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Investigation on the reduction of sulfonyl chlorides with sulfur dioxide in water as solvent

Qian Zhao · Chao Qian · Xin-zhi Chen

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Abstract An operationally simple and environmentally benign method for reductive coupling of sulfonyl chlorides to the corresponding disulfides has been developed. Sulfonyl chlorides can be rapidly reduced with $SO_2/KI/H_2SO_4$ system in moderate to good yields at 80 °C in water.

Keywords Reduction · Catalyst · Acidity · Sulfur dioxide · Disulfides · Sulfonyl chlorides

Introduction

Organic disulfides can serve as valuable intermediates in various organic transformations especially in natural product synthesis as well as intermediates of functional additives and/or auxiliary agents [1–3]. They are also very important precursors for synthesis of sulfenyl, sulfinyl, thiols, and so on [4, 5]. Nowadays, the synthesis of organic disulfides is attracting much attention in both academia and industry.

The interconversion of disulfides and thiols is a fundamental transformation in organosulfur chemistry and such switching plays important roles in biological systems. Conversion of thiols to disulfides by oxidation often serves as a convenient technique in organic synthesis [6]. However, the limited commercial availability of structurally various thiols always restricted its industrial application. In addition, thiols are very odorous compounds and their handing needs special precaution. Since sulfonyl chlorides are easily prepared by the reaction of chlorosulfonation, reductive coupling of sulfonyl chlorides to the corresponding disulfides is an operationally simple alternative protocol, which also provides a procedure to synthesis of thiols.

Many methods concerning the synthesis of disulfides by reductive coupling of sulfonyl chlorides have been reported, such as the use of sodium borohydride ($NaBH_4$) [7], lithium aluminum hydride ($LiAlH_4$) [8], metal/acid [9], hydrazine hydrate [10, 11], and so on. Nevertheless, only a few methods are practically useful for the rapid and mild reduction. Olah et al. [12] reported the reduction of sulfonyl chlorides and their derivatives with iodide in the presence of boron halides in weakly or noncoordinating solvents. However, long reaction time (16 h) limits its application. More recently, low-valent oxophilic d-block metals have become very important in deoxygenation of different types of organic substrates. The successful utilization of the lower valent complexes of Ti, Mo, and W in effecting the deoxygenation of certain organic molecules is the result of the usually high thermodynamic stability of Ti-, Mo-, and W-oxo bonds [13]. Among the low-valent oxophilic d-block metals $TiCl_4/Al$ [14], $MoCl_5/NaI$ [15], $ZrCl_4/NaI$ [16], $SmI_2/HMPA$ [17], WCl_6/Zn, and WCl_6/NaI [18] systems have been used for coupling of different kinds of sulfonyl chlorides. Though they are very useful reducing reagents, their application is limited. Their storage is difficult because they are very sensitive to air oxidation, which seriously restricts their application in large scale reactions. Although a variety of reagents have

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Q. Zhao · C. Qian · X. Chen (✉)
Department of Chemical and Biological Engineering, Zhejiang University, Hangzhou 310027, People's Republic of China
e-mail: chemtec@163.com

Q. Zhao
e-mail: zhaoqian@zju.edu.cn

been reported, a safe, simple, green, and high-yielding procedure is still in demand.

In this paper, we report a water solvent method to complete the reduction of sulfonyl chlorides with sulfur dioxide or sodium bisulfite in the presence of iodide in acid media (Scheme 1), which can potentially ease cost and simplify the procedures. The experimental parameters are optimized for yield of the final product.

Results and discussion

To find the optimum reaction conditions, the reductive coupling of 4-chlorobenzenesulfonyl chloride as a model compound with $NaHSO_3$/KI/acid as a reducing system under neat conditions was examined firstly. The desired product was easily isolated by filtration. The influence of different factors was studied, as shown in Table 1.

Different acids such as HCOOH, H_2SO_4, CH_3COOH, and HCl were tested. The reaction proceeded smoothly in the presence of HCOOH (Table 1, entries 1–5). Increasing the reaction temperature and the amount of acid did not affect the yield of the final product. It should be mentioned that HCOOH itself is capable of reduction. A similar result was given by H_2SO_4 and HCl (Table 1, entries 6–7). A principal advantage of H_2SO_4 or HCl as acid lies in that it was the product of the chlorosulfonation reaction, which provided a possibility to reuse it. With CH_3COOH, the reaction proceeded at a relatively slower rate, the reduction of 4-chlorobenzenesulfonyl chloride being completed after 4 h at 80 °C, as the yield did not exceed 90 % (Table 1, entry 8). It provided us the clue that relative strong acid favors this reaction.

