Oxidation of Thiols to Disulfides Using Silica Chloride as a Heterogeneous Catalyst

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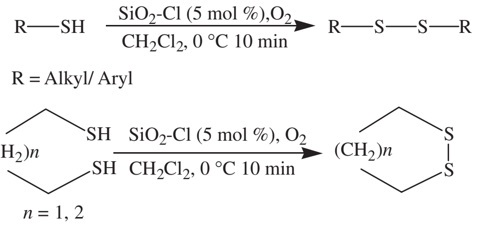
Silica chloride is used as a selective and effective heterogeneous catalyst for the rapid conversion of thiols to disulfides with quantitative yields in a very short period of time.

Disulfides are versatile building blocks for the synthesis of various organosulfur compounds[1] and they play an important role in biological and chemical processes.[2] Disulfides are also used in the sulfenylation of enolates and other anions.[3] Several methods have been reported in the literature[4] for the synthesis of disulfides from thiols, which make use of various oxidizing agents ranging from molecular oxygen[5] to halogens,[6] metal oxides,[7] oxo- and peroxosalts.[8] However, most of the reported methods involve the use of strong oxidants that are capable of reacting with other oxidizable functionalities such as aldehyde and amino groups present in the substrate. These methods also suffer from one or other disadvantages. Therefore, efforts were made to develop new reagents/catalyst with high activity, selectivity, and broad substrate generality, which can lead to practical, efficient, and environmentally friendly chemical synthesis of the disulfides.

Recently, we have initiated work in the field of solid supported reagents for various chemical transformations in organic synthesis.[9] Silica gel is one of the extensively used surface material for different chemical transformations in organic chemistry.[10] One such modified silica is silica chloride (SiO_2–Cl), which has been reported to be an efficient reagent for the synthesis of many organic compounds.[11] The efficiency of silica chloride, under operationally simple conditions has prompted us to explore the possibility of this catalyst for the synthesis of disulfides. Herein, we report a rapid, efficient, economic, environmentally benign, and easy to scale-up method for the effective conversion of alkane/arenethiols to their corresponding disulfides at room temperature using silica chloride as heterogeneous catalyst Scheme 1.

The developed method has allowed us to obtain quantitative yields of the products in reduced reaction times.[12] The room temperature (20–25 °C) reaction of alkane/arenethiols in the presence of silica chloride and air afforded the corresponding dialkyl/diaryl disulfide in 10 min with excellent yields, Table 1.

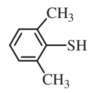
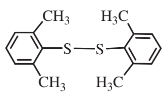
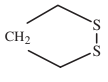
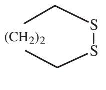
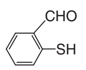
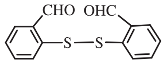
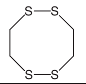


Scheme 1.

We have found that this procedure is suitable for rapid and efficient oxidation of thiols and dithiols to the disulfides. Filtration is only required to remove the catalyst and evaporation of the filtrate afforded pure products. Several examples of silica chloride assisted couplings of aliphatic, aromatic, and heteroaromatic thiols into disulfides are presented in Table 1. In case of 2-aminobenzenethiol (Entry 12) the amino hydrochloride salt was obtained which was basified with cold saturated sodium bicarbonate solution followed by the extraction with diethyl ether to afford bis (2-aminophenyl) disulfide. A simple filtration at the end of the reaction followed by removal of the solvent from the filtrate allows product isolation in quantitative yields.

The extent of chlorination of the silica surfaces was determined by suspending 1 g of silica chloride in 25 mL of boiled distilled water and titrating with 0.1 M (9.3 mL) NaOH using

Table 1.

Entry	Substrate	Product[a]	Yield/%[b]
1	C_2H_5SH	$(C_2H_5S\text{-})_2$	98
2	$(CH_3)_2CHSH$	$((CH_3)_2CHS\text{-})_2$	99
3	C_4H_9SH	$(C_4H_9S\text{-})_2$	98
4	$C_5H_{11}SH$	$(C_5H_{11}S\text{-})_2$	97
5	C_6H_5SH	$(C_6H_5S\text{-})_2$	99
6	$C_6H_{11}SH$	$(C_6H_{11}S\text{-})_2$	96
7	4-CH_3-C_6H_4SH	4-$(CH_3$-$C_6H_4S\text{-})_2$	97
8	C_6H_5-CH_2SH	$(C_6H_5$-$CH_2S\text{-})_2$	99
9	4-NO_2-C_6H_4SH	(4-NO_2-$C_6H_4S\text{-})_2$	97
10	2-Cl-C_6H_4SH	(2-Cl-$C_6H_4S\text{-})_2$	98
11			99
12	2-NH_2-C_6H_4SH	(2-NH_2-$C_6H_4S\text{-})_2$	98
13	$SHCH_2CH_2CH_2SH$		92
14	$SHCH_2CH_2CH_2CH_2SH$		97
15			98
16	$SHCH_2CH_2SH$		95

