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# A highly efficient magnetic solid acid catalyst for synthesis of 2,4,5-trisubstituted imidazoles under ultrasound irradiation

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### ABSTRACT

Fe<sub>3</sub>O<sub>4</sub> nanoparticles were prepared by chemical coprecipitation method and subsequently coated with 3-aminopropyltriethoxysilane (APTES) via silanization reaction. Grafting of chlorosulfuric acid on the amino-functionalized Fe<sub>3</sub>O<sub>4</sub> nanoparticles afforded sulfamic acid-functionalized magnetic nanoparticles (SA-MNPs). SA-MNPs was found to be a mild and effective solid acid catalyst for the efficient, one-pot, three-component synthesis of 2,4,5-trisubstituted imidazoles under ultrasound irradiation. This protocol afforded corresponding imidazoles in shorter reaction durations, and in high yields. This green procedure has many obvious advantages compared to those reported in the previous literatures, including avoiding the use of harmful catalysts, easy and quick isolation of the products, excellent yields, short routine, and simplicity of the methodology.

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### 1. Introduction

During the past decades, advances in nanoscience and nanotechnology have pushed forward the synthesis of functional magnetic nanoparticles (MNPs), which is one of the most active research areas in advanced materials. MNPs that have unique magnetic properties and other functionalities have enabled a wide spectrum of applications [1]. Iron oxide magnetic nanoparticles ( $Fe_3O_4$ -MNPs) are approximately 20–30 nm in size containing a single magnetic domain with a single magnetic moment and exhibit superparamagnetism [2]. Surface functionalized iron oxide magnetic nanoparticles (MNPs) are a kind of novel functional materials, which have been widely used in biotechnology and analysis. Magnetic nanocatalysts can easily be separated and recycled from the products by an external magnet. Moreover, their catalytic performance is enhanced, for the available surface area of the nonporous MNPs is external and the internal diffusion is practically avoided [3].

On the other hand, solid acid catalysts such as clays, zeolites, sulfated metal oxides or carbons and heteropolyacids have already attracted extensive research interests [4–7]. Among these solid acid catalysts, magnetically recyclable nanocatalyst systems, are unique due to simple work-up procedure, ease of separation, and higher catalytic activity, etc. [1,3].

Imidazole derivatives are a very interesting class of heterocyclic compounds because they have many pharmacological properties and play important roles in biochemical processes [8–10]. A number of methods have been developed for the synthesis of 2,4,5-trisubstituted imidazoles. Several methods are used for synthesis of multi-substituted imidazoles [11–22]. Recently, one-pot condensations of an aldehyde and ammonium acetate with an  $\alpha$ -hydroxy ketone, an  $\alpha$ -keto oxime, or a 1,2-diketone have been achieved by using a variety acid catalysts, for example silica sulfuric acid [23,24], boric acid [25], phosphomolybdic acid [26], H<sub>2</sub>SO<sub>4</sub> [27], H<sub>3</sub>PO<sub>4</sub> [28], oxalic acid [29], *p*-toluenesulfonic acid [30].

Despite their potential utility, some of these methods are not environmentally friendly and suffer from one or more disadvantages, for example hazardous reaction conditions, complex workup and purification, strongly acidic conditions, high temperature, poor yields, occurrence of side reactions, and long reaction time. Therefore, the development of a mild general method to overcome these shortcomings remains a challenge for organic chemists in the synthesis of highly substituted imidazoles [10,31].

During the last three decades, ultrasound-accelerated organic chemical reactions have been increasingly developed by researchers across the globe for the synthesis of organic molecules. Ultrasound irradiation offers an alternative energy source for organic reactions which are ordinarily accomplished by heating. Ultrasound- assisted reactions proceed by the formation, growth and collapse of acoustic bubbles in the reaction medium. These directly help in shortening the time span of reactions and increasing the yield of products [32].

In this study, we report immobilization of sulfamic acid groups on the magnetic  $Fe_3O_4$  nanoparticles, as a new heterogeneous



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**Scheme 1.** One-pot synthesis of 2,4,5-trisubstituted imidazoles catalyzed by SA-MNPs under ultrasound irradiation at ambient temperature.

catalyst for the synthesis of trisubstituted imidazoles via one-pot condensation of 1,2-diketone 1 with aldehyde 2 and NH<sub>4</sub>OAc under ultrasound irradiation (Scheme 1). This method is an efficient and rapid ultrasonic assisted route for the synthesis of a range of trisubstituted imidazoles.

