Magnetic Nano-Fe₃O₄ Supported Ionic Liquids: A Recoverable Phase Transfer Catalyst for C-N Cross Coupling Reaction

LIN TANG*, YU SUN, LINGYUN ZHOU and TAILI SHAO

Department of Pharmacology, Wannan Medical College, Wuhu 241002, P.R. China

*Corresponding author: Tel: +86 553 2932492; E-mail: jerry19860506@163.com

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Magnetic nanoparticles-supported quaternary ammonium salts were prepared and evaluated as phase transfer catalysts. Some of them exhibited good activities in CuCl-catalyzed *N*-arylation of aryl amines and *N*-heterocycles with aryl iodides in aqueous solution without any ligands. They could be readily separated from reaction solution using an external magnet and reused three times with a little loss in activity.

Key Words: Copper catalyst, C-N coupling, Nanometre supported, Ionic liquid, Cyclic utilization.

INTRODUCTION

C-N bond formation is considered to be an important strategy in organic synthesis¹, but many toxic organic solvents and expensive ligands were used in this field², which resulted in the high cost. Since more and more attentions have been focused on green chemistry, it is necessary to develop more friendly reaction conditions for C-N cross coupling reactions. Ionic liquids could make organic reaction system simpler and milder as phase transfer catalysts³, but they are also expensive. Magnetic nano-Fe₃O₄ could be an excellent and recyclable support for easy separation by an external magnet⁴. The synthetic approach of magnetic nano-Fe₃O₄ supported quaternary ammonium salts was shown in Fig. 1.

Fig. 1. Synthetic approach of magnetic nano-Fe₃O₄ supported quaternary ammonium salts

EXPERIMENTAL

Nano-Fe₃O₄ was prepared by co-precipitation method according to literature⁵. The Fe₃O₄ nanoparticles obtained were in the average size of about 20 nm. Then the collected magnetic

nanoparticles were dispersed in ethanol. Magnetic nano-Fe₃O₄ supported ionic liquids was prepared by reported method⁶. The catalyst loading was determined to be 0.452 mmol/g by elemental analysis.

To evaluate the catalytic activity of **b3**, the reaction of PhI with imidazole was selected as a model reaction. The results were summarized in Table-1. It was demonstrated that almost all nano-Fe₃O₄ supported ionic liquids exhibited good catalytic activities, **b3** is the best one but **b6** did not catalyze the reaction (Table-1, Entries 2-7). The catalytic activities of them changed with the length change of middle carbon chain. It suggested that steric effect affect the catalytic activity⁷.

TABLE-1 COMPARISON OF THE ACTIVITY OF NANO-Fe ₃ O ₄ SUPPORTED IONIC LIQUIDS ^a		
Entry	Fe ₃ O ₄ -IL	Yield (%) ^b
1	None	Trace
2	b1	35
3	b2	89
4	b3	96
5	b4	87
6	b5	41
7	b6	Trace

^aReaction conditions: iodobenzene (1 mmol), imidazole (1.5 mmol), CuCl (5 mol %), Fe₃O₄-ionic liquid (0.01 g), K₂CO₃ (1.5 mmol), H₂O (1 mL), Ar, ^bIsolated yield

Easy and rapid separation of nano-Fe₃O₄ supported ionic liquids by an external magnetic field is the most advantageous feature of them. After the reaction, they were concentrated on the bottom of the reaction vessel, the aqueous or organic phases were separated by magnetic decantation. Moreover, the residual catalyst in the reaction vessel could be washed and dried and then subjected to the next run directly. We examined the lifetime of **b3** in the *N*-arylation of imidazole and iodobenzene. As shown in Table-2, **b3** could be recycled three times with a little loss in activity.

