



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 activity⁸ 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 $(\text{NH}_4)_2\text{S}_2\text{O}_8$,¹¹ potassium peroxymonosulfate,¹² hydrazine hydrate,¹³ I_2 ,¹⁴ Amberlite IR 120 resin,¹⁵ $\text{H}_3\text{BO}_3\text{--H}_2\text{O}_2$,¹⁶ NaClO_2 .¹⁷ Recently, many scientists have carried out *ipso*-hydroxylations using CNT-chitosan,¹⁸ ascorbic acid,¹⁹ $\text{Fe}_2\text{O}_3@\text{SiO}_2$ 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} $\text{Cu/SB-Fe}_3\text{O}_4$,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 ^1H NMR and ^{13}C NMR spectroscopy without any further purification.

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

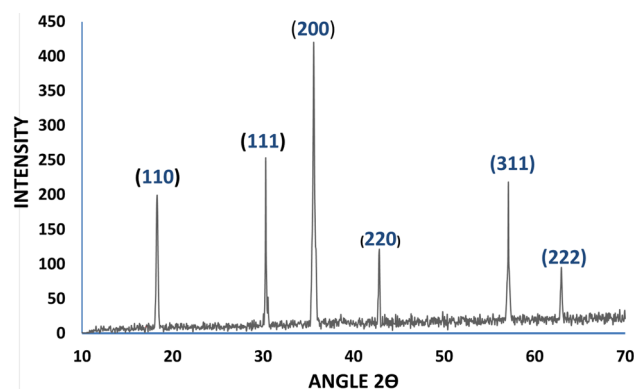


Figure 1. Powder XRD pattern of CuFe_2O_4 MNPs.

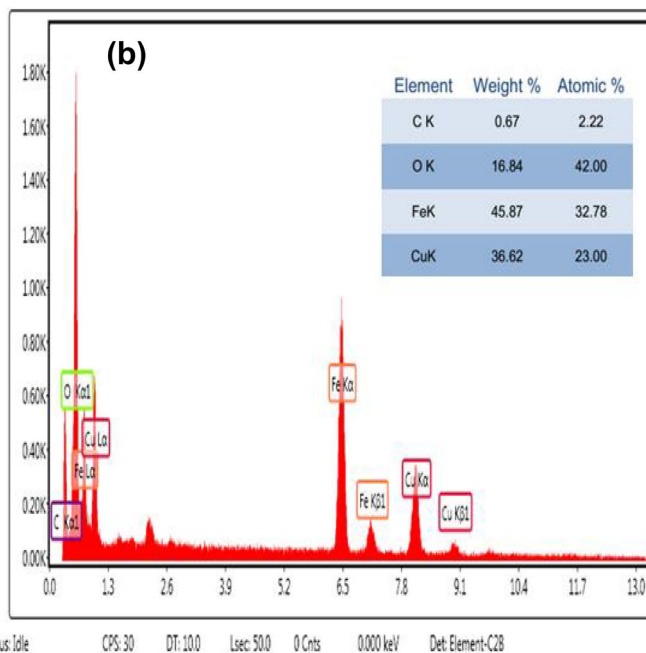
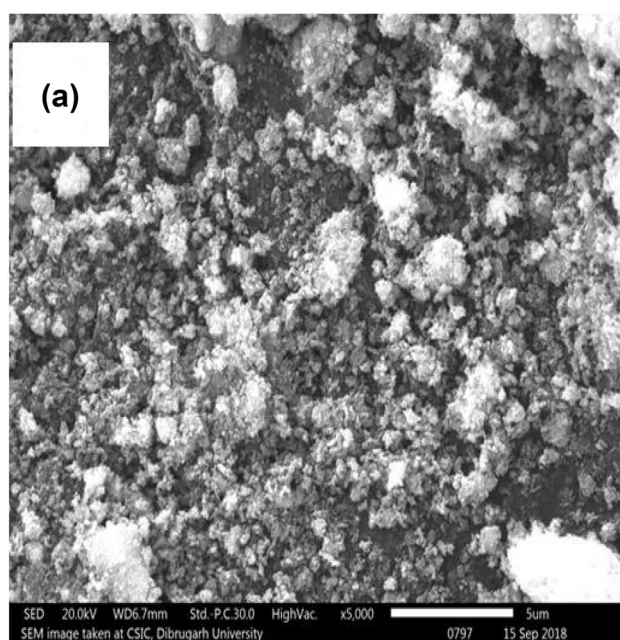


Figure 2. (a) SEM image; (b) EDX image of CuFe_2O_4 MNPs.

