

Nickel-catalyzed Suzuki–Miyaura cross-coupling reactions in deep eutectic solvents

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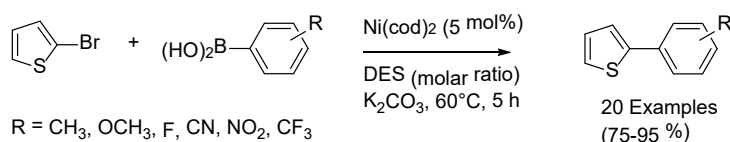
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Abstract:

A highly efficient and ligand-free approach for the Suzuki–Miyaura cross-coupling reaction (SMR) of aryl halides with arylboronic acid under the catalysis of Ni(cod)₂/K₂CO₃ in DES has been developed. Under the described conditions, a category of bromothiophene, whether electron-rich or electron-deficient, were coupled with arylboronic acid to give the excellent yields of biaryls. DES and catalyst can be recovered and reused in this system.



Keywords:

Deep eutectic solvents, Cross-coupling, Nickel, Boron

Introduction:

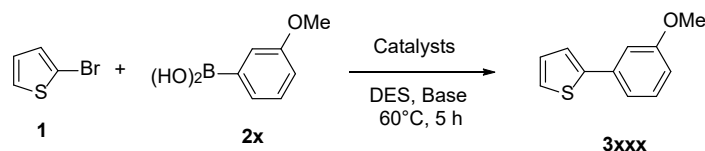
Recently, deep eutectic solvents (DES) have been received great attention and considered as greener and environmentally benign solvent system because they have indispensable advantages to replace conventional organic solvents and ionic liquids in scientific domain.¹ They are low cost, ease of synthetic accessibility, environmentally benign nature, negligible volatility, non-flammable, renewability, and biodegradability. Generally, DES are obtained through the complexation of hydrogen-bond acceptors such as quaternary ammonium salts with a hydrogen bond donor such as urea, carboxylic acids, amino acids, sugars, and glycerol.² Moreover, DESs have been intensively used for many chemical processes including organic functional group transformations and metal catalyzed cross-coupling reactions. Among them, the Suzuki-Miyaura coupling reactions continue to play a vital role in the construction of biaryl and polyaryl compounds that are frequently found in natural products, pharmaceuticals, and functional materials.

In this context, various phosphine-based palladium catalytic systems have been developed for the cross-coupling of arylboronic acids with a range of electrophilic partners, including aryl chlorides, bromides, iodides, triflates, and sulfonates. To avoid high-cost palladium catalysts, Miyaura and co-workers explored for the first time Ni-catalyzed system for the coupling of arylboronic acids with aryl chlorides. Since then, various cheaper nickel complexes have also been investigated for the Suzuki-Miyaura coupling reaction. Among them, transition-metal-catalyzed cross-coupling reactions are one of the most powerful and widely used transformation in organic chemistry for the formation of carbon-carbon and carbon-heteroatom bonds. However, to the best of our knowledge, there are few methods are reported the use of DESs for the Suzuki coupling reaction.³ Although the significant results are observed in the reported methods, there is a need to develop a facile and efficient catalytic system for metal catalyzed Suzuki-Miyaura reactions under DES medium and ligand-free conditions. Here, we have introduced an efficient and straightforward Ni-catalyzed system for the Suzuki coupling of arylboronic acids with aryl chlorides in choline chloride: urea as medium reusable solvent medium.

Results and Discussions:

Here, we have used easily available mixture of choline chloride (ChCl) and urea in 1:2 molar ratio as a suitable reaction system with lower environmental impact than conventional organic solvents. A model reaction of bromo-thiophene (1) and phenylboronic acid (2) was chosen to screen the suitable reaction conditions and the results are compiled in Table 1. From Table 1, it can be noted that the best result was obtained when we used Ni(cod)₂ (5 mol%) as a catalyst, K₂CO₃ as a base (3.0 equiv.) in ChCl/urea (1:2) as reaction medium. To test feasibility of this method, variety of boronic acids were well tolerated with 2-bromo thiophene under these reaction conditions to give the desired products in good to high yields.

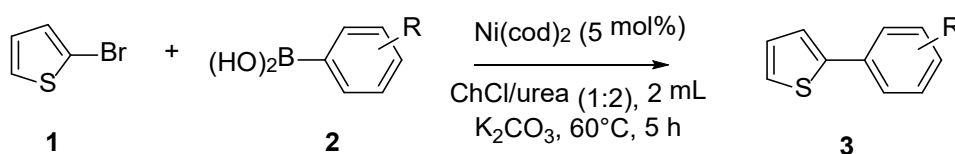
Table 1. Optimization of the reaction conditions for the one-pot synthesis of 3a^a

