# An Easy and Practical Synthesis of Symmetrical Thiosulfonic S-Esters

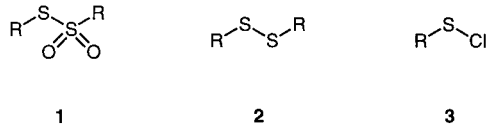
Fabrice Chemla

Laboratoire de Chimie des Organo-Eléments, URA 473 CNRS, Université Pierre et Marie Curie, 4, Place Jussieu, Tour 44-45, 2e étage, Boîte 183, 75252 Paris Cedex 05, France - FAX : (33) 01 44 27 75 67 - Email : fchemla@ccr.jussieu.fr

*Received 15 June 1998*

**Abstract:** Symmetrical alkyl and aryl thiosulfonic S-esters were prepared in good to excellent yields by the acetyl chloride-activated zinc reduction of sulfonyl chlorides.

Thiosulfonic S-esters[1] of the general formula **1** (Figure 1) are powerful sulfenylating reagents,[2] more reactive than the commonly used disulfides **2**, and more stable than the very reactive sulfenyl halides **3**. In addition, they have found wide industrial applications as biologically active compounds or in polymer production.[1]

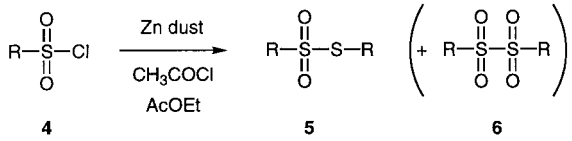


**1** **2** **3**

**Fig. 1**

However, their use has been limited by the lack of easy and practical preparations. The most often used procedures involve the oxidation of thiols or disulfides,[1,3] and then the use of chlorine, bromine or peroxides (MCPBA, hydrogen peroxide or dinitrogen tetroxide) is often necessary. Few methods are reported starting from sulfur compounds in higher oxidation state, involving easily available starting materials.[4] Among these methods the reduction of sulfonyl halides with potassium iodide[5] or with copper/bronze,[6] the reaction of potassium thiosulfonates and diaryliodonium salts[7] and the thermolysis of sulfonylhydrazines[8] deserve attention. We would like to report here an alternative method for the easy preparation of both arene- and alkanethiosulfonic S-esters from easily available sulfonyl chlorides.

In the course of our studies toward the formation of acylzinc species,[9] we were very surprised to observe that a mixture of benzenesulfonyl chloride **4a** and acetyl chloride react exothermically with zinc dust in ethyl acetate at room temperature. To our surprise, the resulting product did not incorporate the acyl choride moiety. As depicted in Scheme 1, a mixture of benzenethiosulfonic S-phenylester (**5a** : R = Ph, 90%) and benzene disulfone (**6a**[10] : R = Ph, 10%) were obtained.



