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REGULAR ARTICLE

A simple, fast and excellent protocol for the synthesis of phenols using $CuFe_2O_4$ magnetic nanoparticles

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Abstract. This paper describes a very mild, quick and simple protocol for the synthesis of phenols using $CuFe_2O_4$ magnetic nanoparticles as a catalyst. The nanosized catalyst has an average diameter of 17.63 nm. The magnetic nanoparticles were characterized by SEM, EDX, VSM, XRD and TEM analysis. The synthesis of phenols from phenylboronic acids using H_2O_2 as an oxidant proceeded very well with excellent yields. Heterogeneous catalyst, easy recyclability, mild reaction conditions, short reaction time added as an advantage for the present protocol.

Keywords. Phenols; $CuFe_2O_4$ magnetic nanoparticles; short reaction time; heterogeneous catalysis; easy recyclability.

1. Introduction

Phenolic compounds are produced as secondary metabolites by most plants. These compounds play an important role in the growth and reproduction of plants, and provide protection against pathogens and predators,[1] besides contributing towards the colour and sensory characteristics of fruits and vegetables.[2] Phenols exhibit a wide range of physiological properties, such as anti-allergenic, anti-atherogenic, anti-inflammatory, anti-microbial, anti-thrombotic, cardioprotective and vasodilatory effects.[3–7] Phenolic compounds also have a wide range of applications both in the industrial world and in nature. Antioxidant activity[8] is a beneficial effect derived from phenolic compounds.

The production of phenols has begun since the 1860s. Moreover, towards the end of the 19th century, phenols have been used in the synthesis of dyes, explosives i.e., picric acid, etc. Formaldehyde resins are the basis of the oldest plastics and are still used in electrical equipment to make low-cost thermosetting plastics such as melamine and bakelite.

Looking at the immense value of phenols, scientists have tried to synthesize it through various reaction pathways. The laboratory scale synthesis of phenols uses nucleophilic substitution of aryl halides activated by electron-withdrawing substituents catalysed by copper, palladium,[9] etc. These conditions suffer from several drawbacks like harsh reaction condition, poor functional group compatibility, less substrate scope, etc. Among them, the synthesis of phenols from arylboronic acids to phenols has received significant attention in organic synthesis, because arylboronic acids are diverse, less toxic, and highly stable under air. The transformations of aryl boronic acids to phenols *via ipso*-hydroxylation have been reported by several scientists using different reaction conditions. Several research groups have reported different catalysts for the synthesis of phenols using arylboronic acids which includes iron(III)oxide,[10] $(NH_4)_2S_2O_8$,[11] potassium peroxymonosulfate,[12] hydrazine hydrate,[13] I_2,[14] Amberlite IR 120 resin,[15] H_3BO_3–H_2O_2,[16] $NaClO_2$.[17] Recently, many scientists have carried out *ipso*-hydroxylations using CNT-chitosan,[18] ascorbic acid,[19] Fe_2O_3@SiO_2 nanoparticles,[20] Cu_2O nanoparticles,[21] etc. But these conditions suffer one or more disadvantages like longer reaction time and/or high amount of catalyst loading. Nowadays, the use of nanoparticles as a catalyst is growing over other catalyst systems, but because of their nanosize, the isolation and recovery of the nanocatalyst from the reaction mixture has been one of the major drawbacks.

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To overcome all these difficulties, the use of magnetic nanoparticles (MNPs) as a catalyst is preferred over choosing other catalysts because of their stability, easy synthesis, better selectivity, excellent surface area to the volume ratio, and easy recyclability. Various magnetic nanoparticles have been synthesized in the laboratory which include Fe_3O_4,[22,23] Cu/SB-Fe_3O_4,[24] etc.

Herein we have synthesized $CuFe_2O_4$ MNPs by a very convenient and simple procedure and used it as a catalyst in the production of phenols from aryl boronic acids.

