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An Efficient Synthesis of Unsymmetrical Sulfides from Organic Disulfides and Aromatic Compounds

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In the presence of an active acidic catalyst generated from $SbCl_5$ and $AgSbF_6$, the sulfenylation reaction of aromatic compounds with organic disulfides smoothly proceeds in refluxing 1,2-dichloroethane to afford the corresponding unsymmetrical sulfides in high yields.

Several synthetic methods for unsymmetrical sulfides are known; for example, the nucleophilic displacement of aryl halides with sodium alkanethiolates$^{1)}$ or with aromatic thiols catalyzed by a nickel (0) complex,$^{2)}$ the reaction between 1-alkylthioethaniminium halides and organic halides using a phase-transfer catalyst,$^{3)}$ the reaction between naphthols and organic thiols,$^{4)}$ and the thermolysis of diaryl disulfides in the presence of aryl iodides at high temperature$^{5)}$ have been reported.

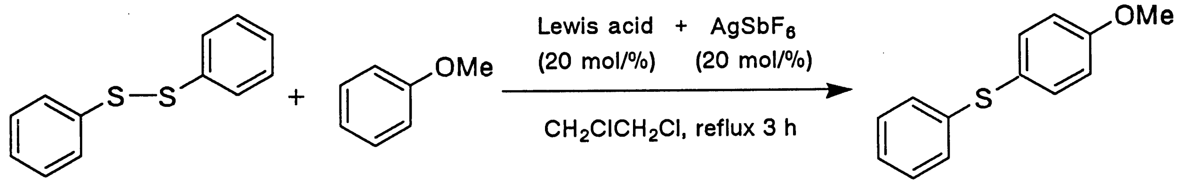
Recently, we focused our attentions on the utilization of unique characters of some active cationic species generated from Lewis acids and $LiClO_4$ or silver salts such as $AgClO_4$, $AgSbF_6$, AgOTf, etc., and reported the catalytic Beckmann$^{6)}$ and pinacol$^{7)}$ rearrangements, the catalytic Friedel-Crafts acylation reaction,$^{8)}$ the catalytic esterification$^{9)}$ and the catalytic and highly stereoselective glycosylation.$^{10)}$ In this communication, we would like to report a new approach to the sulfenylation reaction of aromatic compounds with organic disulfides by the promotion of $SbCl_5$-$AgSbF_6$ catalyst system.

In the first place, several combinations of Lewis acids and $AgSbF_6$ were examined by taking the reaction of anisole (methoxybezene) with diphenyldisulfide as a model (Table 1). As the result of the screening of Lewis acids, it was found that an active cationic species generated in situ from $SbCl_5$ and $AgSbF_6$ effectively activated the sulfur-sulfur bonds of organic disulfides and gave a good result.

Next, the effect of silver salts was examined using $SbCl_5$ as a Lewis acid in the reaction of anisole and diphenyldisulfide (Table 2). Among several silver salts, the best yield was obtained when $AgSbF_6$ was used.

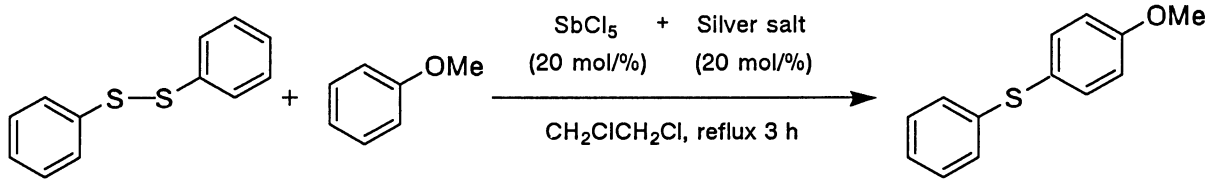
Results of the sulfenylation reaction of some aromatic compounds with organic disulfides catalyzed by 30 mol% of $SbCl_5$-$AgSbF_6$ are listed in Table 3. Anisole or 1-methoxy-2-methylbenzene smoothly reacts with organic disulfides to give the corresponding unsymmetrical sulfides in high yields. 1,3,5-Trimethylbenzene also works well. In these reactions, only para-substituted sulfides were obtained and formation of other isomers (o- or m-) was not observed by ^1H and ^{13}C NMR. In the case of 1,3-dimethoxybenzene, the desired mono-sulfenylated product was obtained in 85% yield by using double molar quantity of 1,3-dimethoxybenzene (Table 3, entry 8), while both of mono- and di-sulfenylated products were obtained in 47% and 52% yield respectively in the reaction of equimolecular amounts of 1,3-dimethoxybenzene and dimethyldisulfide (Table 3, entry 7).

Table 1. Effect of Lewis Acid



Entry	Lewis acid	Yield/%	Entry	Lewis acid	Yield/%
1	$SbCl_5$	76	6	$AlCl_3$	28
2	$SnCl_4$	40	7	$GaCl_3$	23
3	$CuCl_2$	39	8	$InCl_3$	21
4	$FeCl_3$	34	9	$SnCl_2$	17
5	$GeCl_4$	33	10	$TiCl_4$	13

Table 2. Effect of Silver Salt



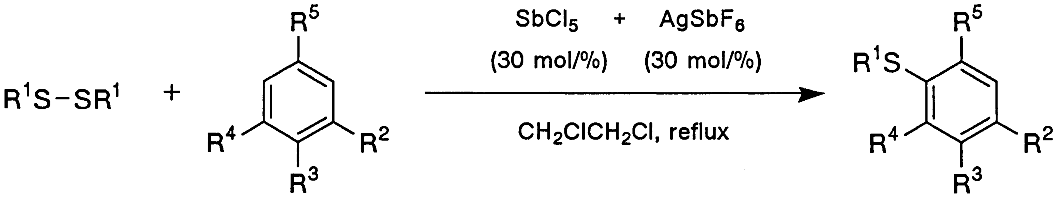
Entry	Silver salt	Yield/%
1 a)	$AgClO_4$	29
2 a)	$AgSbF_6$	38
3	$AgSbF_6$	76
4	$AgBF_4$	31
5	$AgPF_6$	27
6	AgOTf	26

a) The reaction was carried out at room temperature.