By analyzing the system, we found that $NaHSO_3$ is protonated by strong acids applied to form SO_2, so the real attacking agent is SO_2. Meanwhile, more water was needed to wash out the salt produced during the reaction if $NaHSO_3$ was used. According to our experimental result of $NaHSO_3$, it was found that 4-chlorobenzenesulfonyl chloride can be easily reduced with HCOOH, HCl, or H_2SO_4 to afford the corresponding disulfides in moderate to good yield. In an attempt to reuse the waste acid produced during the chlorosulfonation process, we executed the reactions in the presence of HCl or H_2SO_4. Considering the volatility of HCl, we employed the SO_2/KI/H_2SO_4 as reducing system; the result is shown in Table 2.

Scheme 1

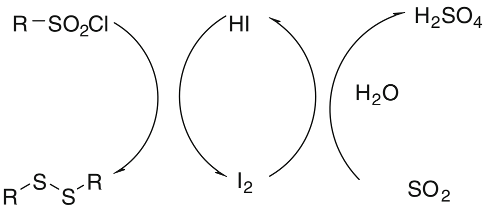


Table 1 Optimization of the conditions in $NaHSO_3$/KI system

Entry	Acid/g	Time/h[a]	Temp/°C	Yield/%[b]
1	HCOOH (5)	3	80	93.5
2	HCOOH (10)	3	80	93.4
3	HCOOH (15)	3	80	93.5
4	HCOOH (5)	3	90	93.6
5	HCOOH (5)	2.5	100	93.5
6	H_2SO_4 (5)	2	80	93.7
7	HCl (5)	2	80	93.2
8	CH_3COOH (5)	4	80	85.9

Reaction conditions: 10 g 4-chlorobenzenesulfonyl chloride, 1 g KI, 20 g $NaHSO_3$ dissolved in water added dropwise at reaction temperature

[a] Reaction time was determined by TLC

[b] Isolated yield

Table 2 Optimization of the conditions in SO_2/KI system

Entry	Acid/g	Water/cm^3	Time/h[a]	Yield/%[b]
1	H_2SO_4 (5)[c]	–	24	53.1
2	H_2SO_4 (5)[d]	–	8	93.1
3	H_2SO_4 (5)[d]	10	2	93.4
4	H_2SO_4 (5)[d]	20	1	94.1
5	H_2SO_4 (5)[d]	30	1	93.8
6	–	30	6	81.9

Reaction conditions: 10 g 4-chlorobenzenesulfonyl chloride, 1 g KI, sulfur dioxide gas was introduced at 80 °C

[a] Reaction time was determined by TLC

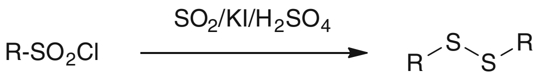
[b] Isolated yield

[c] Sulfur dioxide gas was collected by an aqueous 30 % sodium hydroxide solution

[d] Sulfur dioxide gas was collected by a balloon

Encouraged by the promising results obtained previously, the reduction of 4-chlorobenzenesulfonyl chloride in the presence of sulfur dioxide has also been examined in the same condition. Sulfur dioxide gas was absorbed by an aqueous 30 % sodium hydroxide solution. Unfortunately, a yield of less than 55 % with partial conversion during the long reaction time was achieved (Table 2, entry 1). It seems that sulfur dioxide gas used as a reducing agent would disadvantageously result in a decreased reaction rate. In order to improve the yield and reduce the reaction time, we used a balloon to collect sulfur dioxide gas instead of the sodium hydroxide solution. To our delight, 4,4′-dichlorodiphenyl disulfide was obtained with a yield of 93.1 % in 8 h (Table 2, entry 2). However, compared to the $NaHSO_3$ system, the reaction time is still too long. Finally we found that water played an important role in the reaction. Sulfur dioxide gas and iodide solvated well when