2. Experimental

2.1 *Preparation of the catalyst using Coprecipitation Method*

0.5 g of $FeCl_3$ and 0.5 g of copper acetate were added in a round bottom flask and 70 mL of deionised water was added to it and stirred at room temperature. 5 mL of 0.1 M NaOH was added to the stirring solution. After 30 min 0.1 M $NaBH_4$ was added to the solution and stirred for about 1 h. The resulting solution was centrifuged at 1200 rpm for 10 min and washed with ethanol. The centrifuged product was dried and the desired product of $CuFe_2O_4$ MNPs was obtained.

2.2 *General procedure for the Ipso-Hydroxylation*

In a round bottom flask 1 mmol of phenylboronic acid, 0.03 mmol (3 mol%) of $CuFe_2O_4$ MNPs, 200 µL of H_2O_2 (30%) were added and stirred at room temperature. The desired product was obtained after about 2 min which was monitored by TLC. The reaction mixture was diluted with 20 mL of diethyl ether and the combined organic layer was washed with brine and dried over by anhydrous Na_2SO_4 and evaporated in a rotary evaporator. The products were confirmed by ^{1}H NMR and ^{13}C NMR spectroscopy without any further purification.

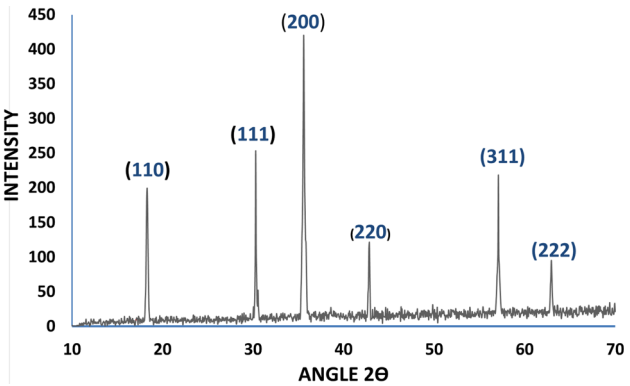


Figure 1. Powder XRD pattern of $CuFe_2O_4$ MNPs.

3. Results and Discussion

3.1 *Characterization of the catalyst*

The powder XRD diffraction pattern of the prepared $CuFe_2O_4$ MNPs is shown in Figure 1. The various diffraction peaks at $2\Theta = 18.3, 30.3, 35.6, 42.8, 57.1, 62.95$ corresponds to the planes (110), (111), (200), (220), (311), (222) respectively. The sharp diffraction peaks clearly shows the highly crystalline nature of $CuFe_2O_4$ MNPs.

The SEM images showed the structure and morphology of the nanoparticles (Figure 2). The SEM images

