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Applied Catalysis A, General



journal homepage: www.elsevier.com/locate/apcata

### Application of sulfonic acid fabricated cobalt ferrite nanoparticles as effective magnetic nanocatalyst for green and facile synthesis of benzimidazoles

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ARTICLE INFO	A B S T R A C T		
Keywords: Benzimidazole Green solvent Heterogeneous catalyst Reusability Solid acid	This work represents the design and synthesis of efficient sulfonated cobalt ferrite solid acid catalyst. The synthesized solid acid green catalyst was characterized using various techniques viz. FT-IR, powder XRD, SEM, TEM and VSM. The obtained catalyst was used to synthesize biologically significant 2-substituted benzimidazole derivatives by condensation between o-phenylenediamine with various aromatic, aliphatic and heterocyclic aldehydes. High yield (up to 98 %), short reaction time (10–25 min), mild reaction condition, wide functional group tolerance, easy work-up procedure and excellent values of green chemistry metrices such as lower E factor (0.126), high RME value (88.83 %), carbon efficiency (100 %) and high atom economy (AE) value (90.65 %), are some salient features of the present catalytic system. Moreover, the catalyst recovery by simply using an external magnet and catalyst reusability up to 7 times without any significant loss in catalytic efficiency are some		

additional remarkable features of the current protocol.

#### 1. Introduction

Heterocyclic compounds containing nitrogen are considered as significant building blocks of various natural products, agrochemicals, pharmaceuticals, and functionalized advanced materials [1]. Among these benzimidazole have emerged as privileged class of N-heterocycles having wide range of applications in pharmaceuticals. They display numerous biological activities and are used as antimicrobial [2], anti-inflammatory [3], antibacterial [4], antibiotic, anti-ulcer [1], anti-cancer [5], anti-helminthic [6], anti-hypertensive [7], topoisomerase IV inhibitors [8] and anti-HIV [1]. Some of the successful clinical drugs containing benzimidazole framework are carbendazim, thiabendazole, omeprazole [9] etc. (Fig. 1).

The imidazole ring present in benzimidazole scaffold is also a distinct part of numerous natural products such as histidine, proteins, histamine, purines and biotin [10]. Along with these, benzimidazole analogs have applications in dye and pigment industry, chemical UVB filters, chemo sensors and thermostable membranes used for fuel cells [1,11,12].

Owing to the importance of benzimidazole scaffolds numerous strategies have been made for their synthesis. Various synthetic schemes for their development involves aromatic and heteroaromatic 2-nitroamines, phenylenediamine, carboxylic acids or its derivatives (carbonitriles, orthoesters), arylamino oximes and cyclization of o-bromoaryl derivatives. However, the most efficient and commonly used method is condensation of o-phenylenediamine with aldehyde [9]. Literature survey reveals that there are numerous catalysis like mineral acids (H<sub>2</sub>SO<sub>4</sub>, HNO<sub>3</sub> and HF), Lewis acids (AlCl<sub>3</sub> and BF<sub>3</sub>) [13], silver nanoparticle [14], metal triflate [15], KHSO<sub>4</sub>, Amberlite, L-proline, CoCl<sub>2</sub>, PTSA, solid support catalyst and ionic liquids [16] are used for the synthesis of benzimidazole synthesis. Even after having these umpteen methods of preparation of benzimidazoles, they are linked with various limitations, such as low atom economy, the formation of by-product, harsh reaction conditions, extended reaction period, expensive catalysts, unsatisfactory yield of products as well as toxic solvents.

Taking into consideration of these constraints, there is an urgent need to design a new more simple, efficient, cheap and reusable heterogeneous catalyst which can be recovered easily from reaction medium and the synthesis of 2-substituted benzimidazoles can be done efficiently under mild reaction conditions.

In past few years, nanomaterials have been extensively employed as a solid support material [17] for the designing of heterogeneous catalyst to overcome the economic and environmental issues. Nanoparticles are well-thought-out as semi-heterogeneous support as they can be

https://doi.org/10.1016/j.apcata.2021.118005

Received 11 November 2020; Received in revised form 7 January 2021; Accepted 7 January 2021 Available online 21 January 2021 0926-860X/© 2021 Elsevier B.V. All rights reserved.

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Fig. 1. Benzimidazole scaffold containing commercial drugs.

dispersed easily and exhibit high surface area [18]. Nanocatalysts being stable, durable and cost effective, eliminates the need for harsh reaction conditions, increases energy efficiency, provides high selectivity, and allows the minimal use of substrates. Among these nanomaterials magnetically retrievable nanocatalyst made number of heads turn due to its unique advantages such as easy and fast separation from reaction media simply by the application of external magnetic field.

