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ARTICLE

Ionophore silica-coated magnetite nanoparticles as a recyclable heterogeneous catalyst for one-pot green synthesis of 2,4,5-trisubstituted imidazoles

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Novel multi-SO_3H functionalized strong Bronsted acidic ionic liquid coated magnetite nanoparticles has been prepared for the synthesis of 2,4,5-trisubstituted imidazoles. The results showed that the novel catalyst was very efficient for the reaction and could be magnetically separated and reused at least 5 times with less reduction in its catalytic activity. Operational simplicity, low cost of catalyst used, high yields, environmental friendliness, wide applicability, reusability and easy recovery of the catalyst using an external magnet are the most important features of this methodology. The catalyst was characterized by infrared spectroscopy (FT-IR), X-Ray diffraction analysis (XRD), field emission scanning electron microscopy (FE-SEM), energy dispersive X-ray analysis (EDX), Dynamic Laser scattering (DLS) and vibrating sample magnetometer (VSM).

Introduction

Imidazole has attracted a wide spread attention because of its pharmaceutical properties such as anti-inflammatory[1-4], cardio vascular[5,6], anti neo plastic[7], enzyme inhibitor[8-10], antianthelmintic[11], anticancer[12], antifungal[7,13], antifilarial, antiviral and antiulcer activities. Furthermore, imidazole has been used to prepare ionic liquids that they can function as a solvent and catalyst together. Ionic liquids are well known as green solvents and catalysts.

Many of the synthetic methods for imidazoles have some disadvantages such as low yields, harsh reaction conditions, application of hazardous and expensive catalysts, and prolonged time of reaction. Therefore synthesis of greener, clean and environmentally friendly approaches is still desirable and much in demand [14].

Multicomponent reactions (MCRs) enjoy an outstanding status in organic and medicinal chemistry for high degree of atom economy and application in the diversity oriented convergent synthesis of complex organic molecules from simple and readily available substrates in a single vessel and fulfil some of the objectives of ideal synthesis because the complex products are formed in a single step and diversity can be achieved simply by varying the reaction components[15,16].

Heterogeneous catalysis is more desired than homogenous because of easy recycling of the catalyst, and minimization of the catalyst wastes. It seems that magnetite nanoparticles (MNPs) are good supports for heterogeneous catalysis and when they are modified with an ionic liquid they become so useful and easy to separate and reuse[17]. Naked magnetic nanoparticles tend to aggregate because of their strong inter particle interaction and high specific area but when they are modified they can stabilize against aggregation over a long period. One of these strategies is coating them by a silica shell to protect the inner magnetite core, from oxidation and provide sites for surface functionalizing[18].

Nowadays, ionic liquids have appeared as a group of green solvents with incomparable properties such as: high thermal stability, partial vapour pressure, immiscibility with a type of organic solvents and recyclability[19]. Ionic liquids have been extensively applied as a mild and effective catalyst for various reactions[20,21].

In contrast, on an industrial scale, homogenous catalysts are often expensive, involving troublesome workup, thus reducing their scope. They are not easy to handle, difficult to separate and have limited reuse potential. The new catalyst can cover these disadvantages[17].

In continuation of our previously research on catalytic reactions for synthesis of heterocyclic compounds[20-22] herein, we hope to report efficient multi-SO_3H functionalization of magnetite nanoparticles and the application of resulted Fe_3O_4@SiO_2.HM.SO_3H as a new heterogeneous catalyst for synthesis of 2,4,5-trisubstituted imidazoles. These heterocycles were produced through treatment of benzil, ammonium acetate and various aldehydes under solvent free conditions.

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Experimental

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.

Apparatus

Products were characterized by comparison of their physical data, IR and ^{1}H 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. 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 Expert X-ray powder diffraction diffractometer (Cuk, 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).

Catalyst preparation

New Fe_3O_4@SiO_2.HM.SO_3H was prepared based on the following procedure.

General procedure for preparation of nano-Fe_3O_4

Fe_3O_4 MNPs were synthesized according to the previously reported procedure by chemical co-precipitation method[22]. $FeCl_3.6H_2O$ (2.7 g) and $FeCl_2.4H_2O$ (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. 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-Fe_3O_4@SiO_2 core-shell

The core-shell of Fe_3O_4@SiO_2 nanospheres were prepared by a modified Stober method [23], briefly, Fe_3O_4 (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 of NaOH (10 %wt). This solution was stirred mechanically for 30 min at room temperature. Then the product, Fe_3O_4@SiO_2, was separated by an external magnet, and was washed with the mixture of deionized water and ethanol three times and dried at 80 ^{o}C for 10h. FT-IR (KBr pellets, cm^{-1}): 3400 (O-H), 1000-1150 (Si-O-Si) and 556 (Fe-O) [24].