TABLE-2
LIFETIME OF **b3** FOR THE *N*-ARYLATION OF
IODOBENZENE AND IMIDAZOLE IN WATER^a

Entry	Cycle	Yield (%) ^b
1	1	96
2	2	94
3	3	92

^aReaction conditions: iodobenzene (1 mmol), imidazole (1.5 mmol), CuCl (5 mol %), **b3** (0.01 g), K₂CO₃ (1.5 mmol), H₂O (1 mL), Ar, 80 °C, 24 h. ^bIsolated yield

After obtaining successful result, a brief research on optimal reaction conditions was carried out (Table-3). A series of copper catalysts and inorganic bases were screened extensively. Finally, the best results were obtained when iodobenzene (1.0 mmol) and imidazole (1.5 mmol) were allowed to react with 5 mol % of CuCl, 0.01 g **b3** and 1.5 equiv K₂CO₃ stirred in 1 mL water at 80 °C under argon for 24 h.

With this optimized conditions, we explored the general scope of substrates, a variety of aryl iodides, amines and *N*-heterocycles were introduced to this system. In all reactions, we found that each reaction only had one product without any by-products. It indicated that the nano-Fe₃O₄ supported ionic liquids could not only accelerate coupling reaction, but also enhance selectivity of reaction.

TABLE-3
OPTIMIZED REACTION CONDITIONS OF THE
N-ARYLATION REACTION IN WATER^a

Entry	T (°C)	Gas	Catalyst	Base	Yield (%) ^b
1	60	Ar	CuCl	K ₂ CO ₃	86
2	30	Ar	CuCl	K ₂ CO ₃	25
3	80	Ar	CuCl	K ₂ CO ₃	96
4	80	Air	CuCl	K ₂ CO ₃	-
5	80	Ar	nano CuI	K ₂ CO ₃	96
6	80	Ar	CuI	K ₂ CO ₃	86
7	80	Ar	CuBr	K ₂ CO ₃	93
8	80	Ar	Cu(acac) ₂	K ₂ CO ₃	40
9	80	Ar	CuO	K ₂ CO ₃	92
10	80	Ar	CuCl	NaHCO ₃	21
11	80	Ar	CuCl	Cs ₂ CO ₃	-
12	80	Ar	CuCl	Na ₂ CO ₃	45

^aReaction conditions: iodobenzene (1 mmol), imidazole (1.5 mmol), CuCl (5 mol %), **b3** (0.01 g), base (1.5 equiv), H₂O (1 mL), 24 h.

^bIsolated yield

As shown in Tables 4 and 5, when substituted iodobenzene was used in this system, yield decreased rapidly, substituent group's position and electronic property nearly had no influence.

TABLE-4
N-ARYLATION OF IODOBENZENE AND AMINES
OR *N*-HETEROCYCLES IN WATER^a

Entry	NuH	Product	Yield (%) ^b
1			96
2			90
3			51
4			35
5			95
6			60
7			80
8			99
9			92

^aReaction conditions: iodobenzene (1 mmol), NuH (1.5 mmol), CuCl (5 mol %), **b3** (0.01 g), K₂CO₃ (1.5 mmol), H₂O (1 mL), Ar, 24 h.

^bIsolated yield

TABLE-5
N-ARYLATION OF ARYL IODIDES WITH BENZYLAMINE
AND *N*-HETEROCYCLES IN WATER^a

Entry	R	NuH	Product	Yield (%) ^b
1	4-Cl			13
2	4-Br			10
3	4-F			9
4	4-COOH			11
5	2-Cl			Trace
6	2-CH ₃			Trace

7	4-Cl			12
8	4-Br			9
9	4-Cl			11
10	4-Br			9

^aReaction conditions: aryl iodides (1 mmol), NuH (1.5 mmol), CuCl (5 mol %), **b3** (0.01 g), K₂CO₃ (1.5 mmol), H₂O (1 mL), Ar, 24 h.
^bIsolated yield

RESULTS AND DISCUSSION

Magnetic nano-Fe₃O₄ supported ionic liquids was prepared and used in phase transfer catalysts. **b3** exhibited the best activities in CuCl-catalyzed *N*-arylation of aryl amines and *N*-heterocycles with aryl iodides in aqueous solution without any ligands. And it could be recycled three times with a little loss in activity.

It can be seen in the research that the magnetite nanoparticles restricted reactions to only one product when high efficiency catalyses reactions. It also showed good cycling effect. The narrow substrate scope is disadvantage of the magnetite nanoparticles which lies in steric effect of magnetite nanoparticles in the reaction.

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