Magnetic cobalt ferrite spinel (CoFe<sub>2</sub>O<sub>4</sub>) have attracted a lot of attention owing to the most prominent support demonstrating wide application in numerous fields such as in ferrofluids technology, MRI, biosensors, drug delivery [19], photocatalysis and nanobiotechnology. They also display exceptional properties like simplistic synthesis, rigidity, high surface area, high abundance of surface hydroxyl groups, outstanding thermal stability, high chemical steadiness, relatively high anisotropy, Curie temperature as well as saturation magnetization (Ms) [20,21]. However, the magnetic nanoparticles has a strong tendency of aggregation. Thus in order to prevent aggregation, the core is usually prevented by an external coating of silica, carbon, or gold etc. [22]. The major advantages of the silica coating are admirable thermal as well as chemical steadiness, high surface area, adjustable pore size, ease of handling, and ease of attaching ligands covalently due to high profusion of exposed silanol (Si—OH) groups [20].

The acid catalysts including mineral acids such as H<sub>2</sub>SO<sub>4</sub>, HCl, HF and organic acids like p-toluene sulfonic acid (PTSA) suffer from various drawbacks such as corrosion, toxicity, their tedious separation from homogeneous reaction medium and need of neutralization of waste streams [23]. Among these commonly used acids, sulfonic acid being highly active, is proficiently used for synthesizing different organic compounds. However, owing to its hazardous nature, it is harmful to the environment as well as public health. It is deadly if swallowed/inhaled and also cause eye and skin burn. Being highly reactive, it reacts immediately with water to generate toxic hydrochloride (HCl) and sulfur dioxide [24]. Along with these drawbacks, its difficulty of separation from reaction mixture restricts its pertinency in pharmaceutics and industry. Keeping all these drawbacks of sulfonic acid in mind, we have synthesized heterogeneous solid sulfonic acid fabricated over biguanidine functionalized silica coated cobalt ferrite nanoparticles for its safer use. In addition to these, its immiscibility in organic solvents, high air and thermal stability, chemical stability, easy separation from the reaction medium, facile recyclability, non-hygroscopic nature, and excellent catalytic performance makes its utilization feasible in various fields.

In continuation of our research efforts in designing heterogeneous solid acid magnetic nanocatalyst for organic transformations [25], here, we wish to report the synthesis of biologically important 2-substituted benzimidazoles by condensation between o-phenylenediamine and aryl aldehydes using CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>@NH<sub>2</sub>@BG@SO<sub>3</sub>H (CFNP@SO<sub>3</sub>H) nanoparticles as heterogeneous catalyst.

#### 2. Experimental

#### 2.1. Catalyst preparation

### 2.1.1. Functionalization of silica-coated $CoFe_2O_4$ nanoparticles with amine groups

The cobalt ferrite nanoparticles (CoFe<sub>2</sub>O<sub>4</sub>) were prepared by one-pot solvothermal process [26]. Briefly, CoCl<sub>2</sub>·6H<sub>2</sub>O (297.4 mg, 1.25 mmol) and FeCl<sub>3</sub>·6H<sub>2</sub>O (676 mg, 2.5 mmol) were taken in 20 mL of ethylene glycol and stirred continuously at 50 °C to obtain a homogeneous mixture. After that, 1.8 g of sodium acetate (NaOAc) and 1.0 g of PEG-6000 were added to the above reaction mixture and further stirred for extra 30 min. The obtained liquid was then moved to a sealed Teflon-lined stainless steel autoclave and kept for 16 h at 160 °C. The black product obtained was extracted using an external magnet and then washed several times with double-deionized water. The resultant cobalt ferrite (CoFe<sub>2</sub>O<sub>4</sub>) nanoparticles were then dried for 6 h at 60 °C.

The coating of cobalt ferrite nanoparticles ( $CoFe_2O_4$ ) by silica was achieved using Stöber sol–gel method [27]. For this,  $CoFe_2O_4$  nanoparticles (200 mg, 0.852 mmol) in 200 mL solution (160 mL of ethanol and 40 mL of double deionized water) were sonicated and then 1.5 mL of ammonia solution and 1 mL of TEOS were added to the solution in dropwise manner. The dispersed mixture was then stirred continuously for 6 h at 60 °C. The silica coated nanoparticles ( $CoFe_2O_4@SiO_2$ ) were separated magnetically, washed several times with ethanol and dried under vacuum.

The NH<sub>2</sub> groups onto the surface of CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>, were introduced by the addition of 1 mL of APTES to 0.5 g of silica coated CoFe<sub>2</sub>O<sub>4</sub> nanoparticles dispersed in 100 mL of ethanol. The resultant solution was allowed to stir continuously for 6 h at 80 °C. The obtained CoFe<sub>2</sub>O<sub>4</sub>@-SiO<sub>2</sub>@NH<sub>2</sub> nanoparticles were magnetically collected, washed several times using ethanol for the removal of any unreacted silylating agent, and then allowed to dry under vacuum.

