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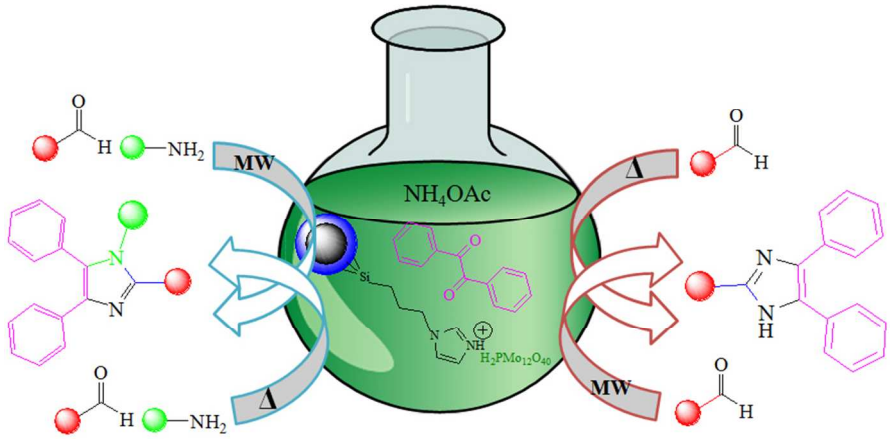

One-pot synthesis of substituted imidazoles by Fe_3O_4@SiO_2-Imid-PMA^n catalyst under solvent-free conditions

One-pot synthesis of multisubstituted imidazoles under solvent-free conditions and microwave irradiation by Fe_3O_4@SiO_2-imid-PMA^n magnetic porous nanosphere as recyclable catalyst

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Abstract

An efficient, green and eco-friendly procedure has been developed using Fe_3O_4@SiO_2-Imid-PMA^n as magnetic catalyst for rapid and an improved synthesis of 2,4,5-trisubstituted and 1,2,4,5-tetrasubstituted imidazoles under solvent-free conditions and microwave irradiation in excellent yields. The reactions in conventional heating conditions were compared with the microwave-assisted reactions. The operational simplicity, practicability and applicability of this protocol to various substrates make it an interesting alternative to previous procedures.
The present approach offers several advantages such as short reaction times, high yields, simplicity of operation, easy work-up, a cleaner reaction and ease of recovery and reusability of the catalyst by magnetic field. Also, nanocatalyst can be easily recovered by a magnetic field and reused for the next reactions for at least 5 times without distinct deterioration in catalytic activity. SEM, BET, DLS and leaching of catalyst after each reaction cycle were investigated.

Keywords

Fe_3O_4@SiO_2-imid-PMA^n magnetic nanocatalyst; Multisubstituted imidazoles; Multicomponent reaction; Solvent-free reaction; Microwave irradiation

1. Introduction

Imidazole and their derivatives, which usually possess diverse biological activities, play important roles as versatile building blocks for the synthesis of natural products and as therapeutic agents. [1,2] In particular, 2, 4, 5-trisubstituted imidazoles are biologically active and occur in structures of a number of anti-inflammatory, [3] anti-allergic, [4] analgesic [5] and glucagon receptor antagonism. [6] This core also has been utilized in diverse pharmaceutical applications such as anti-tumor [7] and anti-thrombotic [8] activities agents.