### 2. Experimental

### 2.1. Chemicals and apparatus

Chemical reagents in high purity were purchased from the Merck Chemical Company. All materials were of commercial reagent grade. Melting points were determined in open capillaries using an Electrothermal Mk3 apparatus and are uncorrected. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded with a Bruker DRX-400 spectrometer at 400 and 100 MHz respectively. NMR spectra were obtained in DMSO- $d_6$  solutions and are reported as parts per million (ppm) downfield from tetramethylsilane as internal standard. The abbreviations used are: singlet (s), doublet (d), triplet (t) and multiplet (m). FT-IR spectra were obtained with potassium bromide pellets in the range 400–4000 cm<sup>-1</sup> with a Perkin–Elmer 550 spectrometer. A mass spectrum was recorded by a QP-1100EX Shimadzu spectrometer. The element analyses (C, H, N) were obtained from a Carlo ERBA Model EA 1108 analyzer carried out on Perkin-Elmer 240c analyzer. The UV-vis measurements were obtained with a GBC cintra 6 UV-vis spectrophotometer. Nanostructures were characterized using a Holland Philips Xpert X-ray powder diffraction (XRD) diffractometer (CuK, radiation,  $\lambda$  = 0.154056 nm), at a scanning speed of 2°/min from 10° to 100°  $(2\theta)$ . Scanning electron microscope (SEM) was performed on a FEI Quanta 200 SEM operated at a 20 kV accelerating voltage. The samples for SEM were prepared by spreading a small drop containing nanoparticles onto a silicon wafer and being dried almost completely in air at room temperature for 2 h, and then were transferred onto SEM conductive tapes. The transferred sample was coated with a thin layer of gold before measurement. Sonication was performed in Shanghai Branson-BUG40-06 ultrasonic cleaner (with a frequency of 35 kHz and a nominal power 200 W) estimated calorimetrically [33]. A circulating water bath (DC2006, Shanghai Hengping Apparatus Factory) with an accuracy of 0.1 K was adopted to keep the reaction temperature at a constant.

### 2.2. Preparation of solid acid catalyst

Fe<sub>3</sub>O<sub>4</sub>-MNPs were prepared using chemical coprecipitation described in the literature [34] and subsequently were coated with 3-aminopropyltriethoxysilane to achieve aminofunctionalized magnetic nanoparticles APTES-MNPs [35]. Sulfamic acid-functionalized magnetic Fe<sub>3</sub>O<sub>4</sub> nanoparticles was prepared by means of a procedure reported elsewhere [3]. In short, The APTES-MNPs (500 mg) were dispersed in dry CH<sub>2</sub>Cl<sub>2</sub> (3 ml) by ultrasonic bath for 10 min. Subsequently, chlorosulfuric acid (1 ml) was added dropwise over a period of 30 min at room temperature. Hydrogen chloride gas evolved from the reaction vessel immediately. Then, the as prepared functionalized MNPs nanoparticles were separated by magnetic decantation and washed three times with dry CH<sub>2</sub>Cl<sub>2</sub> to remove the unattached substrates.

### 2.3. General procedure for the synthesis of 2,4,5-trisubstituted imidazoles under silent condition

A mixture of benzil (1 mmol), aldehyde (1 mmol), ammonium acetate (0.4 g, 5 mmol) and SA-MNPs (0.1 g) in 10 ml ethanol was taken in a 50 ml flask and the reaction mixture was stirred under reflux conditions. After the completion of the reaction (monitored by TLC), the reaction was allowed to cool and the catalyst was separated by an external magnet. The reaction mixture was concentrated on a rotary evaporator under reduced pressure and the solid product obtained was dissolved in acetone and filtered. The product was washed with water and recrystallized from acetonewater 9:1 (v/v) to produce the desired product 5a as white solid in 90% yield.