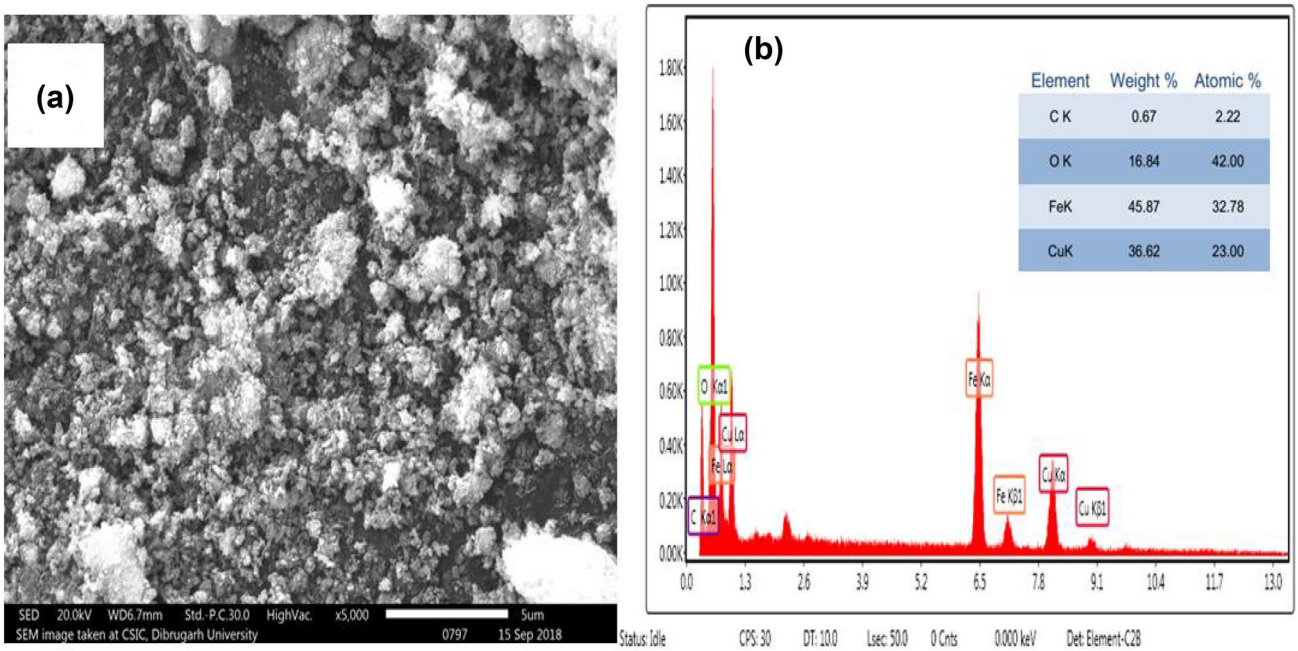


Figure 2. (a) SEM image; (b) EDX image of $CuFe_2O_4$MNPs.

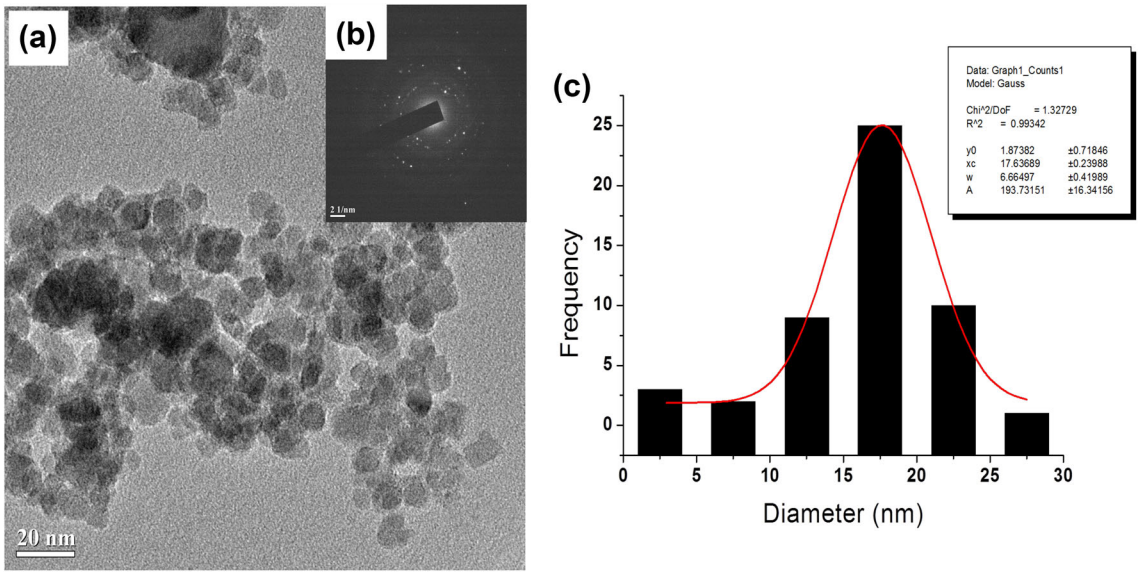


Figure 3. (a) TEM images of the synthesized nanoparticles; (b) the SAED pattern of one nanoparticle (inset) and; (c) grain size distribution of the nanoparticles.

