

# Copper(II)-Catalyzed Single-Step Synthesis of Aryl Thiols from Aryl Halides and 1,2-Ethanedithiol

Yajun Liu,<sup>a,b</sup> Jihye Kim,<sup>a</sup> Heesun Seo,<sup>a</sup> Sunghyoun Park,<sup>b</sup> and Junghyun Chae<sup>a,\*</sup>

<sup>a</sup> Department of Chemistry and Research Institute of Basic Sciences, Sungshin Women's University, Seoul, Korea  
Fax: (+82)-2-920-2547; phone: (+82)-2-920-7660; e-mail: jchae@sungshin.ac.kr

<sup>b</sup> College of Pharmacy, Seoul National University, Seoul, Korea

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Dedicated to Prof. S. L. Buchwald on the occasion of his 60<sup>th</sup> birthday.

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**Abstract:** A highly efficient transition metal-catalyzed single-step synthesis of aryl thiols from aryl halides has been developed employing copper(II) catalyst and 1,2-ethanedithiol. The key features are use of readily available reagents, a simple operation, and relatively mild reaction conditions. This new protocol shows a broad substrate scope with excellent functional group compatibility. A variety of aryl thiols are directly prepared from aryl halides in high yields. Furthermore, the aryl thiols are used *in situ* for the synthesis of more advanced molecules such as diaryl sulfides and benzothiophenes.

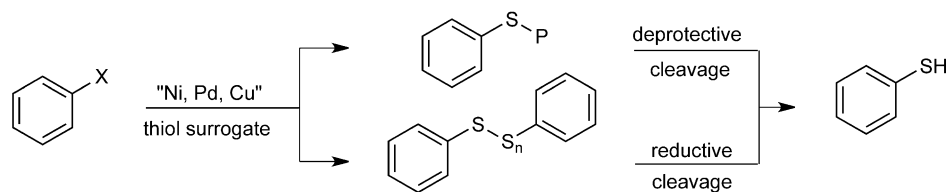
**Keywords:** alkanedithiols; aryl thiols; benzothiophenes; copper(II) catalysts; C–S cross-coupling; diaryl sulfides

Aryl thiols are important structural motifs and building blocks for both natural products and synthetic compounds that show diverse activities ranging from pharmaceuticals to polymers and functional materials.<sup>[1]</sup> Yet, effective synthetic methods for aryl thiols are still much needed due to the scarcity of concise and mild conditions leading to a wide spectrum of aryl thiols. Most of conventional methods including Leuckart thiophenol synthesis,<sup>[2]</sup> Newman–Kwart reaction,<sup>[3]</sup> and Schoenberg reaction<sup>[4]</sup> require multistep syntheses involving diazotization and/or thermal rearrangement at 200–300 °C. Reduction of arylsulfonyl chlorides<sup>[5]</sup> or diaryl polysulfides<sup>[6]</sup> is often employed, but it is also unfavorable due to the laborious preparation of the specific precursors as well as harsh conditions. Synthetic route from readily available aryl halides has been reported using either H<sub>2</sub>S<sup>[7]</sup> or excess alkyl thiolates<sup>[8]</sup> *via* aromatic nucleophilic substitution.

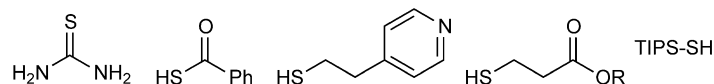
However, this reaction also runs at very high temperature, and it is narrowly applicable to simple aryl halides.

Attempts at the direct introduction of a thiol group into aromatic rings *via* transition metal-catalyzed reactions have been unfruitful, whereas the corresponding formations of amine<sup>[9]</sup> and hydroxy<sup>[10]</sup> groups are known. Apart from the well-known ‘poisonous’ character of sulfur to metal catalysts,<sup>[11]</sup> it is presumably due to the high reactivity of aryl thiols, producing side products; even if aryl thiols are generated, they further react with aryl halides and/or they are easily oxidized during the coupling process.<sup>[1c]</sup> In fact, metal sulfides such as NaSH and Na<sub>2</sub>S always gives diaryl sulfides and diaryl disulfides in the coupling reaction with aryl halides.<sup>[12]</sup> Therefore, surrogates for the sulfide ion, which can cross-couple with aryl halides and later liberate thiols by additional transformation, have been sought over the past few decades (Scheme 1). In the earlier work published by Takagi,<sup>[13]</sup> thiourea reacted with aryl iodides in the presence of a nickel(0) catalyst and the resulting *S*-aryl-isothiuronium salt was further hydrolyzed to give aryl thiols. Other thiol surrogates later reported are mostly based on the protection chemistry of thiols:<sup>[14]</sup> thiobenzoic acid, pyridine-ethanethiol, isooctyl 3-mercaptopropionate, and triisopropylsilanethiol. While these reports provided proof-of-concepts for aryl thiol preparation with a few examples, more reliable synthetic methods were developed very recently. Ma<sup>[12b]</sup> and Feng<sup>[15]</sup> employed sulfur powder and Guo<sup>[16]</sup> applied sodium thiosulfate with copper and palladium catalysts, respectively. Their coupling products are polysulfides, which need to be reduced to afford the desired aryl thiols. Although these transition metal-catalyzed protocols are milder than the traditional methods, they still have much room for improvement. First of all, more efficient single-step reactions with an atom-economical