#### 2.1.2. Preparation of biguanidine functionalized nanocomposite (CFNP's)

In order to increase the catalytic sites, biguanidine moiety was incorporated on the surface of the nanocomposite. For this, 0.5 g of  $CoFe_2O_4@SiO_2@NH_2$  nanoparticles, 125 mg of dicyanodiamide, 0.3 mL of triethylamine were added to 10 mL of ethanol and the mixture was stirred continuously for 6 h at reflux conditions. The resulting  $CoFe_2O_4@SiO_2@NH_2@BG$  (CFNP) nanoparticles were separated magnetically, washed several times with ethanol and dried under vacuum for 6 h.

# 2.1.3. Preparation of final sulfonated CFNP@SO<sub>3</sub>H nanocatalyst (CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>@NH<sub>2</sub>@BG@SO<sub>3</sub>H)

The final nanocatalyst (CFNP@SO<sub>3</sub>H) was synthesized by sulfonation of surface amino groups present on CFNP's (Scheme 1 and Fig. S1). Briefly, 0.5 g of CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>@NH<sub>2</sub>@BG (CFNP) nanoparticles were added in 25 mL of dry DCM followed by addition of 2 mL of chlorosulfonic acid dropwise within 30 min. The reaction mixture obtained was subjected to continuous stirring until HCl evolution stops and then further stirring at room temperature for 12 h to certify complete functionalization. After this, the obtained solid acidic nanocatalyst was separated using an external magnet and washed several times with ethanol and deionized water. The resultant nanocatalyst (CFNP@SO<sub>3</sub>H) was dried under vacuum for 6 h.

### 2.2. General method for synthesis of 2-substituted benzimidazole derivatives

To a equimolar mixture of o-phenylenediamine (1.0 mmol), benzaldehyde (1.0 mmol) in 3 mL of ethanol, 20 mg of nanocatalyst (CFNP@SO<sub>3</sub>H) was added and the reaction solution was subjected to continuous magnetic stirring at room temperature. The reaction progress was closely monitored using TLC and after the verification of



Scheme 1. Systematic representation for the synthesis of CFNP@SO3H magnetic nanoparticles.

completion of reaction, the catalyst was removed from reaction mixture using an external magnet. After this, ice cold water was added to the reaction mixture leading to the formation of a precipitate. The crude product in form of precipitate formed was filtered off and dried. The crude product was then recrystallized using ethanol to afford the pure product.

#### 3. Results and discussion

#### 3.1. Catalyst characterization

#### 3.1.1. FT-IR spectroscopy

FT-IR spectra of  $CoFe_2O_4$ ,  $CoFe_2O_4$ @SiO<sub>2</sub>,  $CoFe_2O_4$ @SiO<sub>2</sub>@NH<sub>2</sub>, CFNP and CFNP@SO<sub>3</sub>H were collected at room temperature within range of 400–4000 cm<sup>-1</sup>, as depicted in Fig. 2.

The spectra of CoFe<sub>2</sub>O<sub>4</sub> nanoparticles visibly shows two absorption bands appearing at 881 and 547 cm<sup>-1</sup>, that can be allocated to the Co—O and Fe—O vibrations, whereas, the broad bands appeared around 3404 and 1648 cm<sup>-1</sup> are attributed to the stretching and bending vibrations respectively of the surface hydroxyl groups present (Fig. 2a). Further, the bands appearing at 792, 950, and 1068 cm<sup>-1</sup> in the spectra of CoFe<sub>2</sub>O<sub>4</sub>@Si can be assigned to the Si—O—Si symmetric, Si—O symmetric, and Si—O—Si asymmetric stretching modes, confirming existence of silica over the surface of CoFe<sub>2</sub>O<sub>4</sub> nanoparticles (Fig. 2b). For amine functionalized CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub> nanoparticles, two new bands appearing at 2920 and 1642 cm<sup>-1</sup>, can be ascribed to the CH<sub>2</sub> and amine groups, respectively, further confirming the functionalization of silica coated nanoparticles with NH<sub>2</sub> groups (Fig. 2c). Further, Fig. 2d and e



Fig. 2. FT-IR spectra results of (a)  $CoFe_2O_4$ , (b)  $CoFe_2O_4@SiO_2$ , (c)  $CoFe_2O_4@SiO_2@NH_2$ , (d) CFNP and (e) CFNP@SO<sub>3</sub>H.

signifies the FT-IR spectra of CFNP and CFNP@SO<sub>3</sub>H nanoparticles respectively. The appearance of two new peaks at 1087 cm<sup>-1</sup> and 985 cm<sup>-1</sup> corresponds to the asymmetrical and symmetrical stretching vibration of S $\equiv$ O bond in CFNP@SO<sub>3</sub>H, respectively (Fig. 2e). Thus the obtained results confirmed the successful functionalization with desired amino moiety along with the sulfonic acid group in silica coated cobalt ferrite nanoparticles.

