



## An efficient iron-catalyzed S-arylation of aryl and alkylthiols with aryl halides in the presence of water under aerobic conditions



K. S. Sindhu, Amrutha P. Thankachan, Anns Maria Thomas, Gopinathan Anilkumar\*

School of Chemical Sciences, Mahatma Gandhi University, PD Hills PO, Kottayam 686 560, India

### ARTICLE INFO

#### Article history:

Received 5 June 2015

Revised 25 June 2015

Accepted 26 June 2015

Available online 2 July 2015

#### Keywords:

C–S coupling

Iron catalysis

Green chemistry

Thioetherification

Cross coupling

### ABSTRACT

In this study, an environmentally benign  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}/L$ -proline catalytic system in the presence of TBAB was employed as a catalyst for the coupling reactions of aryl halides with aryl and alkyl thiols in water under aerobic conditions. The versatility, low cost, and environmental friendliness, in combination with high yields, makes the procedure noteworthy. This protocol offers a simple and efficient thioetherification method for aryl halides.

© 2015 Elsevier Ltd. All rights reserved.

### Introduction

Transition metal catalyzed carbon–heteroatom cross-coupling reactions have found widespread popularity in synthetic chemistry, as several biologically active compounds with wide ranges of activity contain carbon–heteroatom bonds.<sup>1</sup> Whereas many C–N and C–O cross-coupling reactions are reported over the years, C–S bond formation leading to diaryl thioethers has received comparatively less attention, despite of the prevalence of these bonds in many molecules which are widely used for biological, pharmaceutical, and material science applications.<sup>2</sup> In 1978, Migita and co-workers reported the first C–S cross-coupling of aryl halides with thiols using tetrakis(triphenylphosphine)-palladium as catalyst.<sup>3</sup> Later, several transition metal catalysts in which palladium,<sup>4</sup> nickel,<sup>5</sup> cobalt,<sup>6</sup> copper,<sup>7</sup> rhodium,<sup>8</sup> indium,<sup>9</sup> and zinc<sup>10</sup> serve as the metal sources in combination with appropriate ligands have been developed. Out of these transition metals, iron is more attractive over other metals, owing to its cheap price, less toxicity, and environmentally benign properties. In 2008, Bolm et al. reported the first iron-catalyzed thioetherification of aryl thiols with aryl iodides using  $\text{FeCl}_3/\text{DMEDA}$  as the catalyst and  $\text{NaO}^t\text{Bu}$  as the base in toluene under argon atmosphere.<sup>11</sup> Thereafter, only a few reports appeared on iron-catalyzed thioetherification reactions. However, most of these approaches were limited to systems with aryl iodides and aryl thiols and were ineffective for aryl bromides, aryl chlorides, and alkyl thiols.<sup>12</sup>

Moreover, in most cases, the catalytic systems comprised of expensive catalysts, phosphine-based ligands, moisture sensitive bases, and organic solvents.<sup>13</sup>

On the other hand, in recent years the design of green chemistry approaches for the thiol S-arylation reactions has received much attention. The use of water as a solvent for organic reactions is of high practical value, since water is cheap, non-toxic, safe, and environmentally benign as compared to organic solvents.<sup>14</sup> Furthermore, the catalyst-containing aqueous solution can be easily separated from the organic products.

Although several methods are available for the formation of aryl sulfides, those employing green chemistry approaches are very limited for iron-catalyzed C–S coupling reactions and confined to a report by Tsai et al. which utilizes a cationic 2,2'-bipyridyl system as the catalyst. Therefore, it is highly desirable to develop a cheap and greener methodology for the iron-catalyzed C–S cross-coupling reactions with wide range of substrate scope. Herein, we present a green, efficient, and versatile protocol for the synthesis of thioethers based on  $\text{FeCl}_3$  and  $L$ -proline as catalyst system by the coupling of aryl halides including bromides and chlorides with aryl and alkyl thiols in water under air.

### Result and discussion

In this study, we wish to report an efficient  $\text{FeCl}_3$ -catalyzed S-arylation of aryl halides with thiols using  $L$ -proline as the ligand in water under aerobic conditions. Compared to phosphine-based ligands,  $L$ -proline is very cheap, non-toxic, and readily

\* Corresponding author.

available. It is proven that in the absence of the catalyst and ligand, the C–S coupling product was obtained in lesser amounts, and diphenyl disulfide, which arises from an iron-catalyzed oxidation reaction of the thiol, was the main product. When our present protocol for the formation of C–S bond is compared with other existing methods, the following features are worth mentioning: (i) the methodology makes use of an environmentally benign and inexpensive catalytic system that is a combination of readily available iron salt and a universal ligand; (ii) in this approach, a broader scope of substrates, various substituted aryl halides including bromides and chlorides as well as both aryl and alkyl thiols can be applied (iii) the most important aspect is that the most environmentally friendly and cheapest reagent, water, is used as the solvent for the reaction.