Previously reported methods: **two-step reaction**

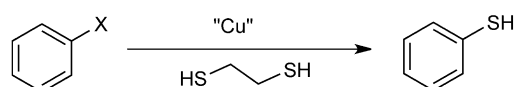


(a) thiol surrogates removed by deprotective cleavage:



(b) thiol surrogates removed by reductive cleavage:  $S_8$ ,  $Na_2S_2O_3$

This work: **single-step reaction**

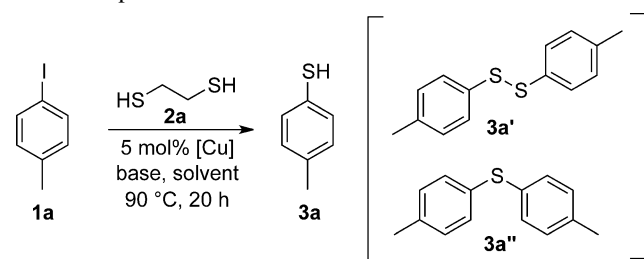


**Scheme 1.** Synthesis of aryl thiols *via* transition metal-catalyzed C–S cross-coupling reactions.

sulfur source would be desirable, as the extra reaction steps and/or by-products from the surrogates make these methods less attractive. The isolation of aryl thiols from the reaction mixture is also problematic due to their highly oxidizable nature, unless the yield is high in each step and the reaction mixture contains only readily separable by-products. Copper is often the metal of choice but it generally works only with aryl iodides. One may broaden the substrate scope to aryl bromides by using an expensive palladium-phosphine system, but both palladium and copper catalytic methods still show limited tolerance for functional groups. Herein, we report a highly efficient transition metal-catalyzed *single-step* synthesis of aryl thiols from aryl halides using a copper(II) catalyst and 1,2-ethanedithiol. Our newly developed protocol requires no additional steps or reagents, and is applicable to a broad range of aryl iodides and bromides. Moreover, the generated aryl thiols can be used *in situ* for the synthesis of more advanced molecules.

In search for a suitable thiol surrogate for aryl thiol synthesis, we discovered that alkanedithiols can cross-couple with aryl halides under copper catalytic conditions. Intriguingly, we found that aryl thiols are directly obtained when certain alkanedithiols are employed, which is especially so with 1,2-ethanedithiol. Thus, we set out to investigate the optimal conditions with 1,2-ethanedithiol and 4-iodotoluene, studying factors such as copper salt, solvent, base, equivalents of reagents, reaction time, and temperature (Table 1). Our initial attempt using 5 mol% of CuI and 5 equivalents of KOH in DMSO at 90 °C for 20 h resulted in the formation of 4-methylbenzenethiol (**3a**) in 87% (entry 2). To our delight, undesired by-products in-

cluding *para*-tolyl disulfide (**3a'**) and di-*para*-tolyl sulfide (**3a''**) were not observed. Diarylated 1,2-ethanedithiol, which was expected from a C–S coupling reaction at both thiol groups, was not detected, either. However, di-*para*-tolyl sulfide was formed in small amount (*ca.* 5%) when DMF was used as solvent (entry 3). Polar solvents other than DMSO usually showed low conversion and yield (entries 3–5), and non-polar solvents such as toluene were essentially ineffective (entry 6). Adding water seems to help solubilize the inorganic base, thereby slightly improving the yield (entry 7). Further optimization with various copper salts revealed that both copper(I) and copper(II) salts are generally effective and quantitative conversion from **1a** into **3a** can be achieved with  $Cu(OH)_2$  and  $CuSO_4 \cdot 5H_2O$  (entries 8–14).  $CuSO_4 \cdot 5H_2O$  was chosen as the catalyst for further studies because it is air- and moisture-stable, readily available, and easily removed during aqueous work-up. Strong bases such as KOH, NaOH and CsOH were necessary for the transformation (entries 13, 15, and 16) while weak bases such as  $K_2CO_3$ ,  $K_3PO_4$ , and  $Cs_2CO_3$  showed poor results and a small amount of *para*-tolyl disulfide (1–3%) was detected (entries 17–19). However, when  $Cs_2CO_3$  was used at the elevated temperature up to 110 °C, complete conversion of starting material and 90% yield of the desired thiol was achieved, suggesting that  $Cs_2CO_3$  can be used in place of KOH for those substrates sensitive to strong bases (entry 19). Reducing the amount of 1,2-ethanedithiol and/or base, shortening the reaction time, and lowering the reaction temperature caused negative effects (entries 20–24). Nonetheless, **1a** was effectively converted into **3a** with reduced loading of 1,2-ethane-

