Journal of Organometallic Chemistry 723 (2013) 137–142

Contents lists available at SciVerse ScienceDirect

Journal of Organometallic Chemistry

journal homepage: www.elsevier.com/locate/jorganchem

Note

Copper(I)-catalyzed tandem reaction of 2-iodophenols with isothiocyanates in room temperature ionic liquids

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ARTICLE INFO

Article history:
Received 20 July 2012
Received in revised form
13 September 2012
Accepted 18 September 2012

Keywords:
Copper(I) catalysis
2-Iminobenzo-1,3-oxathiole
Tandem reaction
Ionic liquid
2-Iodophenol

ABSTRACT

A copper(I)-catalyzed tandem reaction of 2-iodophenols with isothiocyanates in hydrophobic [bmim][PF_6] ionic liquid was described, which proceeded smoothly and generated a variety of 2-iminobenzo-1,3-oxathioles in good to excellent yields. The tandem reaction that was carried out in [bmim][PF_6] has some obvious advantages such as reaction rate acceleration and yield increasing as compared with the reaction run in volatile solvents such as toluene. Furthermore, the CuI/1,10-phenanthroline catalytic system can be reused up to 6 times without loss of activity and efficiency.

1. Introduction

The benzo-1,3-oxathiole motifs are found in a variety of useful heterocyclic compounds that exhibit remarkable pharmaceutical or biochemical activities [1–3]. In particular, the significant importance of the 2-iminobenzo-1,3-oxathioles has stimulated the development of efficient routes for their preparation [4–8]. For example, Ibata et al. discovered a feasible approach to 2-iminobenzo-1,3-oxathioles utilizing rhodium(II) acetate-catalyzed reaction of α-diazocarbonyl compounds with isothiocyanates [5]. Nair et al. found that the heterocyclic scaffolds could be constructed via [4+1] cycloaddition reaction of *o*-thioquinones with isocyanides [6]. Kulka reported a facile synthesis of *N*-acyl-2-imino-1,3-oxathioles from *O*-alkyl acylcarbamothioates and 2-chloro ketones in the presence of sodium alkoxide [9]. However, in many cases, the applications of these methodologies often suffered from some limitations such as narrow substrate scopes, expensive or toxic metal catalysts and reagents, unsatisfactory efficiencies, as well as the tedious multistep manipulation. Recently, Bao et al. reported a highly efficient method for the synthesis of 2-iminobenzo-1,3-oxathioles via a copper(I)-catalyzed one-pot tandem reaction of 2-iodophenols with isothiocyanates in toluene [10]. However, the one-pot tandem reaction of 2-iodophenols with isothiocyanates proceeds in the presence of a homogeneous CuI (10 mol%) using 1,10-phenanthroline (20 mol%) as a ligand in toluene, which makes the recovery of the catalytic system tedious if not impossible and might result in unacceptable copper contamination of the product. Ideally, one would like to be able to recover and recycle the entire catalyst system but avoid the challenges presented by either mounting the catalyst on a solid support or by preparing designer ligands for use in aqueous or fluorous biphasic systems.

Recently, a new alternative solution for catalyst recycling has been reported. This involves the use of room temperature ionic liquids (RTILs), in essence salts that are liquid at or below room temperature [11]. Room temperature ionic liquids, especially those based upon the 1,3-dialkylimidazolium cation, have attracted growing interest in recent years [12–15]. They offer an alternative and ecologically sound medium compared to conventional organic solvents, as they are non-volatile, recyclable, thermally robust and excellent solvents for a wide range of organic and inorganic materials. Furthermore, their high compatibility with transition metal catalysts and limited miscibility with common solvents, enables easy product and catalyst separation with the retention of the stabilized catalyst in the ionic phase [16]. These and related ionic liquids have been successfully applied to hydrogenations [17], alkene dimerizations [18], Friedel–Crafts reactions [19,20], Diels–Alder reactions [21], Heck reactions [22,23], Bechmann

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http://dx.doi.org/10.1016/j.jorganchem.2012.09.010

condensations [24], Suzuki reactions [25–27], Baylis–Hillman reactions [28,29], Stille reactions [30,31], and Sonogashira reactions [32]. However, copper-catalyzed cross-coupling reactions in ionic liquids have received less attention [33,34]. The emerging importance of the imidazolium-based ionic liquids in organic synthesis, motivated us to test the efficacy of ionic liquids for C–S coupling reaction. In this paper, we describe the copper(I)-catalyzed one-pot tandem reaction of 2-iodophenols with isothiocyanates in room temperature ionic liquids. The developed methodology has important practical advantages deserving special note.

2. Experimental

2.1. General remarks

All chemicals were reagent grade and used as purchased. The products were purified by flash chromatography on silica gel. IR spectra were determined on a Perkin–Elmer 683 instrument. ^{1}H NMR spectra were recorded on a Bruker Avance (400 MHz) spectrometer with TMS as an internal standard in $CDCl_3$ as solvent. ^{13}C NMR spectra were recorded on a Bruker Avance (100 MHz) spectrometer in $CDCl_3$ as solvent. Melting points are uncorrected. [bmim][PF_6] was prepared according to the procedure reported in the literature and the purity was confirmed by ^{1}H NMR [35,36].