Table 3 Scope and limitations of the protocol



Entry	R	Time/h	Yield/%[a]	M.p./°C	Lit. m.p./°C
1	C_6H_5	1	93.7	58–60	59 [19]
2	4-F-C_6H_4	1	94.0	47.9–49	49–51 [20]
3	4-Cl-C_6H_4	1	94.1	71.5–71.8	70–72 [7]
4	4-Br-C_6H_4	1	94.3	88.9–89.7	89–91 [17]
5	4-Me-C_6H_4	1.5	93.3	44.6–45.1	45–46 [19]
6	3-NO_2-C_6H_4	2	83.5	78.9–80	75.6–78.6 [21, 22]
7	2-Naphthyl	4	91.6	136.3–137.5	137–138 [7]
8	CH_3	1	92.9	–	–

Reaction conditions: 10 g substrate, 1 g KI, 5 g H_2SO_4 (98 wt%), 20 cm^3 H_2O, sulfur dioxide gas was introduced at 80 °C

[a] Isolated yield

water was added. As listed in Table 2, 20 cm^3 water was optimized for the yield and the minimization of the reaction time (Table 2, entry 4). Increasing the amount of water had no effect (Table 2, entry 5). Since H_2SO_4 was produced during the reaction, we executed the reactions in the absence of H_2SO_4 (Table 2, entry 6). However, the result was unsatisfactory.

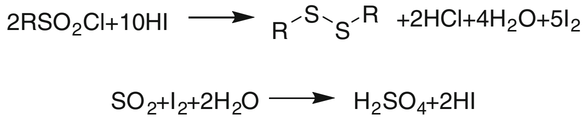
The optimal condition was screened (Table 2, entry 4). H_2SO_4 (5 g, 98 % wt) and 20 cm^3 H_2O gave a satisfactory yield and a minimum of reaction time at 80 °C for 1 h using water as the solvent in the 4,4′-dichlorodiphenyl disulfide synthesis.

Having gained an understanding of the factors that influence the reduction process, we explored the scope and limitation of this method. Further reduction results are summarized in Table 3.

As listed in Table 3, this protocol could be equally applicable to both aliphatic and aromatic sulfonyl chlorides. All reactions proceeded smoothly and quickly under the optimal conditions. The corresponding disulfides were isolated in good to excellent yields. It was observed that the substituents on the arenesulfonyl chlorides and steric hindrance played a significant role in these reactions. Electron-withdrawing groups on the aromatic ring induced the reduction of arenesulfonyl chlorides more easily than electron-donating groups. We also observed the negative influence of steric hindrance upon the reaction times (Table 3, entry 7).

The reaction which takes place when reducing sulfonyl chlorides to produce the corresponding disulfides may be represented by the equation as shown in Scheme 2. The function of SO_2 in conducting the reaction is to regenerate the hydriodic acid by reduction of the iodine produced.

Scheme 2



Conclusion

In conclusion, we have successfully developed a facile, convenient, and efficient process for preparing both aliphatic and aromatic disulfide using sulfonyl chloride as a starting material via use of an iodide as a catalyst in the presence of sulfuric acid under mild reaction conditions. Availability of the reagent, efficiency of the reactions, and high yields of the products make this simple procedure an attractive and a practical alternative to the known methods. The reaction seems to offer a promising strategy for large-scale preparations. In addition, compared to the organic solvent, water was characterized with low toxicity, low cost, and ready availability. The use of water as solvent is very important for eco-friendly demand.

Experimental

All chemicals were of reagent grade and used without further purification. All yields refer to isolated products after purification. Products were characterized by comparison with authentic samples and by spectroscopy data (^1H NMR and ^{13}C NMR spectra) and melting point. Melting points were determined using WRR melting point apparatus. NMR spectra were recorded in DMSO-d_6 or $CDCl_3$ using a Bruker AV 400 spectrometer (400 MHz for ^1H). The progress of the reactions was monitored by thin-layer chromatography (TLC).

General procedure for the synthesis of 4,4′-dichlorodiphenyl disulfide

To a mixture of 10 g 4-chlorobenzenesulfonyl chloride (0.047 mol) in 20 cm^3 water was added 5 g sulfuric acid (98 wt%) and 1 g KI. The mixture turned purple when heating to 80 °C. Sulfur dioxide gas was introduced under vigorous stirring and a balloon was used to collect it. Then the reaction mixture became colorless. The reaction mixture was monitored by TLC. After completion of the reaction, 4,4′-dichlorodiphenyl disulfide was obtained by filtration.

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