A typical experimental procedure is described for the reaction of anisole with dimethyldisulfide; $SbCl_5$ (0.15 mmol) and $AgSbF_6$ (0.15 mmol) were stirred for 1 h in 1,2-dichloroethane (2.0 ml) at rt, and then a

solution of dimethyldisulfide (0.5 mmol) in 1,2-dichloroethane (2.0 ml) and a solution of anisole (1.0 mmol) in 1,2-dichloroethane (2.0 ml) were successively added at rt. The reaction mixture was heated for 3 h under reflux, and then quenched with aq. sat. $NaHCO_3$. After usual work up, the crude product was purified by preparative TLC on silica gel to afford 1-methoxy-4-methylthiobenzene in 92% yield.

Table 3. The Sulfenylation Reaction Catalyzed by $SbCl_5$-$AgSbF_6$



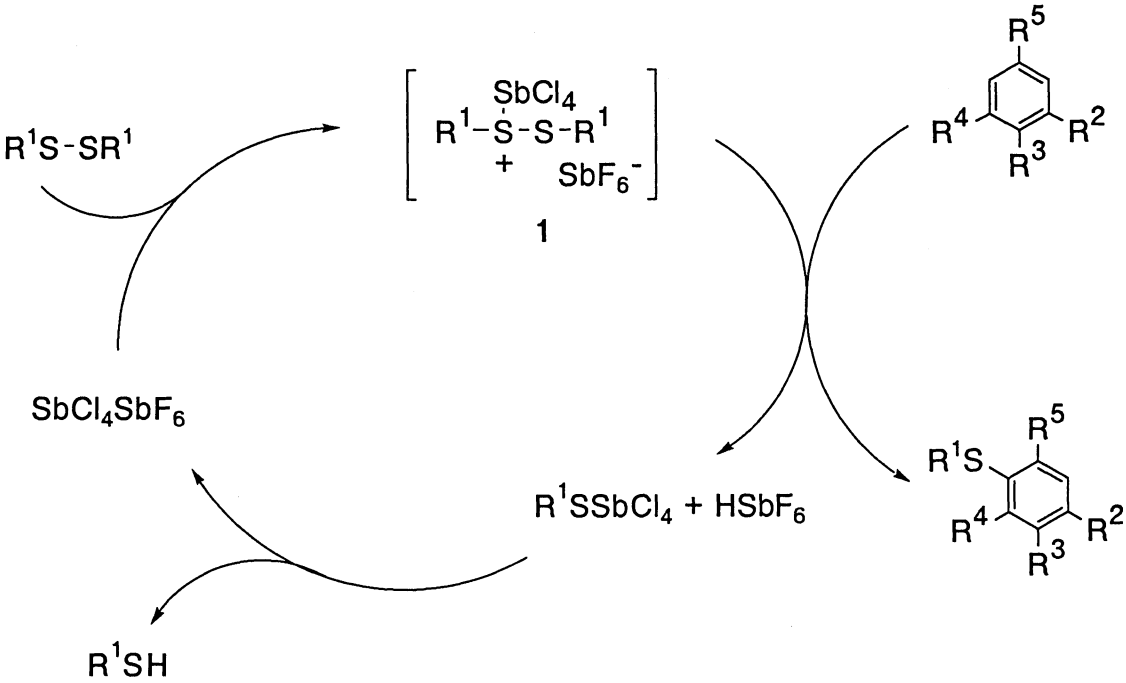
Entry[a)]	R^1	R^2	R^3	R^4	R^5	Time/h	Yield/%
1	Ph	MeO	H	H	H	3	quant.
2[b)]	Ph	MeO	H	H	H	3	81
3	Me	MeO	H	H	H	3	92
4	Ph	MeO	Me	H	H	3	quant.
5	Me	MeO	Me	H	H	3	97
6	Me	MeO	MeO	H	H	4	0 (94)[c)]
7[b)]	Me	MeO	H	MeO	H	3	47 (52)[c)]
8	Me	MeO	H	MeO	H	3	85 (14)[c)]
9	Me	Me	H	Me	Me	3	89

a) Disulfides and aromatic compouds were used in a ratio of 1:2.
b) Disulfides and aromatic compouds were used in a ratio of 1:1.
c) The yields of di-sulfenylated products.

Although the mechanism of the present reaction is not yet made clear at this stage, it is assumed that an organic disulfide forms a reactive intermediate 1 with the active catalyst $SbCl_4SbF_6$ (Scheme 1). Then 1 reacts with an aromatic compound to give the desired sulfide along with $HSbF_6$, which in turn reacts with $R^1S\ SbCl_4$ to regenerate the catalyst along with R^1SH.

Thus, further successful use of the combination of $SbCl_5$ and $AgSbF_6$ as a potential catalyst system in organic synthesis[6-8)] was demonstrated.

Further investigations concerning the scope of the present reaction as well as the mechanism are now in progress.



Scheme 1. The catalytic cycle.

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