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# CuI/TBAB as a novel efficient catalytic system for Heck reaction in water†

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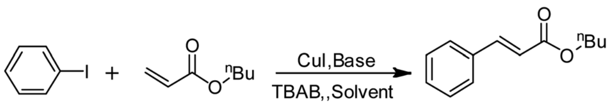
**A novel efficient ligand-free CuI/TBAB catalytic system has been developed for Heck reaction in water without the protection of an inert atmosphere. Both aryl iodides and aryl bromides containing electron-deficient and electron-donating groups reacted smoothly and afforded the corresponding products in moderate to good yields.**

## Introduction

The palladium-catalyzed Mizoroki–Heck cross-coupling reaction represents one of the most valuable methods for carbon–carbon bond formation in organic synthesis.[1] As a result, many efforts have been devoted to develop more efficient and selective catalytic systems for the Heck cross-coupling reaction.[2,3] Soluble palladium compounds, generally phosphine palladium complexes, are employed most frequently and efficiently in controlling the reactivity and selectivity of the Heck reaction.[4] However, most phosphine ligands have some drawbacks such as expensive, toxic, unrecoverable and sensitive to oxygen and water, and these drawbacks prevented their large-scale application. In addition, the palladium catalyst is expensive and recovery of it is difficult.[5–7] Therefore, Heck reactions catalyzed by inexpensive transition metals have attracted more interests of researchers, including Fe, Co, Ni and Cu.[8,9] Nevertheless, only a few papers on Cu-catalyzed Heck cross-coupling reaction have been reported.[10] Thus, the development of mild and efficient copper catalytic systems for the Heck cross-coupling reaction still remains a challenging area for organic chemists.

On the other hand, the Heck reaction is traditionally carried out in organic solvents such as dimethyl formamide (DMF), *N*-methylpyrrolidone (NMP) and acetonitrile, which often bring about significant safety, health and environmental problems due to their flammability, toxicity and volatility.[11,12] The media of water has many merits, such as low cost, safety and environmentally benign nature, and only a few examples of Mizoroki–Heck reactions have been reported in aqueous media[13,14] and most of them need the organic ligands. Sometimes, development of methods in water is strongly limited by the low solubility of organic substrates in water and the sensitivity of chemical groups towards hydrolytic degradation. One of the



**Scheme 1**

**Table 1** Optimization of reaction conditions[a]

| Entry | Base | Solvent | TBAB/mol | Time/h | Yield[b]/% |
|---|---|---|---|---|---|
| 1 | $K_2CO_3$ | NMP | 1 | 20 | 57 |
| 2 | $K_2CO_3$ | DMA | 1 | 20 | 37 |
| 3 | $K_2CO_3$ | DMSO | 1 | 20 | 14 |
| 4 | $K_2CO_3$ | DMF | 1 | 20 | 93 |
| 5 | $K_2CO_3$ | $H_2O$ | 1 | 20 | 70 |
| 6 | $Et_3N$ | $H_2O$ | 1 | 20 | 31 |
| 7 | KOH | $H_2O$ | 1 | 20 | 20 |
| 8 | $K_3PO_4$ | $H_2O$ | 1 | 20 | 49 |
| 9 | NaOH | $H_2O$ | 1 | 20 | 95 |
| 10 | NaOH | $H_2O$ | 1 | 20 | 67[c] |
| 11 | NaOH | $H_2O$ | 1 | 18 | 75 |
| 12 | NaOH | $H_2O$ | 1 | 24 | 95 |
| 13 | NaOH | $H_2O$ | 0.5 | 20 | 54 |
| 14 | NaOH | $H_2O$ | — | 20 | 36 |
| 15 | NaOH | $H_2O$ | 1 | 20 | 64[d] |
| 16 | NaOH | $H_2O$ | 1 | 20 | 57[e] |

[a] *Reaction conditions*: iodobenzene (1.0 mmol), *n*-butyl acrylate (1.2 mmol), CuI (10% mol), base (1.0 mmol), TBAB (1.0 mmol), solvent (3 mL), 100 °C. [b] GC yield determined by using methoxybenzene as internal standard. [c] Reaction temperature is 80 °C. [d] CTAB as PTC. [e] TBAH as PTC.