General procedure for preparation of ionic liquid intermediate

To create an active site for binding to Fe_3O_4@SiO_2, on the ionic liquid, initially Hexamethylenetetramine (HM) (0.14g, 1mmol) was mixed with 3-chloropropyl-trimethoxysilane (0.18 ml, 1 mmol) and the mixture was stirred for 6h and heated to 60 ^{o}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 ^{o}C), white solid zwitterions was formed and the solid was washed repeatedly with ethyl ether. Then it was dried in vacuum (110 ^{o}C, 0.01 torr). The white solid zwitterions was obtained in a good yield (>90%) and sufficient purity [26].

Ionic liquid Intermediate (viscose liquid): IR (KBr)/ν (cm^{-1}): 3354, 2987, 2875, 1578, 1456, 1340, 1115, 1045; ^{1}H NMR (D_2O, 400 MHz) δ (ppm): 0.78 (t, 2H, *J*= 4.7 Hz, CH_2 near Si), 1.19-1.28 (m, 6H, CH_2), 1.61-1.75 (m, 8H, CH_2), 2.45-2.56 (m, 8H, CH_2), 3.22 (m, 2H, CH_2), 3.65 (s, 9H, OCH_3), 4.35 (s, 6H, CH_2-HMT), 5.38 (s, 6H, CH_2-HMT); ^{13}C NMR (D_2O, 100 MHz) δ (ppm): 13.3, 15.1, 22.5, 23.7, 52.1, 57.5, 58.9, 59.8, 75.5, 85.6, 59.0, 98.5.

A procedure for joining IL to Fe_3O_4@SiO_2 and functionalization of IL

1.0 g of SiO_2-coated Fe_3O_4 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 H_2SO_4 (0.154 ml, 3 mmol) 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.

General procedure for synthesis of substituted imidazoles in the presence of Fe_3O_4@SiO_2.HM.SO_3H as catalyst

The reported synthesis of 2,4,5-trisubstituted imidazoles involve the reaction of 0.21 g benzil (1 mmol), 0.35 g ammonium acetate (2 mmol) and a substituted benzaldehyde (1mmol). These reagents were mixed in a 50 ml round bottom flask, heated under neat condition in the presence of catalyst, in an oil bath. Progress of the reaction was monitored by TLC (petroleum ether 7: ethyl acetate 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 (**2a**); white solid; mp 274-277 °C, mp 273-276 °C [26]; IR (KBr)/ν (cm^{-1}): 3426 (NH), 3041(C=C-H), 1490(C=N), 1460, 1598 (C=C aromatic); ^{1}H NMR (Acetone-d_6, 400 MHz) δ (ppm): 7.36-8.15 (m, 15H, Ar-H), 11.73(s, 1H, NH); ^{13}C NMR (DMSO-d_6, 100 MHz) 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 (**2b**); white solid; mp 260-262 °C, mp 259-262 °C [27]; IR (KBr)/ν (cm^{-1}): 3425 (NH), 3059(C=C-H), 2925 (C-C-H), 1482 (C=N), 1444, 1593 (C=C aromatic), 1239 (C-O); ^{1}H NMR (DNSO-d_6, 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); ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm): 55.67, 110.68, 114.70, 118.11, 126.59, 126.94, 127.69, 128.16,

