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Electrophilic substitution reactions using an electrogenerated ArS(ArSSAr)$^+$ cation pool as an ArS$^+$ equivalent

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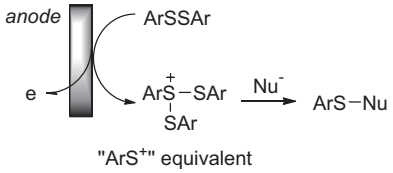
ABSTRACT

Arylbis(arylthio)sulfonium ions (ArS(ArSSAr)$^+$), which were generated and accumulated by the low-temperature electrolysis of diaryl disulfide (ArSSAr), were found to serve as ArS$^+$ equivalent in electrophilic substitution reactions of aromatic compounds, enolizable ketones, enol acetates, ketene silyl acetals and allylsilanes to give the corresponding arylthiolated products.

Introduction

The arylthio (ArS) substituted organic compounds are widely utilized in the organic synthesis, because of the easy generation of carbanions adjacent to the sulfur atom and easy removal of the ArS group.[1] ArS-substituted compounds, especially aromatic compounds have also received significant research interest in the functional materials.[2] Various methods for the synthesis of ArS-substituted compounds have been developed so far. Among them, the direct introduction of ArS group to the organic molecule is one of the most straightforward methods. Arylsulfenium ions[3] (ArS$^+$) seem to be suitable reagents for this purpose, because the reactions of ArS$^+$ with carbon nucleophiles should lead to the formation of ArS-substituted organic compounds. A popular method to generate ArS$^+$ is heterolysis of ArS-X (X = halogen) using silver salts.[4] However, the method suffers from the problems of instability of ArS-X, high cost of silver salts, and wastes of silver halides.

Recently, we have revealed that highly reactive arylbis(arylthio)sulfonium ions[5] (ArS(ArSSAr)$^+$) can readily be generated and accumulated in the solution by the low-temperature electrochemical oxidation[6] of diaryl disulfide (ArSSAr)[7] in CH_2Cl_2 using Bu_4NBF_4 or $Bu_4B(C_6F_5)_4$ as a supporting electrolyte. The ArS(ArSSAr)$^+$ cation pool was found to serve as an effective reagent for introducing the ArS group into alkenes and dienes, as well as generating alkoxycarbenium ions from thioacetals.[8,9] In this Letter, we report that ArS(ArSSAr)$^+$ cation pool serves as an effective reagent for introducing the ArS group in electrophilic substitution reactions of aromatic compounds, enolizable ketones, enol acetates, ketene silyl acetals, and allylsilanes (Scheme 1).



Scheme 1. The generation and accumulation of ArS(ArSSAr)$^+$ cation pool and its reactions with carbon nucleophiles (electrophilic substitution reactions).

Results and discussion

We first focused on the reactions of ArS(ArSSAr)$^+$ with aromatic compounds. A typical procedure is as follows. In the first step, a solution of ArS(ArSSAr)$^+BF_4^-$ (Ar = *p*-FC_6H_4) was generated and accumulated by the anodic oxidation of ArSSAr (0.40 mmol) in 0.3 M Bu_4NBF_4/CH_2Cl_2 (8.0 mL) at −78 °C (0.67 F/mol). 0.67 F/mol is the theoretical amount of electricity to convert ArSSAr into ArS(ArSSAr)$^+$. In the second step, 1,3,5-trimethoxybenzene

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(0.20 mmol) was added to the anodic solution containing ArS(ArSSAr)$^+BF_4^-$ (ca. 0.27 mmol) at −78 °C, and the solution was stirred at the same temperature for 3 min. Then, Et_3N (1 mL) was added to quench the reaction. The work-up followed by chromatography gave 2-ArS-1,3,5-trimethoxybenzene in an 84% yield (Table 1, entry 1). It is noteworthy that the reaction was completed within 3 min at −78 °C, indicating that ArS(ArSSAr)$^+$ is highly reactive.[10]

The reactions with other aromatic compounds were examined. As shown in Table 1, *m*-methoxytoluene and 3,5-dimethoxychlorobenzene reacted with ArS(ArSSAr)$^+$ quickly at −78 °C to give the corresponding mono ArS-substituted products in high yields (entries 2 and 3).