**Table 1.** Optimization of thiolation conditions.<sup>[a]</sup>


Entry	[Cu]	Solvent	Base	Yield [%] <sup>[b]</sup>
1	–	DMSO	KOH	< 5
2	CuI	DMSO	KOH	87
3	CuI	DMF	KOH	31
4	CuI	H <sub>2</sub> O	KOH	37
5	CuI	dioxane	KOH	< 5
6	CuI	toluene	KOH	0
7	CuI	DMSO/H <sub>2</sub> O	KOH	92
8	CuBr	DMSO/H <sub>2</sub> O	KOH	97
9	Cu <sub>2</sub> O	DMSO/H <sub>2</sub> O	KOH	76
10	CuCl <sub>2</sub>	DMSO/H <sub>2</sub> O	KOH	96
11	Cu(OAc) <sub>2</sub>	DMSO/H <sub>2</sub> O	KOH	96
12	Cu(OH) <sub>2</sub>	DMSO/H <sub>2</sub> O	KOH	99
13	CuSO <sub>4</sub> ·5 H <sub>2</sub> O	DMSO/H <sub>2</sub> O	KOH	99
14	CuO	DMSO/H <sub>2</sub> O	KOH	92
15	CuSO <sub>4</sub> ·5 H <sub>2</sub> O	DMSO/H <sub>2</sub> O	NaOH	91
16	CuSO <sub>4</sub> ·5 H <sub>2</sub> O	DMSO/H <sub>2</sub> O	CsOH	98
17	CuSO <sub>4</sub> ·5 H <sub>2</sub> O	DMSO/H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	35
18	CuSO <sub>4</sub> ·5 H <sub>2</sub> O	DMSO/H <sub>2</sub> O	K <sub>3</sub> PO <sub>4</sub>	67
19	CuSO <sub>4</sub> ·5 H <sub>2</sub> O	DMSO/H <sub>2</sub> O	Cs <sub>2</sub> CO <sub>3</sub>	70, 90 <sup>[c]</sup>
20 <sup>[d]</sup>	CuSO <sub>4</sub> ·5 H <sub>2</sub> O	DMSO/H <sub>2</sub> O	KOH	86, 96 <sup>[c]</sup>
21 <sup>[e]</sup>	CuSO <sub>4</sub> ·5 H <sub>2</sub> O	DMSO/H <sub>2</sub> O	KOH	87
22 <sup>[f]</sup>	CuSO <sub>4</sub> ·5 H <sub>2</sub> O	DMSO/H <sub>2</sub> O	KOH	69
23 <sup>[g]</sup>	CuSO <sub>4</sub> ·5 H <sub>2</sub> O	DMSO/H <sub>2</sub> O	KOH	95
24 <sup>[h]</sup>	CuSO <sub>4</sub> ·5 H <sub>2</sub> O	DMSO/H <sub>2</sub> O	KOH	66

<sup>[a]</sup> Reaction conditions: **1a** (1 mmol), **2a** (2 mmol), [Cu] (5 mol%), base (5 equiv.), DMSO (2 mL) or DMSO/H<sub>2</sub>O (2 mL/0.2 mL), 90 °C, 20 h.

<sup>[b]</sup> GC yields using *n*-dodecane as internal standard.

<sup>[c]</sup> At 110 °C.

<sup>[d]</sup> With 1.2 equiv. of **2a**.

<sup>[e]</sup> With 4 equiv. of KOH.

<sup>[f]</sup> With 1.2 equiv. of **2a** and 3 equiv. of KOH.

<sup>[g]</sup> For 12 h.

<sup>[h]</sup> At 70 °C.

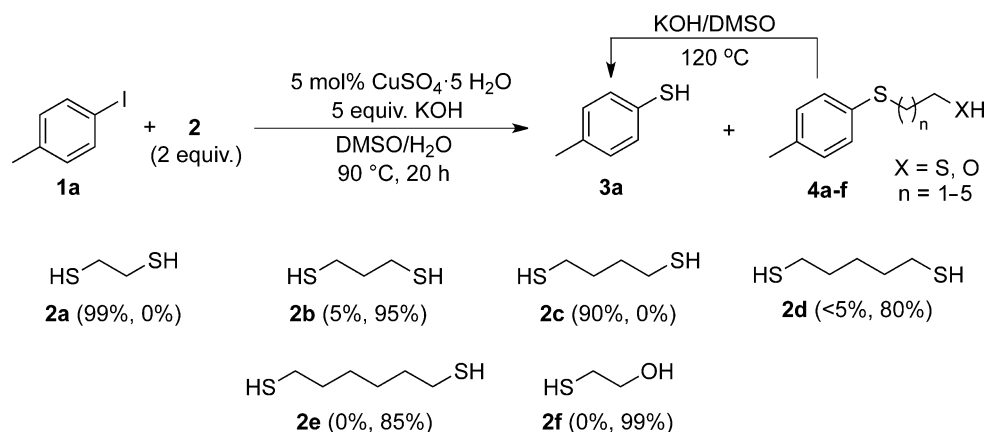
dithiol (1.2 equiv.) at higher temperature (110 °C) (entry 20). These optimization experiments led to the following reaction conditions: ArI (1 mmol), 1,2-ethanedithiol (2 mmol), CuSO<sub>4</sub>·5H<sub>2</sub>O (5 mol%), KOH (5 mmol), DMSO/H<sub>2</sub>O (2 mL/0.2 mL), 90 °C, 20 h.