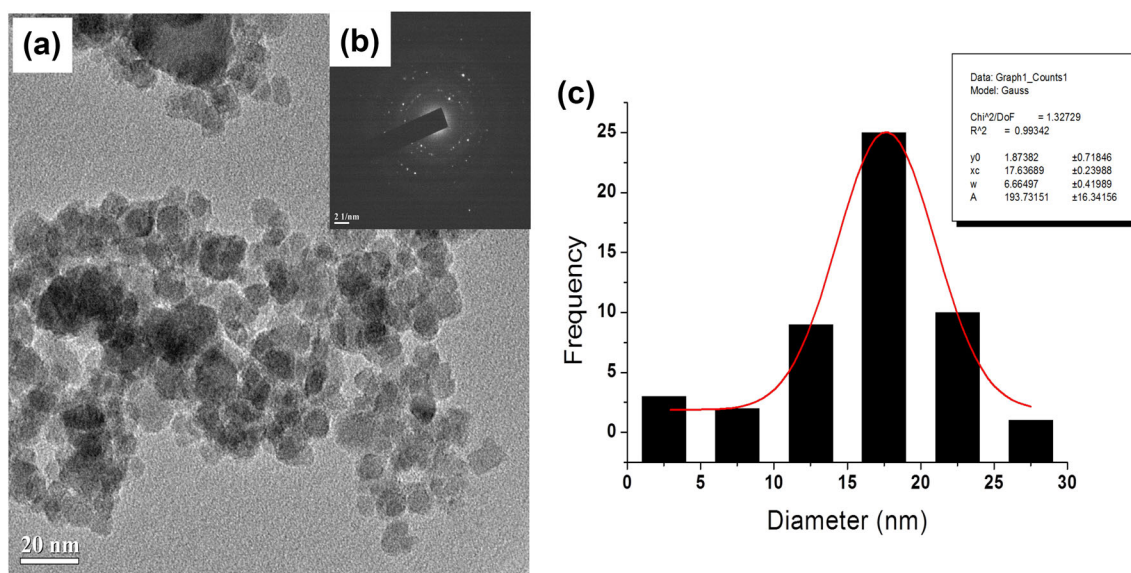


Figure 3. (a) TEM images of the synthesized nanoparticles; (b) the SAED pattern of one nanoparticle (inset) and; (c) grain size distribution of the nanoparticles.

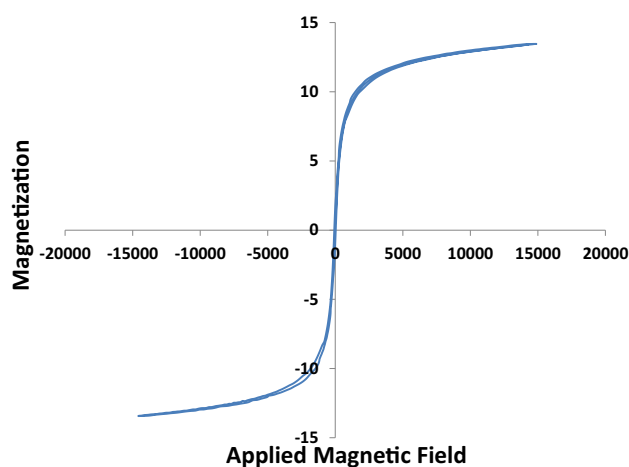


Figure 4. VSM study of the CuFe_2O_4 MNPs.

