

# Nature of the Copper-Oxide-Mediated C–S Cross-Coupling Reaction: Leaching of Catalytically Active Species from the Metal Oxide Surface

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**Supporting Information** 

**ABSTRACT:** Copper-oxide-catalyzed cross-coupling reaction is a well-known strategy in heterogeneous catalysis. A large number of applications have been developed, and catalytic cycles have been proposed based on the involvement of the copper oxide surface. In the present work, we have demonstrated that copper(I) and copper(II) oxides served as precursors in the coupling reaction between thiols and aryl halides, while catalytically active species were formed upon unusual leaching from the oxide surface. A powerful cryo-SEM



technique has been utilized to characterize the solution-state catalytic system by electron microscopy. A series of different experimental methods were used to reveal the key role of copper thiolate intermediates in the studied catalytic reaction. The present study shows an example of leaching from a metal oxide surface, where the leaching process involved the formation of a metal thiolate and the release of water. A new synthetic approach was developed, and many functionalized sulfides were synthesized with yields of up to 96%, using the copper thiolate catalyst. The study suggests that metal oxides may not act as an innocent material under reaction conditions; rather, they may represent a source of reactive species for solution-state homogeneous catalysis.

**KEYWORDS:** C-S cross-coupling, copper oxide, nanoparticles, catalysis, leaching, mechanism

## ■ INTRODUCTION

Cu-catalyzed C–S bond formation is a flexible synthetic tool that is in high demand in research and industrial fields. A simple protocol allows the coupling of an impressive variety of S-nucleophiles with functionalized aryl and alkyl halides including hindered, electron-poor, electron-rich, and heterocyclic compounds.<sup>1–3</sup> The key advantages of copper-based catalytic systems are (i) the commercial availability and relatively low toxicity of copper species; (ii) the high catalytic activity; and (iii) the possibility to carry out reactions under ligand-free conditions, often with the use of nontoxic solvents or recyclable ionic liquids.<sup>1–6</sup> In some cases, Cu-mediated transformations may be superior to the well-known Pd-catalyzed reactions.<sup>7</sup>

A large number of copper compounds have been found to be suitable catalysts for C–S cross-coupling reactions. Copper salts promote the S-arylation and S-alkylation of a wide range of Snucleophiles including potassium thiocyanate,<sup>8</sup> carbon disulfide,<sup>9</sup> sulfur,<sup>10</sup> alkyl and aryl disulfides,<sup>11</sup> and thiourea<sup>12</sup> under mild conditions. Homogeneous catalytic reactions with the use of soluble copper salts or complexes<sup>13</sup> involving one metal center are believed to proceed via the Cu(I)/Cu(III) oxidative addition of aryl halide<sup>14</sup> or the Cu(I)/Cu(II) single electron transfer.<sup>15</sup> Mechanistic studies suggest Cu(I) compounds as the active catalytic species, regardless of which copper source (Cu(0), Cu(I), or Cu(II)) was used initially. Surprisingly, CuO and Cu<sub>2</sub>O nanoparticles showed high catalytic activity in the cross-coupling reactions with various sulfur-containing organic compounds.<sup>16</sup> Supported copper-containing nanoparticles—CuO/GO,<sup>17</sup> CuO/Si,<sup>18</sup> CuO/C,<sup>19</sup> Cu/Cu<sub>2</sub>O,<sup>20</sup> Cu/chitosan,<sup>21</sup> and Cu/polymer<sup>22</sup>—were used as highly efficient and recyclable heterogeneous catalysts. The mechanistic aspects of these copper-catalyzed C–S cross-coupling reactions have raised several questions. The available mechanistic studies have proposed copper oxide nanoparticles as the catalytically active species.<sup>19,23–25</sup> Note that the direct involvement of a metal oxide surface in a cross-coupling reaction is rather unusual and intriguing.