2.2. General procedure for copper(I)-catalyzed tandem reaction of 2-iodophenols with isothiocyanates in [bmim][PF_6]

A two-necked flask equipped with a magnetic stirring bar were placed Cs_2CO_3 (2.0 mmol), CuI (0.1 mmol), 1,10-phenanthroline (0.2 mmol), 2-iodophenol (1.0 mmol) and [bmim][PF_6] (2.0 mL) under an argon atmosphere. The mixture was pre-stirred at 40 °C for 1 h, then isothiocyanate (1.0 mmol) was added and the mixture was allowed to stir at 80–90 °C. After completion of the reaction as monitored by TLC, the reaction was cooled down to 25 °C and extracted with diethyl ether (3 × 10 mL). The recovered ionic liquid phase containing CuI/1,10-phenanthroline complex was concentrated in vacuo (5.0 Torr/r.t. for 1 h) and reused in the next run. The combined ether solution was concentrated under vacuum, and the residue was purified by flash chromatography on silica gel to give the desired product.

2.2.1. N-(Benzo[d][1,3]oxathiol-2-ylidene)benzenamine, **3a**

White solid [10], mp 76–78 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.07 (d, J = 7.6 Hz, 2H), 7.12–7.19 (m, 2H), 7.21–7.28 (m, 3H), 7.38 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 111.4, 120.9, 122.2, 122.7, 124.5, 125.0, 127.1, 129.6, 148.0, 150.4, 160.3.

2.2.2. N-(Benzo[d][1,3]oxathiol-2-ylidene)-4-methylbenzenamine, **3b**

White solid [10], mp 78–80 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (s, 3H), 6.97 (d, J = 8.4 Hz, 2H), 7.13 (dt, J = 2.0, 7.6 Hz, 1H), 7.19 (d, J = 8.0 Hz, 2H), 7.21–7.28 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 111.4, 120.6, 122.1, 122.7, 124.4, 127.1, 130.1, 134.5, 145.4, 150.3, 159.9.

2.2.3. N-(Benzo[d][1,3]oxathiol-2-ylidene)-2-methylbenzenamine, **3c**

White solid [10], mp 62–64 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.28 (s, 3H), 6.98 (d, J = 7.6 Hz, 1H), 7.10–7.18 (m, 2H), 7.21–7.28 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.7, 111.4, 119.5, 122.1, 122.9, 124.4, 124.9, 127.1, 130.0, 130.9, 146.9, 150.6, 159.8.

2.2.4. N-(Benzo[d][1,3]oxathiol-2-ylidene)-4-methoxybenzenamine, **3d**

White solid [10], mp 110–112 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3H), 6.93 (d, J = 9.2 Hz, 2H), 7.03 (d, J = 8.8 Hz, 2H), 7.14 (dt, J = 2.0, 7.6 Hz, 1H), 7.21–7.28 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.5, 111.3, 114.8, 121.9, 122.1, 122.7, 124.4, 127.1, 141.1, 150.3, 157.0, 159.9.

2.2.5. N-(Benzo[d][1,3]oxathiol-2-ylidene)-4-nitrobenzenamine, **3e**

Yellow solid [37], mp 162–164 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18–7.35 (m, 6H), 8.27 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 111.7, 121.7, 122.3, 125.1, 125.6, 127.6, 144.7, 150.3, 153.6, 161.7.

2.2.6. N-(Benzo[d][1,3]oxathiol-2-ylidene)-4-chlorobenzenamine, **3f**

White solid [37], mp 91–93 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.90 (d, J = 8.4 Hz, 2H), 7.05 (dt, J = 2.0, 7.6 Hz, 1H), 7.12 –7.20 (m, 3H), 7.25 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 111.5, 122.2, 122.3, 122.4, 124.6, 127.3, 129.8, 130.1, 146.5, 150.4, 160.8.

2.2.7. N-(Benzo[d][1,3]oxathiol-2-ylidene)-4-fluorobenzenamine, **3g**

White solid [37], mp 101–103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.01–7.10 (m, 4H), 7.14 (dt, J = 2.0, 7.6 Hz, 1H), 7.20–7.28 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 111.4, 116.4 (d, $^2J_{CF}$ = 22 Hz), 122.2 (d, $^2J_{CF}$ = 23 Hz), 122.4, 122.5, 124.6, 127.3, 144.2, 150.3, 160.1 (d, $^1J_{CF}$ = 243 Hz), 160.7.

2.2.8. N-(5-Methylbenzo[d][1,3]oxathiol-2-ylidene)benzenamine, **3h**

White solid [10], mp 83–85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.33 (s, 3H), 7.02–7.12 (m, 5H), 7.17 (t, J = 7.6 Hz, 1H), 7.38 (t, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 110.9, 120.9, 122.3, 122.4, 124.9, 127.7, 129.6, 134.4, 148.0, 148.4, 160.6.