In order to obtain an insight into our reaction pathway, several aliphatic dithiols of different chain lengths and 2-mercaptoethanol were tested under the standard conditions (Scheme 2). Depending on the sulfur sources (**2a–f**), either aryl thiol **3a** or aryl alkyl sulfide **4** was produced; 1,2-ethanedithiol (**2a**) and 1,4-butanedithiol (**2c**) gave **3a** as the only product, but

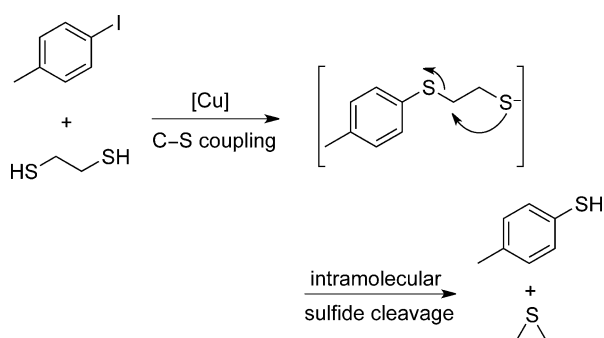
other aliphatic dithiols (**2b**, **2d**, **2e**) and 2-mercaptoethanol (**2f**) gave **4** as the major product.<sup>[17]</sup> When these aryl alkyl sulfides such as **4b**, **4d**, **4e** and **4f** were isolated and treated with KOH in DMSO at 120 °C, **3a** was generated in 30–80% yields. Such a conversion seems to proceed *via* intramolecular S<sub>N</sub>2 cleavage reaction as 6- and 7-membered cyclic thioethers were detected by GC-MS in the reaction of **4d** and **4e**, respectively. In addition, it was observed that tetrahydrothiophene was formed along with aryl thiol **3a** when 1,4-butanedithiol (**2c**) was reacted with **1a**.<sup>[18]</sup>

Inspired by these experimental results, we reached a plausible reaction pathway for the formation of aryl thiols (Scheme 3). The C(aryl)–S bond between aryl halide and aliphatic dithiols is formed in the presence of copper catalyst to afford aryl alkyl sulfide, and then the S–C(alkyl) bond is cleaved *via* an intramolecular S<sub>N</sub>2 reaction by the terminal alkyl thiolate under the basic conditions. Presumably, the driving forces of the cleavage reaction are intramolecular thioether ring formation and the innate character of thiophenolate as a good leaving group. Whether aryl thiol can be obtained in a single-step or not would depend on the efficiency of the intramolecular S<sub>N</sub>2 reaction. Therefore, the results shown in Scheme 2 are consistent with the fact that 3- and 5-membered ring formation is more favored than ring formation of other sizes. Weaker nucleophilic alkoxides as in case of **4f** are less efficient than the corresponding thiolates for the cleavage reaction.

We then explored the scope of our developed transformation and the results are summarized in Table 2. Good to excellent yields were obtained for a broad range of substrates. Aryl iodides were readily converted into aryl thiols regardless of electronic and steric effects of substituents, while aryl bromides possessing electron-neutral and electron-withdrawing groups were transformed at an elevated temperature (110 °C). Simple alkyl substituted aryl iodides, biphenyl iodide, 1- and 2-iodonaphthalenes, and some of their bromo equivalents reacted in very good to excellent yields (**3a–3f**). Free amine, phenolic hydroxy and aliphatic hydroxy groups were compatible under the reaction conditions (**3g–3l**) while competitive N- or O-arylation did not occur. In case of alkoxy-substituted substrates such as **3m**, **3n**, and **3o**, cleavage of alkyl group by thiolate was observed in less than 5%. The preparation of 3-hydroxythiophenol (**3j**) using our single-step catalytic system is noteworthy because it is an important synthetic intermediate of raloxifene, an osteoporosis drug, but has been prepared *via* a laborious multi-step process.<sup>[19]</sup> In fact, our catalytic system showed an excellent functional group tolerance, thus allowing an access to aryl thiols which are otherwise difficult to obtain. These include aryl thiols possessing carbonyl, aldehyde, ester, and nitrile groups (**3p–3t**, **3v**, and **3-w**). For these aryl thiols, Cs<sub>2</sub>CO<sub>3</sub> in DMSO



**Scheme 2.** Coupling reaction of aliphatic dithiols of different lengths; GC yields in the parentheses refer to **3a** and **4**, respectively, with *n*-dodecane as internal standard.