In the present work, we studied the C–S cross-coupling catalytic system for the S-arylation of organic halides mediated by copper oxide nanoparticles. Mechanistic insight was made using cryogenic scanning electron microscopy (cryo-SEM), field-emission scanning electron microscopy (FE-SEM), dynamic light scattering (DLS), high-resolution electrospray ionization mass spectroscopy (HR-ESI-MS), and nuclear magnetic resonance (NMR) techniques. An unexpected leaching process involving the metal oxide surface was detected.

Received: February 2, 2016 Revised: April 22, 2016 Leaching of metal species from the immobilized metal complexes or metal nanoparticles is a well-known phenomenon; however, substitution of oxygen and leaching of metal species from the surface of metal oxides appears rather unusual.<sup>26</sup> Moreover, some metal oxides are often considered to be stable materials and are widely used as a catalyst support in many catalytic transformations. The mechanistic studies revealed copper thiolates as the active component that leached into solution, and a novel catalyst was developed for an efficient C–S cross-coupling reaction.

## RESULTS AND DISCUSSION

The coupling of thiophenol with 4-iodotoluene was chosen as a model reaction (Scheme 1). Nanosized copper(I) oxide was

Scheme 1. Model Catalytic C–S Cross-Coupling Reaction between Thiophenol and 4-Iodotoluene



used as a catalyst precursor, and the reaction was carried out in dimethyl sulfoxide (DMSO) in the presence of  $Cs_2CO_3$  as a base. The reaction mixture visually appeared as a heterogeneous system. In order to detect and localize active copper-containing species in solution, a cryo-SEM technique in combination with energy-dispersive X-ray spectroscopy (EDS) was applied.

The liquid phase of the model reaction mixture was subjected to cryo-SEM and EDS analyses. Electron microscopy revealed complex structures consisting of round-shaped agglomerates  $(2.6-24 \ \mu m)$  (Figure 1, point "a") covered with crystalline particles (Figure 1, point "b") along the perimeter of the agglomerates. The size of the crystalline particles varied from 85 nm to approximately 2  $\mu$ m. The effect of the radiation damage can also be observed in some sample points (Figure 1, point "c"). Energy-dispersive X-ray spectroscopy revealed the presence of copper in both of the described phases, which confirmed catalyst leaching in solution. The crystalline phase was enriched with cesium and probably contained large amounts of cesium carbonate. On the basis of SEM-EDS observations, a colloidal structure of the liquid phase of the reaction mixture can be proposed. The complex structure of the aggregates, as detected by cryo-SEM, suggests the coexistence of active copper catalyst centers and Cs<sub>2</sub>CO<sub>3</sub> in one colloidal particle.

To elaborate the plausible presence of small nanoparticles in the liquid phase, the reaction mixture was analyzed using DLS. The precipitate was removed by centrifugation, and the liquid phase was analyzed by DLS, which did not detect the presence of nanosized particles in solution. Therefore, the complex structures detected by cryo-SEM were most likely formed from solubilized components of the reaction mixture as a result of the partial crystallization of the vitrified solution.

Homogeneous catalysis, initiated by the transfer of the metal species from the metal oxide surface to the solution, is a rather unusual phenomenon. Leaching is well-known for zerovalent metal nanoparticles and immobilized metal complexes,<sup>26</sup> whereas oxides are usually considered as stable materials. Moreover, metal oxides are routinely used as a catalyst support with typically attributed innocent properties.



**Figure 1.** Cryo-SEM images of the vitrified reaction mixture (top) and one spherical agglomerate at higher magnification (bottom). The labels correspond to round-shaped agglomerates (feature "a"), crystalline particles (feature "b"), and radiation damage (feature "c").

The homogeneous nature of the catalytic system was independently confirmed by a series of experiments. First of all, a set of structurally diverse Cu<sub>2</sub>O and CuO nanoparticles were synthesized according to the literature procedures.<sup>27–30</sup> Synthesized copper oxides (1b–1h), as well as the control sample of Cu<sub>2</sub>O particles from a commercial source (1a), were analyzed using XRD (see the Supporting Information), which confirmed the monophasic composition of all of the samples except sample 1h, which consisted of CuO and Cu(OH)<sub>2</sub>. The morphology of samples 1a–1h was studied using electron microscopy. SEM characterization revealed a variety of shapes and sizes for the synthesized and commercial copper oxides (see Figure 2).