## 2.4. General procedure for the synthesis of 2,4,5-trisubstituted imidazoles ultrasonic irradiation

A 25 mL Erlenmeyer flask was charged with benzil (1 mmol), aldehyde (1 mmol), ammonium acetate (0.4 g, 5 mmol), SA-MNPs (0.1 g) and ethanol (10 mL). The reaction flask was located in the ultrasonic bath, where the surface of reactants is slightly lower than the level of the water, and irradiated under 20, 40, 60, 80 and 100% of the power of the ultrasonic bath and the temperature inside the reactor at 40 °C for the period of time (The reaction was monitored by TLC) separately as indicated in Table 4. After the reaction was completed, the catalyst was separated by an external magnet and reused as such for the next experiment. The reaction mixture was concentrated on a rotary evaporator under reduced pressure and the solid product obtained was dissolved in acetone and filtered. The solid product obtained was washed with water and recrystallized from acetone–water 9:1 (v/v) to offer pure product 3a in 98% vield. All products were known and characterized by comparison of their physical and spectra data with those already reported [31].

### 2.5. Spectroscopic data of selected compounds

2-(3-Nitrophenyl)-4,5-bis(4-methoxyphenyl)-1H-imidazole (**30**). Yellow solid. IR (KBr) ( $v_{max}/cm^{-1}$ ): 3428 (NH), 1615 (C=C), 1523 (C=N), 1460 (N=O), 1348 (N=O), 1249 (C=O); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ ):  $\delta_H$  12.92 (s, 1H, NH), 8.92 (s, 1H, Ar–H), 8.50 (d, 1H, J = 8.2 Hz, Ar–H), 8.20 (d, 1H, J = 8.2 Hz, Ar–H), 7.75 (t, 1H, J = 8.2 Hz, Ar–H), 7.47 (d, 2H, J = 8.4 Hz, Ar–H), 7.43 (d, 2H, J = 8.4 Hz, Ar–H), 7.00 (d, 2H, J = 8.4 Hz, Ar–H), 6.90 (d, 2H, J = 8.4 Hz, Ar–H), 3.80 (s, 3H, OMe), 3.75 (s, 3H, OMe) ppm; <sup>13</sup>C NMR (100 MHz, DMSO- $d_6$ ):  $\delta_C$  159.4, 158.6, 148.8, 143.1, 137.5, 132.5, 131.4, 130.8, 130.2, 128.8, 128.7, 127.9, 123.5, 122.7, 119.7, 114.6, 114.1, 55.7, 55.5 ppm; Anal. Calcd. for C<sub>23</sub>H<sub>19</sub>N<sub>3</sub>O<sub>4</sub>: C, 68.82; H, 4.77; N, 10.47%. Found: C, 68.79; H, 4.75; N, 10.44%.

2-(3-methoxyphenyl)-4,5-bis(4-methoxyphenyl)-1*H*-imidazole (3p). White solid. IR (KBr) ( $v_{max}/cm^{-1}$ ): 3430 (N–H), 1608 (C=C), 1519 (C=N), 1246 (C–O); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ ):  $\delta_H$  12.50 (s, 1H, NH), 7.64 (d, 1H, *J* = 8.0 Hz, Ar–H), 7.62 (s, 1H, Ar–H), 7.36–7.46 (m, 5H, Ar–H), 7.00 (d, 2H, *J* = 8.4 Hz, Ar–H), 6.91 (dd, 1H, *J* = 8.4, 2.2 Hz, Ar–H), 6.87 (d, 2H, *J* = 8.4 Hz, Ar–H), 3.82 (s, 3H, OMe), 3.79 (s, 3H, OMe), 3.74 (s, 3H, OMe) ppm; <sup>13</sup>C NMR (100 MHz, DMSO- $d_6$ ):  $\delta_C$  160.0, 158.9, 158.2, 145.1, 136.2, 132.3, 130.2, 130.2, 128.6, 128.2, 127.2, 124.1, 117.0, 115.5, 114.4, 114.3, 110.5, 55.6, 55.5, 55.5 ppm; Anal. Calcd. for C<sub>24</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub>: C, 74.59; H, 5.74; N, 7.25%. Found: C, 74.58; H, 5.75; N, 7.24%.

