

Mono- or Dichalcogenation of Aryl Iodide with Sulfur or Selenium by Copper Catalyst and Aluminum

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Abstract: The copper-catalyzed mono- or dichalcogenation of aryl halide with sulfur or selenium can be carried out with the addition of aluminum. This method takes advantage of two properties of both the insertion of copper into the chalcogen–chalcogen bond and the reductive ability of aluminum. Furthermore, the addition of MgCl_2 or Na_2CO_3 enables the selective synthesis of diaryl mono-chalcogenides or disulfides.

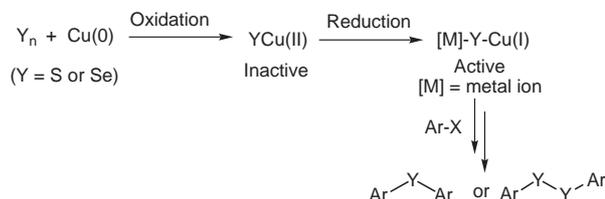
Key words: diaryl chalcogenide, aryl iodide, chalcogen, copper catalyst, aluminum

Transition metal-catalyzed aromatic carbon–chalcogen bond formation is an important reaction in chemical synthesis.¹ The aryl chalcogenides produced by this method are widely used as convenient synthetic intermediates or reagents.²

In general, to achieve chalcogenation of aryl halides by a transition metal catalyst,³ a combination of a copper catalyst with thiol under basic conditions⁴ or sodium sulfide⁵ is often employed. But the reaction using copper with chalcogen itself in one step has not been completely explored to date.

On the other hand, the chalcogen (S or Se) usually has the structure of a polymer possessing the chalcogen–chalcogen bond by catenation. The chalcogen–chalcogen can be easily cleaved by the transition metal,^{6,7} whereas the generated metal–chalcogen complex cannot be used for a reaction such as the chalcogenation of aryl halides, owing to the stability of the metal–chalcogen bond. Similarly, copper(II) chalcogenide or copper(II) diorganochalcogenide is very unreactive.

To exploit these copper(II) chalcogenides for the chalcogenation of aryl halides, it is necessary to convert them into copper(I) chalcogenides by reduction (Scheme 1).⁸ For instance, we have recently reported that Cu(II)(YR)_2 can be reduced by magnesium.⁹ This study indicates that the copper(II) chalcogenide is available for the introduction of chalcogenide groups to aryl halides in the presence of a reducing reagent. Therefore, we anticipated that a copper-catalyzed chalcogenation of aryl halide with chalcogen is a feasible strategy. In this paper, we describe a copper-catalyzed mono- or dichalcogenation of aryl iodide with S or Se using aluminum.



Scheme 1 Strategy for copper-catalyzed chalcogenation of aryl halide using chalcogen.

As an initial attempt to execute a copper-catalyzed synthesis of diaryl chalcogenide from aryl iodide with chalcogen, we investigated the selenation of 2-iodotoluene (**1a**) using CuI and reductive metals (Table 1). It was obvious that the CuI catalyst or aluminum itself could not promote the reaction (Table 1, entries 1 and 2). Fortunately, we found that when both aluminum and CuI–bpy (10 mol%) were added, di-2-tolyl selenide (**2a**) and di-2-tolyl diselenide (**3a**) were obtained in 75% and 6% yield, respectively (Table 1, entry 3). Although other metals (Sm, Mg, and Zn) were examined, no satisfactory results were observed (Table 1, entries 4, 5, and 6). Notably, under the conditions in Table 1 entry 3, the addition of MgCl_2 could selectively synthesize **2a** in 80% yield without the formation of **3a** (Table 1, entry 7). The reaction with sulfur also afforded the mono-sulfide **2** in 71% yield (Table 1, entry 9).

In contrast, the addition of Na_2CO_3 could give the disulfide **3** in 92% yield, however, using Se it was impossible to produce any selenide derivatives (Table 1, entries 8 and 10).

Although other Cu catalysts (Cu_2O , CuCl, CuBr, CuOAc, CuCl_2 , and CuBr_2), ligands (phen, TMEDA, and PPh_3), and solvents (PhCH_3 , NMP, and DMI) were investigated, the results were poor.