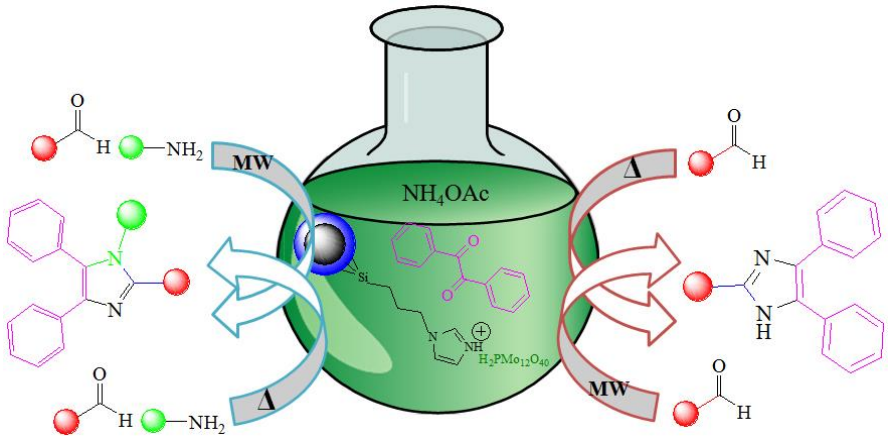
Appropriately substituted imidazoles are extensively used as glucagon receptors [9] and CB1 cannabinoid receptor antagonists, [10] modulators of P-glycoprotein (P-gp)-mediated multidrug resistance (MDR), [11] antibacterial [12] and antitumor [13] agents, and also as pesticides. [14] Recent advances in green chemistry and organometallic catalysis have extended the application of imidazoles as ionic liquids [15] and N-heterocyclic carbenes. [16] This versatile applicability highlights the importance of accessing efficient synthetic routes to well-designed highly substituted imidazole derivatives.

There are many synthetic methodologies that have been developed for assembling and decorating the imidazole ring with diverse functional groups. One of the approaches is using the transition metal catalyzed direct C–H/N–H functionalization [17] and other approaches include using various catalytic systems such as I_2, [18] SiO_2/ $NaHSO_4$, [19] $MgSO_4$, [20] $FeCl_3.6H_2O$ [21] and etc. They can also be obtained by use of microwave irradiation, [22] silica sulfuric acid, [23] $NiCl_2$ -$6H_2O$/ Al_2O_3 [24] and ionic liquids. [25] Many of the reported synthetic protocols for the synthesis of imidazoles suffer from one of the disadvantages or more such as the harsh reaction condition, the poor yields, the prolongation of time in the reaction and the use of heavy metal catalysts hazards. Therefore, the development of a new catalytic system to overcome these shortcomings and fulfill the criteria of a mild, efficient, and environmentally benign protocol for the synthesis of highly substituted imidazoles is still desirable and is in demand.

In recent years, Keggin-type heteropolyacids (HPAs) have been used as efficient catalysts for various organic reactions because of their superacidic and redox properties, low toxicity, ease of handling, low cost and high thermal stability. [26] Although these material are versatile compounds in their acidic form, their main disadvantages are high solubility in polar solvents and low surface area. In previous work, [27]we introduce a simple, repaid, inexpensive and one step

method, solvothermal, for synthesis of $H_3PMo_{12}O_4$ nanoparticles (PMA^n) from $H_3PMo_{12}O_4$ bulk particles (PMA^b). Acidity of as-prepared nanoparticles was investigated by pyridine adsorption method. Results showed rising acidity by declining particle size of HPAs.

Nowadays, Fe_3O_4 nanoparticles, as magnetite nanoparticles, have attracted increasing interest because of their unique properties including a large surface-to-volume ratio, superparamagnetism, low toxicity, biocompatibility and their potential applications in various fields. [28] The Fe_3O_4 nanoparticles are easily synthesized and functionalized by metal and organo-catalysts and they can be easily separated from the reaction mixture by external magnetic field and reused. [29] In our previous study, [30] PMA^n were supported on magnetic Fe_3O_4@SiO_2-imid nanoparticles. Compared to other substrates (silica, acidic ion-exchange resins, active carbon and nano titania), Fe_3O_4@SiO_2-imid nanoparticles have various advantages such as high loading capacity, low leaching and simple and efficient recovery procedure. Fig. 1 presents the procedure for the preparation of Fe_3O_4@SiO_2-imid-PMAn stepwise. In this article, we report a new and efficient method for one-pot synthesis of substituted imidazoles by Fe_3O_4@SiO_2-Imid-PMA^n catalyst under solvent-free conditions and microwave irradiation (Scheme 1).