[a]All compounds have been characterized by IR, NMR, and MS spectroscopy. [b]Isolated yield.

phenolphthalein as an indicator. The amount of immobilized Cl has been found to be 0.93 mol equiv. per gram of SiO_2. Our studies have shown that thionyl chloride is a satisfactory chlorinating agent for silica, if used undiluted. When diluted with dry benzene, a lesser numbers of silanol groups were replaced by chlorine. The extent of reaction with thionyl chloride gives values for active silanols per unit area of silica surface, comparable to other methods, for determining available activities. It was also observed that oxidation of thiol does not take place in the absence of silica chloride and in the presence of silica gel. Advantage of using silica chloride was that it can be prepared[13] by the readily available materials and also can be removed easily from the reaction mixture.

In conclusion, an efficient and simple method for the synthesis of dialkyl/diaryl disulfide has been described using silica chloride as a heterogeneous catalyst. The present procedure is attractive because of its simplicity, general applicability, and excellent yields of the products. It does not require any oxidizing agents. Therefore, the present method is a useful alternative of the existing methodologies.

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References and Notes

1 S. Oae, in *Organic Sulfur Chemistry: Structure and Mechanism*, ed. by F. L. Boca Raton CRC Press, **1991**.

2 R. J. Cremlyn, in *An Introduction to Organo sulfur Chemistry*, John Wiley & Sons, Inc., New York, **1996**.

3 L. Bischoff, C. David, L. Martin, H. Meudal, B. P. Roques, M. C. Fournie-Zaluski, *J. Org. Chem.* **1997**, *62*, 4848.

4 a) R. Sanz, R. Aguado, M. R. Pedrosa, J. F. Arnaiz, *Synthesis* **2002**, 856. b) W. A. Pryor, D. F. Church, C. K. Govindan, G. Crank, *J. Org. Chem.* **1982**, *47*, 156. c) T. J. Wallace, *J. Org. Chem.* **1966**, *31*, 3071. d) M. H. Ali, M. McDermott, *Tetrahedron Lett.* **2002**, *43*, 6271. e) X. Wu, R. D. Rieke, L. Zhu, *Synth. Commun.* **1996**, *26*, 191. f) A. R. Ramesha, S. Chandrasekaran, *J. Org. Chem.* **1994**, *59*, 1354. g) A. McKillop, D. Kuyuncu, *Tetrahedron Lett.* **1990**, *31*, 5007. h) V. Kesavan, D. Bonnet-Delpon, J. P. Begue, *Synthesis* **2000**, 223. i) A. T. S. Shah, M. K. Khan, M. Fecker, W. Voelter, *Tetrahedron Lett.* **2003**, *44*, 6789.

5 K. T. Liu, Y. C. Tong, *Synthesis* **1978**, 669.

6 a) J. Drabowicz, M. Mikolajczyk, *Synthesis* **1980**, 32. b) N. Iranpoor, B. Zeynizadeh, *Synthesis* **1999**, 49.

7 M. Hirao, S. Yakabe, H. Chikamori, J. H. Clark, T. Monmoto, *J. Chem. Res.* **1998**, 310.

8 A. R. Hajipour, S. E. Mallakpour, *J. Chem. Res., Synop.* **2000**, 32.

9 a) A. Cornelis, P. Laszlo, *Synthesis* **1985**, 909. b) B. E. Blass, *Tetrahedron* **2002**, *58*, 9301.

10 a) D. M. Tal, E. Keinan, Y. Mazur, *Tetrahedron* **1981**, *37*, 4327. b) M. A. Zolfigol, *Tetrahedron Lett.* **2001**, *57*, 9509. c) B. Kaboudin, A. Rahmani, *Synthesis* **2003**, 2705.

11 a) F. Mohanazadeh, A. R. Momeni, Y. Ranjbar, *Tetrahedron Lett.* **1994**, *35*, 6127. b) M. Sathe, A. K. Gupta, M. P. Kaushik, *Tetrahedron Lett.* **2006**, *47*, 3107.

12 To a solution of alkane/arenethiol (1 mmol) in dichloromethane, silica chloride (5 mol %) was added at 0 °C and access to atmospheric oxygen. The reaction mixture was stirred for 10 min; the progress of reaction was monitored by TLC and also by gas chromatography. After the completion of reaction, mixture was filtered off and filtrate was concentrated to afford dialkyl/aryl disulfide in a quantitative yield. The physical properties and NMR spectra of compounds agreed with those reported in the literature.

13 Y. Kamitori, M. Hojo, R. Masuda, T. Kimura, T. Yoshida, *J. Org. Chem.* **1986**, *51*, 1427.