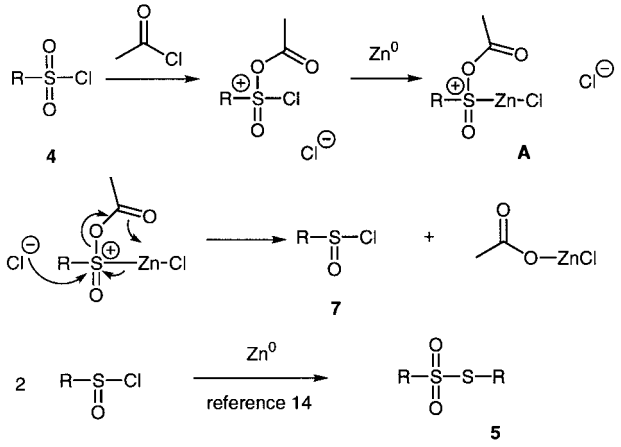

**4** **5** **6**

**Scheme 1**

The reduction of sulfonyl chlorides by zinc dust in acidic water - ether solvent has been reported[11] to give a mixture of sulfinic acids, thiols and disulfides. However, under our conditions, no reaction occurred in the absence of the acyl halide. To obtain good yields of the thiosulfonate, it was necessary to use exactly 1.5 equivalent of zinc dust; the reaction medium had to be kept at room temperature by means of a cooling bath and 1.1 equivalent of acetyl chloride was added dropwise (method A[12]). The reaction was also effective with other arenesulfonyl halides, like p-tolylsulfonyl chloride **4b** and 2,4,6-triisopropylsulfonyl chloride **4c**. For more reactive sulfonyl halides like p-methoxybenzenesulfonyl chloride **4d** as well as for alkanesulfonyl halides (**4e-g**), this method gave a reaction too exothermic to be easily controlled. The sulfonyl halide was then added as a mixture with acetyl chloride (1.1 equivalent) in ethyl acetate (method B[13]). The desired thiosulfonic S-ester was always contaminated with a small amount of the corresponding disulfone, but this was easily removed by flash chromatography. However, from pipsyl chloride **4h**, the disulfone **6**[14] was obtained in good yield instead of the desired product.

Our results are summarized in the Table 1. The products **5** were identified by comparison of their NMR data and/or their physical constants with those previously reported.[12-19]

Concerning the mechanism of this transformation, the fact that the acyl chloride is necessary for the reaction indicates an activation of the sulfonyl halide. The mechanism we propose in Scheme 2 involves an activation similar to the activation of sulfoxides by acyl chlorides in the Pummerer reaction,[20] leading to the corresponding oxosulfonium ion which reacts with zinc dust to give **A**. This species then leads to the sulfinyl chloride **7** and a zinc(II) salt. The reduction of two molecules of sulfinyl chloride by zinc dust has already been well-studied by Freeman[21] and gives the observed symmetrical thiosulfonic ester, through coupling (by an ionic or radical mechanism) and subsequent rearrangement of the resulting disulfoxide.




**4** **A** **7** **5**

**Scheme 2**

In conclusion, we have disclosed here a new, practical and efficient synthesis of symmetrical alkyl and aryl thiosulfonic S-esters. Further studies in this field will be reported in due course.

Thanks are due to F. Prian for his practical assistance and to Pr. J Normant for many helpful discussions.

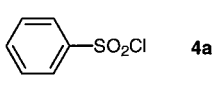
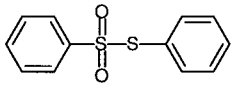
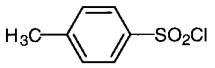
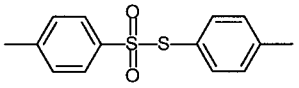
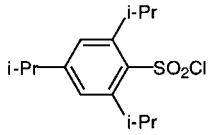
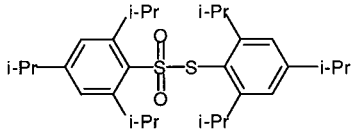
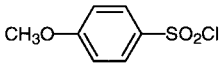
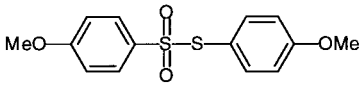
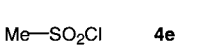
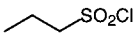
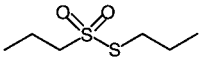
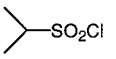
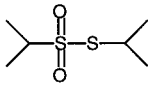
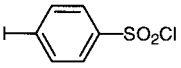
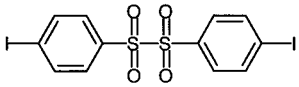
### References and Notes

(1) For a review, see : Zefirov, N.S.; Zyk, N.V.; Beloglazkina, E.K.; Kutateladze, A.G.K. *Sulfur Reports* **1993**, *14*, 223.

(2) Trost, B.M. *Chem. Rev.* **1978**, *78*, 363; Palumbo, G.; Ferreri, C.; D'Ambrosio, C.; Caputo, R. *Phosph. & Sulfur* **1984**, *19*, 235, and references cited therein.

(3) For a recent example, see : Arterburn, J.B.; Perry, M.C.; Nelson, S.L.; Dible, B.R.; Holguin, M.S. *J. Am. Chem. Soc.* **1997**, *119*, 9309.