On the basis of the optimized conditions, the copper-catalyzed mono-chalcogenation of aryl iodide using Se or S was carried out (Table 2). Diaryl mono-chalcogenides **2** were available in 40–84% yields when a mixture of aryl iodide (0.3 mmol), Se or S (0.3 mmol), CuI–bpy (1:1, 10 mol%), Al (0.6 mmol), and MgCl_2 (0.15 mmol) in DMF (0.5 mL) was treated at 110 °C.¹⁰

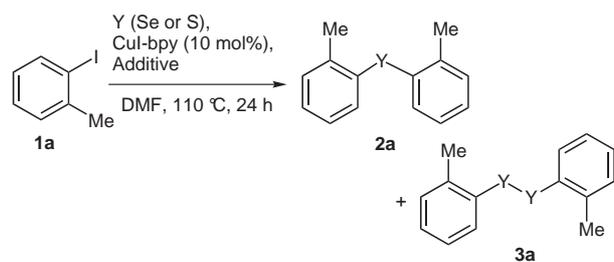
For the selenation, substituents had no effect, however, for sulfidation a long reaction time was often necessary.

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Table 1 Copper-Catalyzed Chalcogenation of 2-Iodotoluene (**1a**) Using Chalcogen^a

Entry	Y	Additive ^b	2a (%) ^c	3a (%) ^c	1a (%) ^c
1	Se	None	0	0	94
2 ^d	Se	Al	0	0	93
3	Se	Al	75	6	5
4	Se	Sm	64	0	32
5	Se	Mg	32	15	0
6	Se	Zn	0	0	95
7 ^e	Se	Al, MgCl ₂	80	0	0
8 ^e	Se	Al, Na ₂ CO ₃	0	0	92
9 ^e	S	Al, MgCl ₂	71	0	trace
10 ^{e,f}	S	Al, Na ₂ CO ₃	0	92	trace

^a The reactions were carried out using **1a** (0.3 mmol), Se or S (0.3 mmol), CuI-bpy (10 mol%), reductive metal (0.6 mmol) in DMF (0.5 mL).

^b Al (53–150 μm), Sm (20 mesh), Mg (212–600 μm) or Zn (75–150 μm) was used.

^c Isolated yields after silica-gel chromatography.

^d CuI-bpy was not added.

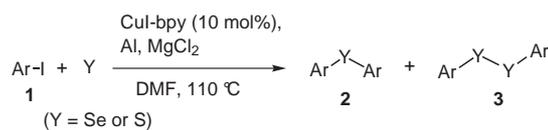
^e MgCl₂ or Na₂CO₃ (0.15 mmol) was added.

^f CuI-bpy (15 mol%) was used.

Thus application of the present method produces symmetrical diarylselenides or sulfides in good yields and by the addition of MgCl₂, it is possible to suppress the formation of other chalcogenide isomers.

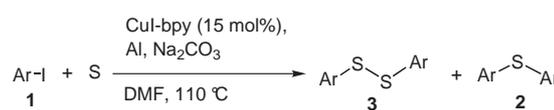
As shown in Table 3, we then performed the disulfidation of aryl iodide with S using Na₂CO₃ (Table 3). Aryl iodides **1** were transformed into the corresponding diaryl disulfides **3** in 72–92% yields by employing CuI-bpy (15 mol%), Al (0.6 mmol), and Na₂CO₃ (0.15 mmol) in DMF (Table 3, entries 1–5).¹¹ For the disulfidation, the reaction time differed depending on the substituent. Regrettably, for 4-bromo-1-iodobenzene, the yield of the expected disulfide decreased to 16% on account of the formation of mono-sulfide **2** (Table 3, entry 6).¹²

To understand the mechanism, we initially researched the role of Cu and aluminum (Table 4). In the selenation of 2-iodotoluene (**1a**), the independent utilization of CuI or aluminum could not promote the reaction and **1a** was recovered (Table 4, entries 1 and 2).^{13,14} Interestingly, the

Table 2 Copper-Catalyzed Mono-Chalcogenation of ArI with Selenium or Sulfur

Entry	ArI	Y	Time (h)	2 (%) ^a	3 (%) ^a
1	C ₆ H ₅ I	Se	24	78	0
2		S	22	75	0
3	2-MeC ₆ H ₄ I	Se	24	80	0
4		S	24	71	0
5	4-MeC ₆ H ₄ I	Se	24	79	0
6		S	43	62	5
7	4-MeOC ₆ H ₄ I	Se	24	77	0
8		S	45	73	trace
9	4-ClC ₆ H ₄ I	Se	24	84	trace
10		S	45	76	0
11	4-BrC ₆ H ₄ I	Se	40	70	0
12		S	40	43	11
13	4-F ₃ CC ₆ H ₄ I	Se	24	74	0
14	4-AcHNC ₆ H ₄ I	Se	18	40	0
15	1-naphthyl-I	Se	18	82	trace

^a Isolated yields after silica-gel chromatography.