2.2.9. 4-Methyl-N-(5-methylbenzo[d][1,3]oxathiol-2-ylidene) benzenamine, **3i**

White solid [10], mp 87–89 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.33 (s, 3H), 2.35 (s, 3H), 6.97 (d, J = 8.0 Hz, 2H), 7.02–7.11 (m, 3H), 7.18 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0 (2C), 110.9, 120.7, 122.3, 122.5, 127.7, 130.2, 134.2, 134.4, 145.5, 148.4, 160.3.

2.2.10. 2-Methyl-N-(5-methylbenzo[d][1,3]oxathiol-2-ylidene) benzenamine, **3j**

White solid [10], mp 56–58 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.27 (s, 3H), 2.36 (s, 3H), 6.98 (d, J = 7.6 Hz, 1H), 7.04–7.15 (m, 4H), 7.22–7.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.7, 21.0, 111.0, 119.7, 122.3, 122.7, 124.9, 127.1, 127.7, 130.1, 130.9, 134.3, 147.1, 148.6, 160.2.

2.2.11. 4-Methoxy-N-(5-methylbenzo[d][1,3]oxathiol-2-ylidene) benzenamine, **3k**

White solid [10], mp 93–95 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.33 (s, 3H), 3.81 (s, 3H), 6.91–6.95 (m, 2H), 7.01–7.05 (m, 3H), 7.09–7.13 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9, 55.4, 110.9, 114.8, 121.9, 122.2, 122.5, 127.7, 134.2, 141.2, 148.3, 156.9, 160.1.

2.2.12. 4-Nitro-N-(5-methylbenzo[d][1,3]oxathiol-2-ylidene) benzenamine, **3l**

Yellow solid [37], mp 160–162 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.37 (s, 3H), 7.08–7.19 (m, 5H), 8.26 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 111.2, 121.7, 122.4, 125.7, 128.2, 135.2, 144.6, 148.5, 153.7, 162.0.

2.2.13. 4-Chloro-N-(5-methylbenzo[d][1,3]oxathiol-2-ylidene) benzenamine, **3m**

White solid [37], mp 100–102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.33 (s, 3H), 6.99 (d, J = 8.8 Hz, 2H), 7.01–7.12 (m,

3H), 7.34 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 111.1, 122.2, 122.3, 122.4, 127.9, 129.7, 130.2, 134.6, 146.5, 148.3, 161.2.

2.2.14. N-(5-methylbenzo[d][1,3]oxathiol-2-ylidene) cyclohexanamine, ***3n***

White solid [10], mp 73–75 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26–1.50 (m, 5H), 1.59–1.64 (m, 1H), 1.76–1.82 (m, 4H), 2.32 (s, 3H), 2.80–2.85 (m, 1H), 6.93–7.04 (m, 2H), 7.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9, 24.5, 25.5, 33.1, 63.4, 110.6, 122.3, 122.6, 127.4, 133.6, 148.2, 156.4.

2.2.15. N-(5-tert-Butylbenzo[d][1,3]oxathiol-2-ylidene) benzenamine, ***3o***

White solid [10], mp 56–58 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (s, 9H), 7.06 (d, J = 7.6 Hz, 2H), 7.16 (t, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 1H), 7.27 (s, 1H), 7.38 (t, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 34.8, 110.7, 118.9, 120.9, 122.3, 124.3, 124.9, 129.6, 148.0, 148.1, 148.3, 160.7.

2.2.16. N-(5-tert-Butylbenzo[d][1,3]oxathiol-2-ylidene)-4-methylbenzenamine, ***3p***

White solid [10], mp 81–83 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.30 (s, 9H), 2.35 (s, 3H), 6.97 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 1H), 7.18 (d, J = 7.6 Hz, 2H), 7.24 (d, J = 8.0 Hz, 1H), 7.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 31.5, 34.8, 110.7, 118.9, 120.8, 122.4, 124.2, 130.2, 134.4, 145.5, 147.9, 148.2, 160.4.

2.2.17. N-(5-tert-Butylbenzo[d][1,3]oxathiol-2-ylidene)-4-methoxybenzenamine, ***3q***

White solid [10], mp 99–101 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 9H), 3.81 (s, 3H), 6.92 (d, J = 8.8 Hz, 2H), 7.02 (d, J = 8.8 Hz, 2H), 7.14 (d, J = 8.8 Hz, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.4, 34.7, 55.4, 110.6, 114.8, 118.9, 122.0, 122.3, 124.2, 141.2, 147.9, 148.2, 156.9, 160.3.

2.2.18. N-(5-tert-Butylbenzo[d][1,3]oxathiol-2-ylidene)-4-nitrobenzenamine, ***3r***

Yellow solid [37], mp 134–136 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 9H), 7.18–7.36 (m, 5H), 8.26 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 34.8, 111.0, 119.1, 121.7, 122.3, 124.8, 125.5, 144.6, 148.2, 148.7, 153.7, 162.1.