#### 3.1.2. XRD analysis

In order to comprehend the structural integrity and crystalline phase structure of synthesized nanoparticles, X-Ray Diffraction patterns of CoFe<sub>2</sub>O<sub>4</sub>, CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>, and CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>@NH<sub>2</sub>@BG@SO<sub>3</sub>H (CFNP@SO<sub>3</sub>H) were obtained in the 2 $\Theta$  range of 5–80° at room temperature (Fig. 3). The distinctive Bragg diffraction peaks appearing at 30.24, 35.62, 43.33, 53.60, 57.27, and 62.79° can be assignable to (220), (311), (400), (422), (511), and (440) planes of the spinel cobalt ferrite nanoparticles. The observed peaks match very well with the standard XRD data of JCPDS card number (22–1086). Furthermore, the Bragg peaks for silica coated CoFe<sub>2</sub>O<sub>4</sub> and CFNP@SO<sub>3</sub>H were observed at same 2 $\theta$  values as for CoFe<sub>2</sub>O<sub>4</sub>, confirming that the structure of CoFe<sub>2</sub>O<sub>4</sub> nanoparticles remained intact even after surface modification.

#### 3.1.3. SEM and TEM analysis

The morphology of nanoparticles and their texture depiction was achieved by SEM and TEM analysis of synthesized CoFe<sub>2</sub>O<sub>4</sub>, CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>, and CFNP@SO<sub>3</sub>H nanoparticles and are shown in Fig. 4. The obtained SEM images for CoFe<sub>2</sub>O<sub>4</sub> corroborated the monodisperse nature as well as the formation of spherically shaped nanoparticles



Fig. 3. Powder XRD spectrum of (a)  $CoFe_2O_4$ , (b)  $CoFe_2O_4@SiO_2$  and (c)  $CFNP@SO_3H$ .



Fig. 4. SEM images of (a) CoFe<sub>2</sub>O<sub>4</sub>(b) CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>, (c) CFNP@SO<sub>3</sub>H and TEM images of (d) CoFe<sub>2</sub>O<sub>4</sub>(e) CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>, (f) CFNP@SO<sub>3</sub>H.

(Fig. 4a). Further, SEM analysis of silica coated and surface modified nanoparticles depicts the spherical shape of these nanoparticles (Fig. 4b and c). TEM analysis of these nanoparticles was also done revealing the spherical shape of  $CoFe_2O_4$  nanoparticles having a diameter approximately 200 nm (Fig. 4d). The EDX was also obtained for  $CoFe_2O_4$  which confirms the presence of Fe, Co and O as represented in (Fig. S1). TEM imaging of silica coated  $CoFe_2O_4$  nanoparticles validates the existence of approximately 30 nm uniform silica layer around the  $CoFe_2O_4$  core (Fig. 4e), preventing them from agglomeration. Furthermore, the TEM image of CFNP@SO<sub>3</sub>H substantiated the intact of similar spherical morphology along with an increase in the size of these nanoparticles (Fig. 4f).

Further, to gain knowledge of the stoichiometric distribution of elements in the synthesized CFNP@SO<sub>3</sub>H nanocatalyst, its EDX spectrum was collected. The obtained EDX spectrum revealed the presence of expected constituent elements like iron, cobalt, oxygen, silicon, carbon, nitrogen and sulfur in the sample (Fig. 5), further confirming the desired fabrication of nanocatalyst by acidic sulfonic group.

#### 3.1.4. Brunauer-Emmett-Teller (BET) surface area analysis

The N<sub>2</sub> adsorption-desorption isotherm was collected using BET analysis of solid acid catalyst (CFNP@SO<sub>3</sub>H) (Fig. 6) to determine the textural properties and to understand its porosity. The nanocatalyst showed BET surface area of 30.966 m<sup>2</sup>/g. The average pore diameter and pore volume determined using Barrett-Joyner- Halenda (BJH) were 4.88 nm and 0.0527 cm<sup>3</sup>/g, respectively (inset, Fig. 6). The pore diameter obtained indicated toward the mesoporous nature of the solid acid catalyst, Further, the existence of hysteresis loop in N<sub>2</sub> adsorption-desorption isotherm for CFNP@SO<sub>3</sub>H confirmed its mesoporous nature. The low pore volume can be due to presence of SO<sub>3</sub>H moieties in the pores of CFNP nanoparticles. Thus, the solid acid catalyst possessed sufficient surface on which the active sites were well dispersed, allowing them easily available to the reactants.

