## DISULFIDES BY REDUCTION OF THIOSULFONIC S-ESTERS

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Abstract: Disulfides are smoothly prepared from thiosulfonic S-esters by chlorotrimethylsilane and sodium iodide. In addition, thiosulfonic S-esters have been shown to be probable intermediates in other already known reactions leading to disulfides.

In a recent paper<sup>1</sup> we have reported that thiosulfonic S-esters can be easily prepared by simple treatment of sulfonyl chlorides with potassium iodide in anhydrous acetone at room temperature. Noteworthy, use of sodium iodide under the same conditions led instead to large amounts of disulfides accompanying the expected thiosulfonic S-esters.

During the investigation of the above results we were concerned with various methods for smoothly converting thiosulfonic *S*-esters to disulfides and, in this context, we have now devised a new procedure for achieving such a conversion under neutral and extremely mild conditions.

The reagent we have utilized is iodotrimethylsilane prepared *in situ* by chlorotrimethylsilane and sodium iodide. The reduction, carried out at r.t. in anhydrous acetonitrile (see below), is very fast, quite clean and affords disulfides in a practically quantitative yield.

The only limitation is that unsymmetric disulfides cannot be prepared in this way from the corresponding thiosulfonic s-esters. In fact S-S bond cleavage and reformation occur during the reaction, so that unsymmetric thiosulfonic s-esters afford a mixture of three different disulfides.

A typical procedure follows: to a magnetically stirred solution of thiosulfonic S-ester (3.0 mmol) in anhydrous acetonitrile (18 ml), kept under dry nitrogen and cooled in a cold water bath, chlorotrimethylsilane (9.3 mmol) and sodium iodide (18.0 mmol) were added in one portion. The solution turned immediately to a red-brown colour and, in all the cases examined (see table), the reaction was complete within one hour (TLC, GLC on capillary columns) and worked up as usually: pouring into water (20 ml), extraction with  $Et_20$  (3x20 ml), washing of the combined ethereal extracts with 5N sodium thiosulfate (20 ml) and finally with water.

Some examples of reduction of symmetric thiosulfonic *S*-esters, performed under our experimental conditions, have been reported in the table beside reaction times and yields.

Thiosulfonic S-ester	Time $^a$	Yield $^{b}$	Disulfide	
R= Methyl	30'	90	b.p.	36-37°
R= Phenyl	15'	94	m.p.	58-60°
R= 4-Methylphenyl	40'	96	m.p.	44-46°
R= 4-Chlorophenyl	60'	96	m.p.	69-71°
R= 4-Methoxyphenyl	40'	98	m.p.	<b>41-4</b> 3°
R= 2,4,6-Trimethylphenyl	50 <b>'</b>	94	m.p.	123-125°
R= 2,4,6-Triisopropylphenyl	45'	92	m.p.	93-95°

Table - Reduction of thiosulfonic S-esters ( $R-SO_2-S-R$ ) by Me<sub>3</sub>SiCl and sodium iodide

<sup>a</sup>TLC or GLC monitored. <sup>b</sup>Yield of crystallized or distilled product. Purity  $\ge$  96% .

In considering the mechanistic course of the reduction, any radical reaction could be first ruled out since *S*-phenyl benzenethiosulfonate (la) was still completely reduced in 15' when treated under the above experimental conditions but in the dark and 2,6-di-t-butyl-p-cresol (DBBC) being added to the reaction mixture.

In order to understand the actual role played by chlorotrimethylsilane and iodide ion, *S*-phenyl benzenethiosulfonate (la) was treated under the above experimental conditions (solvent, temperature) with only sodium iodide, i.e. with exclusion of chlorotrimethylsilane. In fact sulfonyl oxygens in thiosulfonic *S*-esters are too weak bases<sup>2</sup> to afford an adduct with chlorotrimethylsilane (or its iodo analog) so that iodide ion can be regarded as the sole (nucleophilic) reagent initially present in the reaction mixture.

