diaryl sulfoxides by the reaction of thionyl chloride with arenes in the solid-state (Scheme 1).


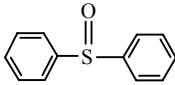
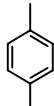
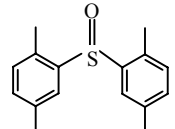
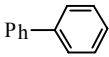
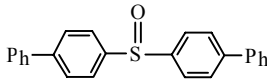
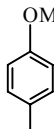
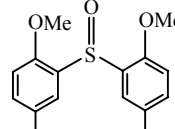
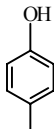
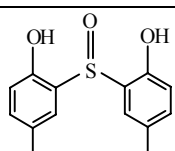
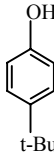
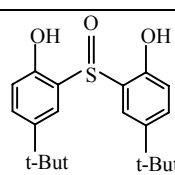
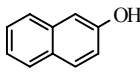
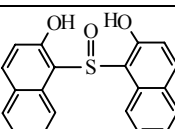
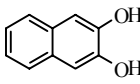
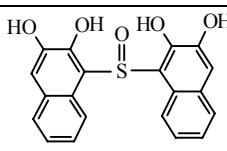
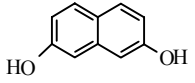
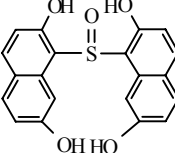

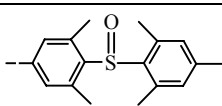
Initially, the synthesis of sulfoxides on SiO<sub>2</sub> in the presence of Lewis acids such as AlCl<sub>3</sub> and FeCl<sub>3</sub> was investigated by grinding the mixtures of reactants at room temperature (Table 1). No reaction was observed in these conditions in the absence of Lewis acid. Only Lewis acids gave us positive results (Mechanism of the reaction in Scheme 2). To generalize the procedure, the reactions were carried out on different arenes. High yields were obtained in almost all cases when the arene, thionyl chloride and Lewis acid were used in the molar ratio which are represented in Tables 1 and 2. The solid-state provided drastic reduction in reaction time. Exclusively a single product was obtained with arenes such as those illustrated in Table 1.

To evaluate the effect of substituents on the isomer distribution of product, we have carried out reactions with mono and unsymmetric disubstituted arenes under the same reaction conditions (Scheme 1). As evident from the results, in all cases the major product was the p, p'-disubstituted sulfoxide, with smaller amounts of o, p- and o, o'- products, respectively (Table 2).

When p-nitrophenol, p-chlorophenol, hydroquinone, nitrobenzene and acetophenone were used, the corresponding sulfoxide was not observed. In addition, when Al<sub>2</sub>O<sub>3</sub> was used as solid support, lower yields of sulfoxides were obtained in all the reactions. Also, when these reactions were carried out under microwave irradiation no reliable difference was observed in the yields of sulfoxides (data are not reported).

In conclusion, the solid-states are useful medium for

Table 1: Synthesis of diaryl sulfoxides in solvent-free conditions.

Entry <sup>c</sup>	Y <sup>d</sup>	Substrate	Product	Yield <sup>a</sup> (%)	
				AlCl <sub>3</sub>	FeCl <sub>3</sub>
1 <sup>19a</sup>	2:1:2			88	91
2 <sup>19b</sup>	2:1:2			89	95
3 <sup>8d</sup>	2:1:2			81	85
4	2:1:2			82	86
5 <sup>8a,b</sup>	2:1:2			85 <sup>c</sup>	b
6	2:1:2			71 <sup>c</sup>	b
7	1:1:1			86	b
8	1:1:1			88	b
9	1:1:1			85	b
10 <sup>8d,19a</sup>	2:1:2			91	96

a) Isolated yields ; b) See reference [18]; c) A trace of oxidative coupling of phenols were formed [18];