#### 3.1.5. VSM analysis

Magnetization of synthesized  $CoFe_2O_4$ ,  $CoFe_2O_4$ @SiO<sub>2</sub>,  $CoFe_2O_4$ @SiO<sub>2</sub>@NH<sub>2</sub>, CFNP and CFNP@SO<sub>3</sub>H were assessed using vibration sample magnetometer (VSM) at room temperature (Fig. 7). The magnetization values of the bare as well as functionalized nanoparticles



Lsec: 200.0 0 Cnts 0.000 keV Det: Octane Plus Det

**Fig. 5.** EDX of CFNP@SO<sub>3</sub>H.



Fig. 6.  $N_2$  adsorption-desorption isotherm of CFNP@SO<sub>3</sub>H. Inset: pore size distribution of CFNP@SO<sub>3</sub>H nanoparticles.



**Fig. 7.** Magnetization curves obtained through VSM at room temperature for (a)  $CoFe_2O_4$ , (b)  $CoFe_2O_4@SiO_2$ , (c) amine functionalized  $CoFe_2O_4@SiO_2$ , (d) CFNP and (e) CFNP@SO<sub>3</sub>H. Inset: Separation of nanocatalyst using an external magnet.

were measured in the presence of an external field sweeping between -10,000 and 10,000 Oe at room temperature. The absence of hysteresis phenomenon and coercivity in all cases illustrated the superparamagnetic nature of these synthesized nanoparticles. The value of saturation magnetization (Ms) for CoFe<sub>2</sub>O<sub>4</sub>, CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>, CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>@NH<sub>2</sub>, CFNP nanoparticles and for the final catalyst (CFNP@SO<sub>3</sub>H) were found to be 63, 52, 47, 34 and 27 emu/g, respectively. The decrease in values of saturation magnetization was observed on going from bare to surface modified nanoparticles. This decrease in the value of magnetism is owing to the fact of presence of non magn nonmagnetic silica and immobilization of various functional groups which results in reduction of the surface moments of individual particles [27]. In spite of the lower Ms value for the final catalyst, it is still significant and sufficient to attract CFNP@SO3H NPs from solution quickly upon application of the external magnetic field. The magnetic hysteresis measurement of recovered catalyst was also performed at room temperature and Ms value for these came out to be  $\sim 19$  emu/g, meaning that their recovery can be done efficiently and easily using an external magnet. Further, the magnetic solid acid catalyst (CFNP@SO3H) in reaction mixture can be dispersed easily simply by shaking resulting in the production of black coloured suspension. While, when an external magnet was used, the nanoparticles aggregates quickly within 30 s. Once the external magnet was detached, the nanoparticles redispersed quickly

with a slight shaking. Thus, the present solid acid catalyst demonstrates fast response to an external magnetic force and as a result, it can be collected effortlessly from the reaction medium, making it favourable for practical applications.

# 3.2. Catalytic activity evaluation of the sulfonated cobalt ferrite nanocatalyst in the synthesis of benzimidazoles

The catalytic ability of the synthesized sulfonated magnetic nanocatalyst (CFNP@SO<sub>3</sub>H) was explored in the synthesis of benzimidazole via a one-pot condensation reaction between o-phenylenediamine and benzaldehyde taking them as model substrates. Thereafter, the impact of various conditions such as amount of catalyst (CFNP@SO<sub>3</sub>H), solvent, and time period for the completion of reaction were studied in order to attain the best reaction conditions.

#### 3.2.1. Effect of catalyst amount on synthesis of benzimidazoles

In order to optimize our reaction conditions we started our investigation by exploring the role of synthesized sulfonated nanocatalyst in the synthesis of 2-substituted benzimidazoles. For achieving this goal, an equimolar mixture (1 mmol) of both the substrates were taken in the absence of nanocatalyst. The product was observed in trace amounts when the reaction was performed in the absence of catalyst suggesting the importance of catalyst to afford the high yield of desired benzimidazole product. Afterwards, to investigate the effect of amount of catalyst on the reaction, the chosen reaction of o-phenylenediamine and benzaldehyde was performed in the presence of a varying amount of synthesized sulfonated cobalt ferrite nanocatalyst (CFNP@SO3H). A remarkable increase in the yield with the reduction in time period for formation of benzimidazole product was observed when the amount of catalyst was increased from 5 mg to 20 mg which is attributed to the increase in number of the active catalytic sites (Fig. 8). Further, no such increase in conversion percentage was observed after additional increment up to 25 mg, owing to the exhaustion of active catalytic sites. Thus, 20 mg of catalyst was fixed for the maximum conversion and for further experiments.

