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Temperature-controlled selective reduction of arenesulfonyl chlorides promoted by samarium metal in DMF

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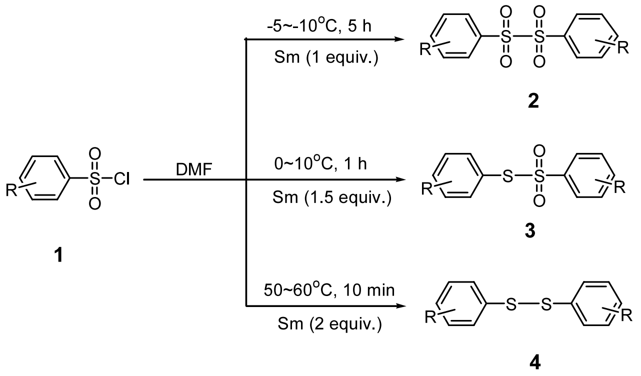
Abstract—Promoted by samarium in DMF, arenesulfonyl chlorides can be selectively reduced to diaryldisulfones, diarylthiosulfonates and diaryldisulfides in good to excellent yields by reaction temperature control without the need to pretreat or activate the metallic samarium. © 2003 Elsevier Science Ltd. All rights reserved.

Diaryldisulfones and diarylthiosulfonates have interesting properties and have been exploited in synthetic, pharmaceutical and polymer chemistry.[1,2] Diaryldisulfides are important intermediates in various organic transformations especially in natural product synthesis.[3] There are many reports involving the syntheses of diaryldisulfides[4] and diaryldisulfones;[5] however, most of these methods require unusual substrates and relatively harsh reaction conditions. In addition, reports concerning the synthesis of diarylthiosulfonates are rare.[6]

Though samarium diiodide (SmI_2) is a useful reducing reagent,[7] its application in organic synthesis is limited. Its storage is difficult because it is very sensitive to air oxidation, which seriously restricts its application in large scale reactions. Furthermore, Sm^{2+} can only donate one electron. Therefore, the direct use of metallic samarium as a reducing agent in organic transformations has attracted the attention of many organic chemists.[8] However, in most cases, reactions promoted by samarium are usually carried out in THF,[9] and metallic samarium has to be activated or pretreated by various methods so as to ensure the reactions proceed smoothly. Generally, metallic samarium is activated by other reagents such as iodine, hydrochloric acid, alkyl halides, etc.[9,10] Until now, only a few reports can be found concerning organic reactions promoted efficiently by metallic samarium without any activator or pretreatment.[11]

In our investigations on the applications of metallic samarium, we found that when *N*,*N*-dimethylformamide (DMF) is used as the solvent instead of THF, metallic samarium, without the need to be activated or pretreated, can selectively reduce arenesulfonyl chlorides **1** to diaryldisulfones **2**, diarylthiosulfonates **3** or diaryldisulfides **4**, by controlling the reaction temperature over three different temperature ranges (Scheme 1).[12]

A variety of diaryldisulfones **2**, diarylthiosulfonates **3** and diaryldisulfides **4** were obtained in good to excellent yields in the Sm/DMF system, as shown in Table 1.[13] We found that the substituents on the arenesulfonyl



Scheme 1.

Keywords: samarium; DMF; arenesulfonyl chloride; diaryldisulfone; diarylthiosulfonate; diaryldisulfide.

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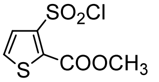
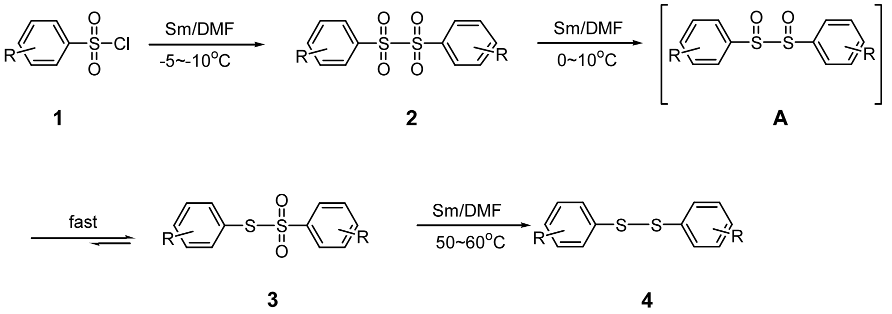
Table 1. Samarium-promoted temperature-controlled selective reduction of arenesulfonyl chlorides