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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 (**2c**); white solid; mp 213-216 °C; mp 215-219 °C [26]; IR (KBr)/ν (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). ^{1}H NMR (DNSO-d_6, 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, ^{3}J= 7.0 Hz, Ar-H), 7.28 (t, 2H, ^{3}J= 7.6 Hz, Ar-H), 7.20 (t, 1H, ^{3}J= 7.0 Hz, Ar-H), 7.15 (d, 1H, ^{3}J= 7.6 Hz, Ar-H), 3.78 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3); ^{13}C NMR (DMSO-d_6, 100 MHz) 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 (**2d**); bisque solid ; mp 231-232 °C; mp 230-232 °C [28]; IR (KBr) /ν (cm^{-1}): 3423 (NH), 3054 (C=C-H), 2837 (C-C-H), 1459 (C=N), 1447, 1611 (C=C aromatic), 1252 (C-O); ^{1}H NMR (DMSO-d_6, 400 MHz) δ (ppm): 3.27 (s, 3H, OMe), 7.04 (d, 2H, J=8.0 Hz, H-Ar), 7.28-7.51 (m, 10H, Ar-H), 8.01 (d, 2H, J=8.0 Hz, H-Ar), 12.64 (s, 1H, N-H); ^{13}C NMR (DMSO-d_6, 100 MHz) 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 (**2e**); white solid; mp 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); ^{1}H 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 $C_{23}H_{20}N_2O_2$: 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 (**2f**); white solid; mp 232-236 °C; mp 232-235 °C [29]; IR (KBr) /ν (cm^{-1}): 3430 (N-H), 3033 (C=C-H), 2923 (C-C-H), 1482 (C=N), 1448, 1598 (C=C aromatic); ^{1}H NMR (DMSO-d_6, 400 MHz) δ (ppm): 2.34 (s, 3H, Me), 7.21 (d, 2H, J=8.0 Hz, H-Ar), 7.26-7.54 (m, 10H, Ar-H), 7.96 (d, 2H, J=8.0 Hz, H-Ar), 12.98 (s, 1H, N-H); ^{13}C NMR (DMSO-d_6, 100 MHz) 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-hidroxyphenyl)-4,5-diphenyl-1H-imidazole (**2g**); white solid; mp 118-120 °C; mp 117-119 °C [30]; IR (KBr) /ν (cm^{-1}): 3430 (N-H), 3033 (C=C-H), 2923 (C-C-H), 1482 (C=N), 1448, 1598 (C=C aromatic); ^{1}H 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, 100 MHz) 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 (**2h**); light bisque solid; mp 264-267 °C; mp 268-270 °C [31]; 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); ^{1}H NMR (DMSO-d_6, 400 MHz) δ (ppm): 6.84 (d, 2H, J=8.4 Hz, H-Ar), 7.28-7.51 (m, 10H, Ar-H), 7.89 (d, 2H, J=8.4 Hz, H-Ar), 9.69 (s, 1H, OH), 12.40 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm): 115.89, 122.05, 127.35, 128.15, 128.85, 146.55, 158.26.

2-(3-methylphenyl)-4,5-diphenyl-1H-imidazole (**2i**); white solid; mp 296-299 °C; m.p.: 298-299 °C [32]; IR (KBr) /ν (cm^{-1}): 3423 (N-H), 3059 (C=C-H), 2924 (C-C-H), 1483 (C=N), 1448, 1601 (C=C aromatic). ^{1}H 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, 100 MHz) 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 (**2j**); white solid; mp 254-256 °C, m.p 253-252 °C [33]; IR (KBr) /ν (cm^{-1}): 3422 (N-H), 3054 (C=C-H), 2960 (C-C-H), 1493 (C=N), 1446, 1603 (C=C aromatic); ^{1}H NMR (DMSO-d_6, 400 MHz) δ (ppm): 1.22 (d, 6H, J=6.4, Me), 2.92-2.93 (m, 1H, CH), 7.21 (d, 2H, J=8.0, H-Ar), 7.28-7.54 (m, 10H, H-Ar), 7.97 (d, 2H, J=8.0, H-Ar), 12.57 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 100 MHz) 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 (**2k**); light bisque solid; mp 196-199 °C, mp 199-201°C [34]; 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); ^{1}H 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, 100 MHz) 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 (**2l**); white solid; mp 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); ^{1}H 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, 100 MHz) 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 $C_{21}H_{14}Cl_2N_2$: 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 (**2m**); white solid; mp 260-261 °C, mp 262-264°C [35]; IR (KBr) /ν (cm^{-1}): 3420 (N-H), 3062 (C=C-H), 1485 (C=N), 1443, 1604 (C=C aromatic), 1092 (C-Cl); ^{1}H 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, 100 MHz) 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 (**2n**); bisque solid; mp 175-178 °C, mp 176.5-177 °C [36]; IR (KBr) /ν (cm^{-1}): 3437 (N-H), 3063 (C=C-H), 2968 (C-C-H), 1475 (C=N), 1448, 1597 (C=C aromatic); ^{1}H NMR (Acetone-d_6, 400 MHz) δ (ppm): 7.23-8.09 (m, 13H, Ar-H), 11.66 (s, 1H, N-H).

2-(3-nitrophenyl)-4,5-diphenyl-1H-imidazole (**2o**); light brown solid; mp 261-263 °C; mp 264-265 °C [37]; IR (KBr) /ν (cm^{-1}): 3438 (N-H), 3305 (OH), 3037 (C=C-H), 1541 (C=N), 1450, 1618 (C=C aromatic), 1154 (C-O); ^{1}H NMR (DMSO-d_6, 400 MHz) δ (ppm): 7.52-7.93 (m, 11H, H-Ar), 8.29 (d, 1H, J= 7.3 Hz, Ar-H), 8.54 (d, 1H, J= 5.6 Hz, Ar-H), 8.98 (s, 1H, Ar-H), 13.27 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm): 120.07, 121.85, 126.54, 127.79, 129.18, 132.39, 133.08, 142.64, 150.26.

