



Solvent-free copper-catalyzed oxidative S-arylation of 1,2-diaryldisulfides with aryltrimethoxysilane

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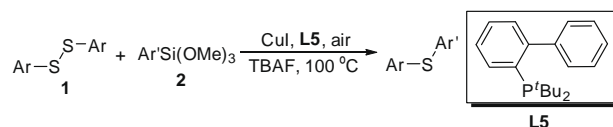
ABSTRACT

A novel and solvent-free protocol for the synthesis of diarylsulfides by the copper-catalyzed oxidative S-arylation of 1,2-diaryldisulfides with aryltrimethoxysilanes is reported. In the presence of CuI, 2-(di-*tert*-butylphosphino)biphenyl, and TBAF (*n*-Bu₄NF), a variety of 1,2-diaryldisulfides underwent the S-arylation reaction with aryltrimethoxysilanes smoothly to afford the corresponding products in moderate to good yield. It is noteworthy that the reaction is conducted under solvent-free conditions.

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Diarylsulfides are an important class of structural units commonly found in many naturally occurring and biologically active compounds¹ as well as are valuable intermediates in organic synthesis.² During the last several years, impressive progress had been made for the synthesis of this class of diarylsulfides.^{1–6} Although many ways have been developed for these purposes, one of the most reliable approaches is transition metal-catalyzed sulfidation reaction.^{3–6} Generally, the sulfidation reaction is conducted between (1) aryl halides and thiols³ or disulfides,⁴ or (2) organoboronic acids and thiols⁵ or disulfides.⁶ The use of organosilicon compounds, initiated by Hiyama and co-workers,⁷ has many advantages in comparison to other organometallic donors, such as organoboronic acids.⁸ Organosilicon compounds present high stability, low toxicity, and high accessibility and are therefore excellent candidates for industrial processes. To the best of our knowledge, however, no paper has been reported on the synthesis of diarylsulfides using organosilicon compounds as the S-arylation reaction partner. Here, we wish to report a simple and solvent-free protocol for the synthesis of diarylsulfides by copper-catalyzed oxidative sulfidation of diaryldisulfides with aryltrimethoxysilanes in the presence of 2-(di-*tert*-butylphosphino)biphenyl and TBAF (*n*-Bu₄NF) (Scheme 1).

As shown in Table 1, S-arylation of 1,2-bis(4-chlorophenyl) disulfane (**1a**) with trimethoxy(phenyl)silane (**2a**) was conducted



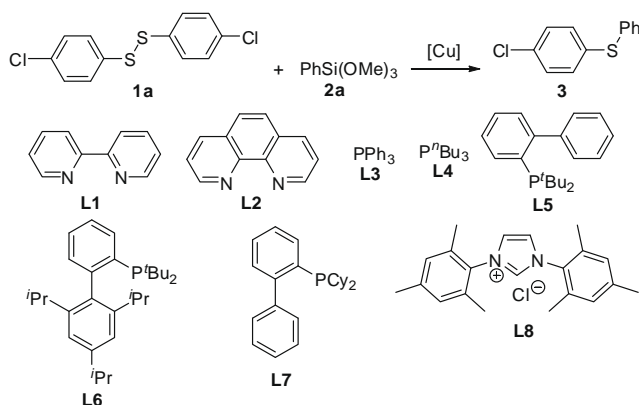
Scheme 1.