Scheme 1 One-pot synthesis of substituted imidazoles by Fe_3O_4@SiO_2-Imid-PMA^n catalyst under solvent-free conditions.

2. Experimental

2.1. Chemicals and instrumentation

Chemical materials were purchased from the Merck Chemical Company in high purity. All the solvents were distilled, dried and purified by standard procedures. Fourier transform infrared (FT-IR) spectra were obtained using a Shimadzu FT-IR 8300 spectrophotometer. The ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) were run on a Bruker Avance DPX-250 using tetramethylsilane (TMS) as an internal reference. All reactions were carried out using a laboratory microwave oven (MicroSYNTH, Milestone Company, Italy). Magnetic characterization was carried out on a vibrating sample magnetometer (Meghnatis Daghigh Kavir Co., Iran) at room temperature. Scanning electron microscopy (SEM) image was obtained on Philips XL-30ESEM and dynamic light scatterings (DLS) were recorded on a HORIBA-LB550. Melting points were measured with an Electrothermal 9100 apparatus. The elemental analyses (C, H, N) were obtained from a Carlo ERBA Model EA 1108 analyzer carried out on a Perkin–Elmer 240c analyzer. Therefore, all of the products were characterized by FT-IR, ^{1}H NMR and ^{13}C NMR, and also by comparison with authentic samples.

2.2. Catalyst preparation

2.2.1. Preparation of Fe_3O_4@SiO_2 core–shell

The core–shell Fe_3O_4@SiO_2 nanospheres were prepared by a modified Stober method in our previous work. [30] In a typical procedure, the mixture of $FeCl_3.6H_2O$ (1.3 g, 4.8 mmol) in water (15 mL) was added to the solution of polyvinyl alcohol (PVA 15000), as a surfactant, and $FeCl_2.4H_2O$ (0.9 g, 4.5 mmol) in water (15 mL), which was prepared by completely dissolving PVA in water followed by addition of $FeCl_2.4H_2O$. The resultant solution was left to be stirred for 30 min in 80 ^{o}C. Then, hexamethylentetr amine (HMTA) (1.0 mol/L) was added drop by drop with vigorous stirring to produce a black solid product when the reaction media reaches pH 10. The resultant mixture was heated on water bath for 2 h at 60 ^{o}C and the black magnetite solid product was filtered and washed with ethanol three times and was then dried at 80 ^{o}C for 10 h. Then Fe_3O_4 nanoparticle (0.50 g, 2.1 mmol) was dispersed in the mixture of ethanol (50 mL), deionized water (5 mL) and tetraethoxysilane (TEOS) (0.20 mL), 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 deionized water and ethanol three times and dried at 80 ^oC for 10 h.

2.2.2. Preparation of $Fe_3O_4@SiO_2$-imid

$Fe_3O_4@SiO_2$ (1 g) was added to the solution of 3-chlorotriethoxypropylsilane (1 mmol, 0.241 g) and imidazole (1 mmol, 0.0680 g) in *p*-xylene (20 mL) and the resultant mixture was under reflux for 24 h under nitrogen atmosphere. After refluxing for about 24 h, the mixture was cooled to room temperature, filtered by an external magnet and the product was washed with xylene to remove any reacted species and dried at 70 ^oC for 6 h. [30]

2.2.3. Preparation of $H_3PMo_{12}O_{40}$ nanoparticles (PMA^n)

PMA^n nanoparticles were prepared in our previous work, [27] which is a simple and single step method. In a typical procedure, 5 mmol of bulk $H_3PMo_{12}O_{40}$ (PMA^b) was dispersed in 50 mL *n*-Octane and the resulting dispersion was stirred vigorously for 30 min at room temperature to form a homogeneous dispersion. This dispersion was transferred into a Teflon-lined stainless autoclave filling 80% of the total volume. The autoclave was sealed and maintained at 150 ^oC for 12 h. The autoclave was then cooled to room temperature. Finally, the resulted powder was filtered and washed for several times by octane, and dried in a vacuum at 80 ^oC for 12 h.