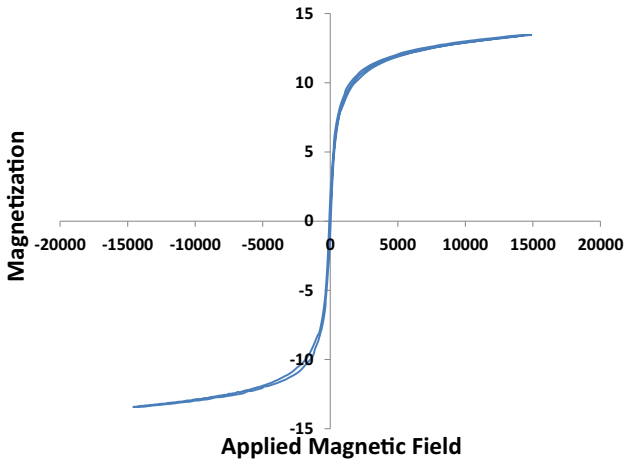


Figure 4. VSM study of the $CuFe_2O_4$ MNPs.

depicted the structure of nanoparticles to be spherical with slight aggregation. The purity of the nanoparticles was observed from the Energy Dispersive X-ray (EDX) spectrum which shows the presence of copper, iron and oxygen element.

The morphology of the nanoparticles was determined from the TEM images (Figure 3a). The selected area electron diffraction (SAED) pattern of the $CuFe_2O_4$ MNPs showed bright fringes, which indicated the crystalline nature of the nanoparticles (Figure 3b). The average diameter of the nanoparticle was found to be 17.636 nm (Figure 3c).

Furthermore, to observe the magnetic behaviour the VSM analysis of the nanoparticles was studied (Figure 4). From the VSM study, the coercivity (Hci) was found to be 53.387 G.

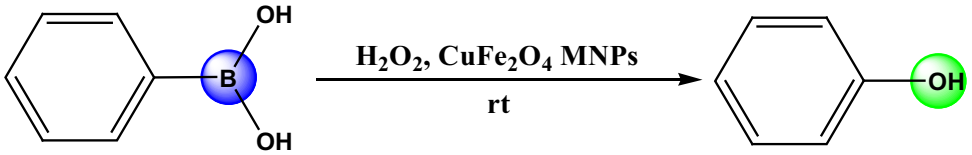
Table 1. Optimization of H_2O_2.

Sl. No	Oxidant (H_2O_2)μL	Time (min)
1	50	30
2	100	5
3	150	3
4	**200**	**2**
5	300	2

Reaction conditions: phenyl boronic acid (1 mmol), $CuFe_2O_4$(3 mol%), rt.

3.2 *Application of the Catalyst*

The prepared catalyst was used for the synthesis of various substituted phenols from arylboronic acids. We began our experiment with the optimization parameter for which we took phenyl boronic acid (1 mmol) as the



Scheme 1. Synthesis of phenol using $CuFe_2O_4$ MNPs.

Table 2. Optimization of the catalyst[a].

