



A highly efficient and widely functional-group-tolerant catalyst system for copper(I)-catalyzed S-arylation of thiols with aryl halides

Yang Feng, Huifeng Wang, Fangfang Sun, Yaming Li^{*}, Xinmei Fu, Kun Jin

State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian 116012, China

ARTICLE INFO

Article history:

Received 15 September 2009

Accepted 22 September 2009

Available online 23 September 2009

ABSTRACT

A mild, general, and efficient copper-catalyzed system for C–S bond formation with high chemoselectivity and wide functional group tolerance is developed. With CuBr as catalyst and 1,2,3,4-tetrahydro-8-hydroxy-quinoline as ligand, the S-arylation of thiols with aryl halides performed well, the activated aryl iodides could take place even at room temperature, and the activated aryl bromides and chlorides give the corresponding products with good to excellent yields as well.

© 2009 Elsevier Ltd. All rights reserved.

1. Introduction

The formation of C–S bond is a key step in synthetic organic chemistry due to the importance of related compounds in pharmaceuticals and functional materials.¹ As a method for the synthesis of sulfides, reduction of aryl sulfones and aryl sulfoxides requires strong reducing agents such as LiAlH₄.² In 1980, Migita and co-workers reported the first palladium-catalyzed C(aryl)–S bond formation from the corresponding aryl halides and thiols.³ From then on, transition-metal-catalyzed C–S bond formation received particular interests. Because sulfur-containing compounds have strong coordinative properties and may poison the metal catalysts, literature reported for the transition-metal-catalyzed C–S cross-coupling reaction was limited since Migita's study, which is in contrast with the C–N and C–O bond formation.⁴ Although several transition metals such as palladium,⁵ nickel,⁶ copper,⁷ cobalt,⁸ iron,⁹ and indium¹⁰ have been reported for this purpose in the past decade, these catalytic systems still suffer from several common problems. For example, the high cost of palladium salts and phosphine ligands, metal toxicity, reagents needed in excess and few types of highly active ligands to choose restrict their applications, especially in large-scale process. Therefore, the development of traditional copper-catalyzed Ullmann-type C–S cross-coupling reactions is still attractive owing to the drawbacks of other metal-catalyzed systems.

In fact, the traditional copper-catalyzed C–S bond formation usually requires harsh conditions such as more than stoichiometric amounts of copper salts, polar solvent such as HMPA, and high temperature above 200 °C. It is noteworthy that only in the last few years attractive copper-catalyzed processes make a great contribution to this reaction. Copper-catalyzed Ullmann-type C–S coupling reaction

could be accelerated by some special ligands such as phosphazene,¹¹ ethylene glycol,¹² neocuproine,¹³ N-methylglycine,¹⁴ oxime-phosphine oxide ligand,¹⁵ tripod ligand,¹⁶ benzotriazole,¹⁷ 1,2-diaminocyclohexane,¹⁸ β-ketoester,¹⁹ L-proline,²⁰ and BINAM.²¹ Indeed, significant progresses have been achieved through the use of the ligands. A popular opinion is that the use of ligands may increase the solubility of copper salts in the solvents. Very recently, copper-catalyzed reactions at high temperature without any ligand were reported.²²

Yet, the development of this copper-catalyzed Ullmann-type reaction is required all the time as most catalytic systems still needed long reaction time (longer than 24 h), relatively high temperature (≥110 °C), sometimes high catalyst loading. Another drawback is that the expensive aryl iodides were used to couple with thiols in most reported systems while cheap aryl bromides were mentioned in countable literatures.^{14,17–21} In addition, high temperature is harmful for both asymmetrical synthesis and pharmaceutical. Therefore a mild, economic, and high-efficient catalytic system is still necessary for C–S coupling reaction aiming to decrease the temperature required for aryl iodides and also to increase the reactivity of aryl bromides.

Recently, we reported that *o*-aminophenol derivatives could accelerate the copper-catalyzed Ullmann-type N-arylation reaction.²³ Encouraged by the success in N-arylation reaction, we have investigated further copper-catalyzed S-arylation using *o*-aminophenol derivatives as ligands. In this paper, we report an extension of our catalytic system, which can catalyze Ullmann-type coupling of thiols with aryl halide for the formation of C–S bond.

