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Article

$\text{Fe}_3\text{O}_4@\text{SiO}_2\cdot\text{HM}\cdot\text{SO}_3\text{H}$ as a recyclable heterogeneous nanocatalyst for microwave-promoted synthesis of 2,4,5-trisubstituted imidazoles under solvent free condition

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Abstract: A simply, highly versatile and efficient synthesis of 2,4,5-trisubstituted imidazoles is achieved through three component one pot reaction of benzil, benzaldehyde and NH_4OAc . This reaction has been catalyzed by $\text{Fe}_3\text{O}_4@\text{SiO}_2\cdot\text{HM}\cdot\text{SO}_3\text{H}$ as a very efficient, novel recyclable heterogeneous catalyst, under microwave irradiation and solvent free condition. The catalyst can be recovered for the subsequent reactions and reused for at least five rounds, without any appreciable loss of its efficiency.

1. Introduction

Imidazole derivatives are very important because of their diverse biological activities in pharmaceuticals as well as agrochemical field¹. Moreover the imidazole nucleus constitutes the core unit of many natural products^{2,3} such as; essential amino acids histidine, histamine and pilocarpine alkaloids. Also, 2,4,5-triaryl imidazoles are popular building blocks for the construction of pharmaceutically interesting compounds like; inhibitors of P38 MAP kinase⁴, B-Raf kinase transforming growth factor b_1 , fungicides and herbicides.

Microwave assisted organic synthesis (MAOS) has had a significant impact on synthetic chemistry since the introduction of controlled, precise microwave reactors. In comparison with conventional thermal heating using microwave irradiation in chemical reactions, has some advantages such as reductions in reaction times, increase in yield and suppression of side product formation, a vast improvement in operations like distillation, and considerable saving in energy⁵.

In comparison between microwave and conventional heating, in case of using microwave the heating is created in the interior of the sample and is then radiated outward, but in conventional heating the heat is generated in the outer region and must then be directed towards the center.

Heterogeneous catalysis has been known for many years and has become strategically vital for the efficient and eco-friendly organic transformations over the past few decades⁶⁻⁸. Magnetite is an ideal oxide support, easy to prepare, having a very active surface for adsorptions or immobilization of metals and ligands, which can be

separated by magnetic separation⁹. Magnetite nanoparticles are not very stable under ambient conditions, and are easily oxidized to magnetite or dissolved in an acidic medium¹⁰.

A silica shell does not only protect the magnetic core, but can also prevent the direct contact of the magnetic core with additional agents linked to the silica surface thus avoiding unwanted interactions. The surfaces of silica coated magnetic nanoparticles can readily modify with functional groups¹¹. In this article, silica coated magnetite nanoparticles have been functionalized with multi- SO_3H functionalized acidic ionic liquid, so it shows strong catalytic activity for one pot green synthesis of 2,4,5-trisubstituted imidazoles under microwave irradiation.

2. Experimental

2.1. Chemicals

All commercially available reagents were used without further purification and purchased from Merck, Chemical Company in high purity. The used solvents were purified by standard procedure.

2.2. Apparatus

Products were characterized by comparison of their physical data; IR and ^1H NMR and ^{13}C NMR spectra with known samples. Fourier transform infrared (FT-IR) spectra were obtained using a Perkin-Elmer 781 spectrophotometer. The NMR spectra were recorded on a Bruker Advance DPX 400 MHz instrument spectrometer at 400 and 100 MHz in DMSO and Acetone as solvent in the presence of tetramethylsilane (TMS) as internal standard. The reaction monitoring was

accomplished by TLC on silica gel Poly Gram SILG/UV 254 nm plates. Field emission scanning electron microscopy (FE SEM) images were obtained by HITACHI S-4160. X-ray diffraction patterns of samples were taken on a Philips Xpert X-ray powder diffraction diffractometer (CuK α , radiation, $k=0.154056$ nm). Melting points were measured on a Yanagimoto micro melting point apparatus. To produce ultrasonic irradiation, the Bandelin ultrasonic HD 3200 with probe model KE 76.6 mm diameter. The amount of ionic liquid coated MNPs was estimated using energy dispersive X-ray spectroscopy (SEM-EDX).

2.3. Catalyst preparation

New Fe₃O₄@SiO₂.HM.SO₃H was prepared based on the following procedure.

General procedure for preparation of nano-Fe₃O₄

Fe₃O₄ MNPs were synthesized according to a previously reported procedure by chemical co-precipitation method¹². FeCl₃.6H₂O (2.7 g) and FeCl₂.4H₂O (1g) were dissolved in 100 ml of 1.2 mmol.L⁻¹ aqueous HCl by ultrasonic bath for 30 min. Then, 1.25 mol.L⁻¹ aqueous NaOH (150 ml) was added under vigorous stirring and heated at 80°C under nitrogen atmosphere and a black precipitate was immediately formed. After 2h, the precipitate was magnetically separated and washed several times with water until the supernatant liquor reached neutrality (pH~7).