**Scheme 3.** Proposed reaction pathway.

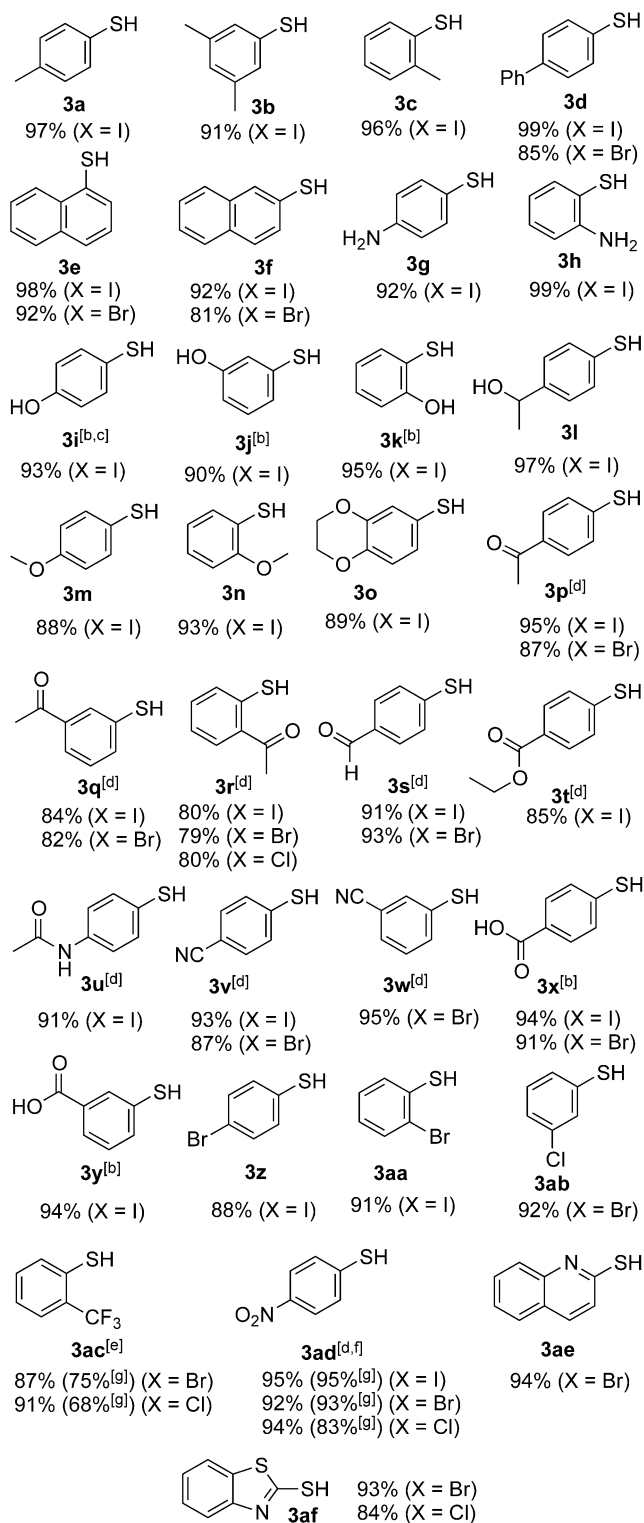
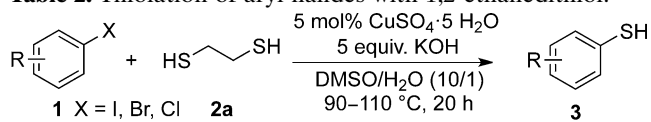
in place of KOH in aqueous DMSO turned out to be more effective: hydrolysis of ester, amide, and nitrile was greatly suppressed. For example, less than 10% of mercaptobenzoic acid was observed in the reaction of a substrate with an ester group (**3t**). Halogen-substituted substrates were also transformed into the desired aryl thiols, and the cross-coupling occurred at the carbon bearing the more reactive halide ( $\text{I} > \text{Br} > \text{Cl}$ ), exhibiting the selectivity of the reaction (**3z–3ab**). Aryl chlorides with strong electron-withdrawing groups such as trifluoromethyl and nitro reacted with 1,2-ethanedithiol without a copper catalyst, but the conversions and yields were improved under the catalytic conditions (**3ac** and **3ad**). Heterocyclic compounds such as 2-bromoquinoline and 2-bromobenzothiazole also afforded the corresponding products in over 90% yield (**3ae** and **3af**). Throughout the study, we observed that the thiolation proceeded smoothly regardless of the substitution position (*ortho* vs. *meta* vs. *para*) as demonstrated with iodophenols (**3i–3k**) and haloacetophenones (**3p–3r**). Moreover, various substituents at the *ortho* position can be tolerated regardless of their electronic nature (**3c**, **3h**, **3k**, **3n**, **3r**, **3aa**, **3ac**). Incidentally, we found that the aryl thiols containing electron-withdrawing groups at the *meta* position such as **3q**, **3w**, **3y** and **3ab** were readily ox-

idized to disulfides during work-up and they required proper handling for the isolation.<sup>[20]</sup>

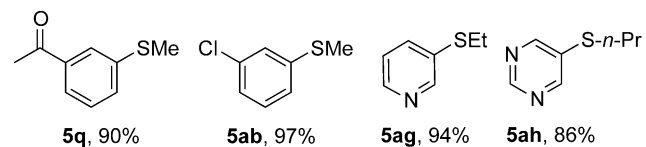
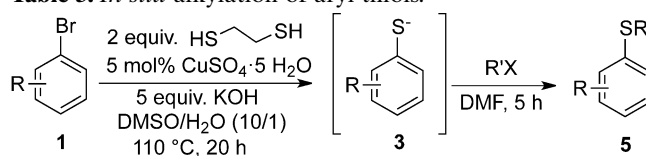
Aryl thiols were directly subjected to alkylation without purification (Table 3). The excellent yields were observed in the one-pot two-step reactions for **5q** and **5ab**. The high yields suggest that the corresponding aryl thiols (**3q** and **3ab**) were produced nearly quantitatively, and the lower isolation yields obtained for these aryl thiols were due to the instability during the work-up process (*vide supra*). Some of the water-soluble heterocyclic thiols were also alkylated *in situ* to afford the corresponding alkyl thioethers (**5ag** and **5ah**), implying these heterocyclic halides are also effective substrates for the conversion to thiols.