2-(2-nitrophenyl)-4,5-diphenyl-1H-imidazole (**2p**); white solid; mp 226-227 °C; mp 224-225 °C [38]; IR (KBr) /ν (cm^{-1}): 3455 (N-H), 3315 (OH), 3032 (C=C-H), 15251 (C=N), 1448, 1624 (C=C aromatic), 1204 (C-O); ^{1}H NMR (DMSO-d_6, 400 MHz) δ (ppm):

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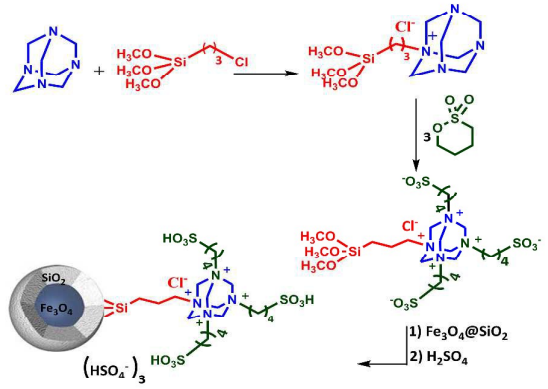
7.25-7.83 (m, 11H, H-Ar), 7.84 (t, 1H, J= 7.1 Hz, Ar-H), 8.04 (d, 1H, J= 6.6 Hz, Ar-H), 8.14 (d, 1H, J= 8.0, Hz, Ar-H), 13.10 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ (ppm): 122.11, 122.90, 125.07, 126.49, 128.54, 130.84, 134.47, 141.07, 151.45.

Results and discussion

Preparation of catalyst

In order to synthesize the catalyst, at first Fe_3O_4 and tetraethoxysilane were mixed together to produce Fe_3O_4@SiO_2. On the other hand, hexamethylentetramine (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 MNP@SiO_2. The Fe_3O_4@SiO_2 and activated ionic liquid joined to each other and after treating H_2SO_4, the final catalyst was obtained (Scheme 1).



Scheme 1. Different steps for the synthesis of Fe_3O_4@SiO_2.HM.SO_3H

Characterization of Fe_3O_4@SiO_2.HM.SO_3H catalyst

The prepared catalyst was characterized using FE-SEM, XRD, FT-IR and VSM. Successful functionalization of the MNPs can be inferred from FT-IR spectrums. 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} we have (S=O stretching). The C-N stretching bond is about 1000-1350 cm^{-1}.

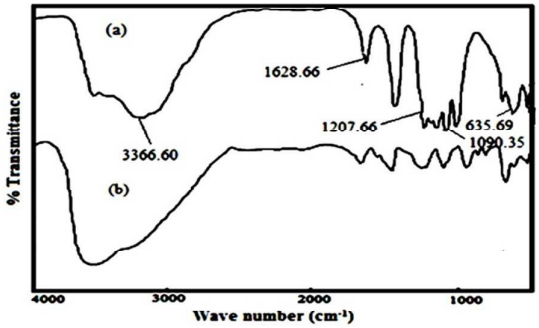


Fig. 1. FT-IR spectrums of (**a**) Fe_3O_4@SiO_2, HM.SO_3H, (**b**) HM.SO_3H (IL)

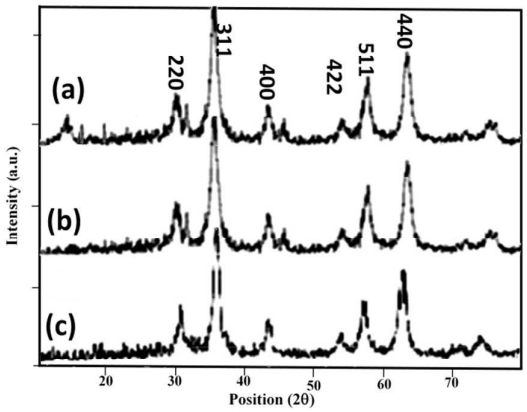


Fig. 2. XRD patterns of (a) Fe_3O_4@SiO_2.HM.SO_3H, (b) Fe_3O_4@SiO_2, (c) Fe_3O_4

The X-ray diffraction patterns of Fe_3O_4, Fe_3O_4@SiO_2 and Fe_3O_4@SiO_2.HM.SO_3H, 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 MNPs[39]. 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 magnetite[40]. Characteristic peak of SiO_2 in core shell structure has been hidden under weak peak of Fe_3O_4 at 2θ=30°[41]. The average diameter for Fe_3O_4@SiO_2.HM.SO_3H from the information obtained from XRD was about 55 nm.