5-[4,5-Bis(4-methoxyphenyl)-1H-imidazol-2-yl]-2- methoxyphenol (**3q**). Ash-gray solid. IR (KBr) ( $v_{max}/cm^{-1}$ ): 3424 (N–H), 3320 (O-H), 1615 (C=C), 1504 (C=N), 1249 (C-O); <sup>1</sup>H NMR (400 MHz. DMSO-*d*<sub>6</sub>): *δ*<sub>H</sub> 12.26 (s, 1H, NH), 9.11 (s, 1H, OH), 7.52 (s, 1H, Ar-H), 7.37-7.46 (m, 6H, Ar-H), 6.98 (d, 2H, J = 8.4 Hz, Ar-H), 6.86 (d, 2H, J = 8.4 Hz, Ar-H), 3.80 (s, 3H, OMe), 3.78 (s, 3H, OMe), 3.73 (s, 3H, OMe) ppm; <sup>13</sup>C NMR (100 MHz, DMSO- $d_6$ ):  $\delta_C$  159.1, 158.7, 148.4, 146.9, 145.6, 129.8, 129.2, 128.4, 126.3, 126.0, 123.5, 124.1, 116.8, 114.3, 114.0, 113.2, 112.5, 56.1, 55.5, 55.1 ppm; Anal. Calcd. for C<sub>24</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub>: C, 71.63; H, 5.51; N, 6.96%. Found: C, 71.61; H, 5.49; N, 6.95%.

### 3. Results and discussion

FeCl<sub>3</sub> + FeCl<sub>3</sub>

NaOH Ar atmosphere

### 3.1. Characterization of SA-MNPs as solid acid catalyst

The magnetite nanoparticles of 18-20 nm were prepared by coprecipitation of iron(II) and iron(III) ions in basic solution at 85 °C using the method described by Massart [34]. For the surface modification, the magnetic nanoparticles coated with 3-aminopropyltriethoxysilane (APTES) to achieve aminofunctionalized magnetic nanoparticles. Ultimately, the reaction of amino groups with chlorosulfuric acid led to sulfamic acid-functionalized magnetic Fe<sub>3</sub>O<sub>4</sub> nanoparticles (SA-MNPs) (Scheme 2).

The number of H<sup>+</sup> sites of SA-MNPs was determined by pH-ISE conductivity titration (Denver Instrument Model 270) and found to be 1.25 H<sup>+</sup> sites per 1 g of solid acid at 25 °C (pH 2.30). Titration carried out under sonication and the number of available H<sup>+</sup> is the same under the silence and the sonication, however, the temperature must be constant. Like any other equilibrium constant, the value of  $K_w$  for H<sub>2</sub>O varies with temperature. Its value is usually taken to be  $1.00 \times 10^{-14} \text{ mol}^2 \text{ dm}^{-6}$  at room temperature. Fig. 1 presents the XRD-diffraction patterns of the prepared Fe<sub>3</sub>O<sub>4</sub>-MNPs, APTES-MNPs, and SA-MNPs. The position and relative intensities of all peaks confirm well with standard XRD pattern of Fe<sub>3</sub>O<sub>4</sub> (JCPDS card No. 79-0417) indicating retention of the crystalline cubic spinel structure during functionalization of MNPs. The XRD patterns of the particles show six characteristic peaks reveal a cubic iron oxide phrase (2*θ* = 30.35, 35.95, 43.45, 53.70, 57.25, 62.88, 71.37, 74.46). These are related to their corresponding indices (220), (311), (400), (331), (422), (333), (440) and (531), respectively [34]. It is implied that the resultant nanoparticles are pure  $Fe_3O_4$  with a spinel structure and that the grafting process did not induced any phase change of Fe<sub>3</sub>O<sub>4</sub>. A weak broad band  $(2\theta = 18-27^{\circ})$  appeared in the the SA-MNPs which could be assigned to the amorphous silane shell formed around the magnetic cores [36].



Fe<sub>3</sub>O<sub>4</sub> nanoparticles.



