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FULL PAPER

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Magnetically Recyclable Metal–Organic Framework@Fe_3O_4 Composite-Catalyzed Facile Reduction of Nitroarene Compounds in Aqueous Medium

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A kind of Metal–organic framework (MOF) composite namely Cu-BTC@Fe_3O_4 (BTC = 1,3,5-benzenetricarboxylate) was prepared and showed good catalytic activity toward the reduction of nitroarenes. This reaction proceeded smoothly under mild reaction conditions in aqueous medium using sodium borohydride as the reduction agent, affording the corresponding anilines in good to excellent yields. In addition, the catalyst could be easily recovered with an external permanent magnet and be reused for successive six runs with slight decrease in its activity.

KEYWORDS
aqueous medium, magnetic catalyst, metal–organic frameworks, nitro reduction

1 | INTRODUCTION

Anilines are very important compounds that found wide applications in organic synthesis, material science, and many other fields.[1] Generally, the reduction of nitroarene compounds in the presence of a catalyst and a reductant is one of the most fundamental and straightforward processes to prepare anilines. Various reductants such as H_2,[2] NH_2NH_2,[3] NH_4Cl,[4] alcohols,[5] acids,[6] $NaHSO_3$,[7] $NaBH_4$,[8] $LiAlH_4$[9] and ammonia-borane[10] have already been successfully employed. Despite these significant progress, there are still some issues to be addressed. For example, (i) highly active and expensive metal catalysts (Pd, Pt, or Au) are usually required for catalytic hydrogenation processes; (ii) in some cases, low selectivity and reaction rates are observed when using alcohols as the hydrogen source; and (iii) some reductants are not readily available or expensive. In this context, $NaBH_4$ turns out to be the most popular reductant since it is commercially available and cheap. Meanwhile, a series of catalysts, particularly the heterogeneous catalysts, have been employed to activate the $NaBH_4$.[11–18] Despite the great advance in this field, the reported procedures still suffered some drawbacks such as long reaction time, poor recyclability of the catalysts as well as tedious work-up.

Recently, the application of metal-organic frameworks (MOFs) in catalysis field has attracted much attention due to their unique structural and catalytic properties.[19,20] Although a large number of MOFs have been successfully developed and applied, we believed that an ideal MOF catalyst should be readily available or prepared, highly stable, cost-effective and easily recoverable. It is worth noting that Cu-BTC (H_3BTC = 1,3,5-benzenetricarboxylic acid) has already been commercially available and also has shown wide applications in diverse organic reactions.[21–24] To further improve its stability and recyclability, Wang *et al.* prepared a well-shaped magnetic Cu-BTC@Fe_3O_4 composite which exhibited good catalytic activity and reusability toward the C-H oxidation of alkylbenzenes.[25] We also successfully applied such

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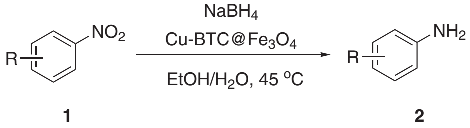


SCHEME 1 Cu-BTC@Fe$_3$O$_4$-catalyzed the reduction of nitroarenes

magnetically recyclable MOF catalyst in one-pot C$_{(aryl)}$-S-P bond formation reaction.[26] Given the importance of aniline derivatives and in continuation of our interest in MOF catalysis, herein, we report a facile reduction of nitroarene compounds in aqueous medium utilizing a magnetically recyclable Cu-BTC@Fe$_3$O$_4$ composite (Scheme 1).

2 | EXPERIMENTAL

2.1 | General remarks

All reagents were obtained from local commercial suppliers and used without further purification. Thin-layer chromatography (TLC) was visualized using UV light. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Advance 300 analyzer in Chloroform-d (CDCl$_3$) using TMS as an internal standard. Fourier transform (FT) Infrared data were recorded on an AVATAR-370 (Nicolet) spectrometer by transmission through the sample deposited on a KBr pellet. Powder X-ray diffraction (PXRD) patterns of the as-synthesized and recycled samples were obtained using a Rigaku D/max 2500 PC X-ray diffractometer with Cu Kα (1.5406 Å) radiation at 10 min^{-1}. Thermogravimetric analysis (TGA) experiments were carried out on a TG/DTA 6300 thermoanalyzer from room temperature to 800 °C under nitrogen atmosphere at a heating rate of 10 °C/min. Field-emission Scanning Electron Microscopy (SEM) images of the samples were taken at 30 kV with a ZEISS Supra 55 microscope. The compositions of samples were analyzed by ICP (inductively coupled plasma) analysis (Varian Vista-AX). N$_2$ adsorption isotherms were obtained using a Micromeritics ASAP 2460 instrument. All the products are known compounds and were identified by comparing of their physical and spectra data with those reported in the literature.