#### 3.2.2. Effect of solvents

It was observed that the nature of solvent has a remarkable effect on the product formation. Solvents possess the ability to alter the reaction environment by changing the solubility of reagents, polarity and dispersing the catalyst. In order to achieve the excellent catalytic conversion, various solvents such as ethanol, acetonitrile,



Fig. 8. Effect of amount of catalyst on the synthesis of benzimidazole. [Reaction conditions: o-phenylenediamine (1.0 mmol), benzaldehyde (1.0 mmol), solvent (3 mL), rt].

dimethylformamide, water, chloroform, and dioxane for various time period were tested for the CFNP@SO3H catalysed formation of benzimidazoles (Fig. 9). After a close inspection of all obtained results, it was concluded that polar solvents such as ethanol, acetonitrile, water etc. resulted in increase of product yield as compared to non-polar solvents such as dioxane. On comparing results, ethanol was found to be the best solvent for the effective conversion of benzimidazoles in a shorter time period. The other reason for increase in yield of product in ethanol medium is better dispersion of nanocatalyst in this solvent. In order to prove that, the size distribution of CFNP@SO3H nanoparticles dispersed in various solvent was also determined using DLS experiment. The average size of these nanoparticles in ethanol determined by DLS studies came about 250 nm (Fig. 10) revealing that well dispersion of nanoparticles in ethanol which resulted in large surface area. The average size of nanoparticles obtained in ethanol medium is in well agreement with TEM results, whereas in case of other solvents like chloroform, water, dioxane etc. the average size was larger due to formation of aggregates (Fig. S6), which resulted in decrease in surface area of nanopartcles and thus decrease in yield of product. Further, ethanol being a green solvent, generation of waste was minimized and green chemistry parameters were followed. Hence, subsequent reactions were performed in an ethanol medium to obtain the desired products.

#### 3.2.3. Green chemistry parameters

The green chemistry metrices for the synthesis of model benzimidazole product were also inspected. Several parameters involved for the assessment of green approach in organic synthesis under optimized conditions are outlined in Table 1. The radar chart diagram among Efactor, atom economy, reaction mass efficiency and carbon efficiency displays a synergistic relationship between all these parameters, indicating the environmental sustainability of the current protocol (Fig. 11). All the calculations related to green chemistry parameters are described in supporting information file.

# 3.2.4. Scope of synthesis of 2-Substitututed benzimidazole derivatives using CoFe<sub>2</sub>O<sub>4</sub>@Si@NH<sub>2</sub>@BG@SO<sub>3</sub>H (CFNP@SO<sub>3</sub>H) nanoparticles

Based on the optimized reaction conditions, the synthesized sulfonated nanocatalyst was used to synthesize benzimidazole derivatives by condensation between o-phenylenediamine and various benzaldehydes. For this a mixture of o-phenylenediamine (1.0 mmol), benzaldehyde (1.0 mmol) and catalyst (20 mg) in 3 mL ethanol were allowed to react at room temperature for a specific period of time. A diverse range of valuable 2-substituted benzimidazole derivatives were synthesized in good to excellent yield by using various substituted benzaldehydes and aliphatic aldehydes. It was observed that the time period for completion of reaction and yield of product depends upon the electronic environment of the benzaldehydes used. The benzaldehyde derivatives having electron donating groups, the reaction proceeded in shorter period of



**Fig. 9.** Effect of various solvents and time period on the formation of benzimidazoles. [Reaction conditions: o-phenylenediamine (1.0 mmol), benzaldehyde (1.0 mmol) and catalyst (20 mg), rt].



Fig. 10. DLS size distribution curve of CFNP $@SO_3H$  nanoparticles dispersed in ethanol.

Table 1

Evaluation of Green	Chemistry Metrices.

Yield	atom economy	reaction mass	E-	carbon efficiency
	(AE)	efficiency (RME)	factor	(CE)
98 %	90.65	88.83 %	0.126	100 %



**Fig. 11.** Radar chart plot of green chemistry metrices calculated for the synthesis of model reaction product "3a" (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

time in comparison to the benzaldehydes having electron withdrawing groups (Scheme 2). Further, along with aromatic aldehydes, aliphatic aldehyde were also used to obtain benzimidazole derivatives in excellent yield (3p and 3q). In addition to benzaldehyde derivatives, the reaction of o-phenylenediamine with heteroatomic aldehyde (2 m) was also performed leading to the formation of the desired product (3 m) in good yield in slight longer reaction time period (25 min).

Further, the synthesis of benzimidazole (3a) was done at gram level for industrial point of view. In order to achieve that o-phenylenediamine (1) (10 mmol), and benzaldehyde (2a) (10 mmol) were allowed to react in ethanol medium in presence of 150 mg catalyst (CFNP@SO<sub>3</sub>H). It was observed that reaction proceeded smoothly and 1.7 g of 2-phenylbenzimidazole product could be synthesized within 1 h. Thus, the ability of the present catalytic system to scale up the reaction under milder reaction conditions and easy workup procedure are the additional advantages of current approach.