Fig. 1. XRD patterns of (a) MNPs, (b) APTES–MNPs and (c) SA-MNPs.

$$D(hkl) = \frac{0.94\lambda}{\beta\cos\theta}$$

NHSO\_H

CISO<sub>3</sub>H, dry CH<sub>2</sub>Cl<sub>2</sub>

where D(hkl) is the average crystalline diameter, 0.94 is the Scherrer's constant,  $\lambda$  is the X-ray wavelength,  $\beta$  is the half width of XRD diffraction lins and  $\theta$  is the Bragg's angle in degree. Here, the (311) peak of the highest intensity was picked out to evaluate the particle diameter of the nanoparticles. MNPs and SA-MNPs were calculated to be 18 nm and 20 nm, respectively. Fig. 2 shows the Fourier transform infrared (FTIR) spectra of both the unfunctionalized and functionalized magnetic nanoparticles. The Fe-O stretching vibration near 580 cm<sup>-1</sup>, O-H stretching vibration near 3432 cm<sup>-1</sup> and O-H deformed vibration near 1625 cm<sup>-1</sup>were observed for both in Fig. 2(a) and (b). The significant features observed for Fig. 2(b) are the appearance of the peaks at  $1002 \text{ cm}^{-1}$  (Si–O stretching) and at  $2800 \text{ cm}^{-1}$  (-CH<sub>2</sub> stretching). The peak at  $3423 \text{ cm}^{-1}$  in Fig. 2(b) was probably attributed to the free amino groups, which is overlapped by the O-H stretching vibration. These



Fig. 2. The comparative FT-IR spectra for (a) MNPs, (b) APTES-MNPs and (c) SA-MNPs.



Fig. 3. Magnetization curves for the prepared MNPs and SA-MNPs at 40 °C.

results provided the evidences that the amino groups were successfully attached to the surface of Fe<sub>3</sub>O<sub>4</sub> nanoparticles [37]. Reaction of APTES–MNPs with chlorosulfuric acid produces SA-MNPs in which the presence of sulfonyl moiety is asserted with 1217 and 1124 cm<sup>-1</sup> bands in FT-IR spectra [3].

The magnetization curve for  $Fe_3O_4$  nanoparticles and SA-MNPs is shown in Fig. 3. Room temperature specific magnetization (*M*) versus applied magnetic field (*H*) curve measurements of the

sample indicate a saturation magnetization value ( $M_s$ ) of 52.3 emu g<sup>-1</sup>, lower than that of bare magnetic nanoparticles (60.7 emu g<sup>-1</sup>) due to the coated shell. In Fig. 4 we can also see that the two magnetization curves both follow a Langevin behavior over the applied magnetic field and the coercivity ( $H_c$ ) could be ignored, which can be considered as superparamagnetism [37].

The sulfamic acid-functionalized magnetic  $Fe_3O_4$  nanoparticles could be separated to the sidewall of the container after 30 s. using a magnet of 2000 Gs, suggesting the obtained magnetic microspheres had an excellent magnetic responsivity, which prevents composite microspheres from aggregation and enables them to redisperse rapidly when the magnetic field is removed.

The SEM image shows that magnetite (Fe<sub>3</sub>O<sub>4</sub>) particles have a mean diameter of about 18 nm and a nearly spherical shape in Fig. 4(a) and (b) shows that APTES–MNPs particles still keep the morphological properties of Fe<sub>3</sub>O<sub>4</sub> except for a slightly larger particle size and smoother surface, which silica are uniform coated on the Fe<sub>3</sub>O<sub>4</sub> particles to form silica shell. Compared to the APTES–MNPs, The SEM image shown in Fig. 4(c) demonstrates that SA-MNPs nanoparticles are nearly spherical with more than 20 nm in size.

### 3.2. Evaluation of the catalytic activity of SA-MNPs through the synthesis of 2,4,5-trisubstituted imidazoles

To achieve suitable conditions for the synthesis of 2,4,5-trisubstituted imidazoles, various reaction conditions have been investigated in the reaction of 4-methoxybenzaldehyde 2b, benzil 1a, and



SEM HV 30.00 kV WD 7 4976 mm LIIIIIII VEGAILTESCAI SEM MAG: 100.00 kx Det SE 200 nm Sav / field: 1.445 µm PC: 19 Performance in nanospace

Fig. 4. The SEM image of (a) MNPs, (b) APTES-MNPs and (c) SA-MNPs.