General procedure for preparation of nano-Fe₃O₄@SiO₂ core-shell

The core-shell Fe₃O₄@SiO₂ nanospheres were prepared by a modified Stober method¹³, briefly, Fe₃O₄ (0.5g, 2.1mmol) was dispersed in the mixture of ethanol (50 ml), deionized water (5ml) and tetraethoxysilane (TEOS) (0.2ml), followed by the addition of 5.0 ml NaOH (10 %wt). This solution was stirred mechanically for 30 min at room temperature. Then the product, Fe₃O₄@SiO₂, was separated by an external magnet, and was washed with the mixture of deionized water and ethanol three times and dried at 80°C for 10 h. FT-IR (KBr pellets, cm⁻¹): 3400 (O-H), 1000-1150 (Si-O-Si) and 556 (Fe-O)¹⁴.

General procedure for preparation of ionic liquid intermediate

To create an active site for binding to Fe₃O₄@SiO₂, on the ionic liquid, initially Hexamethylenetetramine (HM) (0.14g, 1mmol) was mixed with 3-chloropropyltrimethoxysilane (0.18ml, 1mmol) and the mixture was stirred for 6h and heated to 60°C, under nitrogen atmosphere.

Then, this product and 1,4-butane sultone (0.36 ml, 3 mmol) were mixed together without solvent and stirred 72h at room temperature (25°C), and then white solid zwitterions was formed and the solid was washed repeatedly with ethyl ether. Then it was dried in vacuum (110 °C, 0.01 torr). The white solid zwitterions was obtained in a good yield (>90%) and sufficient purity¹⁵.

A procedure for joining IL to Fe₃O₄@SiO₂ and functionalization of IL

1.0 g of SiO₂-coated Fe₃O₄ nanoparticle was dispersed in 50 ml ethanol by sonication for 1h. An ethanol solution of above zwitterions was then added, and the reaction mixture was refluxed for 2 days under nitrogen atmosphere. After cooling to

room temperature, the intermediate was collected by a permanent magnet and rinsed thrice with ethanol (30 ml). The concentrated H₂SO₄ (0.154 ml, 3mmol) was added to the mixture of above intermediate and ethanol as solvent under reflux for 2h to form the ionic liquid. The final catalyst was then washed repeatedly with ethanol to remove nonionic residues and then dried.

2.4. General procedure for synthesis of substituted imidazoles in the presence of Fe₃O₄@SiO₂.HM.SO₃H.

The reported synthesis of 2,4,5-trisubstituted imidazoles involve the reaction of 0.21 g benzil (1mmol), 0.35 g ammonium acetate (2mmol) and a substituted benzaldehyde (1mmol). These reagents were mixed together and treated in the presence of catalyst (0.060 g) under microwave irradiation and solvent free condition. Progress of the reaction was monitored by TLC (petroleum ether ethyl acetate 7: 3) after the reaction completed the mixture was cooled and the substrates separated from the catalyst by dissolving them in acetone. Then the catalyst was separated by using an external magnet. The product recrystallization with ethanol or acetone/water obtained pure 2,4,5-trisubstituted imidazoles.

2,4,5-triphenyl-1H-imidazole (3a), white solid; m.p.: 274-277°C, Lit.¹⁶ m.p.: 273-276°C; IR(KBr)/v (cm⁻¹): 3426 (NH), 3041(C=C-H), 1490(C=N), 1460, 1598 (C=C aromatic);¹H NMR (Acetone-d₆, 400 MHz) δ (ppm): 7.36-8.15 (m, 15H, Ar-H), 11.73(s, 1H, NH); ¹³C NMR(DMSO-d₆, 100MHz) δ (ppm): 122.72, 124.07, 125.67, 127.76, 128.72, 128.87, 129.15, 130.81, 136.93, 145.98.

2-(3-methoxyphenyl)-4,5-diphenyl-1H-imidazole (3b), white solid; m.p.: 260-262 °C, Lit.¹⁷ m.p.: 259-262 °C; IR (KBr)/v (cm⁻¹): 3425 (NH), 3059(C=C-H), 2925 (C-C-H), 1482 (C=N), 1444, 1593 (C=C aromatic), 1239 (C-O); ¹H NMR (DNSO-d₆, 400 MHz) δ (ppm): 3.82 (s, 3H, OMe), 6.94 (s, 1H, Ar-H), 7.30-7.67 (m, 13H, Ar-H), 12.67 (s, 1H, NH); ¹³C NMR (DMSO-d₆, 100MHz) δ (ppm): 55.67, 110.68, 114.70, 118.11, 126.59, 126.94, 127.69, 128.16, 128.89, 129.21, 129.47, 129.67, 130.29, 132.10, 145.85, 160.04.

2-(3,4-dimethoxyphenyl)-4,5-diphenyl-1H-imidazole (3c), white solid; m.p.: 213-216 °C, Lit.¹⁸ m.p.: 215-219 °C; IR (KBr)/v (cm⁻¹): 3427 (N-H), 3048(C=C-H), 2927 (C-C-H), 1602 (C=C), 1500 (C=N), 1258(C-O), 766 (C=C-H), 696(C=C-H).¹H NMR (DNSO-d₆, 400 MHz) δ (ppm): 12.51 (s, 1H, N-H), 7.65 (s, 1H, Ar-H), 7.4- 7.55 (m, 6H, Ar-H), 7.36 (t, 2H, ³J= 7.0 Hz, Ar-H), 7.28 (t, 2H, ³J= 7.6 Hz, Ar-H), 7.2 (t, 1H, 3J= 7.0 Hz, Ar-H), 7.15 (d, 1H, ³J= 7.6 Hz, Ar-H), 3.78 (s, 3H, OCH₃), 3.75 (s, 3H, OCH₃).¹³C NMR (DMSO-d₆, 100MHz) δ (ppm): 148.6, 147.0, 146.3, 137.2, 135.9 131.7, 129.0, 128.8, 128.6, 128.0, 127.5, 126.8, 123.9, 117.0, 113.3, 112.5, 56.1, 55.8 .

