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Copper-Catalyzed Production of Diaryl Sulfides Using Aryl Iodides and a Disilathiane

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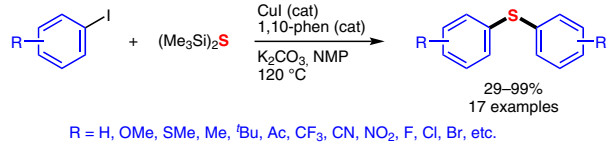

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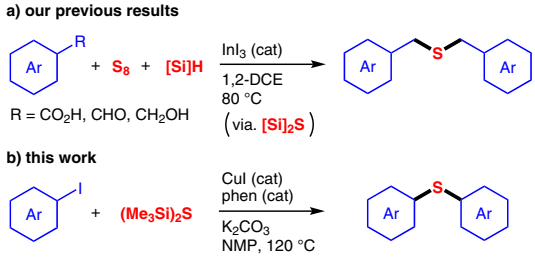
Abstract A disilathiane was found to be a novel S1 source for the copper-catalyzed synthesis of diaryl sulfides using aryl iodides. The reaction of iodoarenes and hexamethyldisilathiane, $(Me_3Si)_2S$, in the presence of a catalytic amount of CuI/1,10-phenanthroline provided various types of diaryl sulfides in good yields.

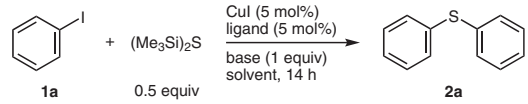
Key words copper catalyst, aryl iodides, disilathiane, carbon–sulfur bond formation, diaryl sulfides

Sulfides (thioethers), R–S–R, are an important class of structural units in organic chemistry, and a number of research groups have devoted extensive effort to the development of novel and efficient synthetic strategies for the construction of these skeletons.[1] Our group has reported the indium-catalyzed reductive construction of thioethers from benzoic acids,[2a] benzaldehydes,[2a] and benzyl alcohols[2b] using a combination of elemental sulfur (S_8) and hydrosilanes. In these reactions, the *in situ* generation of a disilathiane ($[Si]_2S$) from unactivated S_8 and a hydrosilane is considered to be a key activation process for the formation of dibenzyl sulfides (Scheme 1, a). Sulfides obtained by these procedures, however, have primarily been limited to the dibenzyl variety. Also, the protocol could not undertake the formation of the corresponding diaryl alternatives in principle. To produce diaryl sulfides, the transition-metal-catalyzed double formation of a carbon–sulfur bond between two molecules of an aryl halide and an appropriate S1 source has been a reliable and efficient procedure. Various sulfur sources have been utilized for this type of diaryl sulfide synthesis: S_8,[3] thiourea,[4] xanthogenate,[5] thioester,[6] KSCN,[7] Na_2S,[8] CS_2,[9] $Na_2S_2O_3$,[10] and K_2S.[11] To the best of our knowledge, the use of a disilathiane ($[Si]_2S$) as a S1 source for the catalytic construction of diaryl sulfides is unprecedented. Herein, we describe the copper-catalyzed, one-pot synthesis of symmetrical diaryl sulfides using a variety of aryl iodides and hexamethyldisilathiane (Scheme 1, b).



Scheme 1 Catalytic construction of a) dibenzyl sulfides, and b) diaryl sulfides

Table 1 Optimization of the Reaction Conditions[a]



Entry	Ligand	Base	Solvent	Yield (%)[b]
1	none	none	NMP, 120 °C	0
2	phen	none	NMP, 120 °C	trace
3	none	K_2CO_3	NMP, 120 °C	66
4	phen	K_2CO_3	NMP, 120 °C	90 (92)[c]
5	phen	K_2CO_3	NMP, 100 °C	63
6	phen	K_2CO_3	NMP, 80 °C	trace
7	phen	K_2CO_3	DMF, 120 °C	64[d]
8	phen	K_2CO_3	DMSO, 120 °C	40[e]
9	phen	K_2CO_3	toluene, 120 °C	0

[a] Reaction conditions: **1a** (0.5 mmol), $(Me_3Si)_2S$ (0.25 mmol), CuI (0.025 mmol), 1,10-phenanthroline (0.025 mmol), and K_2CO_3 (0.5 mmol) in NMP (0.5 mL) at 120 °C for 14 h.
[b] GC yield.
[c] Isolated yield, 1 mmol scale.
[d] The corresponding disulfide was also generated in a 14% GC yield.
[e] The corresponding disulfide was also generated in a 13% GC yield.