Scheme 3. Standard model reaction.

ammonium acetate as a model reaction (Scheme 3). We examined the effect of different solvents such as EtOH, MeOH, THF, DMF, CH<sub>3</sub>CN, and DCM on a model reaction under ultrasound irradiation (power intensity: 40%) at 40 °C. The results were summarized in Table 1. The use of 0.008 g of SA-MNPs in ethanol afforded a 86% yield (Table 1, entry 1) of the desired product. Therefore EtOH was chosen as solvent of reaction.

After this, the reaction was performed in the presence of 0.005, 0.008, 0.1, 0.12 and 0.15 g of SA-MNPs (Table 2) with and without ultrasonic irradiation. In all cases, the experimental results shows that the reaction times are shorter and the yields of the products are higher under sonication. The reason may be the phenomenon of cavitation produced by ultrasound. Cavitation is the origin of sonochemistry, a physical process that creates, enlarges, and implodes gaseous and vaporous cavities in an irradiated liquid, thus enhancing the mass transfer and allowing chemical reactions to occur. Applying ultrasound, compression of the liquid is followed by rarefaction (expansion), in which a sudden pressure drop forms small, oscillating bubbles of gaseous substances. these bubbles are small and rapidly collapse, they can be seen as microreactors that offer the opportunity of speeding up certain reactions and also allow mechanistically novel reactions to take place in an absolutely safe manner [32,38,39]. The best results were obtained using 0.1 g of the catalyst under both conditions (Table 2, entry 4). As shown, in the absence of catalyst the yield of the product was found to be low (Table 2, entry 1).

In order effect of intensity power of ultrasonic on reaction, the reaction was also performed at 20%, 40%, 60%, 80% and 100% of

#### Table 1

Screening of solvent effect on model reaction.<sup>a</sup>

Entry	Solvent	Time (min)	Yield (%) <sup>b</sup>
1	Ethanol	30	86
2	Methanol	30	60
3	DCM	30	15
4	DMF	30	32
5	THF	30	35
6	Acetonitril	30	48

<sup>a</sup> Reaction of benzil, 4-methoxybenzaldehyde and ammonium acetate (1:1:5) in presence of SA-MNPs (0.008) as a catalyst under ultrasonic irradiation with power intensity of 40% at 40  $^{\circ}$ C.

<sup>b</sup> Isolated yield based on aldehyde.

#### Table 2

Comparison of reaction time and yields with or without sonication for the synthesis of 3b product.

Entry	Catalyst (g)	With sonic	cation <sup>a</sup>	Without sonication <sup>b</sup>		
		Yield (%)	Time (min)	Yield (%)	Time (min)	
1	0	10	35	15 <sup>b</sup> (5) <sup>a</sup>	180	
2	0.005	50	35	30 <sup>b</sup>	180	
3	0.008	70	35	72 <sup>b</sup>	180	
4	0.1	92	35	90 <sup>b</sup>	180	
5	0.12	92	35	90 <sup>b</sup>	180	
6	0.15	93	45	92 <sup>b</sup>	210	

<sup>a</sup> Under ultrasonic waves (power intensity: 40%) at 40 °C.

<sup>b</sup> Reflux condition.

Table 3 The effect of intensity power of ultrasonic on the synthesis of  $3^{\rm b}$ .

Max power	20%	40%	60%	80%	100%
intensity (W)	(40 W)	(80 W)	(120 W)	(160 W)	(200 W)
Time (min) Yields (%)	40 (85)	35 (92)	30 (97)	30 (90)	30 (87)

<sup>b</sup> Isolated yields.

the rate power of the ultrasonic bath (40, 80, 120, 160 and 200 W). The results were showed in Table 3. The intensity of sonication is proportional to the amplitude of vibration of the ultrasonic source and, as such, an increment in the amplitude of vibration will lead to an increase in the intensity of vibration and to an increase in the sonochemical effects. Increase of ultrasonic powerled to relatively higher yield and shorter reaction time before the ultrasound power intensity reached 60%, and then the yield decreased slightly with increasing ultrasound power intensity. Generally, The increase in the acoustic power could increase the number of active cavitation bubbles and also the size of the individual bubbles. Both increases can be expected to result in an increase in the maximum collapse temperature [40], and the respective reaction could be accelerated.