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

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

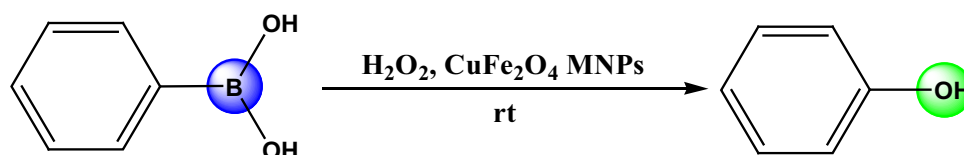
Reaction conditions: phenyl boronic acid (1 mmol), CuFe_2O_4 (3 mol%), rt.

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 (H_{ci}) was found to be 53.387 G.

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

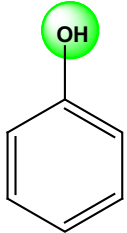
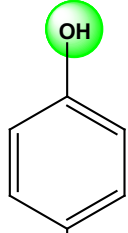
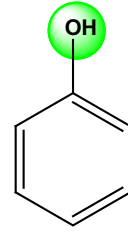
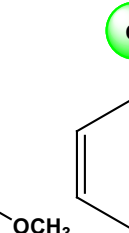
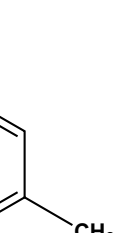
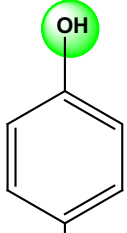
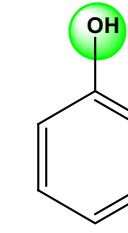
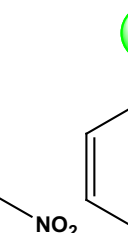
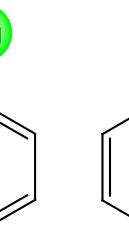
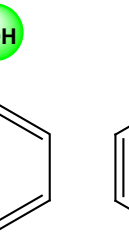
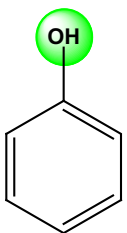
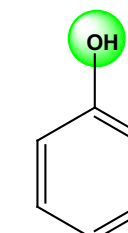

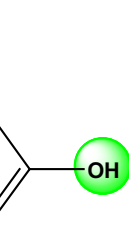
^aReaction conditions: phenylboronic acid (1 mmol), H₂O₂ (200 μL), rt.

^bYields 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 H₂O₂. The reaction preceded very smoothly using only 200 μL of H₂O₂ within 2 min (Table 1, entry 4). After the identification of the proper amount of H₂O₂ the reaction was further optimized for different amount of the catalyst (Table 2). Moreover, with the use of H₂O₂ 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.

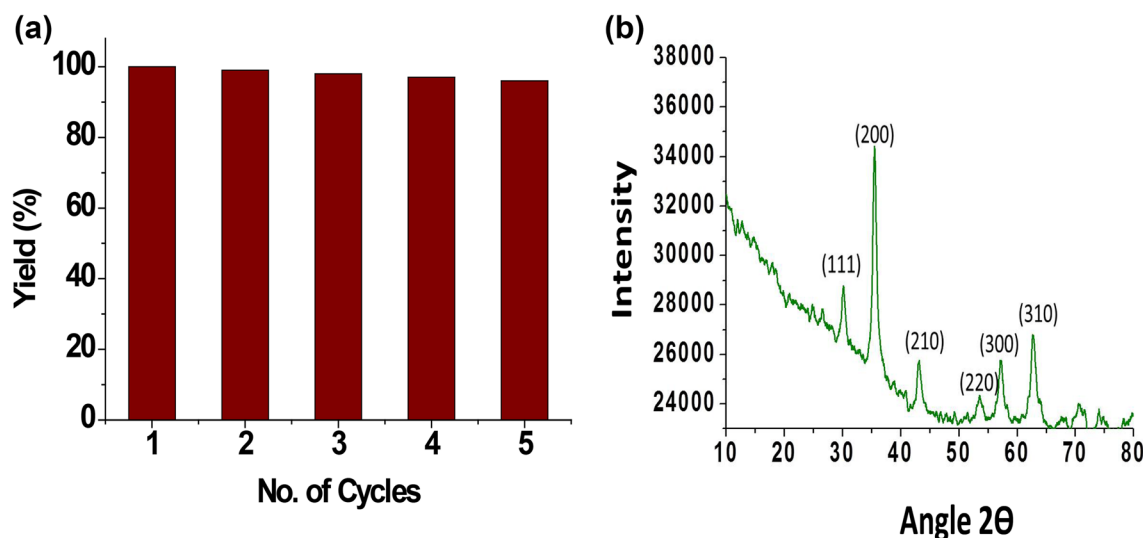
Table 3. CuFe₂O₄ MNPs catalysed *ipso*-hydroxylation of aryl boronic acids to phenols^a.