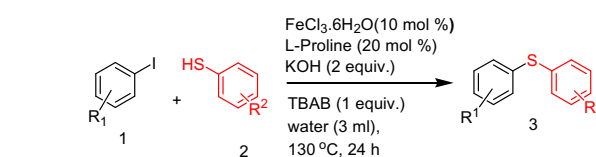
Initially, we carried out a set of experiments using 4-iodoacetophenone (1.2 equiv) and thiophenol (1 equiv) as model substrates in water under air using FeCl<sub>3</sub> as the catalyst and L-proline as the ligand for optimizing the reaction conditions, and the results are summarized in Table 1. As indicated in Table 1 (entries 1–3), in pure water, only low yields of the desired product were obtained. More than half of the reactants were recovered from the reaction mixture which indicated the poor solubility of organic reagents especially aryl halides in water. It is presumed that the reaction occurred through small portions of dissolved solutes in the aqueous–organic interface. Therefore, we added the phase transfer reagent tetrabutylammonium bromide (TBAB). At first we added only 0.2 equiv of TBAB; but no considerable increase in the yield was observed (not shown in table). To our delight, addition of 1 equiv of TBAB to the reaction mixture led to a sharp increase in the conversion rate (Table 1, entries 4 and 5).

In most of the cases, the formation of the undesired phenyl disulfide was observed as a side product. To circumvent this, we used thiol as the limiting reagent. The disulfide formation was predominant at lower temperatures and as the temperature increased,

higher yields of the desired product were detected (Table 1, entries 6 and 7). At 130 °C, formation of the disulfide ceased and the desired product was isolated in 95% yield (Table 1, entry 6).

Further experiments revealed that the thioetherification of **1a** with **2a** has a significant dependence on the nature of the base.

**Table 2**  
Iron-catalyzed carbon–sulfur bond formation of arene thiols and aryl halides<sup>a</sup>



Entry	Aryl halide <b>1</b>	Thiol <b>2</b>	Product <b>3</b>	Yield <sup>b</sup> (%)
1				95
2				61
3				36
4				86
5				55
6				82
7				89
8				58
9				74
10				86
11				79
12				81
13				76
14				65
15				60
16				64

<sup>a</sup> Reaction conditions: aryl halide (1.2 mmol), thiol (1 mmol), KOH (2 equiv), FeCl<sub>3</sub>·6H<sub>2</sub>O (10 mol %), L-proline (20 mol %), TBAB (1 equiv), water (3 ml), 130 °C, 24 h.

<sup>b</sup> Isolated yield.

**Table 1**  
Iron-catalyzed coupling reaction of thiophenol and 4-iodo acetophenone in water<sup>a</sup>

Entry	Catalyst	Base	Additive	Temp (°C)	Yield <sup>b</sup> (%)
1	FeCl <sub>3</sub>	K <sub>2</sub> CO <sub>3</sub>	—	120	38
2	FeCl <sub>3</sub>	KOH	—	120	50
3	FeCl <sub>3</sub> ·6H <sub>2</sub> O	KOH	—	120	53
4	FeCl <sub>3</sub>	KOH	TBAB	120	85
5	FeCl <sub>3</sub> ·6H <sub>2</sub> O	KOH	TBAB	120	88
6	FeCl <sub>3</sub> ·6H <sub>2</sub> O	KOH	TBAB	130	95
7	FeCl <sub>3</sub> ·6H <sub>2</sub> O	KOH	TBAB	110	62
8	FeCl <sub>3</sub> ·6H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	TBAB	130	65
9	FeCl <sub>3</sub> ·6H <sub>2</sub> O	K <sub>3</sub> PO <sub>4</sub>	TBAB	130	19
10	FeCl <sub>3</sub> ·6H <sub>2</sub> O	Cs <sub>2</sub> CO <sub>3</sub>	TBAB	130	36
11	FeCl <sub>3</sub> ·6H <sub>2</sub> O	NaOH	TBAB	130	57
12 <sup>c</sup>	FeCl <sub>3</sub> ·6H <sub>2</sub> O	KOH	TBAB	130	64
13 <sup>d</sup>	FeCl <sub>3</sub> ·6H <sub>2</sub> O	KOH	TBAB	130	69
14	—	KOH	TBAB	130	36 <sup>e</sup>
15 <sup>f</sup>	FeCl <sub>3</sub> ·6H <sub>2</sub> O	KOH	TBAB	130	21 <sup>e</sup>
16	FeCl <sub>3</sub> ·6H <sub>2</sub> O	—	TBAB	130	13 <sup>e</sup>

<sup>a</sup> Reaction conditions: aryl iodide (1.2 mmol), thiophenol (1 mmol), base (2 equiv), catalyst (10 mol %), L-proline (20 mol %), TBAB (1 equiv), water (3 ml), 130 °C, 24 h.

<sup>b</sup> Isolated yield.

<sup>c</sup> 1.5 equiv of KOH.

<sup>d</sup> Use of 5 mol % FeCl<sub>3</sub>·6H<sub>2</sub>O and 10 mol % of L-proline.

<sup>e</sup> GCMS showed the presence of a large peak corresponding to the disulfide.

<sup>f</sup> Absence of L-proline.

Download English Version:

<https://daneshyari.com/en/article/5268693>

Download Persian Version:

<https://daneshyari.com/article/5268693>

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