2.2 | General procedure for the reduction of nitroarenes

In a round-bottomed flask (10 ml) equipped with magnetic stirrer and condenser, nitroarene (1 mmol), EtOH/H$_2$O (3: 1, 4 ml) and Cu-BTC@Fe$_3$O$_4$ (15 mg) were added successively. Then NaBH$_4$ (4 mmol) was added slowly at room temperature. The reaction mixture was then stirred at 45 °C for a given time (monitored by TLC). After completion of the reaction, the Cu-BTC@Fe$_3$O$_4$ was recovered with an external magnet, and washed with EtOAc and water. The reaction mixture was extracted with EtOAc (3 × 5 ml) and dried over Na$_2$SO$_4$. The organic phase was then concentrated under reduced pressure to give the crude product, which was further purified by column chromatography with petroleum ether/ethyl acetate to afford the pure product (if necessary).

3 | RESULTS AND DISCUSSION

The Cu-BTC@Fe$_3$O$_4$ composite was prepared according to our previous report through a secondary growth strategy in non-DMF solvent media.[25,26] The as-prepared composite was well characterized by PXRD, FT-IR, TGA, SEM-EDS and N$_2$ adsorption. The PXRD characterization confirms the combination of the Cu-BTC phase and the Fe$_3$O$_4$ phase within the Cu-BTC@Fe$_3$O$_4$ composite, as

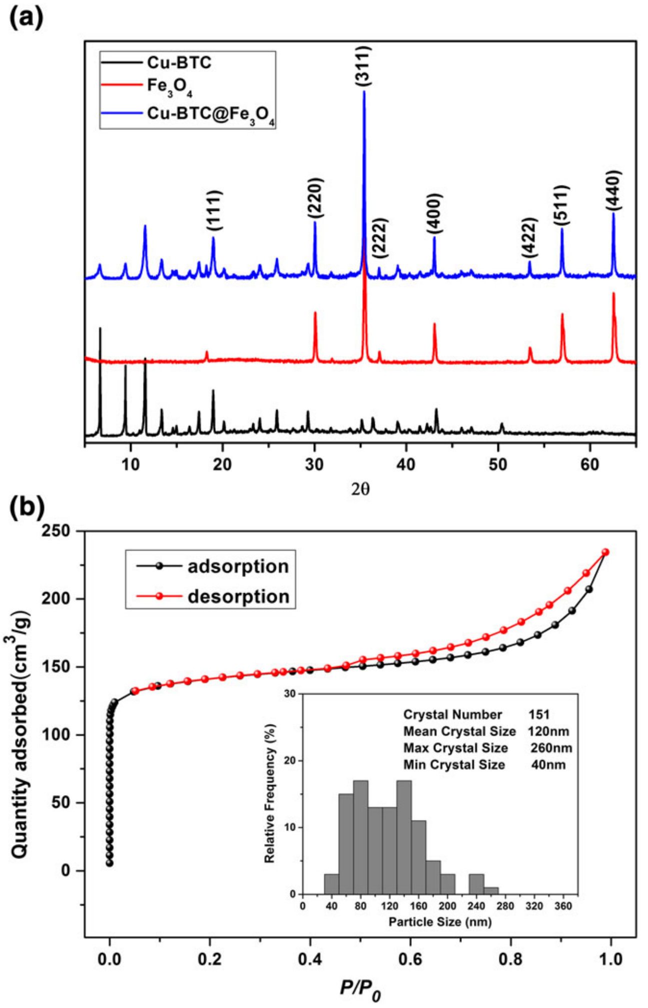


FIGURE 1 (a) the PXRD patterns of Cu-BTC, Fe$_3$O$_4$ and Cu-BTC@Fe$_3$O$_4$ samples. (b) N$_2$ adsorption/desorption isotherms and particle size distribution (insert) of Cu-BTC@Fe$_3$O$_4$