#### 3.2.5. Plausible reaction mechanism

A plausible mechanism for CFNP@SO<sub>3</sub>H catalysed formation of 2substituted benzimidazoles has been depicted in Fig. 12. Firstly, the solid sulfonated acidic catalyst protonates the oxygen atom of the carbonyl group of aromatic aldehyde resulting in an increase of electrophilicity of carbonyl atom. This facilitates the activity of aromatic



Scheme 2. Substrate scope for the synthesis of 2-substituted benzimidazoles.



Fig. 12. Plausible reaction mechanism for the synthesis of 2-substituted benzimidazole using CFNP@SO<sub>3</sub>H nanoparticles.

aldehyde to react with one  $NH_2$  group of o-phenylenediamine to form Schiff's base. Then, the second  $NH_2$  group of o-phenylenediamine donates a lone pair of electron to carbon of the intermediate resulting in formation of five membered ring through intramolecular ring closing. The proton of the positively charged N was abstracted by the negatively charged catalyst resulting in regeneration of sulfonated catalyst. The intermediate thus formed, produces 2-substituted benzimidazole through removal of H<sup>+</sup> ions in presence of atmospheric oxygen. 3.2.6. Quantification of sulfonic acid loading on CFNP@SO<sub>3</sub>H

In order to determine the amount of acid over the surface of catalyst (CFNP@SO<sub>3</sub>H), simple back titration method was employed. Briefly, exactly 10 mg of CFNP@SO<sub>3</sub>H nanocatalyst was added to 10 mL aqueous KCl solution (1 M) and the resultant mixture was subjected to sonication for half an hour. Afterwards, the pH of the resultant solution reduced to 2, demonstrating an ion exchange took place between protons of nanocatalyst and the potassium ions. Later on, the magnetic nanocatalyst was collected from the mixture with the help of an external magnet, and remaining supernatant was subjected to collected supernatant and titrated with standardized 0.1 M KOH solution, till the neutralization point is reached, to evaluate the active acid amount on the magnetic nanocatalyst calculated using back titration method came out to be 2.48 mmol g<sup>-1</sup>.

### 3.2.7. Investigation of recyclability of magnetic sulfonated cobalt ferrite (CFNP@SO<sub>3</sub>H) nanocatalyst

Taking into consideration various parameters of green chemistry, industrial application, recovery and reusability of catalyst are two utmost essential characteristics that lead towards its large scale application. Thus the recyclability of nano catalyst was assayed using ophenylenediamine and benzaldehyde as model substrates. After the completion of the reaction, the catalyst was removed from the reaction medium by utilizing an external magnet followed by washing with ethanol and drying at 60 °C under vacuo. Afterwards, the recovered solid acid catalyst was subjected to consecutive runs of the identical model reaction under the similar reaction conditions. The results of recycling experiment indicated that the nanocatalyst can be recovered



Fig. 13. Recyclability of synthesized CFNP@SO $_3$ H catalyst for the model reaction under same reaction conditions.

effortlessly and also can be reused for seven successive cycles deprived of any considerable loss of its catalytic activity (Fig. 13). The slight decrease in the activity of the catalyst can be attributed to the pore blockage with reactants or products. Further, to confirm the true heterogeneous nature of catalyst and to investigate the leaching of acidic SO<sub>3</sub>H group into the reaction mixture, the solid acid catalyst (CFNP@SO3H) was detached from the reaction medium using an external magnet after 4 min. The remaining reaction solution was permitted to react further under similar reaction conditions. This experiments exhibited that no further reaction progress was detected even after 20 min (Fig. S7), whereas the unperturbed reaction showed the continuous increase in yield of benzimidazole product. Thus leaching experiment results demonstrated the heterogeneous nature of present catalyst and indicated towards the absence of any catalytic active species in the filtrate which proves the stability of sulfonated group over the surface of nanoparticles. The results was further verified by the Powder XRD, SEM and TEM of the catalyst collected after the 7th run (supporting information). On comparing results of fresh and recovered catalyst it was revealed that the structure and morphology of the acidic nanocatalyst remained almost unaffected even after seven runs