2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole (3d); bisque solid ; m.p.: 231-232 °C, Lit.¹⁹ m.p.: 230-232 °C; IR(KBr) / v (cm⁻¹): 3423 (NH), 3054 (C=C-H), 2837 (C-C-H), 1459 (C=N), 1447, 1611 (C=C aromatic), 1252 (C-O); ¹H NMR (DMSO -d₆, 400 MHz) δ (ppm): 3.27 (s,3H,OMe), 7.03-7.05(d, 2H, J=8 Hz, H-Ar), 7.28-7.51 (m, 10H, Ar-H), 8.00-8.02(d, 2H, J=8 Hz, H-Ar),12.64 (s, 1H, N-H); ¹³C NMR(DMSO-d₆, 100MHz) δ (ppm): 54.78, 114.00, 123.26, 126.83, 127.00, 127.87, 128.28, 133.50, 145.96.

2-(2,3-dimethoxyphenyl)-4,5-diphenyl-1H-imidazole (3e); white solid; m.p.: 235-236 °C; IR (KBr) / ν (cm^{-1}): 3421 (NH), 3056 (C=C-H), 2966 (C-C-H), 1483 (C=N), 1442, 1586 (C=C aromatic), 1272 (C-O); ^1H NMR (Acetone- d_6 , 400 MHz) δ (ppm): 2.94(s,3H,OMe), 3.07(s,3H,OMe)7.06-7.92(m, 13H, H-Ar), 11.20 (s, 1H, N-H); ^{13}C NMR(DMSO- d_6 , 100 MHz) δ (ppm): 55.02, 58.49, 118.34, 119.04, 123.14, 123.60, 127.86, 128.04, 128.87, 129.03, 129.60, 136.01, 145.92, 147.23, 150.11; Anal. Calcd. For $\text{C}_{23}\text{H}_{20}\text{N}_2\text{O}_2$: C 77.51, H 5.66, N 7.86, Found C 78.24, H 5.98, N 7.84.

2-(4-methylphenyl)-4,5-diphenyl-1H-imidazole (3f); white solid; m.p.: 232-236 °C, Lit.²⁰ m.p.: 232-235 °C; IR(KBr) / ν (cm^{-1}): 3430 (N-H), 3033 (C=C-H), 2923 (C-C-H), 1482 (C=N), 1448, 1598 (C=C aromatic); ^1H NMR (DMSO- d_6 , 400 MHz) δ (ppm): 2.34 (s,3H, Me), 7.20-7.22(d, 2H, J=8 Hz, H-Ar), 7.26-7.54 (m, 10H, Ar-H), 7.95-7.97 (d, 2H, J=8 Hz, H-Ar), 12.98 (s, 1H, N-H); ^{13}C NMR(DMSO- d_6 , 100MHz) δ (ppm): 21.36, 125.63, 126.94, 127.53, 128.13, 128.16, 128.40, 128.64, 128.86, 129.11, 129.72, 131.59, 135.69, 137.38, 138.17, 146.13.

2-(2-hydroxyphenyl)-4,5-diphenyl-1H-imidazole (3g); white solid; m.p.: 118-120 °C, Lit.²¹ m.p.: 117-119 °C; IR(KBr) / ν (cm^{-1}): 3430 (N-H), 3033 (C=C-H), 2923 (C-C-H), 1482 (C=N), 1448, 1598 (C=C aromatic); ^1H NMR (DMSO- d_6 , 400 MHz) δ (ppm): 12.89 (s,1H, OH), 7.00-7.96(m, 14H, H-Ar), 11.98 (s, NH); ^{13}C NMR(DMSO- d_6 , 100MHz) δ (ppm): 113.82, 117.95, 119.57, 125.27, 127.93, 128.01, 129.09, 129.21, 129.52, 129.61, 130.99.

4-(4,5-diphenyl-1H-imidazole-2-yl)phenol (3h); light bisque solid; m.p.: 264-267 °C, Lit.¹⁸ m.p.: 268-270 °C; IR(KBr) / ν (cm^{-1}): 3408 (N-H), 3200 (OH), 3058 (C=C-H), 1493 (C=N), 1454, 1609 (C=C aromatic), 1254 (C-O); ^1H NMR (DMSO- d_6 , 400 MHz) δ (ppm): 6.83-6.85 (d, 2H, J=8.4 Hz, H-Ar), 7.28-7.51 (m, 10H, Ar-H), 7.88-7.90 (d, 2H, J=8.4 Hz, H-Ar), 9.69 (s, 1H, OH), 12.40(s, 1H, NH); ^{13}C NMR(DMSO- d_6 , 100MHz) δ (ppm): 115.89, 122.05, 127.35, 128.15, 128.85, 146.55, 158.26.

