CHEMISTRY LETTERS, pp. 1483-1486, 1992.

# Convenient One-Pot Synthesis of Sulfonyl Chlorides from Thiols Using Sulfuryl Chloride and Metal Nitrate

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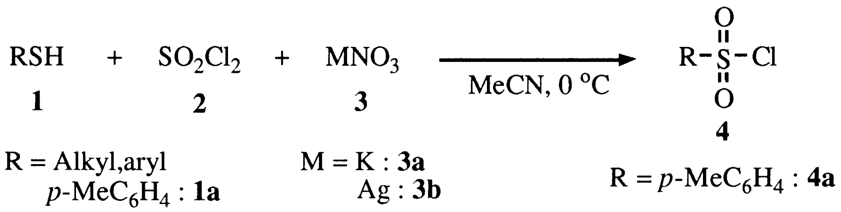
Various sulfonyl chlorides were obtained in excellent yields by the reaction of alkyl and aryl thiols with sulfuryl chloride in the presence of metal nitrate under mild condition in aprotic solvents such as acetonitrile and N,N-dimethylformamide.

The use of sulfonyl chlorides as the important precursors has been frequently encountered for the preparation of many diverse functional groups including sulfonate esters,[1)] amides,[2)] sulfones,[3)] sulfinic acids,[4)] and others.[5)] It has been demonstrated that sulfonyl fluorides are used for the active site probes of chymotrypsin[7)] and best prepared from sulfonyl chlorides.[6)] Recently, extensive studies on organic synthesis using sulfonyl chlorides such as selective protection for carbohydrates,[8)] and addition to olefins,[9)] vinylsulfones,[10)] thiosulfinates,[11)] and thiosulfonates[12)] have been reported. Although a number of methods for the preparation of sulfonyl chlorides[14)] have been developed and successfully utilized for the organic synthesis, the simple methods for the direct conversion of thiols into sulfonyl chlorides are quite few[13)]: most of these methods employ harzardous reagents, such as molecular chlorine and acetic acid, accompanying by hard handling and cautious work-up. Diazotization of aniline followed by treatment with sulfur dioxide and cuprous chloride[15)] and reaction of organo lithium with sulfuryl chloride[16)] were also known to afford the sulfonyl chlorides in moderate yields.

We have now found that various alkyl and aryl thiols (**1**) reacted smoothly with sulfuryl chloride (**2**) in the presence of metal nitrate (**3**) at ca. 0 °C under mild conditions in aprotic solvents such as acetonitrile and DMF to afford the corresponding sulfonyl chlorides (**4**) in excellent yields.



$$\underset{\mathbf{1}}{RSH} + \underset{\mathbf{2}}{SO_2Cl_2} + \underset{\mathbf{3}}{MNO_3} \xrightarrow[\text{MeCN, 0 °C}]{} \underset{\mathbf{4}}{R-\overset{O}{\overset{\|}{\underset{O}{\underset{\|}{S}}}}-Cl}$$

R = Alkyl,aryl
*p*-$MeC_6H_4$ : **1a**

M = K : **3a**
Ag : **3b**

R = *p*-$MeC_6H_4$ : **4a**

In order to find out optimum conditions, the reactions of **1a** with **2** and **3** were examined under various reaction conditions. It is noteworthy that formations of both thiosulfonate (**5a**) and disulfide (**6a**) intermediate together with the product (**4a**) were observed depend on the reaction conditions. When more than 2 equivalent amounts of **2** and **3** were used, **4a** was obtained in high yields without formation of side products( **5a** and **6a** ). Distributions of products obtained are summarized in Table 1.

Table 1. Reactions of thiol (**1a**) with sulfuryl chloride (**2**) and metal nitrate (**3**)

| Entry | **2** (equiv.) | **3** (equiv.) | Time / min | Yield / % [a)] | | |
|---|---|---|---|---|---|---|
| | | | | **4a** | **5a** | **6a** |
| 1 | 1.2 | **3a** ( 1.2 ) | 60 | 36 | 42 | 6 |
| 2 | 2 | **3a** ( 2 ) | 45 | 84 | b) | b) |
| 3 | 2.5 | **3a** ( 2.5 ) | 60 | 93 | - | - |
| 4 | 1.2 | **3b** ( 2 ) | 20 | 63 | 30 | - |
| 5 | 2 | **3b** ( 1.2 ) | 20 | 40 | 32 | 28 |
| 6 | 2.4 | **3b** ( 2.4 ) | 20 | 88 | - | - |

a ) Isolated yields. b) Traceable amount of the product was detected by $^1$H-NMR.

Various thiols (**1**) were converted to **4** in high yields when 2.5 equivalent amounts of **2** and **3a** were used. As a general procedure for preparation of **4** from **1,** potassium nitrate ( **3a**, 253 mg,2.5 mmol ), and sulfuryl chloride ( **2** , 337 mg 2.5 mmol) were added slowly to a solution of thiols (**1**, 1mmol, 10 mL of dry acetonitrile). The reaction mixture was stirred at 0 °C until the starting material disappeared. When the reaction was completed, the product was neutralized with a saturated sodium carbonate solution, extracted with diethyl ether (30 mL x 3), washed twice with a brine solution ( 50 mL ). The organic layer was dried over $MgSO_4$ and then concentrated under reduced pressure. The crude product was purified by a column chromatography ( silica gel, Merk, 70-230 mesh, 2 cm x 30cm, Hexane : $CH_2Cl_2$ = 4 : 1 ). The known products obtained were identified by comparing their $^1$H-NMR, IR, and Mass spectra and mp with those of authentic samples and literature references.The results obtained are summarized in Table 2.