Moreover, when ultrasonic intensity exceeded the optimal value, a large number of gas bubbles exist in the solution and a lesser level of energy is focused on the reaction vessel because of the scattering effect of gas bubbles on the sound waves. The use of high ultrasonic intensity does not always lead to good results. On the other hand, it is possible the coalescence of the cavities in the presence of large number of cavities resulting in the formation of a large cavity which collapses less violently. So with the inordinate increase in the operating intensity, the utilization efficiency of ultrasound would decrease and the reaction yield decreased too [41].

Using the optimized reaction conditions, this process was demonstrated by the wide range of substituted and structurally divers aldehydes to synthesize the corresponding products in high to excellent yields (Table 4, method A). Aldehydes bearing either electron-withdrawing or electron-donating groups perform equally well in the reaction and all imidazoles were obtained in high yields. For more examination of the influence of ultrasound irradiation in this transformation, comparison of the reaction under two methods, ultrasound irradiation at 40 °C (method A) and reflux conditions (method B) was performed. As illustrated in Table 4, method A in comparison with method B is better in both yields and especially in the reaction times (see Table 4).

A plausible mechanism for the formation of trisubstituted imidazoles is envisaged in Scheme 4. A plausible mechanism for these reactions is that aldehyde and 1,2-diketone are first activated by SA-MNPs (H<sup>+</sup>) to afford A and B respectively. Then, imine intermediate (A), condenses further with the carbonyl carbon of 1,2 diketone imine (B) and formation of carbocation (C) followed by attack imine nitrogen to positive center and dehydration to afford the iso-imidazole (E), which rearranges via [1,5] sigmatropic shift to the required imidazole (Scheme 4). The reaction mechanism involves a polar transition state starting from a neutral ground state, that under ultrasonic irradiation ionic reactions are accelerated by physical effects - better mass transport, Typically, in a heterogeneous solid/liquid system, the collapse of the cavitation bubble results in significant structural and mechanical defects. Collapse near the surface produces an asymmetrical inrush of the fluid to fill the void forming a liquid jet targeted at the surface. This effect is equivalent to high-pressure/high-velocity liquid jets. These jets activate the solid catalyst and increase the mass transfer to the surface by the disruption of the interfacial

Table 4 One-pot synthesis of 2,4,5-trisubstituted imidazoles catalyzed by SA-MNPs in EtOH under ultrasound irradiation at 40 °C (method A) and reflux conditions (method B)<sup>a</sup>.

Entry	Benzil	R <sub>1</sub> , R <sub>2</sub>	Aldehyde	R <sub>3</sub>	Product <sup>b</sup>	Method A time (min)/yield (%) <sup>c</sup>	Method B time (min)/yield (%) <sup>c</sup>	$mp_{\rm rep}/mp_{\rm lit.}$ (°C)
1	1a	Н	2a	Н	3a	25/98	120/90	$(271-273)/(270-272)^{31}$
2	1a	Н	2b	p-OMe	3b	30/97	180/89	(230-231)/(228-231) <sup>31</sup>
3	1a	Н	2c	p-Me	3c	35/90	150/84	(229-232)/(230-233) <sup>31</sup>
4	1a	Н	2d	<i>m</i> -Br	3d	30/95	150/92	(302-304)/(301-303) <sup>31</sup>
5	1a	Н	2e	m-OH	3e	30/93	150/90	(260-261)/259 <sup>31</sup>
6	1a	Н	2f	$m-NO_2$	b	30/92	150/91	$(268-270)/(269-271)^{31}$
7	1a	Н	2g	<i>m</i> -OMe	b	30/93	120/93	$(258-260)/(259-262)^{31}$
8	1a	Н	2	<i>т-</i> ОН, <i>p-</i> ОМе	3h	30/97	120/94	(215-216)/(214-216) <sup>31</sup>
9	1a	Н	2i	m-OMe, m-OMe	3i	30/95	120/92	$(255-257)/(256-257)^{32}$
10	1b	OMe	2a	Н	3j	35/97	130/91	$(202-204)/(201-203)^{31}$
11	1b	OMe	2b	p-OMe	3k	45/95	180/80	(184–186)/(183–185) <sup>31</sup>
12	1b	OMe	2c	p-Me	31	40/92	180/90	(187–189)/(186–188) <sup>31</sup>
13	1b	OMe	2d	m-Br	3m	35/95	160/87	$(250-252)/(248-251)^{31}$
14	1b	OMe	2e	m-OH	3n	35/92	160/85	(229–231)/(230–232) <sup>31</sup>
15	1b	OMe	2f	<i>m</i> -NO2	30	35/94	160/87	$(242-244)/(240-242)^{32}$
16	1b	OMe	2g	<i>m</i> -OMe	3р	35/97	160/89	(235-236)/(234-236) <sup>31</sup>
17	1b	OMe	2h	<i>т</i> -ОН, р-ОМе	3q	35/98	140/91	(131–133)/(132–134) <sup>31</sup>
18	1b	OMe	2i	<i>m</i> -OMe, m-OMe	3r	35/94	140/92	(194–196)/(195–197) <sup>31</sup>
19	1c	F	2h	<i>т</i> -ОН, р-ОМе	3s	25/98	90/95	$(249 - 250/(248 - 250)^{10})$
20	1c	F	2d	<i>m</i> -Br	3t	25/96	70/85	$(272 - 274)/(271 - 273)^{10}$