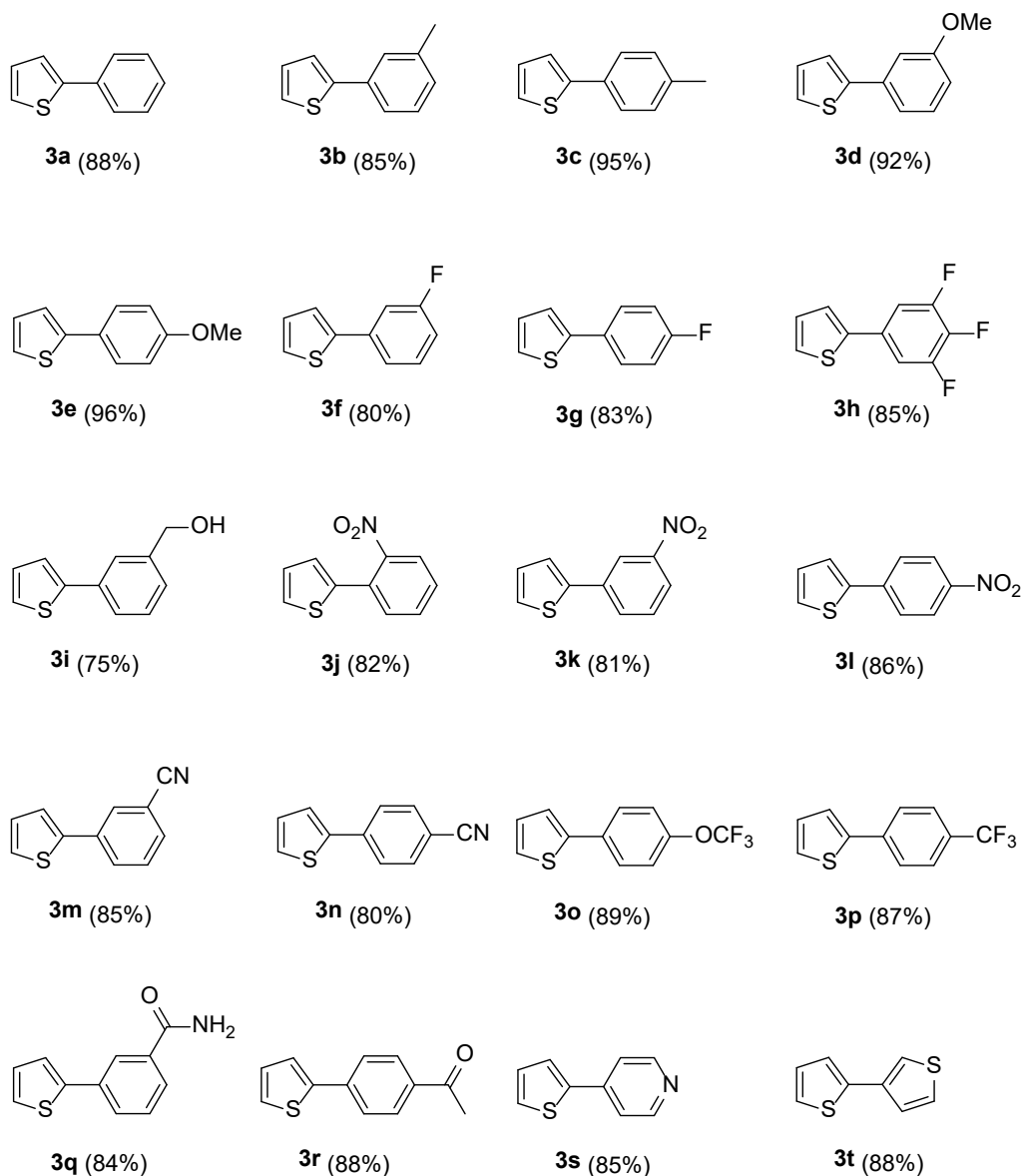


| Entry | Catalyst (5 mol%) | Solvent (molar ratio) | Base | Yield (%) ^b |
|-------|--|-----------------------|---------------------------------|------------------------|
| 1 | Ni(cod) ₂ | ChCl/urea (1:2) | Et ₃ N | 13 |
| 2 | Ni(cod) ₂ | ChCl/urea (1:2) | Cs ₂ CO ₃ | 43 |
| 3 | Ni(cod) ₂ | ChCl/urea (1:2) | Na ₂ CO ₃ | 29 |
| 4 | Ni(cod) ₂ | ChCl/urea (1:2) | K ₂ CO ₃ | 41c |
| 4 | Ni(cod) ₂ | ChCl/urea (1:1) | K ₂ CO ₃ | 54d |
| 5 | Ni(cod) ₂ | ChCl/urea (1:2) | K ₂ CO ₃ | 92 |
| 6 | Ni(cod) ₂ | ChCl/EG (1:2) | K ₂ CO ₃ | 21 |
| 7 | Ni(cod) ₂ | ChCl/Gly (1:2) | K ₂ CO ₃ | 25 |
| 8 | Ni(cod) ₂ | ChCl/OA (1:2) | K ₂ CO ₃ | 13 |
| 9 | NiCl ₂ ·6H ₂ O | ChCl/urea (1:2) | K ₂ CO ₃ | 11 |
| 10 | Ni(PPh ₃) ₂ Cl ₂ | ChCl/urea (1:2) | K ₂ CO ₃ | 8 |
| 11 | Ni(cod) ₂ | Toluene | K ₂ CO ₃ | 36 |
| 12 | Ni(cod) ₂ | DMF | K ₂ CO ₃ | 48 |

^aReaction conditions: Bromothiophene (1a) (1 mmol), phenylboronic acid (2a) (1.5 mmol), K₂CO₃ (3 mmol), DES: molar ratio (1:2), 2 mL. ^bIsolated yield. ^cReaction was performed at 25°C for 12 h. ^dReaction was performed with DES (molar ratio (1:1), 2 mL). ChCl (choline chloride), Ethylene glycol (EG), Glycerol (Gly), and Oxalic acid (OA)

Table 2. Substrate scope.





Conflict of Interest

The authors declare no conflict of interest.

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