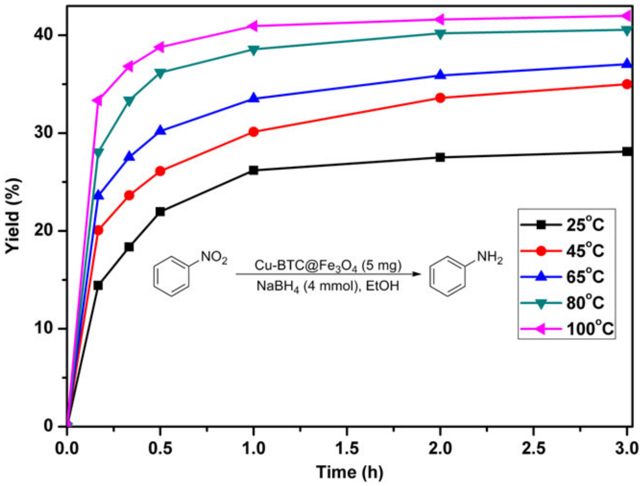


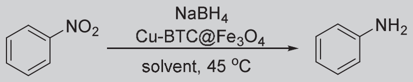
FIGURE 2 Initial survey on the reaction temperature

indicated in Figure 1a. The comparison of PXRD patterns between the as-synthesized composite and Cu-BTC show characteristic peaks of the Cu-BTC moieties. The crystal diffraction peaks of Fe_3O_4 can be observed in the PXRD pattern of Cu-BTC@Fe_3O_4 composite. Meanwhile N_2 adsorption isotherms of Cu-BTC@Fe_3O_4 composite showed the BET surface area of 423 m^2 g^{-1} and the coexistence of microporous and mesoporous adsorption (Figure 1b). The composite shows a spherical morphology with dimensions ranging from 30 to 200 nm and the majority crystal size of 80–140 nm (Figure 1b insert). Moreover, EDS and ICP analysis shows that the weight percentage of Cu-BTC in the composite is *ca*. 38.4% (For details, see Supplementary Material).

With the composite in hand, nitrobenzene (**1a**) was selected as the model substrate to optimize the reaction conditions. Initially, the influence of temperature on the reaction was examined under the following conditions: **1a** (1 mmol), $NaBH_4$ (4 equiv), Cu-BTC@Fe_3O_4 (5 mg) in EtOH (4 ml) under air atmosphere (Figure 2). The results show that a higher reaction temperature could benefit the conversion. However, when the reaction was performed at 100 °C, only 41% yield was obtained (versus 35% yield at 45 °C). Thus 45 °C was chosen as the optimal reaction temperature.

Further optimization of the reaction conditions are listed in Table 1. No reaction occurred in the absence of any catalyst. Catalyst loading survey clearly showed that 15 mg catalyst was the best choice, and further increase of the catalyst loading to 20 mg did not affect the reaction efficiency (entries 3~5). Methanol was also tried as the solvent, however, an inferior result was obtained (47%, entry 6). It was worth noting that addition of water to

TABLE 1 Optimized the reaction conditions[a]



1a **2a**

Entry	Catalyst (mg)	Solvent	$NaBH_4$ (mmol)	Yield(%)[b]
1	-	EtOH	4	n.r.
2	5	EtOH	4	35
3	10	EtOH	4	42
4	15	EtOH	4	66
5	20	EtOH	4	68
6	15	MeOH	4	47
7	15	EtOH/H_2O (1:1)	4	85
8	15	MeOH/H_2O (1:1)	4	78
9	15	EtOH/H_2O (2:1)	4	91
10	15	EtOH/H_2O (3:1)	4	99
11	15	EtOH/H_2O (1:3)	4	70
12	15	H_2O	4	67
13	15	EtOH/H_2O (3:1)	3	84
14	15	EtOH/H_2O (3:1)	5	>99
15[c]	15	EtOH/H_2O (3:1)	4	n.r.

[a]Reaction conditions: **1a** (1 mmol), Cu-BTC@Fe_3O_4 as the catalyst, $NaBH_4$ as the reductant, solvent (4 ml), 45 °C, 3 h, air. [b] GC yields. [c] Fe_3O_4 nanoparticles as the catalyst.