Copper oxides **1a**-**1h** were tested as catalyst precursors in the model C-S cross-coupling reaction between thiophenol and 4-iodotoluene (Scheme 1). All of the tested copper oxides demonstrated high catalytic activity and selectivity. The yields of the C-S cross-coupling products were high (90%-97%) and, surprisingly, almost the same in all cases (see entries 1-8 in Table 1), including initial reaction rate experiments (see the Supporting Information). Neither the morphology nor the metal oxidation state affected the observed yield of the product. Because the morphology and the nature of the catalyst did not influence the exhibited catalytic activity in a substantial manner, the heterogeneous reaction pathway seems to be unlikely. Morphology-independent catalytic activity is in a better agreement with the leaching pathway, followed by homoge-



Figure 2. SEM images of the copper oxide particles: (a) commercial copper oxide 1a and (b-h) synthesized copper oxides ((b) 1b, (c) 1c, (d) 1d, (e) 1e, (f) 1f, (g) 1g, and (h) 1h) (see Table 1 for a detailed morphology description).

neous reaction in solution. The necessary control experiments were carried out, and formation of the product was not observed in the absence of the copper precatalyst or the base (see entries 9 and 10 in Table 1).

The morphology of the solid residue isolated after completion of the reaction provides valuable information about the catalytic process. The catalyst isolated from the reaction mixture was studied using FE-SEM. Electron microscopy showed that all the catalysts lost their initial morphology (see the Supporting Information for details). Modification of the catalyst surface during the reaction also suggests the involvement of a catalyst leaching process, and, consequently, the possibility of a homogeneous nature of the catalytic system.

To confirm the leaching of copper during the cross-coupling reaction, hot centrifugation and hot filtration tests were performed.<sup>31,26</sup> When 20%–30% conversion of thiophenol was reached, the hot reaction mixture was separated. The solution after separation was heated at 110 °C for 19 h. A further increase of the thiophenol conversion (>80%) was observed. Thus, leaching of the copper species and transfer of the catalytically active complexes into solution occurred under the studied reaction conditions.

To establish the composition of the leached copper species, high-resolution electrospray ionization mass spectrometry (HR-ESI-MS) was utilized. HR-ESI-MS analysis in negative ion mode showed the presence of thiolate complexes  $[Cu(SPh)_2]^-$ (m/z = 280.9514) and  $[CuI(SPh)]^{-}$  (m/z = 298.8446) in solution (see the Supporting Information). It is important to note here that a similar species was detected in the CuI/1,10phenanthroline-catalyzed C-S cross coupling reaction, which did not involve copper oxide nanoparticles as precatalysts.<sup>32a</sup> The presence of the oxidative addition product [CuIAr(SPh)<sub>2</sub>]<sup>-</sup> was not observed in the present study nor in the literature.<sup>3</sup> Thus, a soluble copper species were detected in the catalytic reaction initiated with copper oxide nanoparticles as a precatalyst. The copper compounds were confirmed to have a similar nature to that of the previously studied homogeneous catalytic system. The key role of the  $[Cu(SAr)_2]^-$  complex was also recently addressed in the mechanistic study of the photoinduced cross-coupling of an aryl thiol with an aryl halide.<sup>32b</sup>

Finally, the reaction of copper oxide with thiophenol was performed (in the absence of organic halide and base), and the formation of copper thiolate was detected. The formation of  $[CuSPh]_n$  **2** in the reaction of copper(I) oxide **1a** with thiophenol was observed in 81% yield. The expected change in the morphology of copper nanoparticles upon this transformation was detected by FE-SEM (Figure 3). Rod-shaped particles with a length of ~5–25  $\mu$ m and width of ~100–200 nm were observed in the samples obtained in the reaction of Cu<sub>2</sub>O (**1a**) with thiophenol in DMSO after heating at 110 °C for 1.5 h (cf. Figure 2a for initial morphology). XRD (Figure 4)