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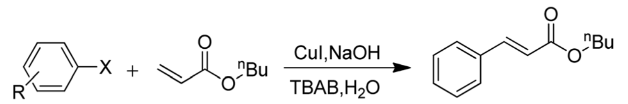
**Table 2** Heck reaction of aryl halides and *n*-butyl acrylate catalyzed by CuI/TBAB[a]



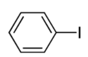
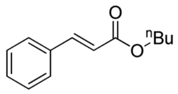
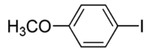
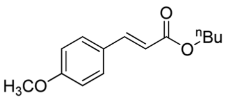
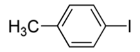
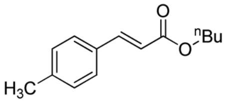
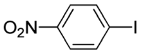
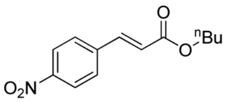
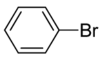
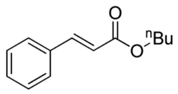
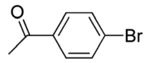
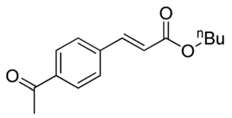
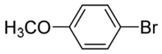
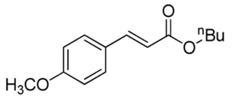
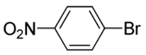
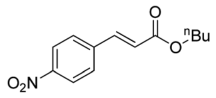
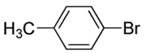
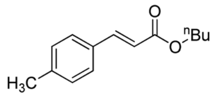
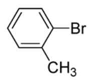
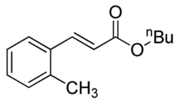
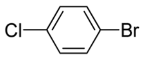
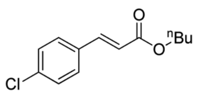
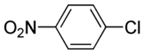
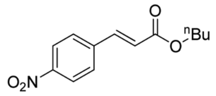
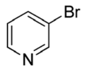
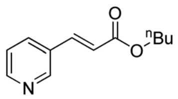
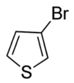
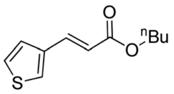
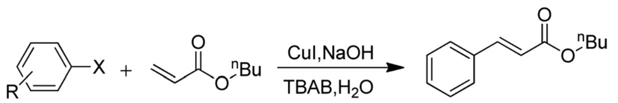
| Entry | ArX | Product | Yield[b]/% |
|---|---|---|---|
| 1 |  |  | 95, 84[c], 77[d] |
| 2 |  |  | 92 |
| 3 |  |  | 91 |
| 4 |  |  | 89 |
| 5 |  |  | 78 |
| 6 |  |  | 84 |
| 7 |  |  | 81 |
| 8 |  |  | 77 |
| 9 |  |  | 74 |
| 10 |  |  | 61[e] |
| 11 |  |  | 69 |
| 12 |  |  | 27 |
| 13 |  |  | 77[f] |
| 14 |  |  | 80[g] |

**Table 2** (*Contd.*)



[a] *Reaction conditions*: iodobenzene (1.0 mmol), *n*-butyl acrylate (1.2 mmol), CuI (10% mol), NaOH (1.0 mmol), TBAB (1.0 mmol), $H_2O$ (3 mL), 100 °C. [b] Isolated yield. [c] The second run. [d] The third run. [e] Reaction time is 22 h. [f] Reaction time is 24 h. [g] Reaction time is 24 h.

solutions to circumvent these issues comprises the addition of a phase-transfer catalyst (PTC).[15,16]

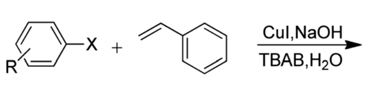
In view of the frame work of green chemistry, we prefer to carry out the cross-coupling reactions in water with tetrabutylammonium bromide (TBAB) as PTC. Herein, we report a simple, cost-effective, environmentally benign, and efficient ligand-free CuI/TBAB catalytic system for Heck reaction in water with good to excellent yields.