Figure 3 shows the FESEM image of Fe_3O_4@SiO_2.HM.SO_3H, nearly spherical morphology with an average diameter of about 60 nm for catalyst has been observed.

The components of this 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) for this catalyst.

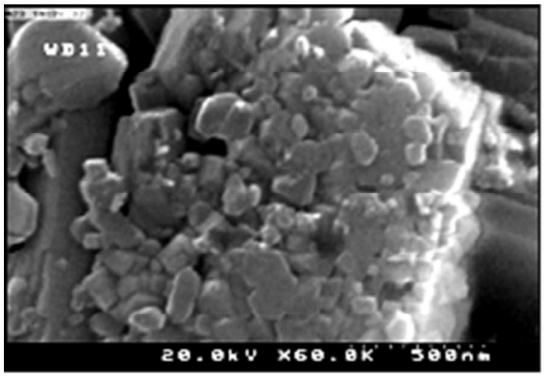


Fig. 3. FE-SEM of Fe_3O_4@SiO_2.HM.SO_3H

Magnetic properties of catalyst and Fe_3O_4@SiO_2 nanoparticles were determined by VSM at room temperature (Figure 5). The magnetization of samples could be completely saturated at high fields of up to 1.0 T and the saturation magnetization of samples changed, because of the functionalization by ionic liquid, from 47 to 7 emu.g^{-1},. Moreover, the room temperature

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magnetization curves, before and after functionalization exhibit no hysteresis which demonstrates its super paramagnetic characteristic[41,42]. The strong magnetization of the catalyst was also revealed by simple attraction with an external magnet.

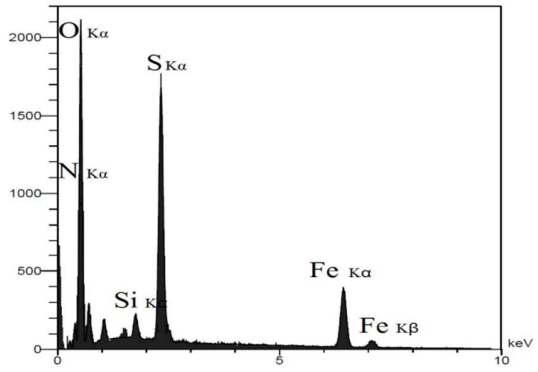

Fig. 4. EDX of Fe_3O_4@SiO_2.HM.SO_3H

The dynamic laser scattering (DLS) measurement of Fe_3O_4@SiO_2.HM.SO_3H nanoparticles was shown in Fig. 6. From this slurry, a stock dispersion (100 ml ethanol at 5 g Fe_3O_4@SiO_2.HM.SO_3H) was prepared using an ultrasonic bath for 30 min. Zeta potential of Fe_3O_4@SiO_2.HM.SO_3H nanoparticles exhibits positive values in ethanol. The value of zeta potential was measured to be 3.03 mV.

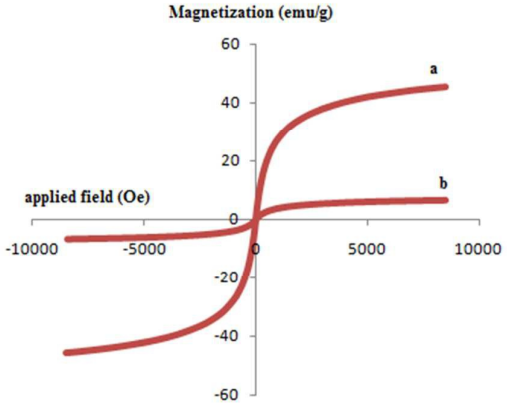

Fig 5. VSM of (**a**) Fe_3O_4@SiO_2, (**b**) Fe_3O_4@SiO_2.HM.SO_3H

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

The efficiency of the supported catalyst was found to be solvent independent and without any solvent good yields observed. To show the merit of Fe_3O_4@SiO_2.HM.SO_3H we have compared this catalyst with the multi-SO_3H functionalized ionic liquid and other catalysts in the synthesis of 2,4,5-trisubstituted imidazoles, under thermal condition. The results are shown in Table 1 (entries 1-6). As it is shown in this Table (entry 6) the reaction with Fe_3O_4@SiO_2.HM.SO_3H is the best choice between these catalysts, other catalysts afforded the desired product in lower yields (Table 1, entries 2-5).