Since sulfuryl chloride (**2**) has been used for the preparation of sulfenyl chlorides (**7**)[17)] and sulfinyl chlorides[18)] from **1**, sulfenyl chlorides can be considered to be an intermediate in the first step. In order to elucidate the route for formation of **5a** , *p*-tolylsulfenyl chloride (**7a**) was carefully prepared by the reaction of **1a** with **2** and then reacted with 1 equivalent of **2** and 2.5 equivalent of **3a** to give 66% of **5a** actually together with 34% of **4a**.

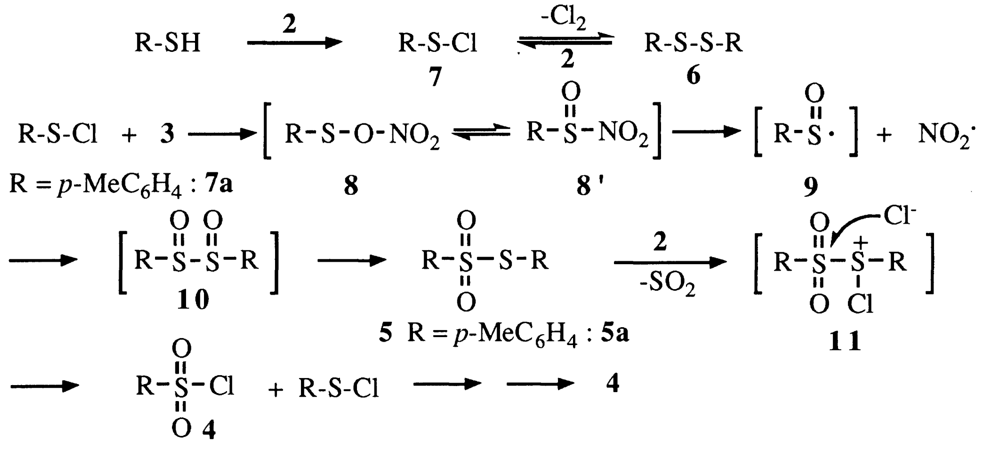


Table 2. Preparation of sulfonyl chlorides (**4**) from thiols (**1**)

| Entry | Thiols (**1**) | Time / min | Products (**4**) | Yields /% [a)] |
|---|---|---|---|---|
| 1 | $p$-$MeC_6H_4SH$ | 60 | $p$-$MeC_6H_4SO_2Cl$ | 100[b)] |
| 2 | $p$-$FC_6H_4SH$ | 40 | $p$-$FC_6H_4SO_2Cl$ | 94 |
| 3 | $p$-$ClC_6H_4SH$ | 30 | $p$-$ClC_6H_4SO_2Cl$ | 95 |
| 4 | $p$-$BrC_6H_4SH$ | 30 | $p$-$BrC_6H_4SO_2Cl$ | 91 |
| 5 | PhSH | 20 | $PhSO_2Cl$ | 82 |
| 6 | $p$-$NO_2C_6H_4SH$ | 60 | $p$-$NO_2C_6H_4SO_2Cl$ | 97 |
| 7 | $PhCH_2SH$ | 60 | $PhCH_2SO_2Cl$ | 73[b,c)] |
| 8 | EtSH | 60 | $EtSO_2Cl$ | 68 |
| 9 | 2-PrSH | 60 | 2-$PrSO_2Cl$ | 87 |
| 10 | 1-BuSH | 120 | 1-$BuSO_2Cl$ | 73 |

a) Isolated yields. b) Determined by $^1$H-NMR. c) Benzyl chloride was obtained in 27% yield as a side product.

This reaction appears to be initiated by chlorination on sulfur atom of **1** to form intermediate (**7**) by following substantial nucleophilic substitution with **3** to form the sulfenyl nitrate (**8**).[19)] The homolysis of **8**' to sulfinyl radical (**9**) and $NO_2^{\cdot}$ may occur. Formation of α-disulfoxide (**10**) by coupling of **9** has been well discussed.[20,21)] Conversion of **10** to **5** has been well documented and recognized.[20-22)] When the unsymmetrical thiosulfonate, phenyl thiomethylsulfonate, was reacted with **2** and **3a** under the same reaction conditions and quenched at the initial step (after 10 min), methanesulfonyl chloride (56%), benzenesulfonyl chloride (20%), phenyl thiobenzenesulfonate (21%), and diphenyl disulfide (13%) together with the starting material (40%) were obtained. Formation of these compounds can be well explained by the S-S bond cleavage reaction. When the same reaction was completed for 2 hours, methanesulfonyl chloride and benzenesulfonyl chloride were obtained in almost quantitative yields.

Conversion of **5** into **4** appears to involve a sulfonium salt intermediate (**11**) following by a subsequent nucleophilic replacement with $Cl^-$ to form the final product **4** and RSCl. The RSCl may also react with **2** and **3** to afford sulfonyl chloride.

This new simple method for the preparation of sulfonyl chlorides by mixing thiols, sulfuryl chloride, and metal nitrate under mild conditions may be widely available particularly for the substrates which are soluble in aprotic organic solvents.

This research was supported by the Basic Science Research Institute Program, Ministry of Education.

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(Received May 18, 1992)