Table 3 Copper-Catalyzed Disulfidation of ArI with Sulfur

Entry	ArI	Time (h)	3 (%) ^a	2 (%) ^a
1	C ₆ H ₅ I	45	85	0
2	2-MeC ₆ H ₄ I	24	92	0
3	4-MeC ₆ H ₄ I	45	82	trace
4	4-MeOC ₆ H ₄ I	65	72	trace
5	4-H ₂ NC ₆ H ₄ I	24	75	0
6	4-BrC ₆ H ₄ I	24	16	71

^a Isolated yields after silica-gel chromatography.

use of Cu(0) (200 mol%) in the absence of aluminum gave **2a** in only 22% yield, the mixture of Cu(0) (10 mol%) and aluminum afforded **2a** in 91% yield (Table 4, entry 4).

Thus, it seems that aluminum does not have the ability to reduce selenium under the conditions employed, but the Cu(0) and Cu(I)-selenide species generated by aluminum serve as the reducing reagent.⁹ In addition, the copper-selenide complex is produced by the reaction of Cu(0) or CuI with Se.¹⁵

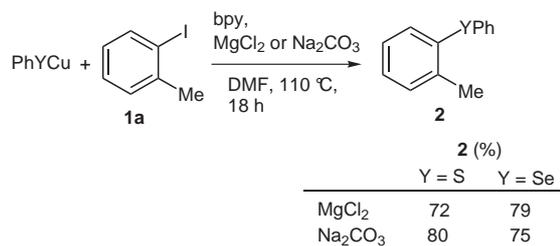
Table 4 Research of the Reaction Mechanism

Entry	Cu (mol%)	Time (h)	Se (0.3 mmol), [Cu]-bpy, Al (0.6 mmol), MgCl ₂ (0.15 mmol)	
			2a (%) ^a	1a (%) ^a
1	None	18	0	96
2 ^b	CuI (100)	18	0	96
3 ^b	Cu (200)	45	22	61
4	Cu (10)	30	91	0

^a Isolated yields after silica-gel chromatography.

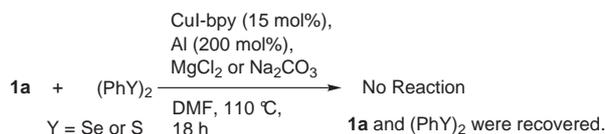
^b Aluminum was not added.

Next, we examined the role of MgCl₂ and Na₂CO₃, we researched the influence of additives on the reactivity of PhYCu considered as an intermediate. However, the reaction of PhYCu with aryl iodide was not affected by additives, and afforded the corresponding chalcogenides in good yields (Scheme 2).



Scheme 2

On the other hand, the reaction of aryl iodide with dichalcogenide did not give the mono-chalcogenide in the presence of additives (Scheme 3). Moreover it was observed that the addition of these salts tends to inhibit the cleavage of the dichalcogenide bond. Thus, diaryl dichalcogenide cannot be used for the mono-chalcogenation.

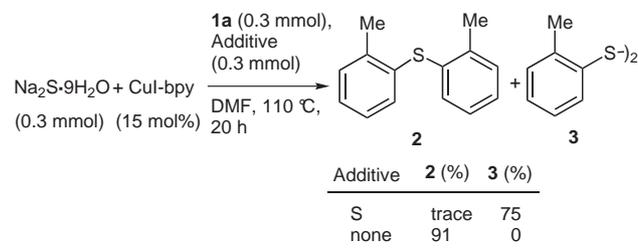


Scheme 3

Therefore, it is estimated that the formation of mono-chalcogenide or disulfide is an independent process, and these additives are involved in the generation of copper-sulfide in the first step.

Actually, after the sulfidation of CuI using Na₂S, the addition of S and **1a** gave disulfide **3** in 75% yield, nevertheless the reaction of Na₂S with ArI produced only mono-sulfide **2** (Scheme 4). These suggest that Cu(I)SSNa is formed in the presence of Na₂CO₃.¹⁶ On the contrary, the addition of MgCl₂ suppresses the generation of CuSS[M].

Consequently, it is considered that in the sulfidation of aryl iodide, the addition of Na₂CO₃ promotes the formation of Cu(I)SSNa, but MgCl₂ or the selenation cannot generate Cu(I)YY[M].

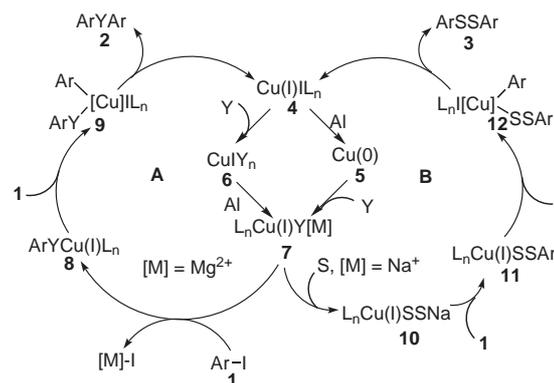


Scheme 4

From these results, the proposed mechanism is outlined in Scheme 5. The reaction of Cu(0) or CuI with chalcogen gave copper(II) chalcogenide or copper(I) chalcogenide [Cu(II) chalcogenide shows no activity, it is reduced to copper(I) chalcogenide **7** by aluminum].⁹ Sequentially, in the presence of MgCl₂, the intermediate **8** is produced from **7** with ArI.⁵ Finally, diaryl chalcogenide **2** is obtained (Cycle A).⁸

On the other hand, by the addition of Na₂CO₃, the copper-disulfide complex **10** is generated, and diaryl disulfide **3** is produced (Cycle B).