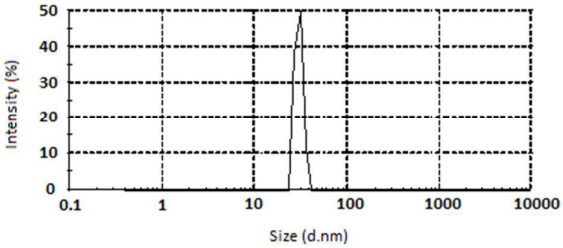

Fig. 6. Dynamic Laser scattering (DLS) measurement of nano Fe_3O_4@SiO_2.HM.SO_3H

The reaction was carried out in the presence of different amounts of the catalyst at constant temperature (100 °C). As can be seen in Table 1, entry 9, the optimum catalyst amount was obtained to equal 40 mg. Then, the reaction temperature was optimized and the results are shown in Table 1 (entries 11-16). As indicated in entry 15, the best operating temperature was found to be 110 °C (Oil bath), and no significant amount of product was produced at room temperature.

Table 1. Optimization of the reaction[a]

Entry	Catalyst	catalyst amount (mg)	Temp. (°C)	Time (min)	Yield (%)[b]
1	*None*	-	110	20	16
2	HCl	55	110	15	60
3	HOAc	90	110	15	40
4	H_2SO_4	47	110	15	60
5	HM-SO_3H (IL)	750	110	10	65
6	Fe_3O_4@SiO_2. HM-SO_3H	30	100	15	85
7	Fe_3O_4@SiO_2. HM-SO_3H	10	100	30	35
8	Fe_3O_4@SiO_2. HM-SO_3H	20	100	25	60
9	Fe_3O_4@SiO_2. HM-SO_3H	40	100	15	76
10	Fe_3O_4@SiO_2. HM-SO_3H	45	100	15	75
11	Fe_3O_4@SiO_2. HM-SO_3H	40	r.t	7h	-
12	Fe_3O_4@SiO_2. HM-SO_3H	40	80	30	60
13	Fe_3O_4@SiO_2. HM-SO_3H	40	90	20	70
14	Fe_3O_4@SiO_2. HM-SO_3H	40	100	15	76
15	Fe_3O_4@SiO_2. HM-SO_3H	40	110	12	95
16	Fe_3O_4@SiO_2. HM-SO_3H	40	120	10	80

[a] Reaction conditions*: benzil (1 mmol), 3,4-dimethoxy benzaldehyde (1 mmol), NH_4OAc (2 mmol), solvent-free*

[b] *Isolated yields.*

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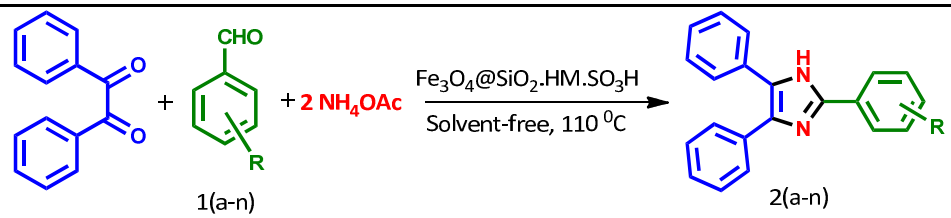
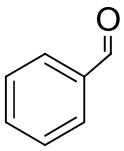
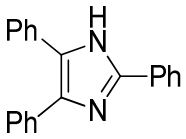
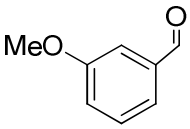
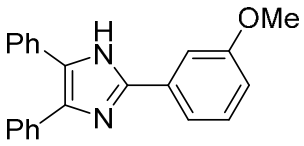
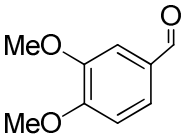
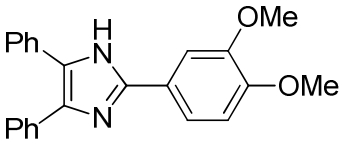
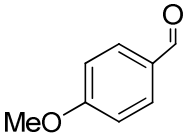
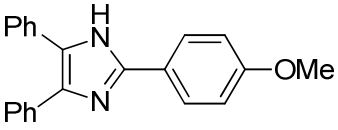
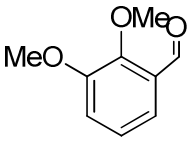
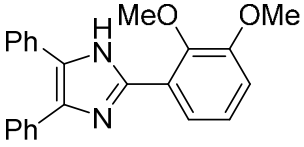
After optimizing the reaction conditions, we used different benzaldehydes as the substrates for this reaction. The corresponding results are summarized in Table 2. As the entries in Table 2 show the catalysis proceeded well for a wide variety of aldehydes, providing the corresponding imidazoles in high yields.