				
96%, 2 min	95%, 5 min	93%, 5 min	91%, 8 min	91%, 8 min
				
92%, 8 min	94%, 4 min	94%, 4 min	92%, 4 min	92%, 8 min
				
93%, 5 min	94%, 8 min	86%, 5 min	91%, 8 min	

^aReaction conditions: phenyl boronic acid (1 mmol), H₂O₂ (200 μL), rt, CuFe₂O₄ MNPs (3 mol%) Yields are isolated yields.

Table 4. Comparison efficiency with other catalysts.

Catalyst	H ₂ O 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 ₂ O NP	0.2	2 (3 mol%)	10	28
CuFe ₂ O ₄ MNPs	0.2	1.05 (3 mol %)	2	This work

**Figure 5.** (a) Recyclability of CuFe₂O₄ 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 CuFe₂O₄ 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 CuFe₂O₄ 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 ¹H NMR of the compounds are available at www.ias.ac.in/chemsci.

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References

- Bravo L 1998 Polyphenols: chemistry, dietary sources, metabolism, and nutritional significance *Nutr. Rev.* **56** 317
- Alasalvar C, Grigor J M, Zhang D and Quantick P C 2001 Comparison of Volatiles, Phenolics, Sugars, Antioxidant Vitamins, and Sensory Quality of Different Colored Carrot Varieties *J. Agric. Food Chem.* **49** 1410
- Ferreira I C F R, Barros L, Soares M E, Bastos M L and Pereira J A 2007 Antioxidant activity and phenolic contents of *Olea europaea* L. leaves sprayed with different copper formulations *Food Chem.* **103** 188
- Manach C, Mazur A and Scalbert A 2005 Polyphenols and prevention of cardiovascular diseases *Curr. Opin Lipidol.* **16** 77
- Middleton E, Middleton E, Kandaswami C, Kandaswami C and Theoharides T C 2000 The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer *Pharmacol. Pharmacol. Rev.* **52** 673
- Puupponen-Pimiä R, Nohynek L and Meier C 2001 Antimicrobial properties of phenolic compounds from berries *J. Appl. Microbiol.* **90** 494
- Samman S, Lyons Wall P M and Cook N C 1998 Flavonoids and coronary heart disease: Dietary perspectives In *Flavonoids in Health and Disease* C A RiceEvans and L Packer (Eds.) (New York: Marcel Dekker) pp. 469–482
- Heim K E, Tagliaferro A R and Bobilya D J 2002 Flavonoid antioxidants: Chemistry, metabolism and structure-activity relationships *J. Nutr. Biochem.* **13** 572
- Yu C W, Chen G S, Huang C W and Chern J W 2012 Efficient microwave-assisted Pd-catalyzed hydroxylation of aryl chlorides in the presence of carbonate *Org. Lett.* **14** 3688
- Sawant S D, Hudwekar A D, Aravinda Kumar K A, Venkateswarlu V, Singh P P and Vishwakarma R A 2014 Ligand- and base-free synthesis of phenols by rapid oxidation of arylboronic acids using iron(III) oxide *Tetrahedron Lett.* **55** 811
- Claudia A, Celedón C, García L C and Corral N J L 2014 An Efficient Synthesis of Phenols via Oxidative Hydroxylation of Arylboronic Acids Using $(\text{NH}_4)_2\text{S}_2\text{O}_8$ *J. Chem.* Article ID 569572
- Webb K S and Levy D 1995 A facile oxidation of boronic acids and boronic esters *Tetrahedron Lett.* **36** 5117