2.2.19. N-(5-tert-Butylbenzo[d][1,3]oxathiol-2-ylidene)-4-chlorobenzenamine, ***3s***

White solid [37], mp 94–96 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (s, 9H), 6.92 (d, J = 8.8 Hz, 2H), 7.07 (d, J = 8.4 Hz, 1H), 7.17–7.25 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.4, 33.7, 109.7, 117.9, 121.0, 121.3, 123.4, 128.7, 129.0, 145.5, 147.1, 160.2.

2.2.20. N-(5-tert-Butylbenzo[d][1,3]oxathiol-2-ylidene) cyclohexanamine, ***3t***

White solid [10], mp 52–54 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (s, 9H), 1.31–1.52 (m, 4H), 1.59–1.65 (m, 2H), 1.76–1.83 (m, 4H), 2.81–2.87 (m, 1H), 7.04 (d, J = 8.4 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 7.31 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.5, 25.6, 31.5, 33.1, 34.7, 63.3, 110.4, 118.9, 122.4, 124.0, 147.2, 148.0, 156.5.

2.2.21. N-(5-Chlorobenzo[d][1,3]oxathiol-2-ylidene)benzenamine, ***3u***

White solid [10], mp 106–108 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.04 (d, J = 7.6 Hz, 2H), 7.12–7.25 (m, 4H), 7.38 (t, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 112.2, 120.8, 121.9, 122.8, 124.5, 125.2, 127.3, 129.7, 147.6, 148.9, 159.4.

2.2.22. N-(5-Chlorobenzo[d][1,3]oxathiol-2-ylidene)-4-methylbenzenamine, ***3v***

White solid [37], mp 120–122 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (s, 3H), 6.94 (d, J = 8.0 Hz, 2H), 7.10–7.23 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 112.1, 120.6, 121.9, 124.6, 127.2, 129.7, 130.3, 134.8, 145.0, 148.9, 159.0.

2.2.23. N-(5-Chlorobenzo[d][1,3]oxathiol-2-ylidene)-4-methoxybenzenamine, ***3w***

White solid [37], mp 100–102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3H), 6.93 (d, J = 8.8 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 7.13 (d, J = 8.4 Hz, 1H), 7.18 (d, J = 8.4 Hz, 1H), 7.24 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4, 112.1, 114.9, 121.8, 121.9, 124.5, 127.2, 129.6, 140.7, 148.9, 157.1, 158.9.

2.2.24. N-(5-Chlorobenzo[d][1,3]oxathiol-2-ylidene)-4-nitrobenzenamine, ***3x***

Yellow solid [37], mp 171–173 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.29 (d, J = 7.6 Hz, 2H), 7.35–7.43 (m, 2H), 7.74 (s, 1H), 8.25 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 112.7, 122.0, 122.7, 123.9, 125.4, 127.6, 129.0, 144.2, 148.8, 152.8, 160.9.

2.2.25. N-(5-Chlorobenzo[d][1,3]oxathiol-2-ylidene)-4-chlorobenzenamine, ***3y***

White solid [37], mp 116–118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.98 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 8.8 Hz, 1H), 7.23 (d, J = 8.8 Hz, 1H), 7.27 (s, 1H), 7.34 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 112.3, 122.0, 122.3, 124.2, 127.4, 129.9, 130.1, 130.5, 146.1, 148.9, 160.1.

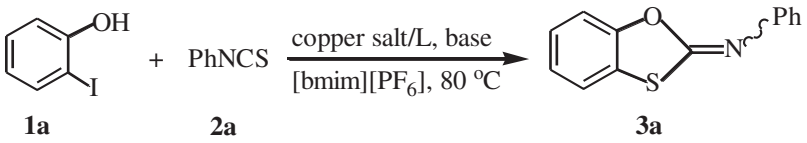
2.3. Recycling of ionic liquid and catalytic system

After completion of the reaction, the reaction mixture was cooled to 25 °C and extracted with diethyl ether (3 × 10 mL). The remaining oily ionic liquid containing CuI/1,10-phenanthroline complex was concentrated in vacuo (5.0 torr/r.t. for 1 h) and a second amount of reactants were added and the process was repeated up to 3 times. After third cycle, the ionic liquid was washed with distilled water (2 × 10 mL), dried in vacuo (5.0 Torr/80 °C for 1 h) and recycled for another three times without addition of CuI and 1,10-phenanthroline.