Table 1. C-S Cross-Coupling Reaction with Various Cu Oxides<sup>a</sup>

entry	catalyst	morphology and size of the catalyst $particles^b$	yield (%) <sup>c</sup>
1	Cu <sub>2</sub> O (1a)	octahedral (20–700 nm, 1–7 µm)	97
2	Cu <sub>2</sub> O (1b)	cubic (0.2–0.8 $\mu$ m)	95
3	$Cu_2O$ (1c)	beveled cubic (0.5–1.5 $\mu$ m)	94
4	$Cu_2O$ (1d)	18-facet polyhedral (0.5–2.0 $\mu$ m)	92
5	Cu <sub>2</sub> O (1e)	octahedral (0.2–2.0 $\mu$ m, rarely up to 7 $\mu$ m)	90
6	CuO (1f)	aggregated spherical (15–80 nm, aggregates > 10 $\mu$ m)	99
7	CuO (1g)	aggregated lamellar (10–15 nm thick, aggregates – 2.5–7.5 $\mu$ m)	94
8	$CuO/Cu(OH)_2$ (1h)	fibrillar (5–15 nm thick, up to 50 nm for bunches)	93
$9^d$	_	-	0
10 <sup>e</sup>	Cu <sub>2</sub> O (1a)	octahedral (20–700 nm, 1–7 µm)	3

<sup>*a*</sup>Reaction conditions: thiophenol (1 mmol), 4-iodotoluene (1.1 mmol), base (1.5 mmol), copper oxide (1 mol %), DMSO (1 mL), Ar, 110 °C. <sup>*b*</sup>Determined by FE-SEM. <sup>*c*</sup>Determined by <sup>1</sup>H NMR. <sup>*d*</sup>The reaction was carried out in the absence of catalyst and base. <sup>*e*</sup>The reaction was carried out in the absence of base.



**Figure 3.** SEM images of  $[CuSPh]_n$  synthesized by the treatment of  $Cu_2O$  (1a) with thiophenol in dimethyl sulfoxide (DMSO).

and elemental analysis confirmed the formation of CuSPh, which, in the case of the nanoparticles, existed as a metal-containing polymer  $[CuSPh]_n$ .<sup>33</sup>



Figure 4. Experimental X-ray diffraction (XRD) data for 2 (blue line) and calculated XRD pattern for CuSPh (red line).

Evidently, the generation of copper thiolate **2** is the first catalyst activation step in the studied Cu<sub>2</sub>O or CuO-catalyzed C-S cross-coupling reaction. If the mechanistic data are correct, these findings open up a new opportunity to develop a novel catalytic system. Easily available and air-stable [CuSPh]<sub>n</sub> particles can be directly used as a catalyst. Thus, we have evaluated the possibility of using [CuSPh]<sub>n</sub> as a catalyst for the coupling of various aryl iodides with thiols (Scheme 2).

The reactions of substituted iodobenzenes and various aromatic, heteroaromatic and aliphatic thiols were performed with moderate to high yields (3a-3f). The developed catalyst showed good tolerance to various functional groups (Scheme 2). In most cases, 1 mol% of the catalyst was enough to perform the reaction (3a-3e, 3g-3j, 3m), with a few exceptions when 5 mol% of the catalyst was employed (3f, 3k, 3l, 3n). Thus, copper thiolate [CuSPh]<sub>n</sub> demonstrated high





<sup>*a*</sup>Reaction conditions: RSH (1 mmol), ArI (1.1 mmol), base (1.5 mmol), [CuSPh]<sub>*n*</sub> (1 mol %), DMSO (1 mL), argon, 21 h, 110 °C; isolated yields are given in parentheses. <sup>*b*</sup>Reaction was conducted in 1,4-dioxane. <sup>*c*</sup>A quantity of 5 mol % of [CuSPh]<sub>*n*</sub> was used. <sup>*d*</sup>A quantity of 1.2 mmol of thiol was used.

