

## An Efficient and New Method on the Oxidative Coupling of Thiols under Mild and Heterogeneous Conditions

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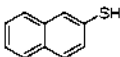
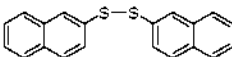
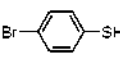
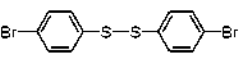
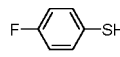
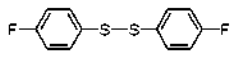
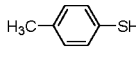
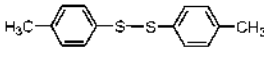

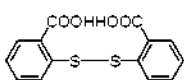
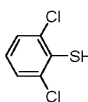
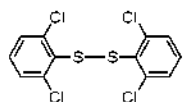
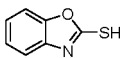
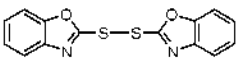
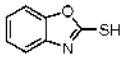
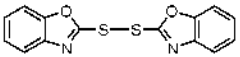
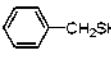
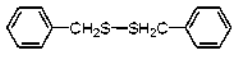
**Key Words:** Thiols, Disulfides, Aluminum nitrate {Al(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O}, Silica sulfuric acid (SiO<sub>2</sub>-OSO<sub>3</sub>H), Heterogeneous

The conversion of thiols to the corresponding disulfides is an important reaction in biological and chemical processes.<sup>1</sup> Oxidation of thiols to disulfides without over-oxidation is an important process in organic synthesis, which has been extensively investigated over the years.<sup>2</sup> Disulfides have found industrial applications as vulcanizing agents and are

important synthetic intermediates with many applications in organic synthesis.<sup>3</sup> Thiols and disulfides are important in living cells being a structural feature of many biomolecules including proteins. In many biochemical redox reactions they are interconverted.<sup>4</sup>

The use of heterogeneous conditions for the organic

**Table 1.** Oxidative coupling of thiols to the corresponding disulfides using combination of Al(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O **I** and silica sulfuric acid **II** in dichloromethane at room temperature.

Entry	Substrate	Product	Time (Min)	Yield (%) <sup>d</sup>	M. P. (°C)	Ref.
1			70	99	142.2-143.5	2,24
2			165	99	87.1-89.4	2,24
3			55	98	oil	24
4			100	98	37.7-39.5	2,24
5			160	97	278-280	2
6			175	99	78.9-89.2	24
7			50	98	77.5-79	24
8			6 h	No reaction <sup>e</sup>	---	---
9			160	64	65-66.1	1,2,4
10	HSCH <sub>2</sub> COOH	HOOCCH <sub>2</sub> S—SCH <sub>2</sub> COOH	155	99	oil	2,15

<sup>a</sup>substrate : **I** : **II** = 1 mmol : 1.1 mmol : 0.2 g. <sup>b</sup>Isolated yield. <sup>c</sup>In the absence of silica sulfuric acid



Scheme 1



Scheme 2

reactions has been attracted much attention in order to reduce waste, thus to develop an environmentally benign chemical process. In recent years, a range of heterogeneous agents have successfully been used to carry out various chemical transformations;<sup>5-10</sup> however, environmental and economical constraints mean that there is still an urgent need to redesign and improve these important processes. Even though several reports for the coupling of thiols have appeared in the recent years,<sup>11-16</sup> unfortunately, some of these reagents are not satisfactory because of several reasons such as overoxidation to sulfoxides and other by-products, low selectivity, low yields of products, toxicity, and expensive reagents or catalysts.

In continuation of our recent studies on the application of new reagents on the organic transformations,<sup>17-22</sup> we became interested to introduce in a new heterogeneous media for the oxidative coupling of thiols by treating aluminum nitrate nine hydrate ( $\text{Al(NO}_3)_3 \cdot 9\text{H}_2\text{O}$ ) and silica sulfuric acid ( $\text{SiO}_2\text{-OSO}_3\text{H}$ ) in dichloromethane as solvent at room temperature.

Initially, we prepared silica sulfuric acid as a non-toxic, powerful and solid source of proton via reported procedure by Zolfigol *et al* (Scheme 1).<sup>23</sup>

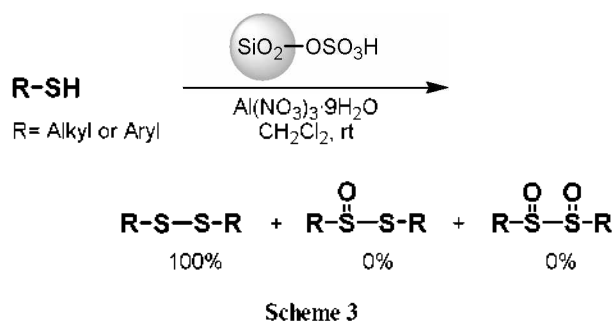
Consequently, we delineated a new heterogeneous and mild protocol for the selective coupling of different types of thiols to the corresponding disulfides using  $\text{Al(NO}_3)_3 \cdot 9\text{H}_2\text{O}$  **I** and  $\text{SiO}_2\text{-OSO}_3\text{H}$  **II** in dichloromethane at room temperature with good to excellent yields (Scheme 2 and Table 1).