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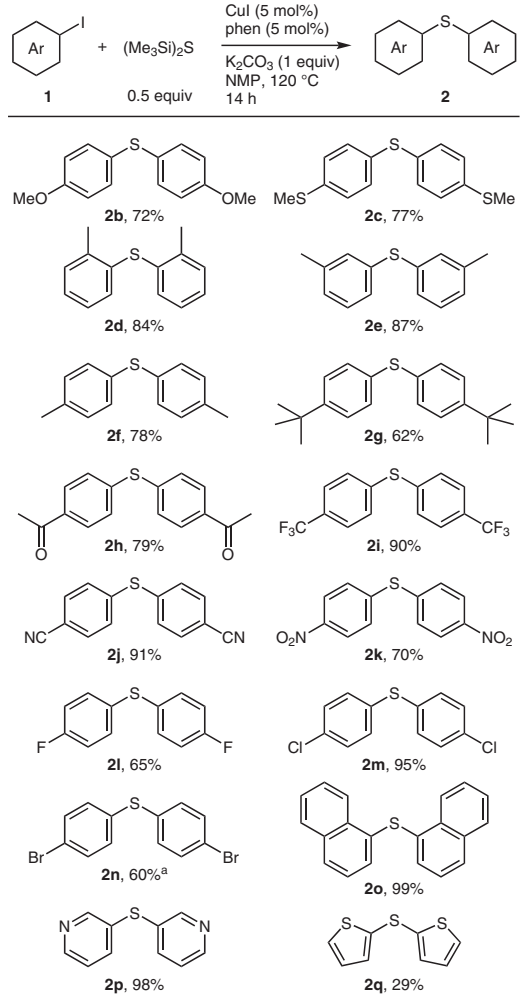
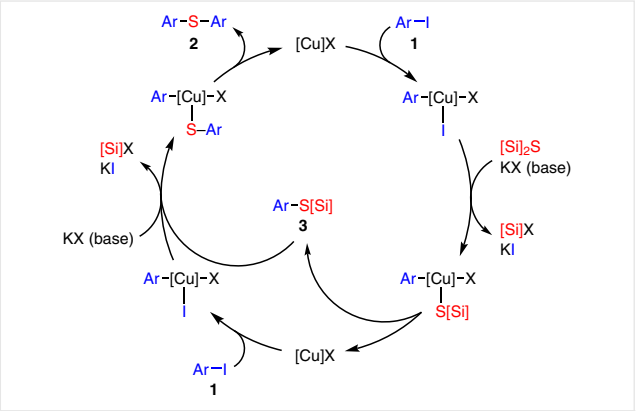
Optimization of the conditions for sulfidation using iodobenzene (**1a**) and $(Me_3Si)_2S$ was initially investigated (Table 1). When the reaction was performed with only a catalytic amount of CuI in *N*-methyl-2-pyrrolidone (NMP) as a solvent at 120 °C for 14 h, the formation of the desired sulfide **2a** was not observed, as determined by GC analysis (Table 1, entry 1). The addition of 1,10-phenanthroline (phen) as a ligand produced a trace amount of **2a** (Table 1, entry 2). Instead, the addition of a stoichiometric amount of K_2CO_3 effectively increased the yield of **2a** to 66% (Table 1, entry 3). The reaction with both the ligand and the base afforded **2a** in a 90% GC yield.[12] Under these conditions, 92% of diphenyl sulfide (**2a**) was isolated using 1 mmol of **1a** (Table 1, entry 4). The reaction temperature was investigated to achieve milder reaction conditions, but the higher reaction temperature (120 °C) was essential to complete the conversion (Table 1, entries 4–6). Next, the solvents were screened. Reactions in either DMF or DMSO proceeded to form sulfide **2a** in moderate yields, but the undesired disulfide, diphenyl disulfide, was simultaneously detected as a byproduct in 14% and 13% GC yields (Table 1, entries 7 and 8). The reaction did not proceed when using toluene as a solvent (Table 1, entry 9).



Scheme 2 Substrate scope for aryl iodides **1**. *Reagents and conditions*: **1** (1 mmol), $(Me_3Si)_2S$ (0.5 mmol), CuI (0.05 mmol), 1,10-phenanthroline (0.05 mmol), and K_2CO_3 (1 mmol) in NMP (1 mL) at 120 °C for 14 h. Isolated yields of diaryl sulfides **2** are shown. [a] NMR yield.

