A Facile Way to Thiosulfonic *S*-Esters

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Thiosulfonic *S*-esters **(2)** have been reported[1] to be powerful sulfenylating agents which react faster and more completely than disulfides; in addition, they are more stable and easier to handle than sulfinyl chlorides. Compounds **2** have also been found to be useful for temporary blocking of mercapto groups in protein chemistry[2]. Unfortunately, the synthetic application of thiosulfonic *S*-esters **(2)** has hitherto been limited by their somewhat difficult preparation. The only practicable method for the preparation of compounds **2** consists of the oxidation of disulfides[3]. The direct reaction of thiols with sulfonyl chlorides, which would possibly lead to "symmetrical" or "unsymmetrical" thiosulfonic *S*-esters, is known[4,5] to fail owing to fast nucleophilic attack of the thiol on the initially formed thiosulfonate whereby disulfides are formed.

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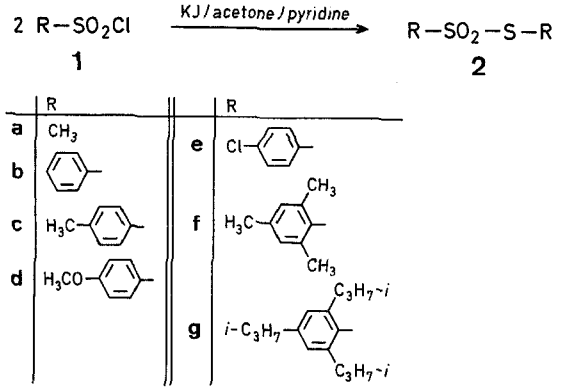
We tried to minimize the undesirable formation of disulfides in the reaction of sulfonyl chlorides **(1)** with thiols and thus favor the formation of thiosulfonic *S*-esters **(2)** by generating the thiol *in situ* by reduction of part of the sulfonyl chlorides **(1)** so that the thiol (or its anion) is present only in low concentration and can thus be trapped by excess sulfonyl chloride to give the desired thiosulfonic *S*-ester **(2)**. We therefore examined the behavior of a series of reducing agents towards benzenesulfonyl chloride **(1b)** under various conditions and found that good yields of *S*-phenyl benzenethiosulfonate **(2b)** are obtained from the reduction of **1b** with potassium iodide in anhydrous acetone containing catalytic[6] amounts of pyridine.

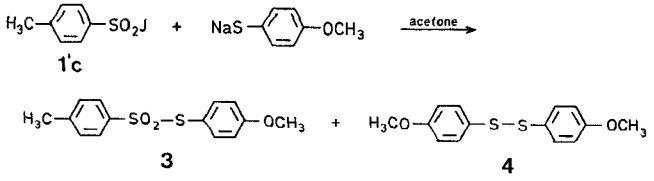


The *S*-ester **2b** was isolated as the only reaction product besides some unreacted sulfonyl chloride **1b**; not even traces of disulfide were found. It is noteworthy, that performance of the reaction with sodium iodide under otherwise identical conditions led to different results (presently under investigation).

The yields obtained using various sulfonyl chlorides **(1)** range from 62 to 84%. They depend strongly on the dryness of the solvent and potassium iodide used since the easily proceeding hydrolysis of the sulfonyl chlorides **1** leads to acetone-insoluble potassium sulfonates which do not participate in the reaction.

The present procedure has the advantage that practically pure thiosulfonic *S*-esters **(2)** are obtained in a fast one-step reaction starting with easily (or commercially) available sulfonyl chlorides, that neither chlorine[7] nor strong oxidizing agents like hydrogen peroxide[3] or peracids[8] have to be used, and that the yields are generally better than those obtained by other methods (20–40%). A serious limitation of the present method is that it can only be applied to the synthesis of "symmetrical" thiosulfonic *S*-esters.

In order to find out if the reaction possibly proceeds via the pattern $R-SO_2-J + {}^{\ominus}S-R$, i.e., via sulfonyl iodides as intermediates, and might thus be modified for the synthesis of "unsymmetrical" thiosulfonic *S*-esters we investigated the reaction of 4-methylbenzenesulfonyl iodide **(1'c)** with sodium 4-methoxybenzenethiolate in anhydrous acetone. In fact, this reaction did afford the "unsymmetrical" thiosulfonic *S*-ester **3** in low (37%) yield, the second product (25%) being, as expected, the disulfide **4** which is formed by the rather fast attack[5] of



thiolate ion on the S-atom of already produced **3** with elimination of 4-methylbenzenesulfinate ion.