<sup>a</sup> Benzil (1 mmol), Aldehyde (1 mmol), NH<sub>4</sub>OAc (5 mmol), SA-MNPs (0.1 g).

<sup>b</sup> All products were characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR and MS spectra.

<sup>c</sup> Isolated yields.

boundary layers as well as dislodging the material occupying the inactive sites. Collapse on the surface, produces enough energy to cause fragmentation. Thus, in this situation, ultrasound can increase the surface area for a reaction and provide additional activation through efficient mixing and enhanced mass transport [42]. Moreover, ultrasound irradiation activates the reaction mixture by inducing high local temperatures and pressure generated inside the cavitation bubble and its interfaces when it collapses and accelerates the reaction rate and shortens the reaction time [42].

The possibility of recycling the catalyst was examined using the reaction of benzil, benzaldehyde, and ammonium acetate under optimized conditions. Upon completion, the catalyst was separated

by an external magnet and was washed with acetone, and the recycled catalyst was saved for the next reaction. The recycled catalyst could be reused five times without any further treatment. No observation of any appreciable loss in the catalytic activity of nanocatalyst was observed (Fig. 5). As observed in Fig. 6 the XRD of the recovered nanocatalyst was indexed according to the magnetite phase (JCPDS card No. 761849), and so there is no considerable change in its magnetic phase. Thus, the magnetite nanocatalyst is stable during synthesis of trisubstituted imidazoles under ultrasound irradiation.

In conclusion, have reported an an efficient and environmentally friendly approach for the synthesis of biologically active trisubstituted imidazoles via condensation of 1,2-diketone with



Scheme 4. Plausible mechanism of the reaction.



Fig. 5. Recyclability of SA-MNPs in the reaction of benzil (1 mmol), benzaldehyde (1 mmol) and ammonium acetate (5 mmol) under ultrasonic waves (35 KHz) at 40  $^\circ$ C.



Fig. 6. XRD patterns of recovered SA-MNPs after five recovery.

various aromatic aldehydes and ammonium acetate using SA-MNPs as a solid acid catalyst under ultrasound irradiation. Corrosiveness, safety, less waste, ease of separation and recovery, replacement of liquid acids with solid acid are all among desirable factors for the chemical industry which we have considered in our green chemistry approach. Furthermore, the catalyst could be magnetically isolated with a permanent magnet and the yields achieved above 90% after reused at least 5 times.

### 4. Conclusions

An ultrasound assisted, efficient and environmentally friendly method has been developed for the preparation of 2-aryl-4,5-diphenyl imidazoles c in the presence of catalytic amounts of SA-MNP. This new method offers several advantages including higher yields, mild reaction conditions, short reaction time, simple workup procedure, ease of separation, and recyclability of the magnetic catalyst, as well as the ability to tolerate a wide variety of substitutions in the reagents.

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746