Entry	Substrate **1**	Product **2**[a]			Product **3**			Product **4**		
		T (°C)	Time (min)	Yield (%)[b]	*T* (°C)	Time (min)	Yield (%)[b]	*T* (°C)	Time (min)	Yield (%)[b]
1	$C_6H_5SO_2Cl$ (**1a**)	−10	5	61 (**2a**)	0	60	87 (**3a**)	50	10	93 (**4a**)
2	4-CH_3-$C_6H_4SO_2Cl$ (**1b**)	−5	5	55 (**2b**)	5	60	85 (**3b**)	60	10	95 (**4b**)
3	4-CH_3O-$C_6H_4SO_2Cl$ (**1c**)	−5	6	58 (**2c**)	10	60	86 (**3c**)	60	10	92 (**4c**)
4	4-Cl-$C_6H_4SO_2Cl$ (**1d**)	−10	4	51 (**2d**)	0	40	83 (**3d**)	50	10	94 (**4d**)
5	4-Br-$C_6H_4SO_2Cl$ (**1e**)	−10	4	49 (**2e**)	0	60	87 (**3e**)	60	10	96 (**4e**)
6	4-I-$C_6H_4SO_2Cl$ (**1f**)	−5	5	54 (**2f**)	5	60	84 (**3f**)	60	10	90 (**4f**)
7	3-NO_2-$C_6H_4SO_2Cl$ (**1g**)	−5	5	–[c]	5	60	62 (**3g**)	60	20	86 (**4g**)
8	4-CH_3CONH-$C_6H_4SO_2Cl$ (**1h**)	−5	5	–[c]	5	60	–[c]	60	30	74 (**4h**)
9	 (**1i**)	−5	5	–[c]	5	60	–[c]	60	30	68 (**4i**)

[a] A considerable amount of product **3** was detected.
[b] Isolated yields based on arenesulfonyl chlorides.
[c] None of the expected product was obtained.



Scheme 2.

chloride influenced this reaction. Electron-withdrawing groups on the aromatic ring (**1d**,**e**) induced the reduction of arenesulfonyl chlorides more easily than electron-donating groups (**1b**,**c**).

Due to the strong electron-withdrawing effect of the nitro group, reaction of the 3-nitrobenzenesulfonyl chloride **1g** could not be stopped at the first step of reduction to the diaryldisulfone, therefore, only the products **3g** and **4g** were obtained (entry 7). On the other hand, the strong electron-donating effect of the thiophene-ring made the initial reduction of **1i** to the diaryldisulfone and diarylthiosulfonate more difficult, but at a relatively higher temperature, the only product obtained was diaryldisulfide **4i** because the diaryldisulfone and diarylthiosulfonate were very reactive toward samarium metal at this temperature (entry 9).

Remarkably, this reaction shows high chemoselectivity. Halo groups (chloro, bromo, iodo), thiophene-rings, esters, amides and nitro groups all remain unaffected by samarium in DMF under the reaction conditions, although these groups, especially the iodo and nitro groups, are usually reactive towards other samarium reagents.[7]

The initial stage of reduction of arenesulfonyl chlorides to afford diaryldisulfones is relatively difficult to control, since the formation of the diarylthiosulfonate **3** is usually unavoidable (generally, **2**:**3** have a ratio of about 70:30 when the initial stage of reduction was finished at a reaction temperature of −5 to −10°C), thus leading to the relatively low yield of disulfone **2**. In contrast, the diarylthiosulfonates **3** can be obtained in high yields after the second stage of reduction. In fact, the three products can be detected in succession when the reaction undergoes a temperature rise from −10 to 60°C (Scheme 2), and the experimental results show that an excess amount of Sm metal has no effect upon this reaction. These results indicate the mechanism of this reaction is as shown in Scheme 2. According to some reports,[13b] the formation of diarylthiosulfonates of type **3** may proceed via an intermediate disulfoxide (intermediate **A**).

In conclusion, the Sm-promoted stepwise reduction of arenesulfonyl chlorides offers a facile, convenient and efficient method for the synthesis of useful diaryldisulfones, diarylthiosulfonates and diaryldisulfides, selectively, by controlling the reaction temperature. The advantages of this method are the readily available starting materials,[14] the mild reaction conditions, the simple operational procedures and high yields of products. In addition, the reaction selectivity of the temperature-controlled procedure seems to offer a promising strategy for large-scale preparations directly promoted by metallic samarium. Finally, because the direct use of samarium in organic synthesis without any activator has rarely been reported, this reaction may become useful.

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12. *Typical procedure*:

    Preparation of diphenyldisulfone: To a mixture of Sm powder (2 mmol) in freshly distilled *N*,*N*-dimethylformamide (DMF, 10 mL), benzenesulfonyl chloride (2 mmol, freshly distilled) was added at −10°C with magnetic stirring under a nitrogen atmosphere. The resulting solution turned yellow-green within 2 h. After the completion of the reaction (about 5 h at −10°C), the reaction was quenched with dilute hydrochloric acid (0.1 mol/L, 5 ml) and the mixture was extracted with diethyl ether (3×30 ml). The organic phase was washed with water (20 ml), saturated brine (15 ml), and dried over anhydrous Na_2SO_4. The solvents were removed under reduced pressure to give the crude product, which was purified by column chromatography to afford diphenyldisulfone in 58% yield.

    Preparation of diphenylthiosulfonate: To a mixture of Sm powder (3 mmol) in freshly distilled *N*,*N*-dimethylformamide (DMF, 10 mL), benzenesulfonyl chloride (2 mmol, freshly distilled) was added at 5°C with magnetic stirring under a nitrogen atmosphere. The resulting solution turned yellow-green within 15 min and an exothermic reaction was observed. After the completion of the reaction (about 1 h at 5°C), a routine workup as mentioned above afforded diphenylthiosulfonate in 87% yield.