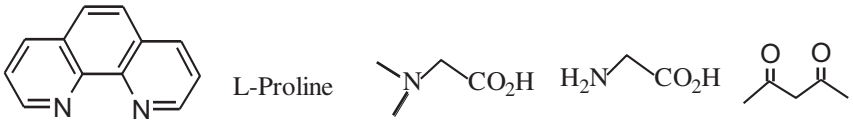
3. Results and discussion

Our choice of solvent was the readily prepared and hydrophobic 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF_6]). In our preliminary experiments, the reaction of 2-iodophenol with phenyl isothiocyanate was chosen as a model reaction. The influences of various reaction parameters such as copper salts, ligands, and bases on the reaction were tested and the results are summarized in Table 1. Among the copper salts such as CuI, CuBr, CuCl, Cu_2O, $CuCl_2$, $CuSO_4$ and $Cu(OAc)_2$ screened in the reaction, CuI was found to be the most effective catalyst, leading to the desired product in 97% yield (Table 1, entry 1). In a blank experiment, the reaction did not occur in the absence of copper catalyst (entry 12). And then, we investigated the influences of various ligands such as 1,10-phenanthroline, L-proline, *N,N*-dimethylglycine, glycine and acac on the model reaction. L-Proline, glycine and acac were not suitable for this process. *N,N*-Dimethylglycine was good, but 1,10-phenanthroline was the best choice. Hardly any desired product was observed without a ligand (entry 13). Among the bases examined, Cs_2CO_3 was found to be the most effective (Table 1, entry 1), K_2CO_3 and K_3PO_4 also afforded good yields (Table 1, entries 14 and 16), but Na_2CO_3 was substantially less effective (Table 1, entry 15). Therefore, the optimized conditions for this tandem reaction

Table 1
Reaction condition screening for the reaction of 2-iodophenol **1a** with phenyl isothiocyanate **2a** in [bmim][PF_6].[a]



1a **2a** **3a**



L1 **L2** **L3** **L4** **L5**

Entry	Copper salt	Ligand	Base	Yield[b] (%)
1	CuI	**L1**	Cs_2CO_3	97
2	CuBr	**L1**	Cs_2CO_3	68
3	CuCl	**L1**	Cs_2CO_3	70
4	Cu_2O	**L1**	Cs_2CO_3	23
5	$CuCl_2$	**L1**	Cs_2CO_3	74
6	$CuSO_4$	**L1**	Cs_2CO_3	65
7	$Cu(OAc)_2$	**L1**	Cs_2CO_3	63
8	CuI	**L2**	Cs_2CO_3	28
9	CuI	**L3**	Cs_2CO_3	87
10	CuI	**L4**	Cs_2CO_3	31
11	CuI	**L5**	Cs_2CO_3	21
12	–	**L1**	Cs_2CO_3	n.d.[c]
13	CuI	–	Cs_2CO_3	Trace
14	CuI	**L1**	K_2CO_3	90
15	CuI	**L1**	Na_2CO_3	78
16	CuI	**L1**	K_3PO_4	88

[a] Reaction conditions: 2-iodophenol **1a** (1.0 mmol), phenyl isothiocyanate **2a** (1.0 mmol), copper salt (0.1 mmol), ligand (0.2 mmol) and base (2.0 mmol) in [bmim][PF_6] (2.0 mL) under Ar at 80 °C for 14 h.
[b] Isolated yield.
[c] The desired product was not detected (n.d.).

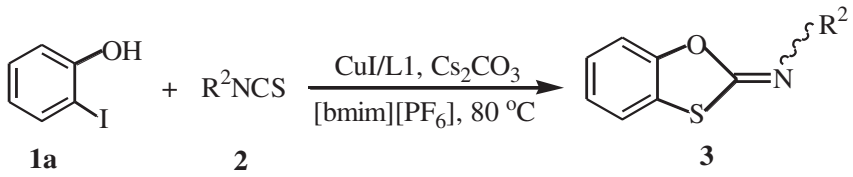
are to use a combination of CuI (10 mol%) and 1,10-phenanthroline (20 mol%) in the presence of Cs_2CO_3 (2.0 equiv.) as base at 80 °C in [bmim][PF_6] (Table 1, entry 1).

With this promising result in hand, we started to investigate the scope of this methodology. Firstly, the scope of isothiocyanates was examined and the results are summarized in Table 2. The optimized reaction conditions were applied to a variety of isothiocyanates giving rise to the corresponding 2-iminobenzo-1,3-oxathioles **3** in good to excellent yields, regardless of the electronic nature of the groups on the aryl isothiocyanate (Table 2, entries 2–7). For example, 2-iodophenol **1a** reacted with 4-methylphenyl isothiocyanate **2b** or 2-methylphenyl isothiocyanate **2c** leading to the desired products in excellent yields (entries 2 and 3). When 4-nitrophenyl isothiocyanate **2e** was used in the reaction of **1a** under the standard conditions, the corresponding product **3e** was formed in 94% yield (Table 2, entry 5). Reaction of **1a** with 4-chlorophenyl isothiocyanate **2f** or 4-fluorophenyl isothiocyanate **2g** gave rise to the corresponding 2-iminobenzo-1,3-oxathioles **3f** or **3g** in 92% or 93% yield, respectively (Table 2, entries 6 and 7). For the strong electron-donating substituents such as methoxy attached on the isothiocyanate the reaction required higher temperature (90 °C) and longer time to promote the completion of the reaction (Table 2, entry 4).