#### Table 2

Previou	sly repo	rted method	s and cata	lyst for	the formation	on of	benzimida	zoles
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S. No.	Catalyst	Solvent/Temp	Reaction time/ Yield (%)	Ref.
1.	[NiL <sub>1</sub> (PPh <sub>3</sub> )] (0.5 mol%)	Ethanol/rt	2-3 h/94 %	[1]
2.	NaHSO <sub>3</sub>	DMF/80 °C	95 %	[28]
3.	Graphene oxide (20 mg)	<sup>°</sup> C	3 h/82 %	[29]
4.	Resin Supported Ionic Liquids/ Iodide and BPO as oxidant (0.2 equiv.)	Water/rt	5 h/95 %	[30]
5.	PBA@SMNP	Ethanol/50 °C	30 min/95 %	[31]
6.	Sulfonated carbon- encapsulated iron nanoparticles	Ethanol/40 °C	50 min/95 %	[9]
7.	{Mo <sub>72</sub> V <sub>30</sub> } (0.05 mol%)	EtOAc, O <sub>2</sub> balloon/ 70 °C	4 h/95 %	[32]
8.	Pd(dppf)Cl <sub>2</sub>	°C	24 h/97 %	[33]
9.	Ce(NO <sub>3</sub> ) <sub>3</sub> .6H <sub>2</sub> O	DMF/80 °C	90 min/93 %	[34]
11.	Cu(II)-TD@nSiO <sub>2</sub>	EtOAc, 50 °C.	15–100 min/ 96 %	[35]
12.	GLR-G2-Cu polymer	Ethanol/air/ 30 °C	1 h/95 %	[36]
13.	GO-VB1 (30 mg)	Ethanol/rt	30 min/95 %	[37]
14.	CuMVs (2 ppm, 20 mL),	Water/30 °C	45 min/96 %	[ <mark>16</mark> ]
15.	MTF-1E (20 mg)	Water/ 40 °C	3 h/97 %	[38]
16.	Fe <sub>3</sub> O <sub>4</sub> @SiO <sub>2</sub> @(NH <sub>4</sub> )6Mo <sub>7</sub> O <sub>24</sub> (0.22 g)	Ethanol/H <sub>2</sub> O <sub>2</sub> (0.2 mL)/rt	30 min/95 %	[39]
17.	CFNP@SO3H (20 mg)	Ethanol/rt	10-25 min/	PW

indicating towards the stability and durability of the catalyst.

### 3.2.8. Comparison of CFNP@SO<sub>3</sub>H catalysed formation of 2-Substituted benzimidazoles with reported precedents

An extensive literature survey suggests that various homogeneous as well as heterogeneous catalysts have been described for the formation of 2-substituted benzimidazoles (Table 2). Despite of all these, magnetic solid acid CFNP@SO<sub>3</sub>H nanocatalyst exhibited its predominance in terms of ambient reaction conditions, catalyst loading, time period, product yield, extensive functional group tolerance, catalytic magnetic retrievability and recyclability. The outstanding performance of the present magnetic solid acid nanocatalyst is due to the existence of large number of sulfonated catalytic sites responsible for the formation of the desired product. Therefore, the present catalytic system presents a clean and green approach using ethanol an environmental benign solvent, easy work up procedure and recyclability of sulfonated nanocatalyst by simply applying magnetic forces.

#### 4. Conclusions

In summary, we have explored the performance of newly developed sulfonated magnetic cobalt ferrite nanocatalyst (CFNP@SO<sub>3</sub>H) for the synthesis of biologically important 2-substituted benzimidazoles. The salient features of the present protocol includes ambient reaction conditions, shorter reaction period (10-25 min), low catalyst loading, broad substrate scope and high yield of products. Along with these, the nanocatalyst can be recovered easily from the reaction mixture by simple magnetic attraction as it displayed saturation magnetization value of 27 emu/g and possess recyclability up to 7 consecutive cycles without any significant loss in activity. In addition, reaction simplicity, the use of non-toxic chemicals, cost, use of environment benign solvent "ethanol", and simple workup procedure make this methodology a green and sustainable approach for the large scale synthesis of 2-substituted benzimidazoles. Further, we are in opinion that the developed nanocatalyst has the flexibility of immobilizing various chemical moieties onto it which could promote several other industrially substantial organic transformation reactions in an environmentally benign conditions.

#### CRediT authorship contribution statement

**Priyanka Yadav:** Conceptualization, Methodology, Software, Visualization, Writing - original draft. **Praachi Kakati:** Software, Validation, Writing - review & editing. **Preeti Singh:** Writing - original draft, Writing - review & editing. **Satish K. Awasthi:** Supervision.

#### **Declaration of Competing Interest**

The authors report no declarations of interest.

#### Acknowledgements

PY and PS acknowledges University Grant Commission, Delhi, India, for awarding Senior Research Fellowship. The authors acknowledges USIC, University of Delhi, Delhi, for providing instrumentation facilities. Authors also acknowledges SAIF, AIIMS New Delhi, for TEM facility. SKA acknowledges financial support from DST-SERB (SERB/F/ 9974T20-17), New Delhi, India.

### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.apcata.2021.118005.

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