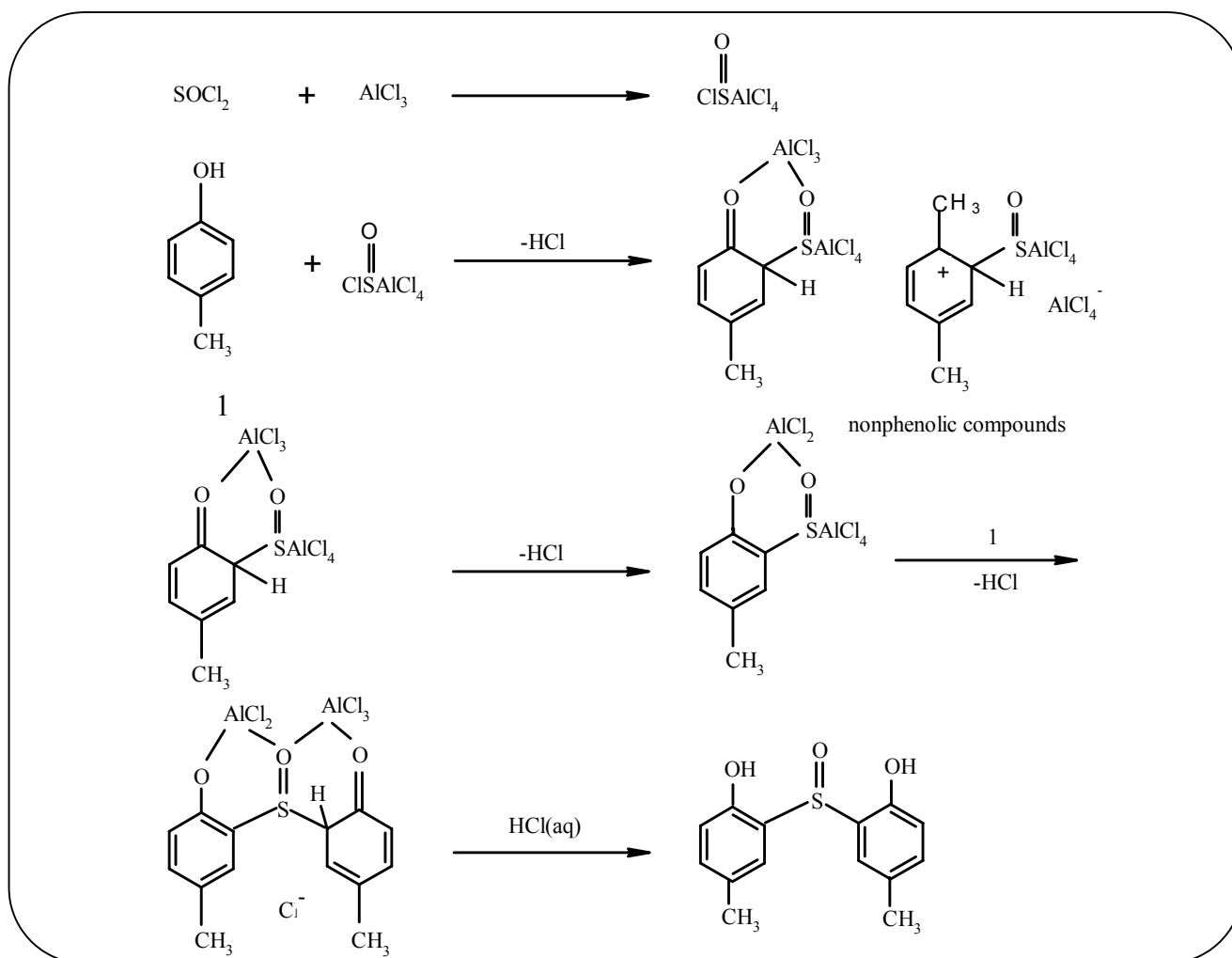
d) Y = Substrate / Thionyl chloride / Lewis acid (mmol); e) References of products.

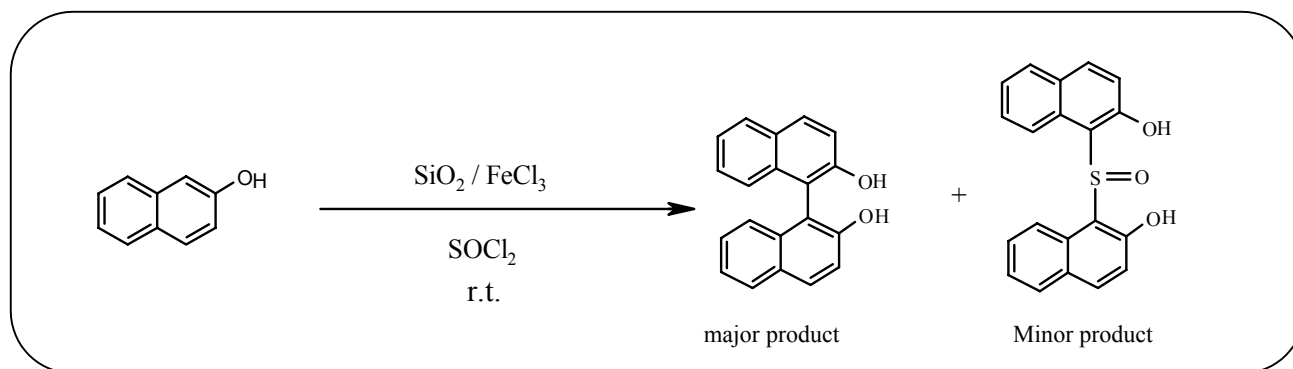
**Table 2: The effects of substituents in the mono- and disubstituted arenes on the isomer distribution of diaryl sulfoxides.**

Substrate <sup>d</sup>	Y <sup>c</sup>	Yield <sup>a</sup> % (AlCl <sub>3</sub> )				Yield <sup>a</sup> % (FeCl <sub>3</sub> )			
		p,p'-	o,p-	o,o'-	Total	p,p'-	o,p-	o,o'-	Total
Toluene <sup>8d, 19a,e</sup>	2:1:2	65	28	5	98	55	32	4	91
Bromobenzene <sup>19c,f</sup>	2:1:2	50	35	5	90	97.5	1	0.5	99
Chlorobenzene <sup>19d,f</sup>	2:1:2	67	27	5	97	94	2	1	92
m-Xylene <sup>8d, 19a</sup>	2:1:2	72	18	1	91	73	15	4	92
Phenol <sup>8d</sup>	1:1:1	55	33	5	93	b	b	b	b
Catechol	1:1:1	50	30	6	86	b	b	b	b
Resorcinol <sup>19g</sup>	1:1:1	60	28	4	92	b	b	b	b

a) The % of p,p'-, o,p- and o,o'- diaryl sulfoxides were determined by GC-MS [8d]; b) See reference [18];

c) Y = Arene / Thionyl chloride / Lewis acid (mmol); d) References of products.

**Scheme 2: Mechanism of the reaction.**



Scheme 3

the synthesis of diaryl sulfoxides employing arenes and thionyl chloride. The experimental procedure is simple and time saving. Further investigations on the synthesis of asymmetric diaryl sulfoxides, sulfones and sulfides in the solid-state are underway, sulfones and sulfides in the solid-state are underway.

Received: 6<sup>th</sup> October 2004 ; Accepted : 1<sup>st</sup> February 2005

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