2-(3-methylphenyl)-4,5-diphenyl-1H-imidazole (3i); white solid; m.p.: 296-299 °C, Lit.²² m.p.: 298-299 °C; IR(KBr) / ν (cm^{-1}): 3423 (N-H), 3059 (C=C-H), 2924 (C-C-H), 1483 (C=N), 1448, 1601 (C=C aromatic). ^1H NMR (DMSO- d_6 , 400 MHz) δ (ppm): 2.37 (s, 3H, Me), 7.17 (s, 1H, Ar-H), 7.19-7.93 (m, 13H, Ar-H), 12.64 (s, 1H, NH). ^{13}C NMR(DMSO- d_6 , 100MHz) δ (ppm): 21.57, 122.86, 126.23, 126.99, 127.58, 128.20, 128.65, 128.87, 129.06, 129.40, 130.73, 131.54, 135.67, 137.54, 138.29, 146.11.

2-(4-isopropylphenyl)-4,5-diphenyl-1H-imidazole (3j); white solid; m.p.: 254-256 °C, Lit.²³ m.p.: 253-255 °C; IR(KBr) / ν (cm^{-1}): 3422 (N-H), 3054 (C=C-H), 2960 (C-C-H), 1493 (C=N), 1446, 1603 (C=C aromatic); ^1H NMR (DMSO- d_6 , 400 MHz) δ (ppm): 1.22-1.23 (d, 6H, J=6.4 Hz, 2Me), 2.92-2.93 (m, 1H, CH), 7.20-7.22 (d, 2H, J=8, H-Ar), 7.28-7.54 (m, 10H, H-Ar), 7.97-7.99(d, 2H, J=8, H-Ar), 12.57(s, 1H, NH); ^{13}C NMR(DMSO- d_6 , 100MHz) δ (ppm): 24.23, 33.72, 125.75, 126.94, 127.06, 127.55, 128.16, 128.41, 128.51, 128.64, 128.86, 129.11, 131.59, 135.69, 137.42, 146.18, 149.06.

2-(2-chlorophenyl)-4,5-diphenyl-1H-imidazole (3k); light bisque solid; m.p.: 196-199 °C, Lit.²⁴ m.p.: 199-201 °C;

IR(KBr) / ν (cm^{-1}): 3433 (N-H), 3062 (C=C-H), 2924 (C-C-H), 1477 (C=N), 1448, 1604 (C=C aromatic), 1054 (C-Cl); ^1H NMR (DMSO- d_6 , 400 MHz) δ (ppm): 7.24-7.78 (m, 14H, Ar-H), 12.64 (s, 1H, NH); ^{13}C NMR(Acetone- d_6 , 100MHz) δ (ppm): 127.15, 127.91, 128.35, 129.88, 130.27, 131.21, 131.34, 143.40.

2-(2,3-dichlorophenyl)-4,5-diphenyl-1H-imidazole (3l); white solid; m.p.: 194-197 °C; IR(KBr) / ν (cm^{-1}): 3436 (N-H), 3059 (C=C-H), 2818 (C-C-H), 1502 (C=N), 1444, 1604 (C=C aromatic), 1049 (C-Cl); ^1H NMR (DMSO- d_6 , 400 MHz) δ (ppm): 7.22-7.74 (m, 13H, Ar-H), 12.75 (s, 1H, NH); ^{13}C NMR(DMSO- d_6 , 100MHz) δ (ppm): 126.67, 127.42, 127.98, 128.08, 128.44, 128.71, 129.70, 130.02, 130.47, 131.17, 132.41, 133.28, 142.93; Anal. Calcd. For $\text{C}_{21}\text{H}_{14}\text{Cl}_2\text{N}_2$: C 69.06, H 3.86, N 7.67, Found C 70.14, H 3.72, N 7.50.

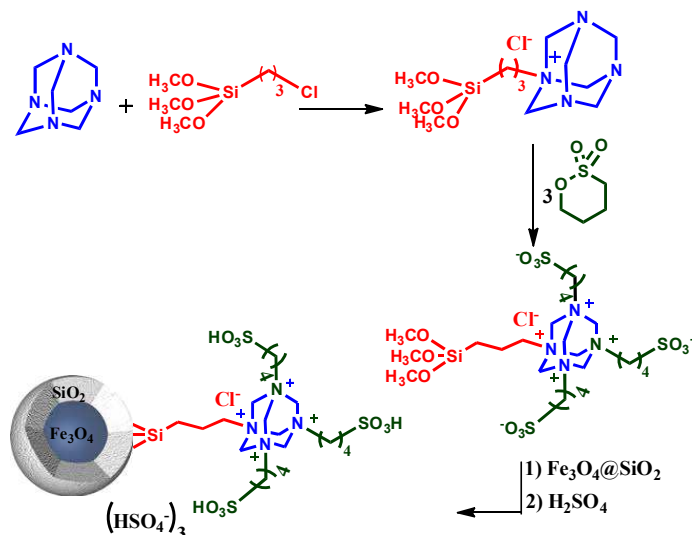
2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole (3m); white solid; m.p.: 260-261 °C, Lit.¹ m.p.: 262-264 °C; IR(KBr) / ν (cm^{-1}): 3420 (N-H), 3062 (C=C-H), 1485 (C=N), 1443, 1604 (C=C aromatic), 1092 (C-Cl); ^1H NMR (DMSO- d_6 , 400 MHz) δ (ppm): 7.20-8.53 (m, 12H, Ar-H), 8.61-8.65 (m, 2H, Ar-H), 12.76 (s, 1H, N-H); ^{13}C NMR(DMSO- d_6 , 100MHz) δ (ppm): 126.59, 126.75, 127.36, 127.84, 128.05, 128.38, 128.67, 135.77, 129.95, 133.46, 144.76.