2. Results and discussion

In a preliminary study, three ligands **A**, **B**, and **C** derived from *o*-aminophenol (see structures in Fig. 1) were tested to find the

^{*} Corresponding author. Tel./fax: +86 411 39893900.

E-mail address: yamingli@chem.dlut.edu.cn (Y. Li).

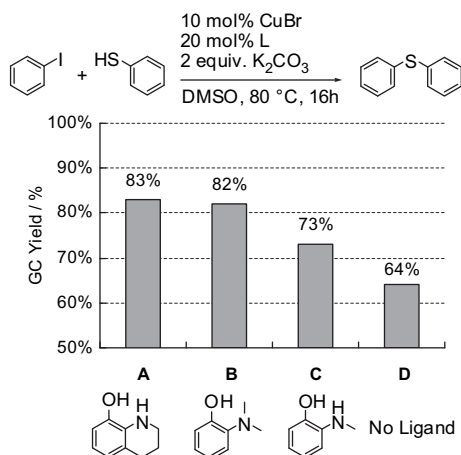


Figure 1. Ligand screening for S-arylation of thiophenol.

optimal ligand for S-arylation reaction under the condition used for N-arylation reaction.²³ K_2CO_3 was used instead of Cs_2CO_3 because the acidity of thiophenol was much stronger than substrates for N-arylation reaction. As shown in Figure 1, all ligands promoted the coupling reaction under the indicated conditions. Ligands **A** and **B** gave the higher GC yields compared with **C**. Without any ligand, the GC yield of diphenyl thioether is 64%, which is in agreement with the literature.^{22c} We speculated that the synergistic electron-donating groups and flexible tetrahedral steric structures of ligands **A**, **B**, and **C** facilitated the oxidative addition and reductive elimination reaction.²³ Thus our study indicated that both ligands **A** and **B** were effective for the copper-catalyzed C–S coupling reaction. Considering the continuity of our research on the copper-catalyzed coupling reaction, the ligand **A** was chosen for the S-arylation reaction due to its low cost and commercial availability.

Some influencing factors, such as the copper salts, solvents, bases, molar ratio of ligand to copper salt, reaction time, etc., were briefly screened using this model reaction. As shown in Table 1, polar solvents CH_3CN , DMF, and DMSO can promote this reaction in a more efficient way compared with weakly polar solvent toluene, and DMSO was found to be the best choice. Although several copper salts could catalyze the reaction, $CuBr$ was superior to others. Similarly, K_2CO_3 gave the best result among the bases examined. It was noted

that the molar ratio of copper to ligand is important in the reaction. The yield of diphenyl thioether was dramatically decreased from 83% to 68% when the molar ratio of copper to ligand increased from 10:20 to 10:10 (Table 1, entries 7 and 12). Perhaps the structure of four-coordinate complex makes the copper ion more stable in reaction system relative to two-coordinate complex. The yield decreased to 51% while the catalyst loading decreased to 5 mol % (Table 1, entry 13). Detected by GC, byproduct diphenyl disulfide ranged from 5% to 15%. In order to avoid this side reaction, the iodobenzene was excess compared with thiophenol. After prolonging the reaction time to 24 h, the reaction gave a GC yield of 97% (Table 1, entry 14). Thus, the optimal reaction condition was obtained as shown in entry 14.