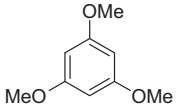
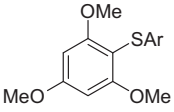
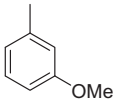
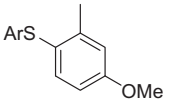
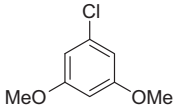
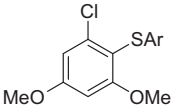
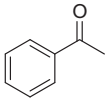
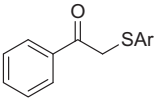
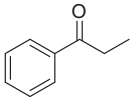
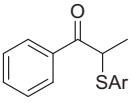
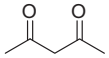
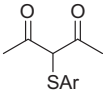
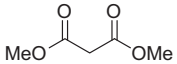
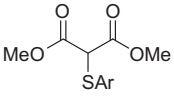
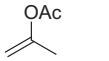
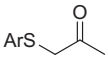
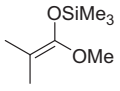
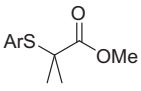
Enolizable ketones also reacted with ArS(ArSSAr)$^+$ and the ArS group was introduced to the α-carbon. The reaction of acetophenone is interesting. ArS was introduced to the methyl carbon selectively. The aromatic ring was not affected, presumably because of electron-withdrawing effect of the carbonyl group (entry 4). Ethyl phenyl ketone also reacted with ArS(ArSSAr)$^+$ and ArS was introduced to the α-carbon selectively, although the yield was moderate (entry 5). 1,3-Dicarbonyl compounds such as acetylacetone reacted with ArS(ArSSAr)$^+$ and the ArS group was introduced into the methylene carbon in a moderate yield (entry 6). In contrast, the reaction of dimethyl malonate with ArS(ArSSAr)$^+$ did not proceed at all (entry 7). Enol acetate reacted with ArS(ArSSAr)$^+$ to give ArS-substituted compounds in a moderate yield (entry 8).

Next, reactions of ArS(ArSSAr)$^+$ with silyl-substituted carbon nucleophile such as ketene silyl acetal was examined. The reaction of ArS(ArSSAr)$^+$ with dimethylketene methyltrimethylsilylacetal gave the corresponding ArS-substituted product in a good yield (entry 9).

The effect of the counter anion is interesting. The reaction of electrogenerated ArS(ArSSAr)$^+X^-$, which was prepared by the anodic oxidation of ArSSAr (0.40 mmol) in $Bu_4N^+X^-/CH_2Cl_2$, with 3-(trimethylsilyl)cyclohexene (1.00 mmol) was examined (X^- = BF_4^- or $B(C_6F_5)_4^-$). The use of BF_4^- as X^-, the reaction gave the allylated product (0.28 mmol) quantitatively (Scheme 2).[11] In contrast, the use of $B(C_6F_5)_4^-$ as X^- led to the formation of the allylated product in a 188% yield based on the electricity (0.506 mmol). Surprisingly, the decrease in the amount of electricity (0.20 F/mol) led to the formation of a significant amount of the allylated product (463% yield based on the electricity, 0.370 mmol), indicating that a catalytic amount of ArS(ArSSAr)$^+$ is sufficient for the reaction.

The following explanation seems to be reasonable (Scheme 3). One mole of ArS(ArSSAr)$^+$ reacted with the 3-(trimethylsilyl)cyclohexene to generate one mole of the arylthiolated product, one mole of ArSSAr, and one mole of $Me_3Si^+B(C_6F_5)_4^-$. Me_3Si^+ $B(C_6F_5)_4^-$ reacted

Table 1
Reactions of ArS(ArSSAr)$^+$ cation pool with carbon nucleophiles (Ar = *p*-FC_6H_4)[a]

Entry	Carbon nucleophile	Conditions	Product	% Yield[b]
1		−78 °C, 3 min		84
2		−78 °C, 3 min		90
3		−78 °C, 3 min		Quant
4		0 °C, 24 h		96[c]
5		0 °C, 24 h		48[c,d]
6		0 °C, 24 h		46
7		0 °C, 24 h		n.d.
8		−78 °C, 3 min		34
9		−78 °C, 3 min		82

[a] A Typical procedure: ArSSAr (Ar = *p*-FC_6H_4, 0.40 mmol, 2 equiv) was oxidized electrochemically in 0.3 M Bu_4NBF_4/CH_2Cl_2 at −78 °C using 0.67 F/mol of electricity. The solution of ArS(ArSSAr)$^+BF_4^-$ (ca. 0.27 mmol) thus obtained was allowed to react with carbon nucleophile (0.20 mmol). Then the reaction was quenched with Et_3N (1 mL).
[b] Isolated yield.
[c] 4.5 equiv of ArSSAr (Ar = *p*-FC_6H_4) was used.
[d] The purity of the product was ca. 80%.