2-(2,4-dichlorophenyl)-4,5-diphenyl-1H-imidazole (3n); bisque solid; m.p.: 175-178 °C, Lit.¹⁹ m.p.: 176.5-177 °C; IR(KBr) / ν (cm^{-1}): 3437 (N-H), 3063 (C=C-H), 2968 (C-C-H), 1475 (C=N), 1448, 1597 (C=C aromatic); ^1H NMR (Acetone- d_6 , 400 MHz) δ (ppm): 7.23-8.09 (m, 13H, Ar-H), 11.66 (s, 1H, N-H).

3. Results and discussion

3.1. Preparation of catalyst

For the synthesis of catalyst, at first Fe_3O_4 and tetraethoxysilane were mixed together to produce $\text{Fe}_3\text{O}_4@\text{SiO}_2$. On the other hand, hexamethylenetetramine (HM) was reacted with chloropropyltrimethoxysilane and the product was mixed to 1,4-butane sultone to produce an ionic liquid intermediate with an active site for binding to the $\text{MNP}@\text{SiO}_2$. The $\text{Fe}_3\text{O}_4@\text{SiO}_2$ and activated ionic liquid joined together, the final catalyst was obtained after treating H_2SO_4 (Scheme 1).



Scheme 1. Different steps for the synthesis of $\text{Fe}_3\text{O}_4@\text{SiO}_2.\text{HM}.\text{SO}_3\text{H}$

3.2. Characterization of catalyst $\text{Fe}_3\text{O}_4@\text{SiO}_2.\text{HM}.\text{SO}_3\text{H}$

The catalyst was characterized using FE SEM, XRD, FT-IR and VSM. Successful functionalization of the MNPs can be characterized by FT-IR spectra. Figure 1 shows the FT-IR spectrum of the catalyst and ionic liquid. The presence of Fe-O stretching vibration is inferred from the peak near 635 cm^{-1} , O-H stretching vibration near 3366 cm^{-1} and O-H deformation vibration near 1628 cm^{-1} . Peaks of (Si-O) stretching are around 1090 cm^{-1} . At about 1207 cm^{-1} and 1136 cm^{-1} , S=O stretching was appeared and the C-N stretching bond is about $1000\text{-}1350\text{ cm}^{-1}$.

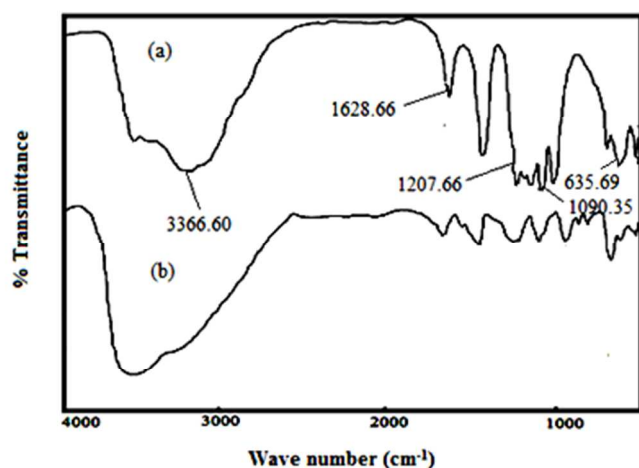


Fig 1. FT-IR spectrums of (a) $\text{Fe}_3\text{O}_4@\text{SiO}_2.\text{HM}.\text{SO}_3\text{H}$, (b) $\text{HM}.\text{SO}_3\text{H}$ (IL)

The X-ray diffraction patterns of Fe_3O_4 , $\text{Fe}_3\text{O}_4@\text{SiO}_2$ and $\text{Fe}_3\text{O}_4@\text{SiO}_2.\text{HM}.\text{SO}_3\text{H}$, are shown in Figure 2. The positions and relative intensities of all the peaks in the XRD pattern of Fe_3O_4 , indicating retention of the crystalline cubic spinel structure during functionalization of the MNPs²⁵. The patterns in both catalysts

indicate a crystallized structure at 2θ : 30.1° , 35.67° , 43.42° , 53.88° , 57.38° and 62.95° , which are assigned to the (220), (311), (400), (422), (511) and (440) crystallographic faces of magnetite²⁶. Characteristic peak of SiO_2 in core shell structure has been hidden under weak peak of Fe_3O_4 at $2\theta=30^\circ$ ²⁷. The average diameter for $\text{Fe}_3\text{O}_4@\text{SiO}_2.\text{HM}.\text{SO}_3\text{H}$ was about 55 nm and the average core diameter was calculated to be about 21 nm from XRD results by Debye-Scherrer equation.