With respect to the electronic nature of the substituents on the 2-iodophenol, we further investigated the scope and the generality of the methodology by varying the 2-iodophenols, which could be easily derived from the *para*-substituted phenols. As shown in Table 3, generally the tandem reactions proceeded smoothly to afford the corresponding products **3** in good to excellent yields, although a higher temperature (85 °C) and slightly longer times were required. For instance, reaction of **1b** or **1c** with a variety of aryl isothiocyanates bearing electron-withdrawing groups as well as weak electron-donating groups led to the corresponding products **3** in good to excellent yields (Table 3, entries 1–3, 5, 6, 8, 9, 11 and 12). The reaction of **1b** or **1c** with **2d** bearing strong electron-donating group was slow and required higher temperature (90 °C) and prolonged times (entries 4 and 10). A slightly drop of yield was observed when the alkyl isothiocyanates were subjected into the copper(I)-catalyzed tandem reaction of 2-iodophenols, which might be due to the less reactivity of the substrates as compared with the aryl isothiocyanates (entries 7 and 13).

We were pleased to notice that the tandem reaction carried out in [bmim][PF_6] has the advantages of rate acceleration and yield increasing as compared with the reaction run in toluene. For example, the reaction of **1b** with **2d** in the presence of CuI (10 mol%) and 1,10-phenanthroline (20 mol%) using Cs_2CO_3 (2.0 equiv.) as base at 90 °C in [bmim][PF_6] afforded **3k** in 82% yield after 24 h (entry 4), however, the same reaction run in toluene at 90 °C for 30 h gave **3k** in 63% yield [10]. The desired products were also isolated in good yields, when 4-chloro-2-iodophenol **1d** was used in the reaction (Table 3, entries 14–18). However, the reaction of 4-chloro-2-iodophenol **1d** with phenyl isothiocyanate **2a** in the presence of CuI (10 mol%) and 1,10-phenanthroline (20 mol%) using Cs_2CO_3 (2.0 equiv.) as base at 90 °C in toluene afforded **3u** in only 52% yield after 40 h [10]. 1-Iodonaphthalen-2-ol was also tried under the same conditions, but no desired product was detected. Probably the steric hindrance of the naphthyl ring inhibited the intramolecular coupling process.

Table 2
CuI-catalyzed tandem reaction of 2-iodophenol **1a** with isothiocyanates **2**.[a]



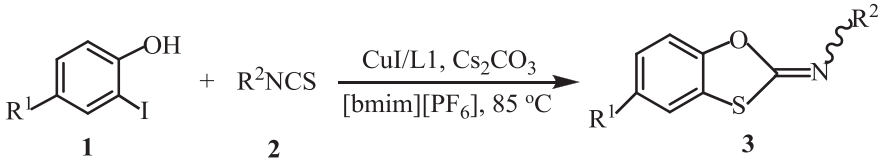
1a **2** **3**

Entry	**2**/R^2	Time (h)	Product	Yield[b] (%)
1	**2a**/Ph	14	**3a**	97
2	**2b**/4-MeC_6H_4	14	**3b**	93
3	**2c**/2-MeC_6H_4	18	**3c**	91
4[c]	**2d**/4-$MeOC_6H_4$	24	**3d**	89
5	**2e**/4-$O_2NC_6H_4$	11	**3e**	94
6	**2f**/4-ClC_6H_4	12	**3f**	92
7	**2g**/4-FC_6H_4	12	**3g**	93

[a] Reaction conditions: 2-iodophenol **1a** (1.0 mmol), isothiocyanate **2** (1.0 mmol), CuI (0.1 mmol), 1,10-phenanthroline (0.2 mmol) and Cs_2CO_3 (2.0 mmol) in [bmim][PF_6] (2.0 mL) under Ar at 80 °C.
[b] Isolated yield.
[c] Reaction was performed at 90 °C.

Isolation of products from the [bmim][PF_6] reaction mixtures can be conveniently achieved by extraction with diethyl ether for three times. To evaluate the possibility of recycling the ionic liquid and CuI/1,10-phenanthroline catalytic system used in the reaction, 2-iodophenol **1a** and phenyl isothiocyanate **2a** were allowed to react in [bmim][PF_6] under the catalysis of CuI and 1,10-phenanthroline for 14 h and then the product **3a** was extracted with diethyl ether for three times affording the cleaned, ionic liquid, catalytic solution. After the recovered ionic liquid containing copper catalyst and the ligand was concentrated in vacuo (5.0 torr/r.t. for 1 h), a second amount of reactants were added and the process was repeated up to 3 times. After third cycle, the ionic liquid was washed with distilled water (2 × 10 mL), dried in vacuo (5.0 torr/80 °C for 1 h) and recycled for another three times without addition of CuI and 1,10-phenanthroline. The results are listed in Table 4. It seemed that there was no obvious effect on the rate and yield of the reaction during those 1–6 cycles. Additionally, this ionic liquid layer could be stored for several weeks with no special precautions to exclude air or moisture and still afford comparable results to the fresh ionic liquid/catalyst system. The result is important from a practical point of view.