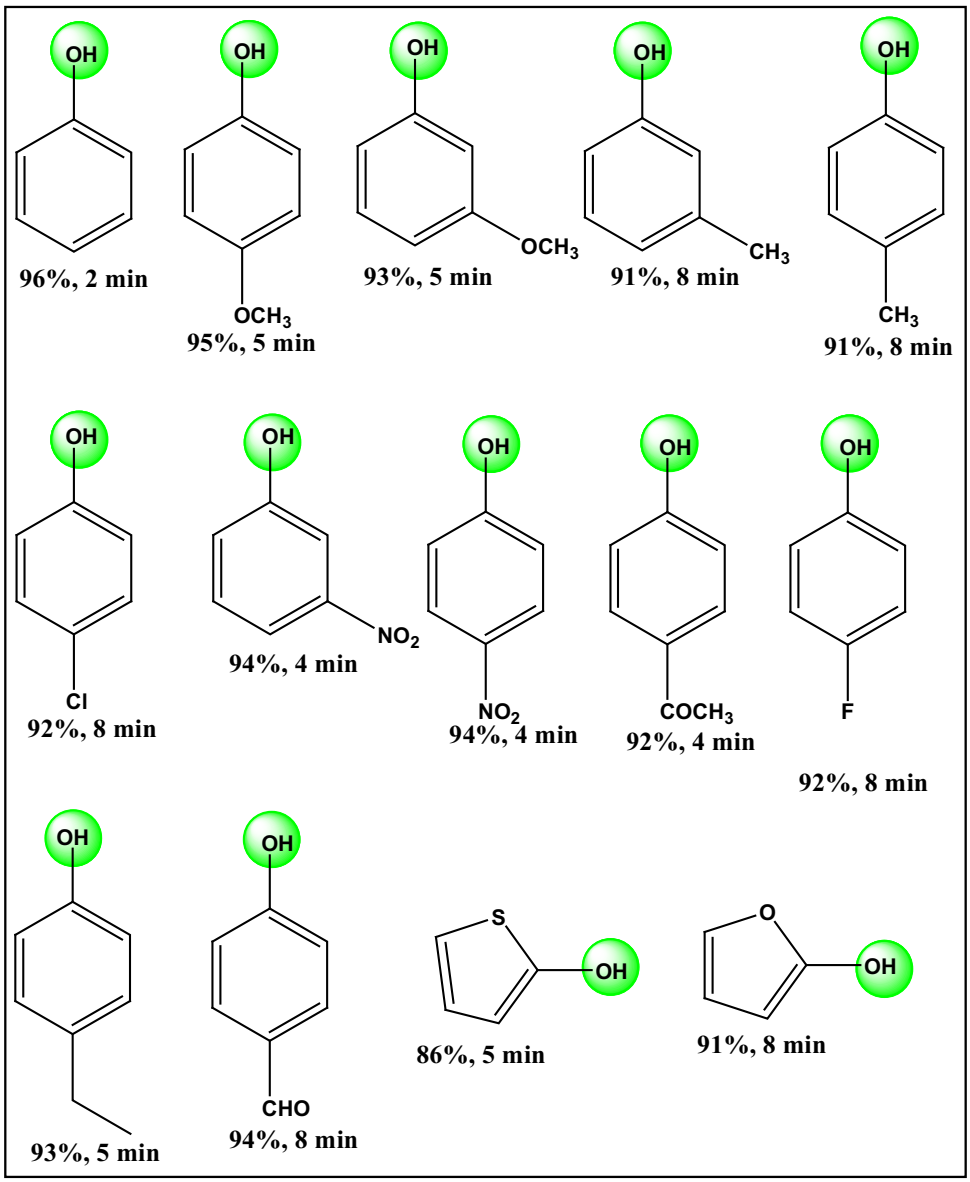
Sl. No	Catalyst (mol %)	Time (min)	Yield (%)[b]
1	-	60	45
2	1	30	80
3	1.5	25	80
4	2	20	85
5	2.5	10	90
6	3	2	95
7	3.5	2	95

[a]Reaction conditions: phenylboronic acid (1 mmol), H_2O_2 (200μL), rt.
[b]Yields are isolated yields.

model substrate and the reaction was carried out at room temperature (Scheme 1). The product was formed within 2 min with 96% yield.

Initially, we optimized our reaction using different amounts of H_2O_2. The reaction preceded very smoothly using only 200 μL of H_2O_2 within 2 min (Table 1, entry 4). After the identification of the proper amount of H_2O_2 the reaction was further optimized for different amount of the catalyst (Table 2). Moreover, with the use of H_2O_2 only as an oxidant, trace amount of yields was obtained after 1 h (Table 2, entry 1). The yield of the product was further increased by using only 3 mol% of the catalyst without the use of any solvent.

Table 3. $CuFe_2O_4$ MNPs catalysed *ipso*-hydroxylation of aryl boronic acids to phenols[a].



[a]Reaction conditions: phenyl boronic acid (1 mmol), H_2O_2 (200μL), rt, $CuFe_2O_4$ MNPs (3 mol%) Yields are isolated yields.

Table 4. Comparison efficiency with other catalysts.