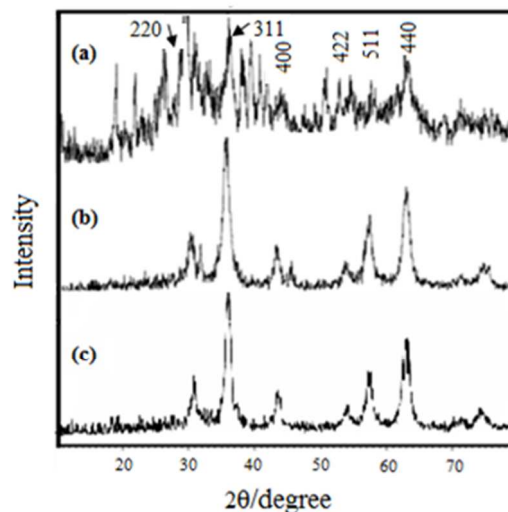


Fig 2. XRD patterns of (a) $\text{Fe}_3\text{O}_4@\text{SiO}_2.\text{HM}.\text{SO}_3\text{H}$, (b) $\text{Fe}_3\text{O}_4@\text{SiO}_2$, (c) Fe_3O_4 .

Figure 3 shows the FE SEM image of $\text{Fe}_3\text{O}_4@\text{SiO}_2.\text{HM}.\text{SO}_3\text{H}$, in that the cubic morphology with an average diameter of about 60 nm for catalyst was observed.

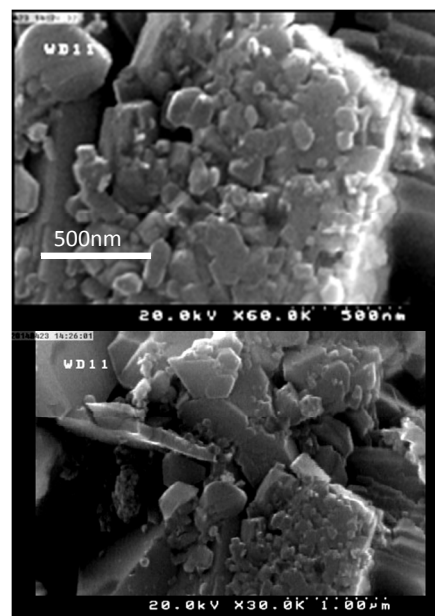


Fig 3. FESEM of $\text{Fe}_3\text{O}_4@\text{SiO}_2.\text{HM}.\text{SO}_3\text{H}$

The components of the catalyst were analyzed by using energy dispersive spectroscopy (EDX). The EDX spectrum in Figure 4

shows the elemental composition (S, O, N, C, Si and Fe) of the catalyst.

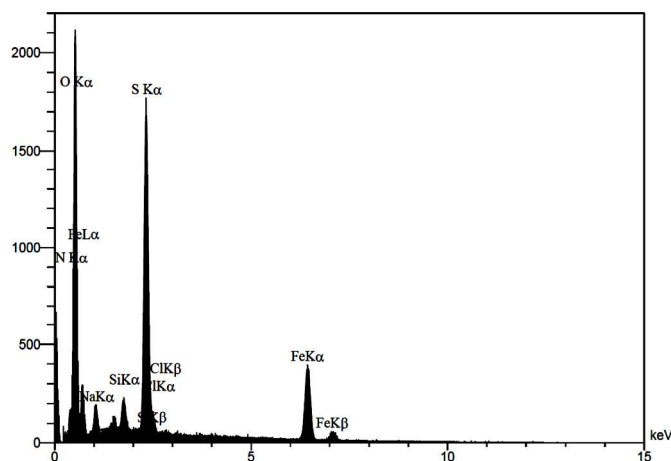


Fig 4. EDX of $\text{Fe}_3\text{O}_4@\text{SiO}_2.\text{HM}.\text{SO}_3\text{H}$

Magnetic properties of catalyst and $\text{Fe}_3\text{O}_4@\text{SiO}_2$ nanoparticles were determined by VSM at room temperature (Figure 5). Magnetization of samples could be completely saturated at high fields of up to 1.0 T and the saturation magnetization of samples changed from 47 to 7 emu g^{-1} , because of the functionalization by ionic liquid. Moreover, the room temperature magnetization curves, before and after functionalization exhibit no hysteresis which demonstrates its super paramagnetic characteristic^{27, 28}. The strong magnetization of the catalyst was also revealed by simple attraction with an external magnet.

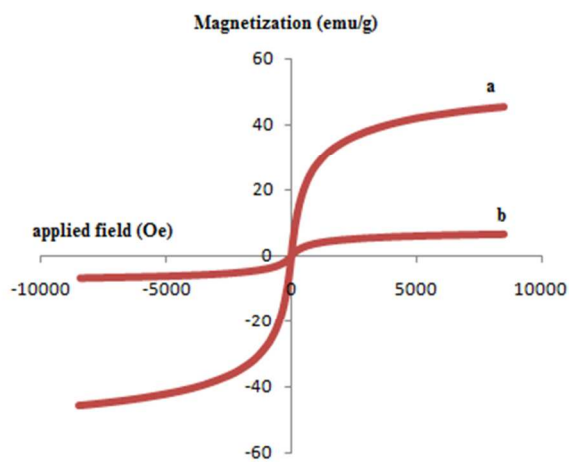


Fig 5. VSM of (a) $\text{Fe}_3\text{O}_4@\text{SiO}_2$, (b) $\text{Fe}_3\text{O}_4@\text{SiO}_2.\text{HM}.\text{SO}_3\text{H}$

3.3. Investigation of catalytic activity for synthesis of 2,4,5-trisubstituted imidazoles

The acidity of the catalyst was measured by an acid-base titration. The pH was calculated to be approximately 1. The efficiency of the supported catalyst was found to be solvent independent and without any solvent good yields observed.