**Table 1. Preparation of Symmetrical Thiosulfonates 5 from Sulfonyl Chlorides 4**

| | Starting material | Method | Product | Yield |
|---|---|---|---|---|
| 1 |  **4a** | A |  **5a** | 90 % |
| 2 |  **4b** | A |  **5b** | 90 % |
| 3 |  **4c** | A |  **5c** | 44 %* |
| 4 |  **4d** | B |  **5d** | 65 % |
| 5 |  **4e** | B |  **5e** | 60 % |
| 6 |  **4f** | B |  **5f** | 60 % |
| 7 |  **4g** | B |  **5g** | 34 % |
| 8 |  **4h** | A |  **6** | 80 % |

* The symmetrical disulfide was also isolated in 39% yield


(4) For a preparation of methanethiosulfonic acid, methyl ester **4e** from DMSO, see : Lazlo, P.; Mathy, A. *J. Org. Chem.* **1984**, *49*, 2281; for a preparation of symmetrical thiosulfonic esters from sulfinyl chlorides, see reference 13.

(5) Palumbo, G.; Caputo, R. *Synthesis* **1981**, 888.

(6) Karrer, P.; Wehrli, W.; Biedermann, E.; dallaVedova, M. *Helv. Chim. Acta* **1928**, *11*, 233.

(7) Xia, M.; Chen, Z. *Synth. Commun.* **1997**, *27*, 1309.

(8) Meier, H.; Menzel, I. *Synthesis* **1972**, 267.

(9) Chemla, F.; Normant, J.F. *Tetrahedron* **1997**, *53*, 17265.

(10) Disulfones were identified (except for **6**, see ref 14) by comparison with described spectral data : Bartmann, E.A. *Synthesis* **1993**, 490.

(11) Klivenyi, F.; Vinkler, E.; Lazar, J. *Acta Chim. Acad. Sci. Hung.* **1965**, *46*, 357.

(12) Method A : Preparation of phenyl benzenethiosulfonate **4a** : to zinc dust (1g, 16mmol) in ethyl acetate (60mL) were added 1,2-dibromoethane (two drops) and trimethylchlorosilane (three drops). The mixture was heated to reflux, the zinc became brilliant and flakey. After cooling, benzenesulfonyl chloride (1.765g, 10mmol) was added in one portion, following by acetyl chloride (0.79g, 10mmol) dropwise. The mixture became initially green, and then turned to yellow. The reaction was followed by TLC. After disappearance of the starting material, the solution was washed with a 1M solution of hydrochloric acid in water, then with brine and dried over magnesium sulfate. After evaporation of the solvent, purification by flash chromatography over silica gel (eluent : cyclohexane / ethyl acetate 90:10) gave phenyl benzenethiosulfonate **4a** (1.13g, 90%). $^1$H NMR ($CDCl_3$, 400MHz) : δ 7.60-7.20 (m) $^{13}$C NMR ($CDCl_3$, 100MHz): δ 142.77, 136.50, 133.77, 131.48, 129.47, 128.86, 127.80, 127.45; these data are identical to those previously reported : Billard, T.; Langlois, B.R.; Large, S.; Anker, D.; Roidot, N.; Roure, P. *J. Org. Chem.* **1996**, *61*, 7545.

(13) Method B : Preparation of methyl methanethiosulfonate **4e** : to zinc dust (49g, 0.75mol) in ethyl acetate (300mL) were added 1,2-dibromoethane (1mL) and trimethyl-chlorosilane (2mL). The mixture was heated to reflux, the zinc became brilliant and flakey. After cooling, a mixture of methanesulfonyl chloride (57.25g, 0.5mol) and acetyl chloride (39.25g, 0.5mol) in 300mL ethyl acetate was added dropwise at a rate such as the temperature did not rise above 40°C. At the end of the addition, the zinc had totally disappeared. After stirring two hours at room temperature, the solution was washed with a 1M solution of hydrochloric acid in water, then with brine and dried over magnesium sulfate. After evaporation of the solvent, distillation at reduced pressure gave methyl methanethiosulfonate **4e** (18.9g, 60 %, $bp_{0.5}$ = 90°C). $^1$H NMR ($CDCl_3$, 400MHz) : δ 3.32 (s, 3H), 2.70 (s, 3H); ); $^{13}$C NMR ($CDCl_3$, 100MHz): δ 20.70, 18.48; ; these data are identical to those previously reported : : Lazlo, P.; Mathy, A. *J. Org. Chem.* **1984**, *49*, 2281.