    Preparation of diphenyldisulfide: To a mixture of Sm powder (4 mmol) in freshly distilled *N*,*N*-dimethylformamide (DMF, 10 mL) benzenesulfonyl chloride (2 mmol, freshly distilled) was added at 50°C with magnetic stirring under a nitrogen atmosphere. The resulting solution turned yellow-green within 1 min and an exothermic reaction was observed. After the completion of the reaction (about 10 min), a routine workup as mentioned above afforded diphenyldisulfide in 93% yield.

13. (a) All of the products obtained in this study were characterized (^{1}H NMR, MS, IR, EA).

    Diphenyldisulfone ***(2a)*** (Ref. 5e): White solid, mp 193–196°C. $\nu_{\max}$ (KBr)/cm^{-1}: 3062, 1349, 1143. δ_H (CDCl$_3$): 7.84–7.86 (2H, m), 7.74–7.76 (2H, m), 7.58–7.66 (6H, m). m/z (%): 282 (M$^+$, 0.09), 141 (44.97), 77 (100.00). Anal. calcd for $C_{12}H_{10}O_4S_2$: C, 51.05; H, 3.57. Found: C, 51.24; H, 3.60%.

    Di(4-methyl)phenyldisulfone ***(2b)*** (Ref. 5e): White solid, mp >200°C. $\nu_{\max}$ (KBr)/cm^{-1}: 2947, 1344, 1137. δ_H (CDCl$_3$): 7.86–7.88 (4H, m), 7.44–7.46 (4H, m), 2.53 (6H, s). m/z (%): 310 (M$^+$, 0.18), 155 (53.37), 91 (100.00). Anal. calcd for $C_{14}H_{14}O_4S_2$: C, 54.17; H, 4.55. Found: C, 54.22; H, 4.58%.

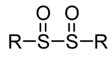
    Diphenylthiosulfonate ***(3a)*** (Refs. 13b and 15a): White solid, mp 44–45°C. $\nu_{\max}$ (KBr)/cm^{-1}: 3054, 1381, 1139. δ_H (CDCl$_3$): 7.57–7.60 (4H, m), 7.37–7.44 (6H, m). m/z (%): 250 (M$^+$, 25.10), 141 (33.15), 125 (82.04), 109 (42.75), 77 (100.00). Anal. calcd for $C_{12}H_{10}O_2S_2$: C, 57.57; H, 4.03. Found: C, 57.28; H, 4.05%.

    Di(4-methyl)phenylthiosulfonate ***(3b)*** (Refs. 13b and 15b): White solid, mp 77–78°C. $\nu_{\max}$ (KBr)/cm^{-1}: 2917, 1378, 1139. δ_H (CDCl$_3$): 7.86–7.88 (2H, m), 7.22–7.28 (4H, m), 7.15–7.17 (2H, m), 2.44 (3H, s), 2.38 (3H, s). m/z (%): 278 (M$^+$, 21.75), 155 (23.76), 139 (100.00), 123 (44.88), 91 (85.90). Anal. calcd for $C_{14}H_{14}O_2S_2$: C, 60.40; H, 5.07. Found: C, 60.59; H, 5.10%.

    Diphenyldisulfide ***(4a)*** (Ref. 4b): White solid, mp 59°C. $\nu_{\max}$ (KBr)/cm^{-1}: 3070, 464. δ_H (CDCl$_3$): 7.52–7.54 (4H, m), 7.24–7.34 (6H, m). m/z (%): 218 (M$^+$, 0.09), 109 (100.00), 77 (11.52). Anal. calcd for $C_{12}H_{10}S_2$: C, 66.01; H, 4.62. Found: C, 66.02; H, 4.60%.

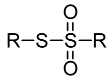
    Di(4-methyl)phenyldisulfide ***(4b)*** (Ref. 4b): White solid, mp 45–46°C. $\nu_{\max}$ (KBr)/cm^{-1}: 2921, 485. δ_H (CDCl$_3$): 7.39–7.41 (4H, m), 7.11–7.13 (4H, m), 2.34 (6H, s). m/z (%): 246 (M$^+$, 100.00), 123 (44.96), 91 (8.94). Anal. calcd for $C_{14}H_{14}S_2$: C, 68.25; H, 5.73. Found: C, 68.47; H, 5.69%.

    (b) The exact structure of the thiosulfonate is debatable. The problem mainly focuses on which structure is the more rational between **I** and **II**[4a,15] shown below:

    $\mathrm{R{-}S({=}O){-}S({=}O){-}R}$

    I

    $\mathrm{R{-}S{-}S({=}O)_2{-}R}$

    II

    Structure **I** was given by Beilstein,[15a,b] while structure **II** was suggested to be more probable in other literature.[15c] In fact, according to more recent literature, disulfoxides of type **I** are known to rearrange readily to thiosulfonate esters of type **II**.[4a,15d,e]

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