to explore the suitable reaction conditions. We have recently demonstrated that TBAF (*n*-Bu₄NF) is an effective base for the solvent-free Pd or Cu-catalyzed cross-coupling reactions.⁹ Thus, we expected to perform the reaction under solvent-free conditions using TBAF as base. As expected, the S-arylation of substrate **1a** with silane **2a** was conducted successfully under solvent-free conditions using CuI as the catalyst and TBAF as the base under air atmosphere. Initially, a series of ligands **L1–L8** were examined, and the results showed that 2-(di-*tert*-butylphosphino)biphenyl (**L5**) provided the best results (entries 1–9). Without ligands, treatment of substrate **1a** with silane **2a**, CuI and TBAF afforded the corresponding product **3** in 53% yield (entry 1), whereas the yield of **3** was enhanced to 77% in the presence of **L5** (entry 6). The other ligand **L2–L4** and **L6–L8** were found to favor the reaction (entries 3–5 and 7–9), but **L1** reduced the yield of the product **3** to some extent (entry 2). Among the effect of catalysts examined, a number of catalysts, including CuBr, CuCl, Cu₂O, (CuOTf)₂·C₆H₆, CuBr₂, and Cu(OTf)₂, were less effective than CuI (entries 6 and 10–16). CuBr, for instance, decreased the yield of the product **3** to 65% (entry 10), and no reaction was observed without Cu catalysts (entry 16). The

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Table 1
Screening optimal conditions^a



Entry	[Cu]	Ligand	Additive	T (°C)	Isolated yield (%)
1	CuI	—	TBAF	100	53
2	CuI	L1	TBAF	100	38
3 ^b	CuI	L2	TBAF	100	65
4	CuI	L3	TBAF	100	60
5	CuI	L4	TBAF	100	65
6	CuI	L5	TBAF	100	77
7	CuI	L6	TBAF	100	58
8	CuI	L7	TBAF	100	50
9	CuI	L8	TBAF	100	55
10	CuBr	L5	TBAF	100	65
11	CuCl	L5	TBAF	100	61
12	Cu ₂ O	L5	TBAF	100	35
13	(CuOTf) ₂ ·C ₆ H ₆	L5	TBAF	100	56
14	CuBr ₂	L5	TBAF	100	59
15	Cu(OTf) ₂	L5	TBAF	100	60
16	—	L5	TBAF	100	0
17	CuI	L5	TBAF	80	63
18	CuI	L5	TBAF	120	71
19 ^b	CuI	L5	TBAF	100	63
20 ^b	CuI	L5	CsF	100	Trace
21 ^b	CuI	L5	Cs ₂ CO ₃	100	Trace
22 ^c	CuI	L5	TBAF	100	72

^a Reaction conditions: **1a** (0.3 mmol), **2a** (0.9 mmol), CuI (5 mol %), ligand (10 mol %), and base (3 equiv) under air atmosphere for 24 h.

^b DMSO (1 mL) was added.

^c Under oxygen atmosphere.

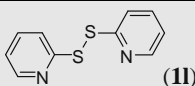
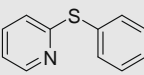
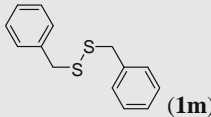
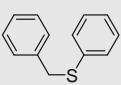
controlled experimental results demonstrated that the reaction temperature had a fundamental influence on the reaction, and 100 °C gave the best results (entries 6, 17, and 18). The reaction could also be carried out smoothly in DMSO, but the yield was reduced to some extent (entry 19). Two other bases, CsF and Cs₂CO₃, were also investigated, and both were inferior than TBAF even in DMSO (entries 20 and 21). It is worth noting that the reaction can be conducted efficiently under pure oxygen atmosphere (entry 21).

With the optimal reaction conditions, we decided to explore scope of both 1,2-diaryldisulfides and trimethoxysilanes for the reaction (Table 2).¹⁰ As demonstrated in Table 2, a number of trimethoxysilanes were firstly examined by reacting with diphenyldisulfane (**1b**), CuI, **L5**, and TBAF (entries 1–5). We found that aryltrimethoxysilanes **2a–c**, bearing either electron-donating or electron-deficient groups on aromatic ring, all work well with disulfane **1b** in good yields under the standard condition (entries 1–3), but the reactions of vinyltrimethoxysilane (**2d**) or allyltrimethoxysilane were unsuccessful (entries 4 and 5). Next, a variety of disulfanes were evaluated. The results indicated that a series of functional groups on the aryl moiety, including methyl, methoxy, fluoro, chloro, bromo, nitro, amino, and cyano groups, were perfectly tolerated. However, aliphatic disulfane, 1,2-dibenzyldisul-