## Results and discussion

As a model, the Heck reaction of PhI with *n*-butyl acrylate (Scheme 1) was chosen to optimize the reaction conditions.[18]

The effects of solvent, base, temperature and reaction time were examined and the results are summarized in Table 1. Several different solvents (Table 1, entry 1–5) such as DMF, NMP, DMA, DMSO and water were tested. The results showed that the reaction catalyzed by CuI/TBAB catalyst system succeeded in performing in DMF with $K_2CO_3$ as base at 100 °C for 20 h with good yield, 93%. To our great delight, the reaction proceeded in aqueous media gave 70% yield under the same condition. Encouraged by this result, several bases were investigated to find a best base for the reaction in water. As depicted in Table 1, $Et_3N$ and KOH provided very low yield, (31% and 20%, respectively). $K_3PO_4$ as base gave a moderate yield 49%. Surprisingly, NaOH was found to give a satisfactory yield, 95% (Table 1, entry 9). As the results showed in Table 1, entry 13–14, TBAB plays an important role in the copper-catalyzed Heck-type reaction in water. In the absence of any TBAB, only 36% coupling product was obtained after 20 h and only 54% yield product was observed when 50 mol% of TBAB was added, but with 1 mmol TBAB added the yield increased to 95% significantly. It is because that TBAB could improve the solubility of the reagent in water. Hexadecyl trimethyl ammonium bromide (CTAB) and tetra-*n*-butylammonium hydroxide (TBAH) were also tested as the PTC, but the results indicated that they were less effective (Table 1, entry 15 and 16). Heterogeneous Heck reactions can run better at higher temperatures if reagents, products and catalyst can survive such a harsh treatment.[13] To our great delight, the yield significantly increased from 67% to

**Table 3** Heck reaction of aryl halides and styrene catalyzed by CuI/TBAB[a]



| Entry | ArX | Product | Time/h | Yield[b]/% |
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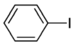
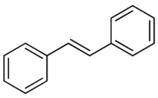
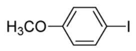
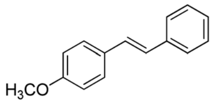
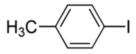
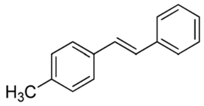
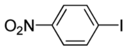
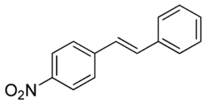
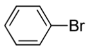
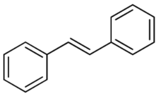
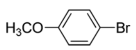
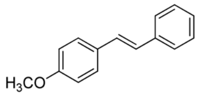
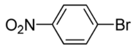
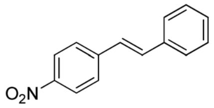
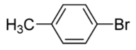
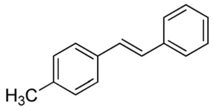
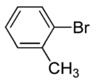
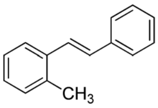
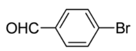
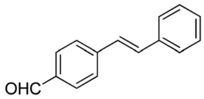
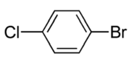
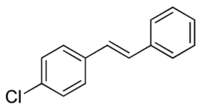
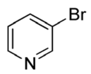
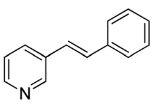
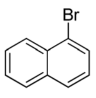
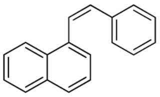
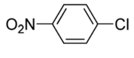
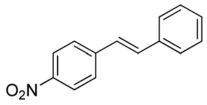
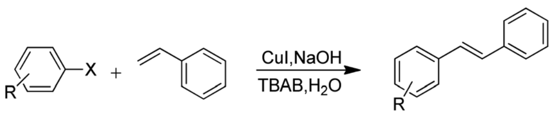
| 1 |  |  | 20 | 91 |
| 2 |  |  | 20 | 89 |
| 3 |  |  | 20 | 85 |
| 4 |  |  | 20 | 87 |
| 5 |  |  | 22 | 76 |
| 6 |  |  | 22 | 74 |
| 7 |  |  | 22 | 81 |
| 8 |  |  | 22 | 78 |
| 9 |  |  | 22 | 69 |
| 10 |  |  | 22 | 85 |
| 11 |  |  | 22 | 73 |
| 12 |  |  | 24 | 82 |
| 13 |  |  | 22 | 75 |
| 14 |  |  | 24 | 34 |

**Table 3** (*Contd.*)



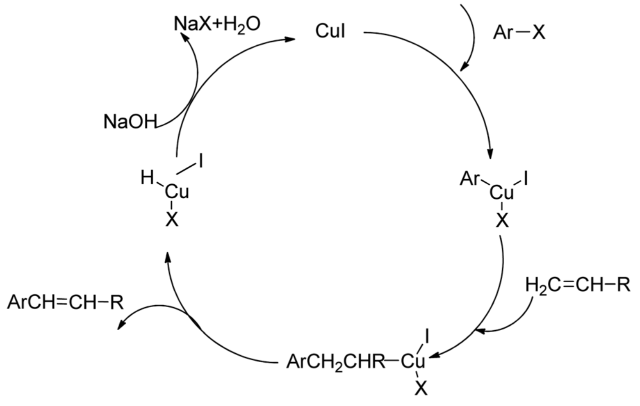
[a] *Reaction conditions*: iodobenzene (1.0 mmol), styrene (1.2 mmol), CuI (10% mol), NaOH (1.0 mmol), TBAB (1.0 mmol), $H_2O$ (3 mL), 100 °C. [b] Isolated yield.