Table 2. Synthesis of 2,4,5-trisubstituted imidazoles in the presence of Fe_3O_4@SiO_2.HM.SO_3H catalyst [a]



Entry	Aldehyde	Product	Time (min)	Yield (%)
1	 1a	 2a	15	93
2	 1b	 2b	10	88
3	 1c	 2c	12	95
4	 1d	 2d	14	90
5	 1e	 2e	13	90

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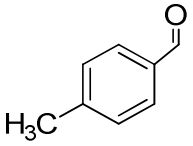
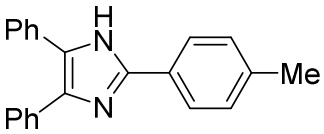
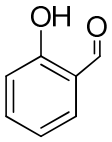
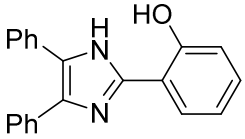
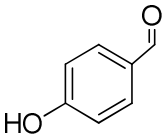
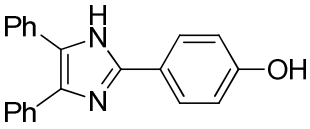
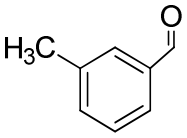
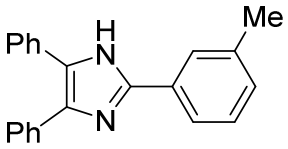
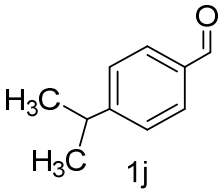
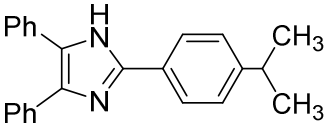
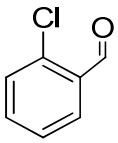
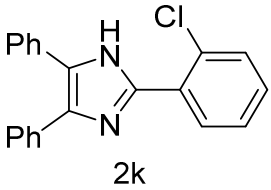
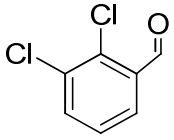
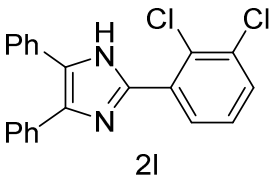
6	 1f	 2f	10	85
7	 1g	 2g	15	82
8	 1h	 2h	10	85
9	 1i	 2i	15	80
10	 1j	 2j	15	93
11	 1k	 2k	10	89
12	 1l	 2l	10	92

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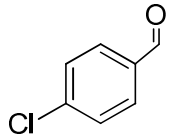
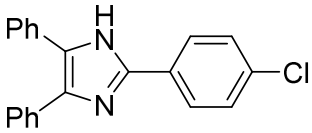
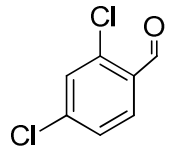
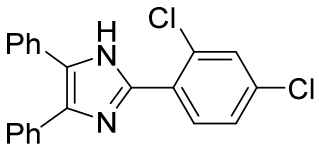
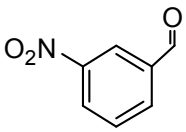
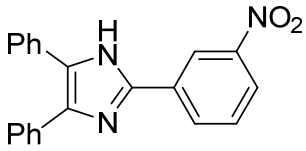
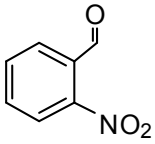
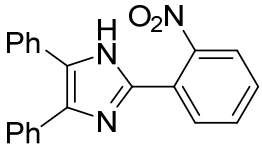
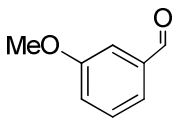
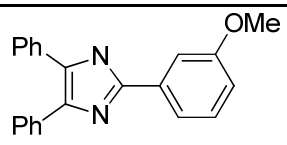
13	 1m	 2m	10	92
14	 1n	 2n	10	95
15	 1o	 2o	14	86
16	 1p	 2p	15	88

a) Reaction condition: benzil (1 mmol), 3,4-dimethoxy benzaldehyde (1mmol), NH_4OAc (2 mmol) was heated at 110°C, Catalyst amount: 40 mg.

A comparison of the present method with previously reported works [40,41] is reported in Table 3. As shown in this Table, the reaction of some aldehydes with benzyl and ammonium acetate in the presence of Fe_3O_4@SiO_2.HM.SO_3H as catalyst the excellent yields of related products were achieved in shorter reaction times under solvent free conditions Table 3, entries 2, 4, 6). While, in the previously reported works [43, 44], the similar reaction in the presence of other catalysts were afforded the corresponding products in lower yields and longer reaction times (Table 3, entries 1, 3, 5).