fane (**1m**), was not suitable for the reaction (entry 16). 1,2-Di(*p*-tolyl)disulfane (**1c**), for instance, underwent the S-arylation reaction with silane **2a**, CuI, **L5**, and TBAF smoothly to afford the target product **9** in 75% yield (entry 6). To our delight, the reaction conditions were also compatible with ether, halides, and carbonitrile that could be readily substituted and decomposed under harsh conditions (entries 7–11 and 14). It is noted that free NH₂ group is also tolerated well under the standard condition (entries 13 and 14). Disulfane (**1c**) bearing an amino group, for example, was treated with silane **2a**, CuI, **L5**, and TBAF successfully to afford the corresponding fipronil analog (**15**) in moderate yield (entry 14).¹¹ Interestingly, diheteroaryldisulfane (**1l**) was still a suitable substrate for the reaction under the same conditions (entry 15).

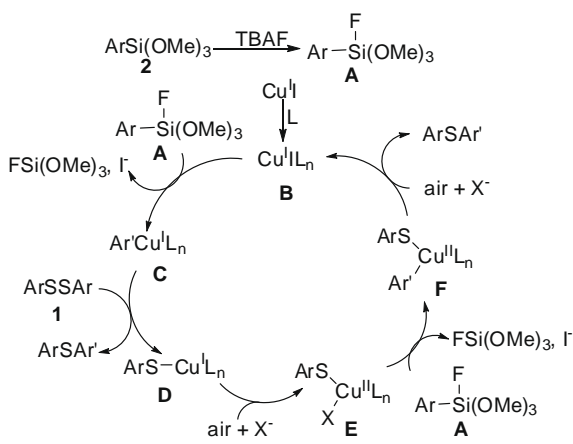
A working mechanism was proposed as outlined in Scheme 2 on the basis of the earlier proposed mechanism.^{5–8} Aryltrimethoxysilane **2** can readily react with TBAF to afford a pentavalent silicate intermediate **A**.^{7,8,12} The pentavalent silicate **A** undergoes transmetalation with intermediate **B**, which is obtained from the coordination of ligand with CuI catalyst, to generate intermediate **C**. Intermediate **C** subsequently reacts with ArSSAr **1** to generate intermediate **D** and the target product. In the presence of air and I[−], intermediate **D** is oxidated to give intermediate **E**, followed by the second transmetalation with aryltrimethoxysilane **2** to yield

Table 2 (continued)

Entry	Disulfide 1	R ²	Product	Yield ^b (%)
15	 (11)	(2a)		36 (17)
16 ^c	 (1m)	(2a)		Trace (18)

^a Reaction conditions: **1** (0.3 mmol), **2** (0.9 mmol), CuI (5 mol %), **L5** (10 mol %), and TBAF·3H₂O (3 equiv) at 100 °C for 24 h.

^b Isolated yield based on disulfide **1**.



Scheme 2. A working mechanism.

intermediate **F**. Finally, reductive elimination of intermediate **F** takes place to afford the target product and regenerate the active Cu(I) species. We deduced that ligand **L5** displayed the highest activity due to its steric and electronic effects. Study on the real role of ligand is in progress.

In summary, we describe here the first example of the synthesis of diarylsulfides by the copper-catalyzed oxidative S-arylation of 1,2-diaryldisulfides with aryltrimethoxysilanes. In the presence of CuI, 2-(di-*tert*-butylphosphino)biphenyl, and TBAF (*n*-Bu₄NF), a variety of 1,2-diaryldisulfides underwent the S-arylation reaction with aryltrimethoxysilanes smoothly to afford the corresponding products in moderate to good yield. Noteworthy is that the reaction is conducted under solvent-free conditions. Further application of the present system in organic synthesis and study of the detailed mechanism are underway.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.12.066.

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