Copper-catalyzed production of diaryl sulfides **2** using a disilathiane was then conducted with several iodoarenes **1** (Scheme 2). When the reaction of iodobenzene bearing a 4-methoxy group **1b** was performed under the optimal conditions, the corresponding product **2b** was obtained in a 72% isolated yield. Sulfur-containing iodoarene **1c** was also converted into product **2c**, and the reactions with the alkyl-substituted versions **1d–g** proceeded to form the corresponding diaryl sulfides **2d–g**, regardless of the position of the substituent on their benzene rings. Substrates bearing electron-withdrawing acetyl **1h**, trifluoromethyl **1i**, cyano **1j**, and nitro **1k** groups were also suitable for the sulfidation and provided products **2h–k** in excellent isolated yields. When using halogen-substituted iodobenzenes such as 1-fluoro-4-iodobenzene (**1l**), 1-chloro-4-iodobenzene (**1m**), and 1-bromo-4-iodobenzene (**1n**), each activation occurred at the carbon–iodine bond selectively over C–F, C–Cl, and C–Br bonds, giving 4-halo-diaryl sulfides **2l–n**. The reaction of an iodoarene bearing a 1-naphthyl moiety **1o** proceeded to give the corresponding sulfide **2o**. Heteroaromatic substrates 3-iodopyridine (**1p**) and 2-iodothiophene (**1q**) were also applicable to the conversion to afford products **2p** and **2q**, respectively.

A plausible catalytic cycle for the present reaction is illustrated in Scheme 3. The starting copper(I) inserts to the C–I bond of iodoarene **1** to afford the Ar–Cu–I species, which undergoes a ligand exchange between a disilathiane and a base. The first C–S bond formation occurs by reductive elimination and provides benzenethiol derivative **3** with a regeneration of copper(I). Again, the oxidative addition of **1** to copper(I) occurs to form an Ar–Cu–I species, followed by transmetalation between **3** and the formed Ar–



Scheme 3 Proposed mechanism for the preparation of diaryl sulfides

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Cu–I to generate an Ar–[Cu]–SAr species. Finally, the second reductive elimination of the species occurs to provide diaryl sulfide **2**.[13]

In summary, we described an efficient copper catalytic system for the production of diaryl sulfide using iodoarenes and a disilathiane via a double carbon–sulfur bond formation.[14] A variety of iodobenzene derivatives were applied to this protocol with highly functional group tolerance, which yielded the corresponding sulfides.[15] The results of a preliminary mechanistic study supported the plausibility of using benzenethiol as an intermediate.[16]

Funding Information

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1591723.

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(12) See the Supporting Information for more details on the screening of the ligands.

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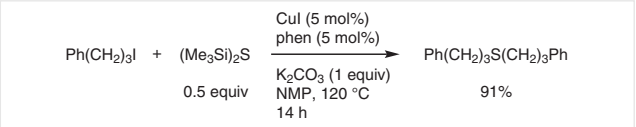
(14) **General Procedure**
To a screw-capped test tube under a nitrogen atmosphere, 1,10-phenanthroline (0.05 mmol, 9.0 mg), iodobenzene **1** (1 mmol), K_2CO_3 (1 mmol, 138.2 mg), CuI (0.05 mmol, 9.5 mg), *N*-methyl-2-pyrrolidone (1 mL), and 1,1,1,3,3,3-hexamethyldisilathiane (0.5 mmol, 89.2 mg) were added. After the tube was sealed with a cap, the mixture was heated at 120 °C for 14 h. After the reaction, H_2O was added to the mixture, which was then extracted with EtOAc three times. The combined organic phases were evaporated under reduced pressure. The crude material was purified by silica gel column chromatography to give the corresponding diaryl sulfide **2**.
Diphenyl Sulfide (2a)
The general procedure was followed with iodobenzene (**1a**, 202.7 mg, 0.99 mmol) for 14 h. Column chromatography (hexane) afforded **2a** as a colorless oil (85.0 mg, 92%). ^{1}H NMR (500.2 MHz, $CDCl_3$): δ = 7.23 (t, *J* = 7.5 Hz, 2 H, ArH), 7.29 (t, *J* = 7.5 Hz, 4 H, ArH), 7.34 (d, *J* = 7.5 Hz, 4 H, ArH). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 127.0, 129.2, 131.0, 135.8. LRMS (EI): *m/z* (% relative intensity) = 187 (17) $[M + 1]^+$, 186 (100), 185 (69), 184 (27), 154 (14), 134 (14), 77 (15), 51 (20).

(15) An alkyl iodide was also applicable for this reaction (Scheme 4).



Scheme 4

(16) See the Supporting Information for further results to support the proposed mechanism.

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