Table 3. Comparative study the present method with previous works

Entry	Aldehyde	Product	Time (min)	Yield(%)[b]	Ref.
1[a]			60	85	[40]

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2	10	88	This work
3[b]	120	92	[41]
4	12	95	This work
5[a]	90	87	[41]
6	10	95	This work

a) Reaction condition: Aromatic aldehyde (5 mmol), benzil (5 mmol), ammonium acetate (10 mmol), $[BPy]H_2PO_4$ (15 mol%) at 130°C under solvent-free conditions.

b) Reaction condition: benzaldehyde (1 mmol), benzil (1 mmol) and ammonium acetate (5 mmol), 0.05 g of Fe_3O_4@chitosan as nanocatalyst in EtOH.

The recyclability of the catalyst is an important benefit especially for commercial applications. The reusability of used catalyst was investigated using the reaction of benzil, 3,4-dimethoxy benzaldehyde and NH_4OAc in the presence of Fe_3O_4@SiO_2.HM.SO_3H under optimized conditions (Figure 7).

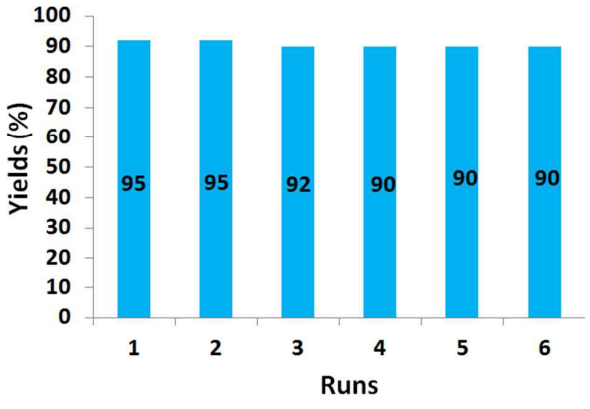

Fig. 7. Reusability of catalyst for synthesis of 2,4,5-trisubstituted imidazoles

The catalyst was recovered by an external magnet and washed thrice with acetone, dried and then reused for subsequent reactions for at least 6 times with less reduction in its catalytic activity.

Conclusions

Generally, catalytic activity is increased with magnetite nanoparticles of smaller size, as they contain a large amount of active catalytic sites compared to bigger particles. But in this case we have seen that the SiO_2 shell increases active sites for binding the functional group also it decreases the magnetization. In organocatalyzed reactions, typically 10 to 30 mol% of a catalyst, often an amino acid is needed. A great challenge is to reduce the quantity of organocatalysts and exploit them with higher efficiency, *i.e.* in a more economical way. In the synthesis, only 1mmol loading of ionic liquid on 1g of Fe_3O_4@SiO_2 was sufficient to achieve high catalytic activities from low amounts of catalyst was used; because of multi SO_3H functionalized ionic liquid the catalytic activity was remarkable.

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Acknowledgements

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1. F. Suzuki, T. Kuroda and T. Tamura, *J. Med. Chem.*, 1992, **35**, 2863-2870.
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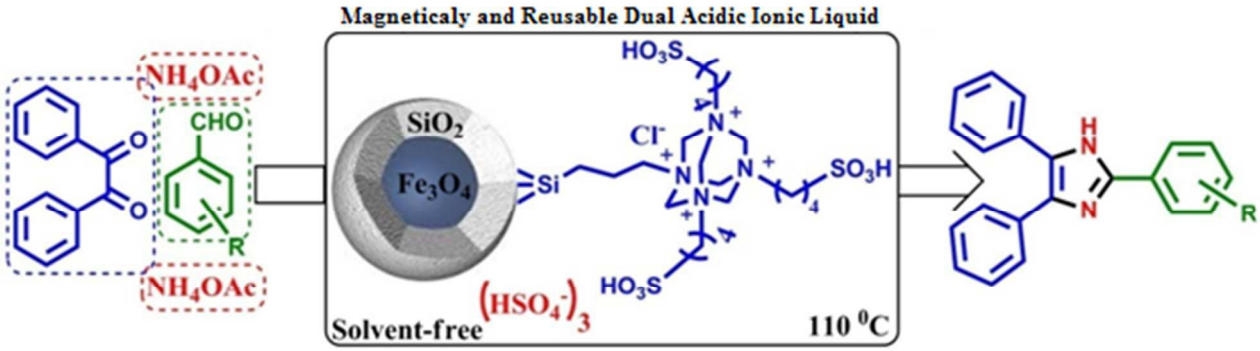
Graphical abstract

Ionophore silica-coated magnetite nanoparticles as a recyclable heterogeneous catalyst for one-pot green synthesis of 2,4,5-trisubstituted imidazoles



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