Table 3
CuI-catalyzed tandem reaction of 2-iodophenols **1** with isothiocyanates **2**.[a]

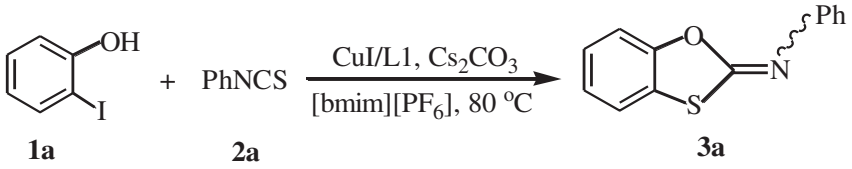


1 **2** **3**

Entry	**1**/R^1	**2**/R^2	Product	Time (h)	Yield[b] (%)
1	**1b**/4-Me	**2a**/Ph	**3h**	15	95
2	**1b**/4-Me	**2b**/4-MeC_6H_4	**3i**	17	92
3	**1b**/4-Me	**2c**/2-MeC_6H_4	**3j**	20	87
4[c]	**1b**/4-Me	**2d**/4-$MeOC_6H_4$	**3k**	24	82
5	**1b**/4-Me	**2e**/4-$O_2NC_6H_4$	**3l**	13	90
6	**1b**/4-Me	**2f**/4-ClC_6H_4	**3m**	15	91
7	**1b**/4-Me	**2h**/cyclohexyl	**3n**	24	65
8	**1c**/4-^{t}Bu	**2a**/Ph	**3o**	15	94
9	**1c**/4-^{t}Bu	**2b**/4-MeC_6H_4	**3p**	16	90
10[c]	**1c**/4-^{t}Bu	**2d**/4-$MeOC_6H_4$	**3q**	24	85
11	**1c**/4-^{t}Bu	**2e**/4-$O_2NC_6H_4$	**3r**	13	88
12	**1c**/4-^{t}Bu	**2f**/4-ClC_6H_4	**3s**	15	89
13	**1c**/4-^{t}Bu	**2h**/cyclohexyl	**3t**	24	72
14	**1d**/4-Cl	**2a**/Ph	**3u**	24	83
15	**1d**/4-Cl	**2b**/4-MeC_6H_4	**3v**	24	85
16[c]	**1d**/4-Cl	**2d**/4-$MeOC_6H_4$	**3w**	36	67
17	**1d**/4-Cl	**2e**/4-$O_2NC_6H_4$	**3x**	20	82
18	**1d**/4-Cl	**2f**/4-ClC_6H_4	**3y**	24	86

[a] Reaction conditions: 2-iodophenol **1** (1.0 mmol), isothiocyanate **2** (1.0 mmol), CuI (0.1 mmol), 1,10-phenanthroline (0.2 mmol) and Cs_2CO_3 (2.0 mmol) in [bmim][PF_6] (2.0 mL) under Ar at 85 °C.
[b] Isolated yield.
[c] Reaction was performed at 90 °C.

Table 4
Ionic liquid and catalyst recycling in the reaction of 2-iodophenol **1a** and phenyl isothiocyanate **2a**.[a]



1a **2a** **3a**

Cycle	Yield[b] (%)	Cycle	Yield[b] (%)
1	97	4	96
2	96	5	96
3	94	6	95

[a] Reaction conditions: 2-iodophenol **1a** (1.0 mmol), phenyl isothiocyanate **2a** (1.0 mmol), CuI (0.1 mmol), 1,10-phenanthroline (0.2 mmol) and Cs_2CO_3 (2.0 mmol) in [bmim][PF_6] (2.0 mL) under Ar at 80 °C for 14 h.
[b] Isolated yield.

4. Conclusion

In summary, we have described an environmentally benign, simple, and highly efficient method for the synthesis of 2-iminobenzo-1,3-oxathioles via a CuI-catalyzed tandem reaction of 2-iodophenols with isothiocyanates in [bmim][PF_6]. A variety of 2-iminobenzo-1,3-oxathioles have been synthesized in moderate to excellent yields. Easy product isolation, the ionic liquid and catalyst system recycling, enhanced reaction efficiency as well as avoiding the use of easily volatile and toxic toluene as solvent are important advantages of this developed methodology.

Acknowledgment

We thank the National Natural Science Foundation of China (gs1) (Project No. 20862008) and the Natural Science Foundation of Jiangxi Province (gs2) (Project No. 2010GZH0062).