95% when the temperature increased from 80 °C to 100 °C (Table 1, entry 10). In addition, when the reaction performed for 18 h, only 75% product was observed (Table 1, entry 11). However, even the reaction time was prolonged to 24 h, the yield did not increase markedly (Table 1, entry 12).

With the optimized reaction conditions in hand, various types of aryl halide coupled with *n*-butyl acrylate were investigated, as shown in Table 2. The coupling reactions with styrene were performed under the same reaction conditions as used for *n*-butyl acrylate and moderate to high yields of the coupled products were obtained in Table 3.

The results revealed that the CuI/TBAB catalytic system is remarkably active and tolerant of a range of functionalities. Both aryl iodides and aryl bromides bearing electron-deficient as well as electron-donating groups afforded the corresponding products in moderate to good yields. But aryl iodides performed better and reacted more quickly than aryl bromides under the same conditions as shown in Tables 2 and 3. Besides, the coupling selectivity was also tested and 1-chloro-4-bromobenzene was converted to *n*-butyl-4-chlorocinnamate and (*E*)-1-chloro-4-styrylbenzene as the only product, respectively (Table 2, entry 11 and Table 3, entry 11). The comparison of the yields (Table 2, entry 9 and10; Table 3, entry 8 and 9) showed that the reaction was influenced somewhat by steric hindrance. It was worth noting that even 3-bromopyridine coupled with *n*-butyl acrylate and styrene could performed well and get the desired products in 77% and 82% yield, respectively (Table 2, entry 13 and Table 3, entry 12). Besides, the reaction between 3-bromothiophene and *n*-butyl acrylate also works well to give product in 80% yield (Table 2, entry 14) and a 75% yield product was obtained by coupling with 1-bromonaphthol and styrene (Table 3, entry 13). Unfortunately, aryl chlorides did not perform as well under the same condition and lower yields coupling products were observed (Table 2, entry 12 and Table 3, entry 14). Furthermore, the catalytic system can be reused for several times with less decreasing catalytic activity (Table 2, entry 1).

A possible mechanism was proposed as shown in Scheme 2.[10,17] It starts with oxidative addition of aryl halide includes oxidation of Cu(I) to Cu(III), insertion of olefin, and finally β-hydride elimination.



**Scheme 2** A possible mechanism for the copper-catalyzed Heck reaction.

## Conclusion

In summary, we have developed a novel efficient ligand-free CuI/TBAB catalytic system for Heck reaction in water without the protection of an inert atmosphere. Both aryl iodides and aryl bromides containing electron-deficient and electron-donating groups performed smoothly and afforded the corresponding products in moderate to good yields. This reaction will provide a novel environmentally friendly and economical route for Heck reaction. Our further investigations to understand the mechanism concerning the origin of the broad scope and high activity of the catalysts featured herein are currently ongoing in our laboratory.

## Acknowledgements

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18 Procedures for the Heck reaction: all reactions were carried out under air. Aryl halide (1.0 mmol), olefins (1.2 mmol), CuI (10 mol%), NaOH (1.0 mmol), TBAB (1.0 mol) and 3 mL $H_2O$ were continuously added to a sealed tube. The reaction mixture was stirred at 100 °C for 20 h. The progress of the reaction was monitored by GC. After completion of the reaction, the catalyst was filtered easily and the product was extracted with EtOAc, the combined organic layers was dried over $MgSO_4$ for 2 h. The solvent was evaporated under reduced pressure and the desired product purified by flash chromatography on a silica gel column using hexane/ethyl acetate (5 : 1). $^1H$ NMR and $^{13}C$ NMR spectra (see ESI†) were recorded in $CDCl_3$ on a JEOL 300 MHz spectrometer with tetramethyl silane (TMS) as internal standard.