S-Phenyl Benzenethiosulfonate (2b); Typical Procedure:
To a stirred solution of benzenesulfonyl chloride (**1b**; 0.883 g, 5 mmol) in anhydrous acetone (20 ml) containing dry pyridine (1 ml), dry potassium iodide (3.4 g, >20 mmol) is added portionwise over 30 min at room temperature [in the preparation of **2e** and **2g**, potassium iodide is added in smaller portions over 2–3 h]. The clear solution immediately turns red-brown. Stirring is continued for 30 min, most of the solvent is then evaporated under reduced pressure [a precipitate present should be filtered off before evaporation], and the oily residue is dissolved in ether (200 ml). The ether solution is washed with aqueous 5 normal sodium thiosulfate (50 ml) and with water (20 ml), dried with sodium sulfate, and evaporated. The residual semicrystalline product is recrystallized from hexane; yield: 0.338 g (76%); m.p. 40–41 °C.

S-(4-Methoxyphenyl) 4-Methylbenzenethiosulfonate (3):
To a stirred solution of freshly prepared[10] 4-methylbenzenesulfonyl iodide (**1'c**; 0.564 g, 2 mmol) in anhydrous acetone (15 ml), sodium 4-methoxybenzenethiolate (0.324 g, 2 mmol) is added in one portion and the suspension is vigorously stirred for 3 h under nitrogen at room temperature. Then, aqueous 5 normal sodium thiosulfate (80 ml) is added and the resultant solution extracted with ether (3 × 25 ml). The organic extract is washed with water (3 × 20 ml), dried with sodium sulfate, and evaporated in vacuo. Column chromatography of the residual crude product (369 mg) on silica gel using hexane as eluent gives two fractions:

Bis[4-methoxyphenyl] Disulfide **(4)**, obtained as the first fraction; yield: 145 mg (25%); m.p. 41–43 °C (from hexane).

$C_{14}H_{14}O_2S_2$	calc.	C 60.50	H 5.01	S 22.94
(278.4)	*found*	*60.43*	*5.07*	*23.00*

I.R. ($CHCl_3$): ν = 1245, 815 cm^{-1}.

S-(4-Methoxyphenyl) 4-Methylbenzenethiosulfonate **(3)**, obtained as the second fraction; yield: 220 mg (37%); m.p. 53–55 °C (from methanol).

$C_{14}H_{14}O_3S_2$	calc.	C 57.34	H 4.74	S 21.57
(294.4)	found	57.14	4.80	21.74

I.R. ($CHCl_3$): ν = 1320, 1136 cm^{-1}.

Table. Thiosulfonic *S*-Esters **(2)**

2	Yield[a] [%]	m.p. or b.p./torr [°C]	Molecular formula[b] or lit. data	I.R. ($CHCl_3$) ν [cm^{-1}]
a	67	b.p. 122°/16	b.p. 114°/13[7]	1310, 1130
b	76	m.p. 41–42°	m.p. 41–43°[8]	1310, 1133
c	82	m.p. 73–75°	m.p. 78°[9]	1325, 1138
d	84	m.p. 92–94°	$C_{14}H_{14}O_4S_2$ (310.4)	1328, 1136
e	62	m.p. 134–136°	$C_{12}H_8Cl_2O_2S_2$ (319.2)	1332, 1142
f	72	m.p. 133–134°	$C_{18}H_{22}O_2S_2$ (334.5)	1318, 1133
g	70	m.p. 110–113°	$C_{30}H_{46}O_2S_2$ (502.8)	1315, 1135

[a] Yield of pure isolated product; purity: >90% (as determined by ^{1}H-N.M.R. and T.L.C. or G.L.C. analysis.

[b] *The microanalyses were in satisfactory agreement with the calculated values: C, ±0.35; H, ±0.31; S, ±0.27. Exception: **2c** (C, −0.44). The analyses were performed by Mikroanalytisches Laboratorium E. Thommen, Bettingen (Switzerland).*

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