The coupling reaction was performed under completely heterogeneous conditions at room temperature with high yields. The mixing of the  $\text{Al(NO}_3)_3 \cdot 9\text{H}_2\text{O}$ ,  $\text{SiO}_2\text{-OSO}_3\text{H}$  and a thiol in dichloromethane and stirring the resulting heterogeneous mixture at room temperature can selectively produce corresponding disulfide. Consequently, pure products can be easily obtained by simple filtration and evaporation of reaction solvent. Because of mild conditions of described heterogeneous system, there is no overoxidation was observed (Scheme 3).

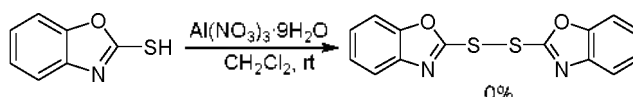
To show the role of silica sulfuric acid as a source of proton in the described system 2-mercaptobenzoxazole, as a typical example, we performed the coupling reaction without  $\text{SiO}_2\text{-OSO}_3\text{H}$ , however the reaction didn't occur after 6 hours (Table 1, entry 8 and Scheme 4).

A suggested mechanism of this oxidation is outlined in Scheme 5 based on our previously reported papers,<sup>7,8,10,21,22</sup> our observations and obtained results.

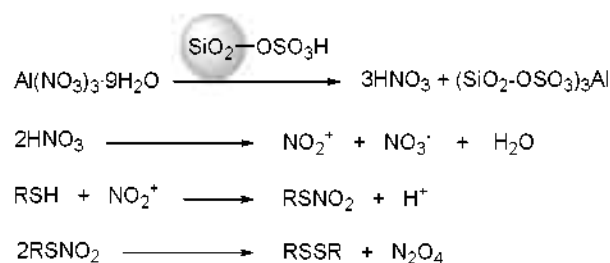
In summary, herein we report an efficient protocol for the



Scheme 3



Scheme 4



Scheme 5

selective oxidative coupling of thiols to the disulfides under mild and heterogeneous conditions. Also chemoselectivity, the cheapness and availability of the reagents, easy and clean work-up and high yields make this method attractive for chemists.

## Experimental

**General.** The chemicals and solvents were supplied by Fluka, Merck and Aldrich chemical companies without further purifications. The products were characterized by comparison of their spectral (IR, <sup>1</sup>H NMR, and <sup>13</sup>C NMR) and physical data with authentic samples.

**Coupling of 2-naphthylthiol to 1,2-di(naphthalen-2-yl)-disulfane: As a typical procedure.**  $\text{Al(NO}_3)_3 \cdot 9\text{H}_2\text{O}$  (0.412 g, 1.1 mmol) and silica sulfuric acid (0.2 g) was added to a solution of 2-naphthylthiol (0.160 g, 1 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL). The resulting reaction mixture was stirred at room temperature for 70 min (the reaction progress was monitored by TLC) and then filtered. The residue was washed with  $\text{CH}_2\text{Cl}_2$  (4 × 5 mL). Finally  $\text{CH}_2\text{Cl}_2$  was removed and 1,2-di(naphthalen-2-yl)disulfane was obtained in 99% yield (0.315 g). White solid; mp 142.2-143.5 °C; <sup>1</sup>H NMR (90 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.23-7.98 (m); IR (KBr):  $\bar{\nu}$  3020, 1585, 1497, 1342, 1215, 757, 669  $\text{cm}^{-1}$ .

**Spectral data for selected products.** **1,2-Bis(4-bromophenyl)disulfane:** White solid; mp 87.1-89.4 °C; <sup>1</sup>H NMR (90 MHz, DMSO):  $\delta$  7.25-7.48 (m); IR (KBr):  $\bar{\nu}$  3072, 1555, 1466, 1382, 1066, 1004, 811  $\text{cm}^{-1}$ .

**1,2-Bis(4-methylphenyl)disulfane:** White solid; mp 37.7-

39.5 °C; <sup>1</sup>H NMR (90 MHz, DMSO): δ 7.06-7.40 (dd, 4H, *J* = 23.0, 8.4 Hz), 2.31 (s, 3H).

**1,2-Dibenzylidene-sulfane:** White solid; mp 65-66.1 °C; <sup>1</sup>H NMR (90 MHz, DMSO): δ 7.27-7.91 (m, 10H), 4.26 (s, 4H); IR (KBr):  $\bar{\nu}$  3031, 2929, 1601, 1495, 1265, 1120, 1072, 766, 738, 698 cm<sup>-1</sup>.

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