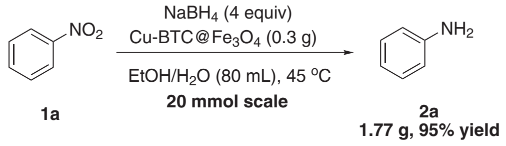
TABLE 2 Reduction of nitroarene compounds catalyzed by Cu-BTC@Fe_3O_4[a]

$$\underset{\mathbf{1}}{R{-}NO_2} \xrightarrow[EtOH/H_2O,\ 45\ ^{\circ}C]{NaBH_4 \\ Cu\text{-}BTC@Fe_3O_4} \underset{\mathbf{2}}{R{-}NH_2}$$

Entry	R	Product	Time (h)	Yield (%)
1	C_6H_5	**2a**	3	99
2	*p*-$CH_3C_6H_4$	**2b**	3	97
3	*p*-$MeOC_6H_4$	**2c**	3	94
4	*p*-ClC_6H_4	**2d**	3	93
5	*p*-BrC_6H_4	**2e**	3	93
6	*p*-FC_6H_4	**2f**	3	90
7	*p*-OHC_6H_4	**2g**	2	98
8	*p*-$NH_2C_6H_4$	**2h**	2	99
9	*p*-$HOCH_2C_6H_4$	**2i**	2	96
10	*p*-$NO_2C_6H_4$	**2j**	3	95[b]
11	*p*-$MeCOC_6H_4$	**2k**	3	99,[c] 95[d]
12	*m*-$NO_2C_6H_4$	**2l**	3	94[b]
13	*o*-OHC_6H_4	**2m**	3	96
14	*o*-BrC_6H_4	**2n**	3	93
15	*o*-$CH_3C_6H_4$	**2o**	3	95
16	1-naphthyl	**2p**	2	99
17	Cyclohexyl	**2q**	3	93[e]
18	*n*-hexyl	**2r**	3	91[e]

[a]Reaction conditions: **1** (1 mmol), Cu-BTC@Fe_3O_4 (15 mg), $NaBH_4$ (4 equiv), EtOH/H_2O (3:1, 4 ml), 45 °C, air, isolated yields. [b] $NaBH_4$ (6 equiv), both the two nitro groups were reduced. [c] $NaBH_4$ (1 equiv), 20 min, 1-(2-nitrophenyl)ethan-1-ol was isolated as the product. [d] $NaBH_4$ (6 equiv), 3 h, 1-(2-aminophenyl) ethan-1-ol was isolated as the product. [e] GC yields.

the solvent greatly accelerated the reaction, and almost quantitative yield was obtained in EtOH/H_2O (3:1) medium (entry 10). This result could be attributed that water could promote the hydrolysis of amino-borate intermediate during the reaction.[8] However, reaction using water as the solvent afforded a moderate yield (entry 12). The amount of $NaBH_4$ was then examined and 4 equivalents of reductant were enough for this transformation. Finally, to confirm the role of the catalyst, a blank experiment was carried out by using Fe_3O_4 nanoparticles as the catalyst. The result clearly indicated that the copper component was the actual catalyst center (entry 15).



SCHEME 2 Gram-scale synthesis of **2a**

The scope and limitations of the present protocol was then evaluated under the optimized reaction conditions. As shown from Table 2, nitroarenes bearing with either electron-withdrawing or electron-donating substituents such as halide (Cl, Br and F), alkyl, methoxy, hydroxy, amino groups underwent the reaction smoothly to afford the corresponding products in excellent yields (90~99%). Sterically hindered nitroarenes such as **1m**~**1o** also survived the reaction conditions to deliver to the corresponding anilines in excellent yields (**2m**~**2o**, entries 13~15). It should be pointed out that chemoselective reduction of keto group over nitro group was observed for substrate **1k** in the presence of only one equivalent of $NaBH_4$. Both keto group and nitro group were reduced by employing six equivalents of $NaBH_4$, affording 1-(2-aminophenyl)ethan-1-ol as the major product in 95% yield (entry 11). Moreover, this protocol was also suitable for the reduction of dinitroarenes in the presence of six equivalents of $NaBH_4$ (entries 10 and 12). Finally, this protocol was also extended to aliphatic nitro substrates such as nitrocyclohexane and 1-nitrohexane. The results showed