efficiency as a catalyst in the C–S coupling reaction involving a wide scope of substrates. Typically, 5–20 mol % of copper catalyst is employed in similar reactions, and efficient synthetic applications with <5 mol % of the catalyst are rare.<sup>4–12,16–19,34</sup>

Based on the experimental results, a plausible mechanism for the C-S cross-coupling reaction, with copper oxides as the catalyst precursor, can be proposed (Scheme 3).

The reaction between copper oxide nanoparticles and thiol leads to the formation of Cu thiolate complex and release of water.<sup>35</sup> In the presence of thiol and base, copper precursor

Scheme 3. Proposed Mechanism of C-S Cross-Coupling Reaction with Copper Oxide Particles as a Catalyst Precursor



dissolves with the generation of the  $[Cu(SR)_2]^-$  species (step "A").<sup>36</sup> In the next step, ArI reacts with the thiolate complex, leading to the formation of the product and the generation of the  $[Cu(SR)I]^-$  intermediate (step "B"). The reaction of the  $[Cu(SR)I]^-$  species with thiol and base regenerates the anionic thiolate species  $[Cu(SR)_2]^-$  and the catalytic cycle repeats (step "C"). The presence of a Cu(III) species, which may appear due to oxidative addition or radical pathways, was not experimentally confirmed. However, the involvement of a Cu(III) intermediate cannot be ruled out, although a typical exchange reaction (concerted or stepwise) seems to be a probable pathway.

Thus, the catalytic system in solution (Scheme 3) can be initiated from the copper oxide nanoparticles. Transformation of the metal oxide to metal thiolate and leaching to solution has been observed in the present study. The findings clearly indicate that the metal oxide particles can undergo substantial transformations prior to entering the catalytic cycle. The possibility of using the coordination polymer [CuSPh]<sub>n</sub> (instead of the copper oxide catalyst precursor) has been successfully demonstrated in many examples (Scheme 2). In such cases, the catalytic cycle directly started with the generation of the active thiolate species.

## CONCLUSIONS

In the present study, we addressed the nature of copper-oxidecatalyzed C–S cross-coupling reaction. A set of Cu<sub>2</sub>O and CuO particles with different morphologies was synthesized and tested in the catalytic C–S cross coupling reaction. It was shown that the morphology of the catalyst did not play a significant role in the catalytic process. Indeed, all the synthesized copper oxides demonstrated similar catalytic activity. Cryo-SEM-EDX provided evidence of the presence of copper species in the liquid phase, and the corresponding  $[Cu(SPh)_2]^-$ and  $[Cu(SPh)I]^-$  intermediates were detected in solution by HR-ESI-MS. The homogeneous pathway was initiated by the leaching of the copper thiolate species from the copper oxide nanoparticle precursors. Copper thiolate complexes in solution, rather than copper oxide nanoparticles, were found to be the catalytically active species.

The product of the reaction between copper oxide particles and thiol—the coordination polymer  $[CuSAr]_n$ —was synthesized and studied in the C–S cross-coupling reaction as a catalyst. The developed novel catalyst has shown high catalytic activity and good functional group tolerance. The catalytically active coordination polymer  $[CuSAr]_n$  is a material that is inexpensive, easy to synthesize and handle, and has good potential areas of application.

The present study provides an example of leaching from a metal oxide surface. The leaching process involved the formation of a metal thiolate and release of water. The findings are of great importance in rethinking the application of metal oxides as catalysts and catalyst supports. The possibility of leaching from a metal oxide surface may have substantial influence on several catalytic systems, with a key influence on the nature of the catalytic system, stability of the catalyst and ability to recycle.