3.3.1. Optimization of the microwave power

Power of the microwave instrument was optimized and the best operating power was found to be 450 watt.

Table 1. Microwave power optimization^{a, b}

Entry	Power (w)	Time (min)	Yield (%)
1	180	7	45
2	360	7	70
3	450	7	91
4	600	7	84
5	650	7	83
6	700	7	78

^a Reaction condition: benzil (1 mmol), 3,4-dimethoxy benzaldehyde (1 mmol), NH_4OAc (2 mmol)

^b amount of catalyst (30 mg)

3.3.2. Optimization reactions of catalyst amount

The reaction has been done in the presence of different catalyst amounts under optimized power.

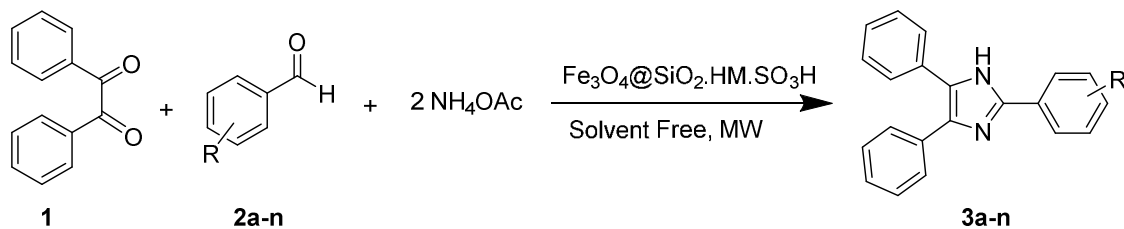
Table 2. Optimization of the catalyst amount^a

Entry	Amount of catalyst (g) ^b	Time (min)	Yield (%)
1	0.010	15	42
2	0.020	10	77
3	0.030	7	91
4	0.040	7	87
5	0.045	7	87
6	0.050	7	85

^a Benzil (0.5mmol), 3,4-dimethoxy benzaldehyde (0.5mmol), NH_4OAc (1mmol), microwave power 450 W.

^b The amount of $\text{Fe}_3\text{O}_4@\text{SiO}_2.\text{HM}.\text{SO}_3\text{H}$

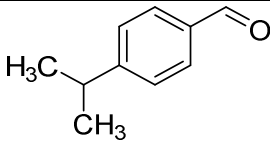
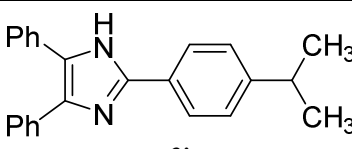
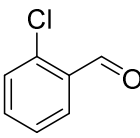
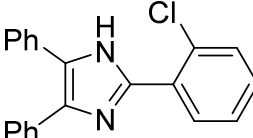
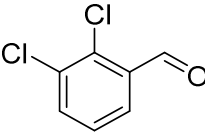
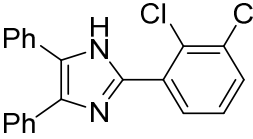
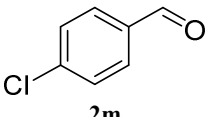
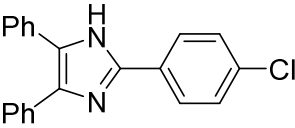
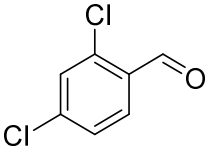
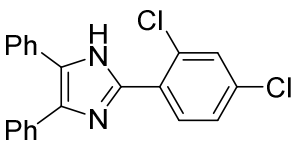
After optimizing the reaction conditions, it was used different benzaldehydes as the substrates for this reaction. The results are summarized in Table 3. As the entries in Table 3 show, the catalysis proceeded well for a wide variety of aldehydes, providing the corresponding imidazoles in high yields and short reaction times.



Scheme 2. Synthesis of 2,4,5-trisubstituted imidazoles from benzil, benzaldehyde and NH₄OAc

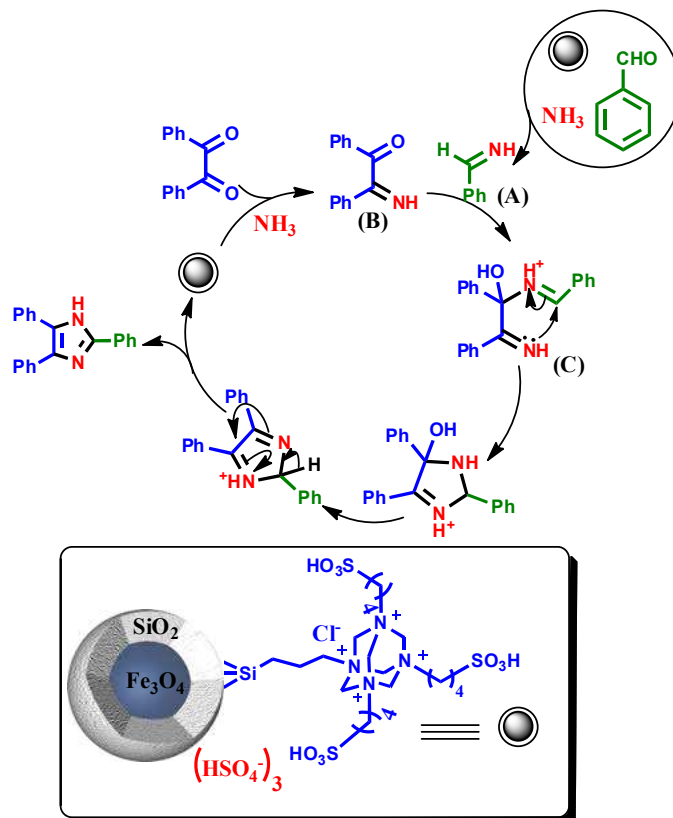
Table 3. Synthesis of 2,4,5-trisubstituted imidazoles in the presence of catalyst Fe₃O₄@SiO₂.HM.SO₃H^a