Investigation of the detailed process for the formation of diaryl mono-chalcogenides or disulfides is now in progress.



Scheme 5 A plausible reaction mechanism.

In conclusion, we have achieved a copper-catalyzed synthesis of symmetrical diaryl chalcogenide from aryl iodide with chalcogen by the addition of aluminum. Furthermore, the use of MgCl₂ or Na₂CO₃ could selectively synthesize diaryl mono-chalcogenide or disulfide.

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- (10) **Typical procedure for the preparation of diaryl sulfide**: To a mixture of S (10.6 mg, 0.3 mmol), CuI (5.7 mg, 0.03 mmol), aluminum powder (53–150 μ m) (16.2 mg, 0.6 mmol), MgCl₂ (14.3 mg, 0.15 mmol), bpy (4.6 mg, 0.03 mmol), and DMF (0.5 mL) was added 2-iodotoluene (**1a**) (65.4 mg, 0.3 mmol), and the mixture was stirred at 110 °C for 24 h. After the reaction mixture was diluted with Et₂O, the solution was washed with H₂O and saturated NaCl, and dried over anhydrous MgSO₄. Chromatography on silica gel (hexane) gave di-2-tolyl sulfide (22.8 mg, 71%). ¹H NMR (270 MHz, CDCl₃): δ = 2.38 (s, 6 H), 7.04–7.25 (m, 8 H); ¹³C NMR (67 MHz, CDCl₃): δ = 20.1, 126.7, 127.1, 130.4, 131.1, 134.3, 138.9; Anal. Calcd for C₁₄H₁₄S: C, 78.45; H, 6.58. Found: C, 78.71; H, 6.61. **Di-2-tolyl selenide**: ¹H NMR (270 MHz, CDCl₃): δ = 2.39 (s, 6 H), 7.02–7.07 (m, 2 H), 7.14–7.25 (m, 6 H); ¹³C NMR (67 MHz, CDCl₃): δ = 22.2, 126.8, 127.5, 130.2, 132.7, 133.2, 139.8; Anal. Calcd for C₁₄H₁₄Se: C, 64.37; H, 5.40. Found: C, 64.21; H, 5.17.
- (11) **Typical procedure for the preparation of diaryl disulfide**: To a mixture of sulfur (10.6 mg, 0.3 mmol), CuI (8.5 mg, 0.045 mmol), aluminum powder (53–150 μ m) (16.2 mg, 0.6 mmol), Na₂CO₃ (15.9 mg, 0.15 mmol), bpy (7.0 mg, 0.045 mmol), and DMF (0.5 mL) was added 2-iodotoluene (**1a**) (65.4 mg, 0.3 mmol), and the mixture was stirred at 110 °C for 24 h. The reaction mixture was diluted with Et₂O, the solution was washed with H₂O and saturated NaCl, and dried over anhydrous MgSO₄. Chromatography on silica gel (hexane) gave bis(2-tolyl) disulfide (34.0 mg, 92%). ¹H NMR (270 MHz, CDCl₃): δ = 2.42 (s, 6 H), 7.10–7.15 (m, 6 H), 7.49–7.52 (m, 2 H); ¹³C NMR (67 MHz, CDCl₃): δ = 20.0, 126.7, 127.3, 128.7, 130.3, 135.4, 137.4; Anal. Calcd for C₁₄H₁₄S₂: C, 68.24; H, 5.73. Found: C, 68.19; H, 5.70.
- (12) It is considered that because the disulfide bond of bis(4-bromophenyl) disulfide is easy to cleave, the monosulfide was obtained selectively. The reaction of this disulfide with 2-iodotoluene in the presence of Na₂CO₃ gave 4-bromophenyl 2-tolyl sulfide in 50% yield.
- (13) Selenium was recovered in 90–92% yields.
- (14) The reaction of CuI (100 mol%) with Se gave a green precipitate. The structure of this compound is now under investigation.
- (15) In the reaction using Cu(II)Se or Cu(II)₂Se in the presence of Al and MgCl₂: Cu(II)Se afforded **2a** in 45% yield after 40 h, and Cu(I)₂Se resulted in a 5% yield after 80 h.
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