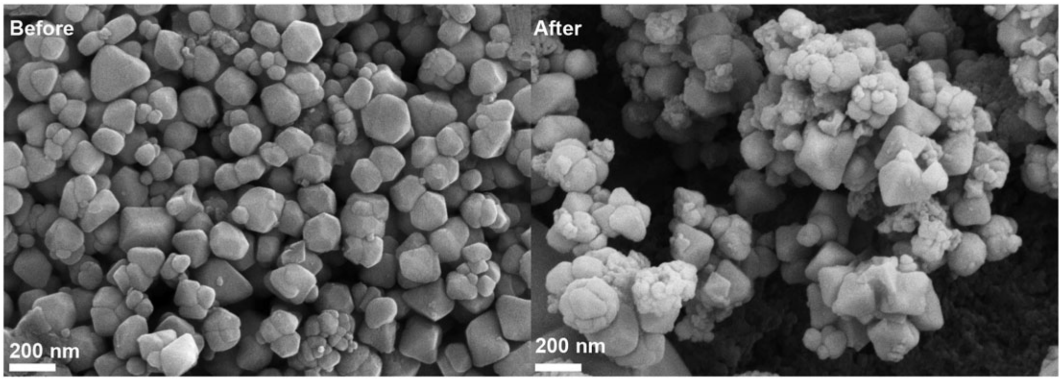


FIGURE 3 SEM images of Cu-BTC@Fe_3O_4 before and after the catalysis

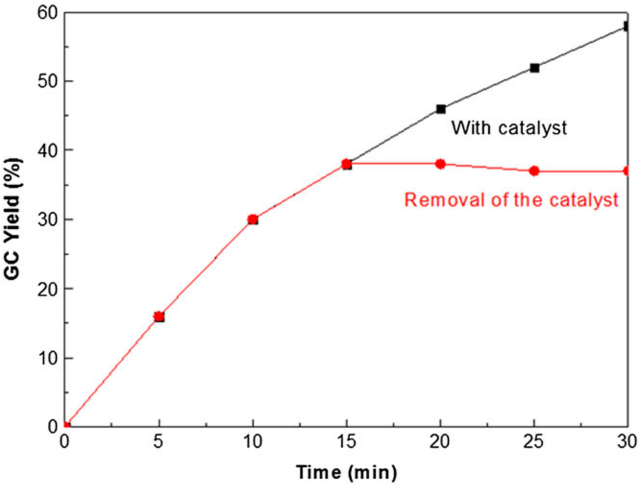


FIGURE 4 Hot-filtration experiment

that aliphatic nitro substrates were also well tolerated under the reaction conditions to provide the corresponding products in excellent yields (entries 17 and 18).

To demonstrate the practicality of the present protocol, a scale-up reaction (20 mmol) was carried out under the optimized conditions (Scheme 2). To our delight, this reaction provided the desired product **2a** in 95% yield (1.77 g), showing a high potential application for industry scale-up.

The reusability of the catalyst is also an advantage of the present protocol. Generally, after reaction, the catalyst was recovered with an external magnet, and washed by EtOAc and water. Using substrate **1a** as example, the results showed that the catalyst could be reused without obvious loss in activity in six consecutive runs (99%, 99%, 99%, 95%, 93% and 92%, respectively). Moreover, the recovered catalyst was further examined by scanning electron microscopy (SEM). Results clearly showed that no obvious aggregation of the catalyst was observed, which might account for the good reusability of the catalyst (Figure 3).

Finally, hot-filtration experiment was performed using the model reaction to investigate whether the reaction proceeded via a heterogeneous or homogeneous fashion (Figure 4). The catalyst was removed after 15 min while the filtrate was kept stirring. The result showed that the reaction was completely terminated after removal of the catalyst. Meanwhile, the ICP analysis showed that copper contents in the reaction mixture was less than 8 ppm, indicating this catalytic system could be a heterogeneous fashion.

4 | CONCLUSION

In summary, we have developed a facile and environmentally benign protocol for reduction of nitroarenes using Cu-BTC@Fe_3O_4 composite in aqueous medium. The catalyst is readily prepared and cost-effective. A broad scope of nitroarenes survived the reaction conditions to afford the aniline derivatives in good to excellent yields under mild reaction conditions. Excellent yields, good group compatibility, as well as the reusability of the catalyst are the major features of the present catalytic system.

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SUPPORTING INFORMATION

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