We then wished to examine whether the reaction mixtures containing copper(II) catalyst and aryl thiols can be directly used for the coupling reaction with aryl iodides to afford diaryl sulfides. A good deal of experiments led us to develop the efficient process for both symmetrical and unsymmetrical diaryl sulfides which are shown in Table 4. Diaryl sulfides are often synthesized from aryl thiols and aryl halides using metal catalysts,<sup>[21]</sup> but the product diversity is greatly limited by the availability of aryl thiols. Alternative methods employing double C–S couplings between two aryl halides and H<sub>2</sub>S equivalents such as thioacetate, thiourea, ethyl xanthogenate, TIPS-SH, KSCN, Na<sub>2</sub>S have been reported,<sup>[12a,14c,22,23]</sup> and all these methods essentially endeavor to generate aryl thiols *in situ* in various indirect ways. However, contrary to symmetrical diaryl sulfides, the one-pot sequential preparation of unsymmetrical diaryl sulfides still suffers from either expensive operations using palladium and/or costly ligands or limited substrate scope. In this regard, the direct synthesis of aryl thiols and their *in situ* use for diaryl sulfides under ligand-free copper-catalytic conditions developed by us is indeed a gratifying advance. Aryl iodides reacted with 0.55 equiv. 1,2-ethanedithiol with 5 mol% copper sulfate in DMF

**Table 2.** Thiolation of aryl halides with 1,2-ethanedithiol.<sup>[a]</sup>



**Table 3.** *In situ* alkylation of aryl thiols.<sup>[a]</sup>



<sup>[a]</sup> *Reaction conditions:* After thiolation is completed, R'X (3 mmol) and DMF (1 mL) were added and the mixture was stirred for 5 h at room temperature; overall two-step yields of isolated products.

and H<sub>2</sub>O at 120 °C, furnishing a variety of symmetrical diaryl sulfides with various functional groups in good to excellent yields (**6c–6ag**). More significantly, unsymmetrical diaryl sulfides were readily prepared by adding the second aryl iodide in DMF into the reaction mixture after the first aryl halide was transformed to aryl thiol (**7a–7ap**). Addition of DMF was beneficial for the second C–S coupling and each step reaction required a higher temperature for the completion. Under the developed conditions, the order of adding aryl iodides was not important because most aryl iodides can be used either at the first or second step regardless of their electronic nature, providing more freedom when designing sulfides. As demonstrated in the synthesis of the aryl thiols in Table 2, many functional groups including amine, hydroxy, nitrile, carboxyl, and halo groups were also compatible with these one-pot reaction conditions. Heteroaryl aryl sulfides were readily synthesized as well.

In addition, the *in situ* use of aryl thiols was further explored for the synthesis of benzothiophenes.<sup>[24]</sup> Several 2-arylbenzothiophenes, as examples, were synthesized from aryl bromides bearing a phenylethynyl group at the *ortho* position using the same protocol for the aryl thiol synthesis (Scheme 4).

In summary, we have developed a highly efficient transition metal-catalyzed *single-step* synthesis of aryl thiols from aryl halides employing a copper(II) cata-

<sup>[a]</sup> *Reaction conditions:* ArX (1 mmol), **2a** (2 equiv.), CuSO<sub>4</sub>·5H<sub>2</sub>O (5 mol%), KOH (5 equiv.), DMSO/H<sub>2</sub>O (2 mL/0.2 mL), 20 h, 90 °C for ArI and 110 °C for ArBr and ArCl; yields of isolated products.

<sup>[b]</sup> With 6 equiv. of KOH.

<sup>[c]</sup> For 30 h.

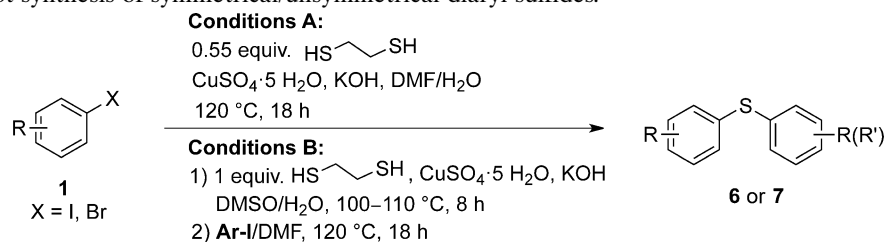
<sup>[d]</sup> With Cs<sub>2</sub>CO<sub>3</sub> as base in DMSO (2 mL).

<sup>[e]</sup> At 90 °C.

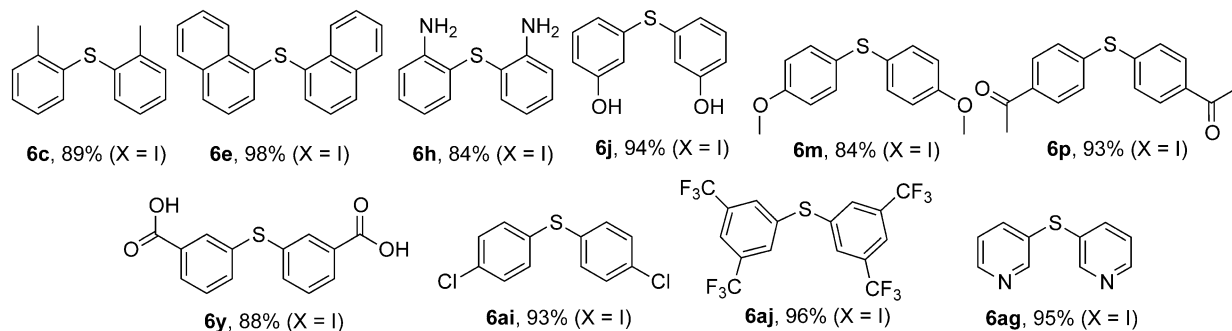
<sup>[f]</sup> At 60 °C.

<sup>[g]</sup> Without copper.