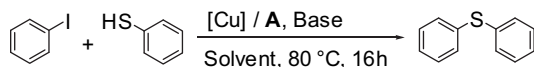
By using the optimized reaction condition, we further investigated the scope of the Ullmann-type C–S coupling reaction of aryl iodides with thiols and the results are summarized in Table 2. As shown in Table 2, various substituted aryl iodides reacted with both aromatic and aliphatic thiols and gave the corresponding products with excellent yields. The aryl iodides with electron-donating groups, which deactivate the aryl iodides gave the desired diaryl thioethers in high yields (Table 2, entries 1–10). Electron-withdrawing groups such as nitro group dramatically increased the reactivity of aryl iodides and the coupling reaction took place even at room temperature (Table 2, entry 2). Whether the substitution of iodobenzene was at the *para*- or *ortho*-position, the C–S bond formation reaction gave excellent yields (Table 2, entries 3–9). Similarly in the case of thiols, both aliphatic and aromatic thiols with *para*- or *ortho*-substituted gave the corresponding products in excellent yields (Table 2, entries 11–17). All the results of *ortho*-substituted iodobenzene and thiophenol relative to the *para*-substitutions indicated that the effect of steric hindrance was unobvious. Moreover, the reaction showed a chemoselectivity to the thiols other than arylation on amino or hydroxyl groups. Monitoring the reaction of *p*-bromo iodobenzene with thiophenol at 80 °C by GC–MS, both *p*-bromo and *p*-iodo diphenyl thioethers were produced at a ratio of 1:1 approximately. It was noted that in the previous reported catalytic system the less reactive bromo group did not react when bromo and iodo groups coexist in the arene ring at 80 °C or above. By decreasing the temperature stepwise to 45 °C for 48 h, *p*-bromo diphenyl thioether became the sole product as we desired through the coupling reaction.

To the best of our knowledge, only few literatures reported that aryl bromides could react with thiols and gave satisfied yields by copper-catalyzed system.^{17,19b,21} Encouraged by the result of *p*-bromo iodobenzene that *p*-iodo diphenyl thioether was formed under our optimized condition, aryl bromides were tried to react with thiophenol. At the initial stage, bromobenzene was tested but failed to form the corresponding product through the coupling reaction even the temperature was increased to 110 °C (Table 3, entry 1). To our delight, bromobenzene with electron-withdrawing groups such as nitro, cyano, keto, and aldehyde could react well under the condition used for aryl iodides, and the results are summarized in Table 3. It was noted that the presence of the electron-withdrawing groups dramatically increased the activity of aryl bromides and gave the good to excellent yields. Heterocyclic bromides such as 3-hydroxyl-2-bromo pyridine could also be applied to this coupling reaction and give a satisfactory yield of 62% (Table 3, entry 6). Even *p*-nitro chlorobenzene reacted well under our condition and an isolated yield of 95% was obtained (Table 3, entry 7).

The results in Tables 2 and 3 showed that various functional groups such as –Br, –Cl, –CN, –NO₂, –Ac, –CHO, and especially free –OH and –NH₂, which were intolerant of Pd catalyzed systems, were tolerated by our catalytic system.

Aiming to obtain diaryl thioethers from less reactive aryl bromides with thiophenol under the reaction condition, we tried to change the base. The desired product was formed with good isolated yield when K_2CO_3 was replaced by the strong base *t*-BuOK

Table 1
Optimization of the reaction condition^a



Entry	[Cu]/L	Solvent	[Cu]	Base	Yield (%)
1	10:20	Toluene	CuCl	K_2CO_3	3
2	10:20	CH_3CN	CuCl	K_2CO_3	73
3	10:20	DMF	CuCl	K_2CO_3	78
4	10:20	DMSO	CuCl	K_2CO_3	80
5	10:20	DMSO	CuI	K_2CO_3	47
6	10:20	DMSO	$CuBr_2$	K_2CO_3	38
7	10:20	DMSO	CuBr	K_2CO_3	83
8	10:20	DMSO	CuBr	Cs_2CO_3	62
9	10:20	DMSO	CuBr	K_3PO_4	60
10	10:20	DMSO	CuBr	KOH	73
11	10:20	DMSO	CuBr	NEt_3	27
12	10:10	DMSO	CuBr	K_2CO_3	68
13	5:10	DMSO	CuBr	K_2CO_3	51
14 ^b	10:20	DMSO	CuBr	K_2CO_3	97

^a Reaction conditions: [Cu] (0.05 mmol), base (2 mmol), solvent (1 mL), iodobenzene (1 mmol), thiophenol (1.5 mmol), N_2 . Yield (GC) was calibrated with diphenyl ether as an internal standard.

^b Thiophenol (1 mmol), iodobenzene (1.5 mmol), 80 °C for 24 h.

Download English Version:

<https://daneshyari.com/en/article/5226362>

Download Persian Version:

<https://daneshyari.com/article/5226362>

[Daneshyari.com](https://daneshyari.com)