Entry	Benzaldehyde	Product	Time (min)	Yield(%) ^b
1			8	77
2			7	85
3			7	90
4			8	87
5			7	89
6			8	80
7			7	85
8			7	85
9			8	76

10	 2j	 3j	8	93
11	 2k	 3k	7	84
12	 2l	 3l	7	89
13	 2m	 3m	7	85
14	 2n	 3n	7	90

^aReaction condition: benzil (1 mmol), 3,4-dimethoxy benzaldehyde (1 mmol), NH₄OAc (2 mmol) was under microwave irradiation (power 450 w) and solvent free condition, Catalyst amount: 30 mg.

^bIsolated product yields



Scheme 4. Proposed mechanism of the reaction

The reusability of the catalyst is an important benefit for catalytic reactions. The reusability was investigated using the reaction of benzil, 3,4-dimethoxy benzaldehyde and NH_4OAc in the presence of $\text{Fe}_3\text{O}_4@\text{SiO}_2\text{-HM.SO}_3\text{H}$ under optimized conditions (Figure 6). The catalyst was recovered by an external magnet and washed thrice with acetone, dried and then reused for subsequent reactions for at least 5 times with less reduction in its catalytic activity.

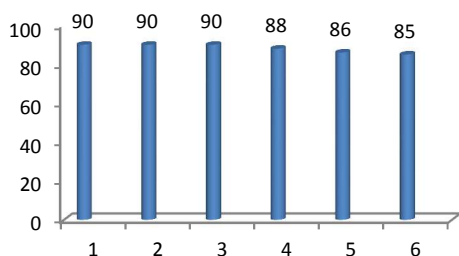


Fig 6. Reusability of catalyst for the synthesis of 2,4,5-trisubstituted imidazoles

Conclusions

A novel ionic liquid coated nano magnetite catalyst was synthesized and tested as a reusable nano catalyst in the one-pot three component reaction of benzil, benzaldehyde and NH_4OAc under microwave irradiation and neat condition to give 2,4,5-trisubstituted imidazoles. Excelling features of the proposed methodology include high efficiency, reusability, short times of reaction, high yields of products and simplicity, making it an attractive alternative for the clean synthesis of 2,4,5-trisubstituted imidazoles as biologically and pharmaceutically relevant material.

Acknowledgements

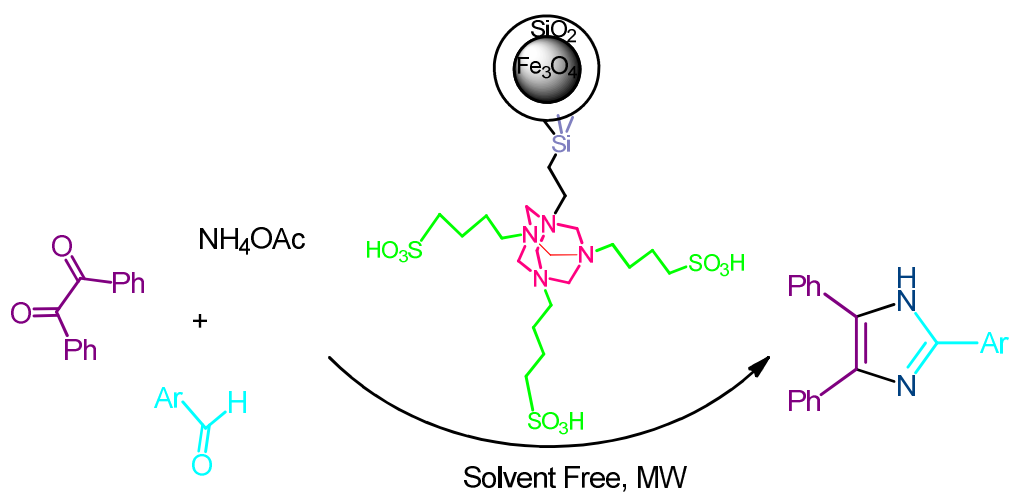
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Graphical abstract



A simply, highly versatile and efficient synthesis of 2,4,5-trisubstituted imidazoles catalyzed by $\text{Fe}_3\text{O}_4@\text{SiO}_2.\text{HM}.\text{SO}_3\text{H}$ is achieved via three component one pot reaction of benzil, benzaldehyde and NH_4OAc .