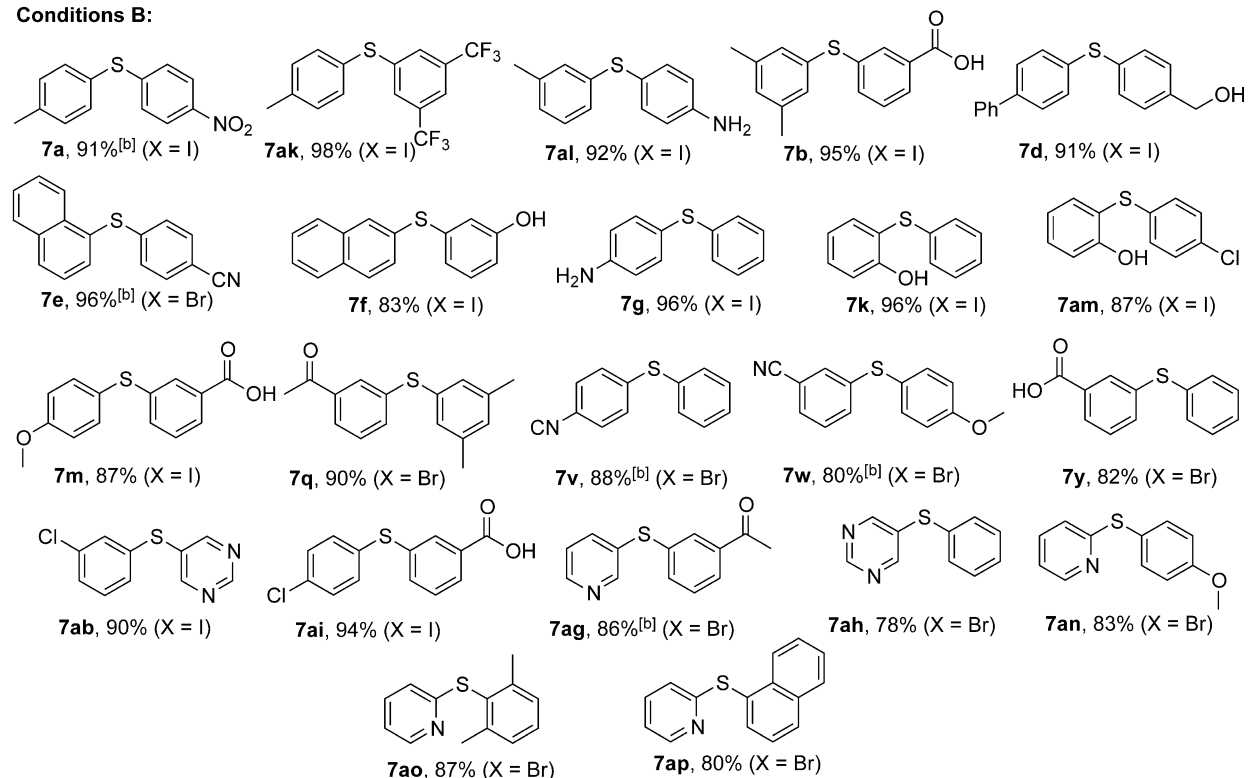
**Table 4.** One-pot synthesis of symmetrical/unsymmetrical diaryl sulfides.<sup>[a]</sup>



**Conditions A:**



**Conditions B:**

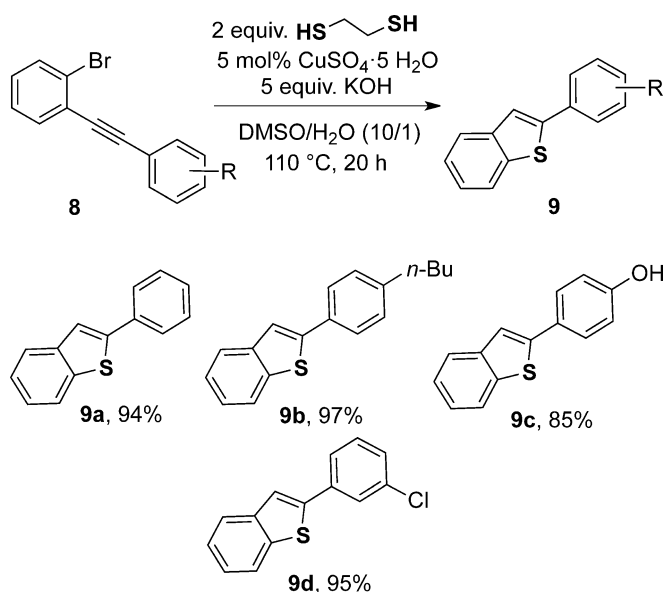


<sup>[a]</sup> Reaction conditions: [A] ArX (1 mmol), HSCH<sub>2</sub>CH<sub>2</sub>SH (0.55 equiv.), CuSO<sub>4</sub>·5H<sub>2</sub>O (5 mol%), KOH (5 equiv.), DMF/H<sub>2</sub>O (2 mL/0.2 mL), 120 °C, 18 h; [B] 1) ArX (1 mmol), HSCH<sub>2</sub>CH<sub>2</sub>SH (1 equiv.), CuSO<sub>4</sub>·5H<sub>2</sub>O (5 mol%), KOH (5 equiv.), DMSO/H<sub>2</sub>O (2 mL/0.2 mL), 8 h, 100 °C for ArI and 110 °C for ArBr; 2) ArI (1.3 equiv.) in DMF (1 mL), 120 °C, 18 h; yields of isolated products.