The formation under such conditions of phenyl disulfide (2a), sodium benzenesulfinate and iodine in the ratio 1:2:1 could be rationalized by the following equations which can be thus assumed to represent the first step in the overall reduction:

 $R-SO_2-S-R + J \xrightarrow{\phantom{a}} R-SJ + R-SO_2 \xrightarrow{\phantom{a}} R-SJ + R-SO_2 \xrightarrow{\phantom{a}} R-S-S-R + R-SO_2 \xrightarrow{\phantom{a}} + J_2$ 

Therefore the reaction proceeds via S-S bond cleavage and reformation. In fact the unsymmetric *s*-(4-methoxyphenyl) 4-methyl-benzenethiosulfonate (lb), when treated under our experimental conditions, afforded a mixture of three disulfides<sup>3</sup>: 4-methylphenyl 4-methoxyphenyl disulfide (2b), bis(4-methoxyphenyl) disulfide (2c) and bis(4-methylphenyl) disulfide (2d).



a, R = R' = Hc, R = R' = OMe



b, R = Me; R' = OMed, R = R' = Me

The almost quantitative yield of disulfides obtained in the presence of chlorotrimethylsilane can be accounted for by considering that the sulfonyl moiety of the starting thiosulfonic *S*-ester released in the first step is then involved in subsequent steps of the reduction.

Actually sodium sulfinates have been reported<sup>4</sup> to undergo reduction by iodotrimethylsilane leading to disulfides although, in the light of our preliminary results (see below), the mechanism which had been proposed does not seem to be anymore tenable. The authors in fact suggested a mechanism involving reduction of sulfinate ion to the corresponding sulfenyl iodide followed by dimerization of this latter to afford disulfides.

Since in our experience sulfenyl halides undergo fast nucleophilic attack by sulfinate ions affording thiosulfonic *S*-esters, it seemed unlikely that the sulfenyl iodide initially formed under the reported experimental conditions could couple with a second molecule of the same species rather than react with the excess sodium sulfinate (eventually silylated)<sup>5</sup> still present thus leading to an intermediate thiosulfonic *S*-ester then reduced as reported above.

In this view we repeated the reaction of sodium 4-methyl-benzenesulfinate under the above authors' conditions to check any presence of S-(4-methylphenyl) 4-methyl-benzenethiosulfonate (ld) beside bis(4-methylphenyl) disulfide (2d) in the reaction mixture. In our hands such a reaction was very fast and complete in only few minutes (reported 16 hr) so that we needed to operate at lower temperature  $(-70^{\circ}\text{C})$ . Indeed under such conditions we succeeded in isolating S-(4-methylphenyl) 4-methyl-benzenethiosulfonate (ld) (identical with an authentic sample, m.m.p. 44-46°), after 5', when about 50% of the starting sodium sulfinate had been consumed affording thiosulfonic *S*-ester (ld) and the corresponding disulfide (2d) in nearly 1:5 ratio.

Many papers dealing with "reductive dimerization" of sulfonic acids and their derivatives have appeared in the recent literature<sup>6</sup>. The results presented in this paper should prompt a reconsideration of the mechanistic course of such reactions.

Work is still in progress to elucidate the mechanistic aspects of the reduction of thiosulfonic *S*-esters and related substances and full details will be published in due course.

## REFERENCES AND NOTES

- <sup>1</sup>. G.Palumbo, R.Caputo, *Synthesis*, 888 (1981).
- <sup>2</sup>. J.L.Kice,G.B.Large, *J.Org.Chem.*, 33, 1940 (1968).
- <sup>3</sup>. Partial equilibration of disulfides may occur under our experimental conditions. However we have found that the process is rather slow if compared with the reduction reaction.
- <sup>4</sup>. G.A.Olah,S.C.Narang,L.D.Field,G.F.Salem, *J.Org.Chem.*, 45, 4792 (1980).
- <sup>5</sup>. Nucleophilic attack of the species  $R-SO_2$ -SiMe<sub>3</sub> onto sulfenyl halide can be expected<sup>7</sup> to be the favoured process in the presence of excess iodide ion which acts as a general base accepting Me<sub>3</sub>Si<sup>+</sup>.
- <sup>6</sup>. G.A.Olah,S.C.Narang,L.D.Field,R.Karpeles, J.Org.Chem., 46, 2408 (1981) and literature therein cited.
- <sup>7</sup>. J.L.Kice, J.P.Cleveland, J.Am. Chem. Soc., 95, 109 (1973).

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