## EXPERIMENTAL SECTION

**General Remarks.** The solvents were dried and purified according to standard procedures. The copper oxides were synthesized using previously described methods.<sup>27–30</sup> XRD

patterns were recorded in the  $2\theta$  range of  $5^{\circ}-80^{\circ}$  on a Bruker D2 Phaser diffractometer with Cu K $\alpha$  radiation. The morphologies of the samples were observed on several SEM systems: Zeiss Merlin, Zeiss Auriga Laser, and Hitachi SU8000. Energy-dispersive X-ray spectroscopy was performed using an Oxford Instruments X-Max 80 system. <sup>1</sup>H and <sup>13</sup>C spectra were recorded on a Bruker Model Avance 400 NMR spectrometer. Electrospray ionization mass spectrometry was performed using a MaXis Bruker Daltonik spectrometer. Elemental analysis was carried out on a Euro EA3028-HT elemental analyzer.

Cryogenic scanning electron microscopy (cryo-SEM) was used to investigate the morphology and size of nanoparticles and soluble clusters in organic solution. The samples for the cryo-SEM studies were prepared in a controlled environment vitrification system (CEVS) Leica EM GP. A small amount of the sample  $(1.2 \ \mu L)$  was placed onto a carbon film on a metal grid support and blotted with filter paper to obtain a thin liquid film on the grid. The grid was quenched in liquid ethane at -180 °C and transferred to liquid nitrogen (-196 °C). The grid was subsequently mounted on a precooled cryo-SEM Leica EM VCT100 shuttle. The shuttle was inserted into the Leica EM BAF060 device against a counter flow of dry nitrogen gas at -120 °C and 1  $\times$  10<sup>-7</sup> Pa for 60 min to remove water. The samples were then transferred to, and examined in, a Tescan MIRA3 LMU SEM system. All the observations were performed at -160 °C using an accelerating voltage between 6 kV and 20 kV. Energy-dispersive X-ray spectroscopy (EDS) was performed using an Advanced Aztec Energy (IE350)/X-Max 80 system.

Light scattering experiments were carried out on a Nano Partica SZ-100 (Horiba Jobin Yvon) nanoparticle analyzer. The light source was a diode-pumped frequency-doubled laser (532 nm, 10 mW). The system determines the particle size distribution of particles in solution with measurement capability from 0.3 nm to 8  $\mu$ m. The measurements were carried out in a cuvette at an angle of 90° at a temperature of 24.9 ± 0.1 °C; after that, the position of the cuvette was changed manually, and the measurements were repeated. The results were analyzed according to the diffusion coefficient using the Stokes–Einstein equation.

Synthetic Procedure for Copper Oxide-Catalyzed Model Reaction. Copper oxide (0.01 mmol, 1.4 mg for Cu<sub>2</sub>O or 0.8 mg for CuO), Cs<sub>2</sub>CO<sub>3</sub> (1.5 mmol, 0.4887 g), 4iodotoluene (1.1 mmol, 0.2398 g), DMSO (1 mL), thiophenol (1 mmol, 0.102 mL) were added to a vessel under inert atmosphere. The reaction vessel was equipped with a magnetic stirrer bar and sealed with a polytetrafluoroethylene (PTFE)lined cap. The mixture was stirred at 110 °C for 21 h.

Synthesis of  $[CuSPh]_n$  (2) using  $Cu_2O$  as a Starting Reagent. Copper(I) oxide (0.1 mmol, 14 mg), DMSO (1.5 mL), and thiophenol (1 mmol, 0.102 mL) were added to a vessel under an inert atmosphere. The reaction vessel was equipped with a magnetic stirrer bar and sealed with a PTFElined cap. The mixture was stirred at 110 °C for 1.5 h. An insoluble yellow precipitate was formed. After cooling to room temperature, 2 was separated by centrifugation and sequentially washed with water (2 × 10 mL), methanol (2 × 10 mL), diethyl ether (10 mL), and dichloromethane (DCM) (10 mL). The residue then was dried in an oven at 105 °C overnight. Yield: 81% (0.028 g). Elemental analysis calculated (%): C 41.72, H 2.92; found (%): C 41.73, H 2.94.