<sup>[b]</sup> With Cs<sub>2</sub>CO<sub>3</sub> as base in DMSO (2 mL).

lyst and 1,2-ethanedithiol in aqueous DMSO. The catalyst of the reaction, CuSO<sub>4</sub>·5H<sub>2</sub>O, is one of the most readily available copper salts. The C–S cross-coupling proceeds with various alkanedithiols, the proper

choice of which is the key for the single-step transformation to aryl thiols. A broad range of aryl iodides and bromides of various functional groups are directly converted into the corresponding aryl thiols without



**Scheme 4.** Synthesis of 2-aryl benzothiophenes.

additional reaction steps or reagents, while by-products such as sulfides and disulfides are not formed. Some of examples include aryl thiols which are commercially unavailable and/or difficult to prepare *via* previously known methods. Furthermore, the generated aryl thiols are used *in situ* for the synthesis of more advanced molecules such as diaryl sulfides and benzothiophenes.

## Experimental Section

### General Procedure for Synthesis of Aryl Thiols (Table 2)

To a test tube containing a magnetic stir bar was added aryl halide (1 mmol), CuSO<sub>4</sub>·5H<sub>2</sub>O (12.5 mg, 0.05 mmol), KOH (280 mg, 5 mmol) or Cs<sub>2</sub>CO<sub>3</sub> (1.62 g, 5 mmol), DMSO (2 mL), and water (0.2 mL; water was not used in case of using Cs<sub>2</sub>CO<sub>3</sub> as base). After flushing with argon, 1,2-ethanedithiol (0.18 mL, 2 mmol) was added. The mixture was stirred in the preheated oil bath at 90 °C or 110 °C for 20 h. After being cooled to ambient temperature, the reaction mixture was distributed in aqueous HCl (5%) and ethyl acetate. The organic layer was separated and washed with water and brine, dried over MgSO<sub>4</sub> and concentrated under vacuum. The crude product was further purified by column chromatography to provide the desired aryl thiol.

### General Procedure for Synthesis of Aryl Alkyl Sulfides (Table 3)

After the above thiolation was complete, the reaction mixture was cooled to ambient temperature and alkyl halide (3 mmol) in DMF (1 mL) was added. Then, the mixture was stirred at room temperature for 5 h. The reaction mixture was distributed in water and ethyl acetate. The organic layer was separated and washed with water and brine, dried over

MgSO<sub>4</sub> and concentrated under vacuum. The crude product was further purified by column chromatography to provide the aryl alkyl sulfide.

### General Procedure for Synthesis of Symmetrical Diaryl Sulfides (Table 4)

To a test tube containing a magnetic stir bar was added aryl halide (1 mmol), CuSO<sub>4</sub>·5H<sub>2</sub>O (12.5 mg, 0.05 mmol), KOH (280 mg, 5 mmol), DMF (2 mL), and water (0.2 mL). After flushing with argon, 1,2-ethanedithiol (0.05 mL, 0.55 mmol) was added. The mixture was stirred in the preheated oil bath at 120 °C for 18 h. After being cooled to ambient temperature, the reaction mixture was distributed in water and ethyl acetate. The organic layer was separated and washed with water and brine, dried over MgSO<sub>4</sub> and concentrated under vacuum. The crude product was further purified by column chromatography to provide the desired symmetrical diaryl sulfide.

### General Procedure for Synthesis of Unsymmetrical Diaryl Sulfides (Table 4)

To a test tube containing a magnetic stir bar was added aryl halide (1 mmol), CuSO<sub>4</sub>·5H<sub>2</sub>O (12.5 mg, 0.05 mmol), KOH (280 mg, 5 mmol), DMSO (2 mL), and water (0.2 mL; water was not used in case of using Cs<sub>2</sub>CO<sub>3</sub> as base). After flushing with argon, 1,2-ethanedithiol (0.09 mL, 1 mmol) was added. The mixture was stirred in the preheated oil bath at 100 °C or 110 °C for 8 h. After cooling to ambient temperature, a solution of the second aryl halide (1.3 mmol) in DMF (1 mL) was added. Then the reaction mixture was reheated to 120 °C for 18 h. After being cooled to ambient temperature, the reaction mixture was distributed in water and ethyl acetate. The organic layer was separated and washed with water and brine, dried over MgSO<sub>4</sub> and concentrated under vacuum. The crude product was further purified by column chromatography to provide the desired unsymmetrical diaryl sulfide.

### General Procedure for Synthesis of 2-Arylbenzothiophenes (Scheme 4)

To a test tube containing a magnetic stir bar under an argon atmosphere was added 1-bromo-2-(phenylethynyl)benzene (1 mmol), CuSO<sub>4</sub>·5H<sub>2</sub>O (12.5 mg, 0.05 mmol), KOH (280 mg, 5 mmol), DMSO (2 mL), water (0.2 mL), and 1,2-ethanedithiol (0.18 mL, 2 mmol). The mixture was stirred in the preheated oil bath at 110 °C for 20 h. After being cooled to ambient temperature, the reaction mixture was distributed in water and ethyl acetate. The organic layer was separated and washed with water and brine, dried over MgSO<sub>4</sub> and concentrated under vacuum. The crude product was further purified by column chromatography to provide the desired 2-arylbenzothiophene.

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Copper(II)-Catalyzed Single-Step Synthesis of Aryl Thiols from Aryl Halides and 1,2-Ethanedithiol

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 Yajun Liu, Jihye Kim, Heesun Seo, Sunghyok Park, Junghyun Chae\*