- Zhong Y, Yuan L, Huang Z, Gu W, Shao Y and Han W 2014 Unexpected Hydrazine Hydrate-Mediated Aerobic Oxidation of Aryl/Heteroaryl Boronic Acids to Phenols with Ambient Air *RSC Adv.* **4** 33164
- Gogoi A and Bora U 2012 An iodine-promoted, mild and efficient method for the synthesis of phenols from arylboronic acids *Synlett.* **23** 1079
- Mulakayala N, Ismail Kumar K M, Rapolu R K, Kanda-gatla B, Rao P, Oruganti S and Pal M 2012 Catalysis by Amberlite IR-120 resin: A rapid and green method for the synthesis of phenols from arylboronic acids under metal, ligand, and base-free conditions *Tetrahedron Lett.* **53** 6004
- Gogoi K, Dewan A, Gogoi A, Borah G and Bora U 2014 Boric Acid as Highly Efficient Catalyst for the Synthesis of Phenols from Arylboronic Acids *Heteroatom Chem.* **25** 127
- Gogoi P, Bezboruah P, Gogoi J and Boruah R C 2013 *Ips*o-hydroxylation of arylboronic acids and boronate esters by using sodium chlorite as an oxidant in water *Eur. J. Org. Chem.* **2013** 7291
- Kim H S, Joo S R, Shin U S and Kim S H 2018 Recyclable CNT-chitosan nanohybrid film utilized in copper-catalyzed aerobic *ipso*-hydroxylation of arylboronic acids in aqueous media *Tetrahedron Lett.* **59** 4597
- Das S K, Bhattacharjee P and Bora U 2018 Ascorbic Acid as a Highly Efficient Organocatalyst for *ipso*-Hydroxylation of Arylboronic Acid *Chem. Select.* **3** 2131
- Saikia I, Hazarika M, Hussian N, Das M R and Tamuly C 2017 Biogenic synthesis of Fe_2O_3 @ SiO_2 nanoparticles for *ipso*-hydroxylation of boronic acid in water *Tetrahedron Lett.* **58** 4255
- Borah R, Saikia E, Bora S J and Chetia B 2016 On-water synthesis of phenols using biogenic Cu_2O nanoparticles without using H_2O_2 *RSC Adv.* **6** 100443
- Chacko P and Shivashankar K 2018 Synthesis of aminomethylphenol derivatives via magnetic nano Fe_3O_4 catalyzed one pot Petasis borono-Mannich reaction *J. Chem. Sci.* **130** 1
- Dadras A, Jamal M R N, Moghaddam M F and Ayati S E 2018 Green and selective oxidation of alcohols by immobilized Pd on triazole functionalized Fe_3O_4 magnetic nanoparticles *J. Chem. Sci.* **130** 1
- Elhamifar D, Mofatehnia P and Faal M 2017 Magnetic nanoparticles supported Schiff-base/copper complex: An efficient nanocatalyst for preparation of biologically active 3,4-dihydropyrimidinones *J. Colloid Interface Sci.* **504** 268
- Begum T, Gogoi A, Gogoi P K and Bora U 2015 Catalysis by mont K-10 supported silver nanoparticles: A rapid and green protocol for the efficient *ipso*-hydroxylation of arylboronic acids *Tetrahedron Lett.* **56** 95
- Mahanta A, Adhikari P, Bora U and Thakur A J 2015 Biosilica as an efficient heterogeneous catalyst for *ipso*-hydroxylation of arylboronic acids *Tetrahedron Lett.* **56** 1780
- Gogoi A and Bora U 2013 A mild and efficient protocol for the *ipso*-hydroxylation of arylboronic acids *Tetrahedron Lett.* **54** 1821
- Borah R, Saikia E, Bora S J and Chetia B 2017 Banana pulp extract mediated synthesis of Cu_2O nanoparticles: An efficient heterogeneous catalyst for the *ipso*-hydroxylation of arylboronic acids *Tetrahedron Lett.* **58** 1211