Synthesis of  $[CuSPh]_n$  (2) Using CuO as a Starting Reagent. A similar procedure was utilized (see above). Yield:

Synthetic Procedure for [CuSPh]<sub>n</sub>-Catalyzed C-S **Cross-Coupling Reaction.**  $[CuSPh]_n$  (0.01 mmol, 1.7 mg for 3a-3e, 3g-3j, 3m, and 0.05 mmol, 8.5 mg for 3f, 3k, 3l, 3n), Cs<sub>2</sub>CO<sub>3</sub> (1.5 mmol, 0.4887 g), aryl iodide (1.1 mmol), DMSO (1 mL) or dioxane (1 mL) and thiol (1 mmol for 3a-3j, 3l, 1.2 mmol for 3k, 3m, 3n) were added to a vessel under an inert atmosphere. The reaction vessel was equipped with a magnetic stir bar and sealed with a PTFE-lined cap. The mixture was stirred at 110 °C for 21 h. The heterogeneous mixture was cooled to room temperature, diluted with water (20 mL) and washed with EtOAc ( $3 \times 10$  mL). The combined organic layers were washed with water  $(5 \times 20 \text{ mL})$  to remove DMSO and then dried over Na<sub>2</sub>SO<sub>4</sub>. The mixture was filtered, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (hexane or hexane/ether or hexane/ethyl acetate) to afford the corresponding product. All the products were characterized by <sup>1</sup>H NMR, <sup>13</sup>C{<sup>1</sup>H} NMR, and high-resolution mass spectroscopy. Efficient MS ionization of sulfides was obtained by the addition of formic acid and AgNO<sub>3</sub> to solutions of 3a-3e, 3g-3k, 3m, 3n and 3f, 3l, correspondently.

**Cryo-SEM-EDS Measurements.** Copper(I) oxide (0.01 mmol, 1.4 mg),  $Cs_2CO_3$  (1.5 mmol, 0.4887 g), 4-iodotoluene (1.1 mmol, 0.2398 g), DMSO (1 mL), and thiophenol (1 mmol, 0.102 mL) were added to a vessel under inert atmosphere. The reaction vessel was equipped with a magnetic stir bar and sealed with a PTFE-lined cap. The mixture was stirred at 110 °C for 3 h and then allowed to cool to room temperature. After 2 h of residue sedimentation, the resulting solution was characterized by cryo-SEM and cryo-SEM-EDS.

Leaching Test Using Hot Centrifugation. Copper(I) oxide (0.01 mmol, 1.4 mg),  $Cs_2CO_3$  (1.5 mmol, 0.4887 g), 4-iodotoluene (1.1 mmol, 0.2398 g), solvent (1 mL), and thiophenol (1 mmol, 0.102 mL) were added to a test tube under an inert atmosphere. The mixture was stirred at 110 °C until the 4-iodotoluene conversion level reached 20% (for 2 h). The test tube then was covered with heat-insulating material and centrifuged until precipitate sedimentation (for 2 min). The solution after centrifugation was transferred into new test tube, fresh portion of  $Cs_2CO_3$  (1 mmol, 0.3258 g) was added and mixture was heated for 19 h at 110 °C. In addition, a standard hot filtration test was performed and similar results were obtained.

#### ASSOCIATED CONTENT

#### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.6b00337.

Details on Cryo-SEM measurements, XRD study, FE-SEM data, ESI-MS data, NMR data, optimization of reaction conditions, spectral parameters, and characterization of products (PDF)

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#### Notes

The authors declare no competing financial interest.

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(35) Reaction of CuO and  $Cu_2O$  with the thiol under studied conditions generated the same copper (I) thiolate species. Reduction of CuO by the thiol most likely occurred and the formation of corresponding disulfides was detected.

(36) For the sake of clarity, the plausible mechanism is shown with monometallic copper species detected in the experiments. Small soluble copper clusters may also be involved in the studied system (see refs 26 and 31 for discussion).