(14) Spectral data for compound **6** : $^1$H NMR ($CDCl_3$, 200MHz) : δ 7.2 (d, 4H, *J*=7Hz), 7.6 (d, 4H, *J*=7Hz); $^{13}$C NMR ($CDCl_3$, 50MHz): 92.6, 129.2, 136.6, 138.1; MS (CI, $NH_3$) : m/z 552, 520(100), 502, 470, 408, 394, 235, 125, 108; IR (KBr) : 1460, 1372, 1320, 1140, 1000, 802, 725 $cm^{-1}$ ; mp = 112°C.

(15) Selected spectral data for compound **5b** : $^1$H NMR ($CDCl_3$, 400MHz) : δ 7.41 (d, 2H, *J* = 8Hz), 7.26 (d, 2H, *J* = 8Hz), 7.23 (d, 2H, *J* = 8Hz), 7.16 (d, 2H, *J* = 8Hz), 2.42 (s, 3H), 2.38 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100MHz): δ 144.78, 142.17, 140.33, 136.49,

130.30, 129.48, 125.58, 124.52, 21.61, 21,43; these data are identical to those previously reported : Davis, F.A.; Reddy, R.E.; Sczewczyk, J.M. *J. Org. Chem.* **1995**, *60*, 7037.

(16) Selected data for compound **5c** : mp 105-106°C; $^{1}$H NMR ($CDCl_3$, 400MHz) : δ 7.1 (s, 2H), 7.0 (s, 2H); 3.72 (hept, 2H, *J*=8Hz), 3.60 (hept, 2H, *J*=8Hz), 2.91 (m, 2H), 1.1-1.3 (m, 24H); these data are consistent with those previously reported : Adlington, R.M.; Barrett, A.G.M. *J. Chem. Soc., Perkin Trans. I* **1980**, 1076.

(17) Selected data for compound **5d** : $^{1}$H NMR ($CDCl_3$, 400MHz) : δ 7.52 (d, 2H, *J* = 9Hz), 7.29 (d, 2H, *J* = 9Hz), 6.89 (d, 2H, *J* = 9Hz), 6.86 (d, 2H, *J* = 9Hz), 3.88 (s, 3H), 3.85 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100MHz): δ 163.65, 163.32, 138.46, 134.98, 129.99, 118.99, 115.03, 113.95, 55.83, 55.59; ; these data are identical to those previously reported : Bell, K.H. *J. Chem. Soc., Perkin Trans. I* **1988**, 1957.

(18) Selected data for compound **5f** : $^{1}$H NMR ($CDCl_3$, 400MHz) : δ 3.29 (td, 2H, *J*=6Hz, *J'*=1Hz), 3.12 (td, 2H, *J*=7Hz, *J'*=2Hz), 1.95 (m, 2H), 1.78 (m, 2H), 1.08 (t, 3H, *J*=7.5Hz), 1.04 (t, 3H, *J*=7.3Hz); $^{13}$C NMR ($CDCl_3$, 100MHz): δ 64.65, 38.47, 23.54, 17.73, 13.50, 13.02; these data are identical to those previously reported : Smith, D.J.; Maggio, E.T.; Kenyon, G.L. *Biochemistry* **1975**, *14*, 766.

(19) Selected spectral data for compound **5g** : $^{1}$H NMR ($CDCl_3$, 400MHz) : δ 3.51 (hept, 1H, *J*=8Hz), 3.25 (quint, 1H, *J*=8Hz), 1.3-1.5 (m, 12H); $^{13}$C NMR ($CDCl_3$, 100MHz): δ 55.55, 38.59, 24.46, 16.49. These data are consistent with those previously reported : Derbesy, G.; Harpp, D.N. *J. Org. Chem.* **1995**, *60*, 1044.

(20) DeLucchi, O.; Miotti, U.; Modena, G. *Org. React.* **1991**, *40*, 157.

(21) Freeman, F.; Bartosik, L.G.; vanBui, N.; Keindl, M.C.; Nelson, E.L. *Phosph. & Sulfur* **1988**, *35*, 375; Freeman, F. *Chem. Rev.* **1984**, *84*, 117; Freeman, F.; Keindl, M.C. *Synthesis* **1983**, 913.