References

[1] M.T. Konieczny, W. Konieczny, M. Sabisz, A. Skladanowski, R. Wakiec, E. Augustynowicz-Kopec, Z. Zwolska, European Journal of Medicinal Chemistry 42 (2007) 729–733.
[2] M.T. Konieczny, W. Konieczny, M. Sabisz, A. Skladanowski, R. Wakiec, E. Augustynowicz-Kopec, Z. Zwolska, Chemical and Pharmaceutical Bulletin 55 (2007) 817–820.
[3] M.T. Konieczny, W. Konieczny, S. Wolniewicz, K. Wierzba, Y. Suda, P. Sowinski, Tetrahedron 61 (2005) 8648–8655.
[4] W. Fathalla, J. Marek, P. Pazdera, Journal of Heterocyclic Chemistry 39 (2002) 1139–1144.
[5] T. Ibata, H. Nakano, Bulletin of the Chemical Society of Japan 65 (1992) 3088–3093.
[6] V. Nair, B. Mathew, A.U. Vinod, J.S. Mathen, S. Ros, R.S. Menon, R.L. Varma, R. Srinivas, Synthesis (2003) 662–664.
[7] M. Noboru, T. Masaaki, M. Osamu, T. Yoshikazu, Y. Shigeo, Tetrahedron Letters 30 (1989) 2259–2262.
[8] L. Raphaelian, H. Hooks, G. Ottmann, Angewandte Chemie International Edition 6 (1967) 363–364.
[9] M. Kulka, Canadian Journal of Chemistry 59 (1981) 1557–1559.
[10] X. Lv, Y. Liu, W. Qian, W. Bao, Advances Synthesis & Catalysis 350 (2008) 2507–2512.
[11] J.P. Hallett, T. Welton, Chemical Reviews 111 (2011) 3508–3576.
[12] A.S. Larsen, J.D. Holbrey, F.S. Tham, C.A. Reed, Journal of American Chemical Society 122 (2000) 7264–7272.
[13] C.E. Song, Chemical Communications (2004) 1033–1043.
[14] W.Z. Wu, B.X. Han, H.X. Gao, Z.M. Liu, T. Jiang, J. Huang, Angewandte Chemie International Edition 43 (2004) 2415–2417.
[15] J. Dupont, R.F. de Souza, P.A.Z. Suarez, Chemical Reviews 102 (2002) 3667–3692.
[16] V.I. Parvulescu, C. Hardacre, Chemical Reviews 107 (2007) 2615–2665.
[17] P.J. Dyson, D.J. Ellis, D.G. Parker, T. Welton, Chemical Communications (1999) 25–26.
[18] B. Ellis, W. Keim, P. Wasserscheid, Chemical Communications (1999) 337–338.
[19] C.J. Adams, M.J. Earle, G. Roberts, K.R. Seddon, Chemical Communications (1998) 2097–2098.
[20] A. Stark, B.L. Maclean, R.D. Singer, Journal of Chemical Society, Dalton Transactions (1999) 63–66.
[21] T. Fischer, A. Sethi, T. Welton, J. Woolf, Tetrahedron Letters 40 (1999) 793–796.
[22] V. Calo, A. Nacci, L. Lopez, A. Napola, Tetrahedron Letters 42 (2001) 4701–4703.
[23] A.J. Carmichael, M.J. Earle, J.D. Holbrey, P.B. McCormac, K.R. Seddon, Organic Letters 1 (1999) 997–1000.
[24] X.R. Rex, D.Z. Larisa, O. Wei, Tetrahedron Letters 42 (2001) 8441–8443.
[25] C.J. Mathews, P.J. Smith, T. Welton, Chemical Communications (2000) 1249–1250.
[26] J.-C. Xiao, B. Twamley, J.M. Shreeve, Organic Letters 6 (2004) 3845–3847.
[27] R. Wang, B. Twamley, J.M. Shreeve, Journal of Organic Chemistry 71 (2006) 426–429.
[28] J.-C. Hsu, Y.-H. Yen, Y.-H. Chu, Tetrahedron Letters 45 (2004) 4673–4676.
[29] M.Y. Machado, R. Dorta, Synthesis (2005) 2473–2475.
[30] S.T. Handy, X. Zhang, Organic Letters 3 (2001) 233–236.
[31] C. Chiappe, G. Imperato, E. Napolitano, D. Pieraccini, Green Chemistry 6 (2004) 33–36.
[32] T. Fukuyama, M. Shinmen, S. Nishitani, M. Sato, I. Ryu, Organic Letters 4 (2002) 1691–1694.
[33] J.S. Yadav, B.V.S. Reddy, K.B. Reddy, K.U. Gayathri, A.R. Prasad, Tetrahedron Letters 44 (2003) 6493–6496.
[34] M.L. Kantam, B. Neelima, C.V. Reddy, V. Neeraja, Journal of Molecular Catalysis A: Chemical 249 (2006) 201–206.
[35] P.A.Z. Suaarez, J.E.L. Dullius, S. Einloft, R.F. de Souza, J. Dupont, Polyhedron 15 (1996) 1217–1219.
[36] S. Park, R.J. Kazlauskas, Journal of Organic Chemistry 66 (2001) 8395–8401.
[37] Q. Ding, X. Liu, B. Cao, Z. Zong, Y. Peng, Tetrahedron Letters 52 (2011) 1964–1967.