Catalyst	H_2O_2 (mL)	Catalyst loading (mg)	Time (min)	Ref.
Ag-NP Mont-K	0.5	5	15	25
Bio-silica	0.2	5	5	26
Acidic alumina	1.5	20	10	27
Cu_2O NP	0.2	2 (3 mol%)	10	28
$CuFe_2O_4$ MNPs	0.2	1.05 (3 mol %)	2	This work

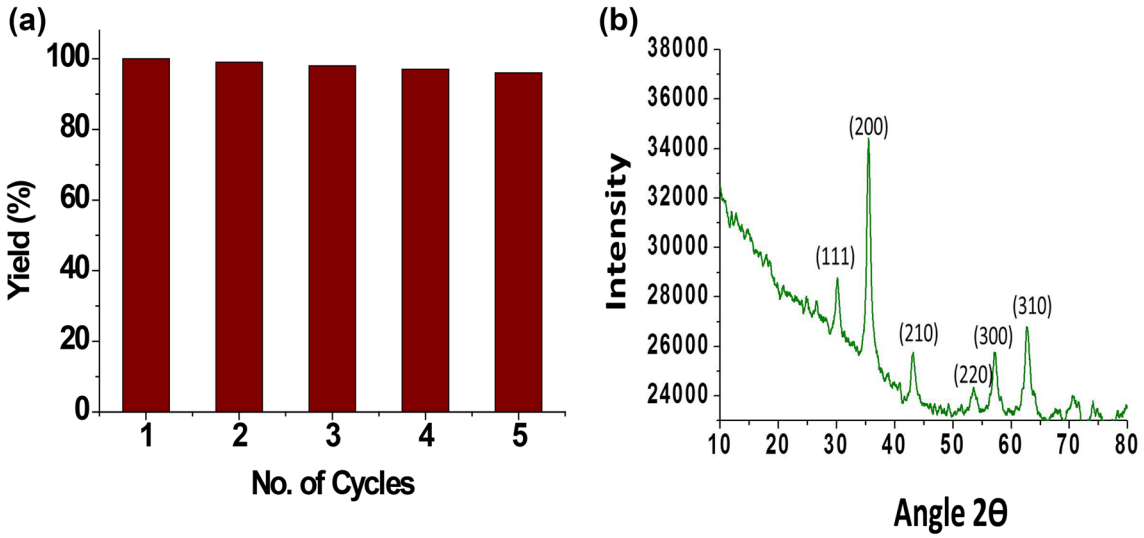


Figure 5. (a) Recyclability of $CuFe_2O_4$ MNPs; (b) XRD of the recycled catalyst after the 5th cycle.

Using the optimized conditions provided in the previous section, the scope of the reaction was studied for a number of phenyl boronic acids to phenols (Table 3). It was observed that both electron withdrawing and electron donating groups had little effect on the reactivity conditions. Moreover, hetero arylboronic acids also gave high yields in less time.

We compared the use of $CuFe_2O_4$ MNPs as a catalyst for the *ipso*-hydroxylation of aryl boronic acids to phenols with other reported catalyst,[25–28] which showed the better catalytic efficiency of our catalyst. The easy recyclability, less amount of catalyst loading, less reaction time, easy preparation of the catalyst proved to be the advantages of the present protocol. The comparison efficiency of phenylboronic acid to phenol with other reported catalyst is shown in Table 4.

3.3 *Recyclability*

Recyclability is one of the main advantages of a heterogeneous catalyst. To test the recyclability, we observed the *ipso*-hydroxylation of phenyl boronic acid to phenol (Figure 5). The catalyst was easily recycled up to 5th cycle without any loss in the catalytic cycle. After the completion of the reaction the catalyst was extracted with the help of an external magnet, centrifuged and washed properly with ethanol. It was then dried and reused for a fresh batch of reaction.

The sharp XRD peaks taken after the 5th cycle (Figure 5b) proved the crystallinity of the nanoparticles. There was no filtration required for the recyclability of the catalyst.

4. Conclusions

Herein we have synthesized phenols using a very mild procedure using a heterogeneous, recyclable $CuFe_2O_4$ MNPs catalyst for the first time. The easy formation of the product in less reaction time proved to be a very significant procedure for the synthesis of phenols. The magnetic nature of the catalyst added as an advantage for the protocol as the product formation required less amount of catalyst.

Supplementary Information (SI)

Characterization methods and ^{1}H NMR of the compunds are available at www.ias.ac.in/chemsci.

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