2.2.4. Preparation of $Fe_3O_4@SiO_2$-imid-PMA^n

Fig. 1 represents the anchoring of PMA^n onto $Fe_3O_4@SiO_2$- imid. $Fe_3O_4@SiO_2$-imid (1.0 g) was added to an acetonitrile solution of PMA^n (1.0 mmol) in 20 mL was taken in a round-bottom flask. The mixture was refluxed for 24 h under nitrogen atmosphere. After 24 h, the mixture was filtered by an external magnet, washed with acetonitrile and dichloromethane, and dried at 70^oC for 6 h. FT-IR spectrum of the catalyst showed the expected bands, including distinctive bands due to anchoring of PMA^n onto $Fe_3O_4@SiO_2$-imid. [30]

2.3. General procedure for the synthesis of 1,2,4,5- tetrasubstituted imidazoles

A mixture of benzil (1 mmol), ammonium acetate (1 mmol), aldehyde (1 mmol), primary aliphatic and aromatic amine (1 mmol) and $Fe_3O_4@SiO_2$-imid-PMA^n catalyst (0.03 g) was

stirred with a glass bar at 110 ^{o}C or irradiated in a microwave oven at 100 W for the appropriate time. The progress of reaction was followed by TLC. 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 dissolved in acetone and filtered. The filtrate was concentrated on a rotary evaporator under reduced pressure and the solid product obtained was washed with water and recrystallized from acetone–water 8:1 (v/v). Pure products were obtained in excellent yields, as summarized in Table 2.

2.4. General procedure for the preparation of 2,4,5-trisubstituted imidazoles

In a 50 mL round bottom flask a mixture of 1,2-diketone (1 mmol), ammonium acetate (3 mmol), aldehyde (1 mmol), and Fe_3O_4@SiO_2-imid-PMA^n catalyst (0.03 g) was stirred at 110 ^{o}C or irradiated in a microwave oven at 100 W for the appropriate time. After completion of the reaction which was monitored by TLC using eluent (1:4 mL, petroleum ether: ethyl acetate), the mixture was washed with water completely and the solid product dissolved in hot ethyl acetate. Then, the mixture was filtered by an external magnet for removing the unsolvable catalyst and the filtrate was cooled to afford the pure product.

3. Results and discussion

First of all, the Fe_3O_4@SiO_2 nanosphere core-shell is synthesized. Then, $H_3PMo_{12}O_{40}$ nanoparticles were synthesized by the treatment of $H_3PMo_{12}O_{40}$ with *n*-Octane as solvent by a solvothermal method and this nano heteropolyacid immobilized onto imidazole functionalized Fe_3O_4@SiO_2 nanoparticles (Fig. 1). [30] The Fe_3O_4, Fe_3O_4@SiO_2 and Fe_3O_4@SiO_2-imid-PMA^n nano catalysts were characterized by various methods such as transmission electron microscopy (TEM), scanning electron microscopy (SEM), dynamic light scattering (DLS), Fourier transform infrared (FT-IR), Vibrating sample magnetometer (VSM) and etc. As shown in Fig. 1 Fe_3O_4@SiO_2-imid-PMA^n nanoparticles have spherical shapes with approximately 50 nm diameters. The size distribution of these is centered at a value of 55 nm. Themagnetic properties of Fe_3O_4, Fe_3O_4@SiO_2, Fe_3O_4@SiO_2-imid-PMA^n nanoparticles were measured by VSM at room temperature. All the samples show a typical superparamagnetic behavior. Hysteresis

phenomenon was not found and the magnetization curves were coincident. The saturation magnetizati magnetization of samples is 63.4, 39.7, 33.2 emu g^{-1}, respectively.

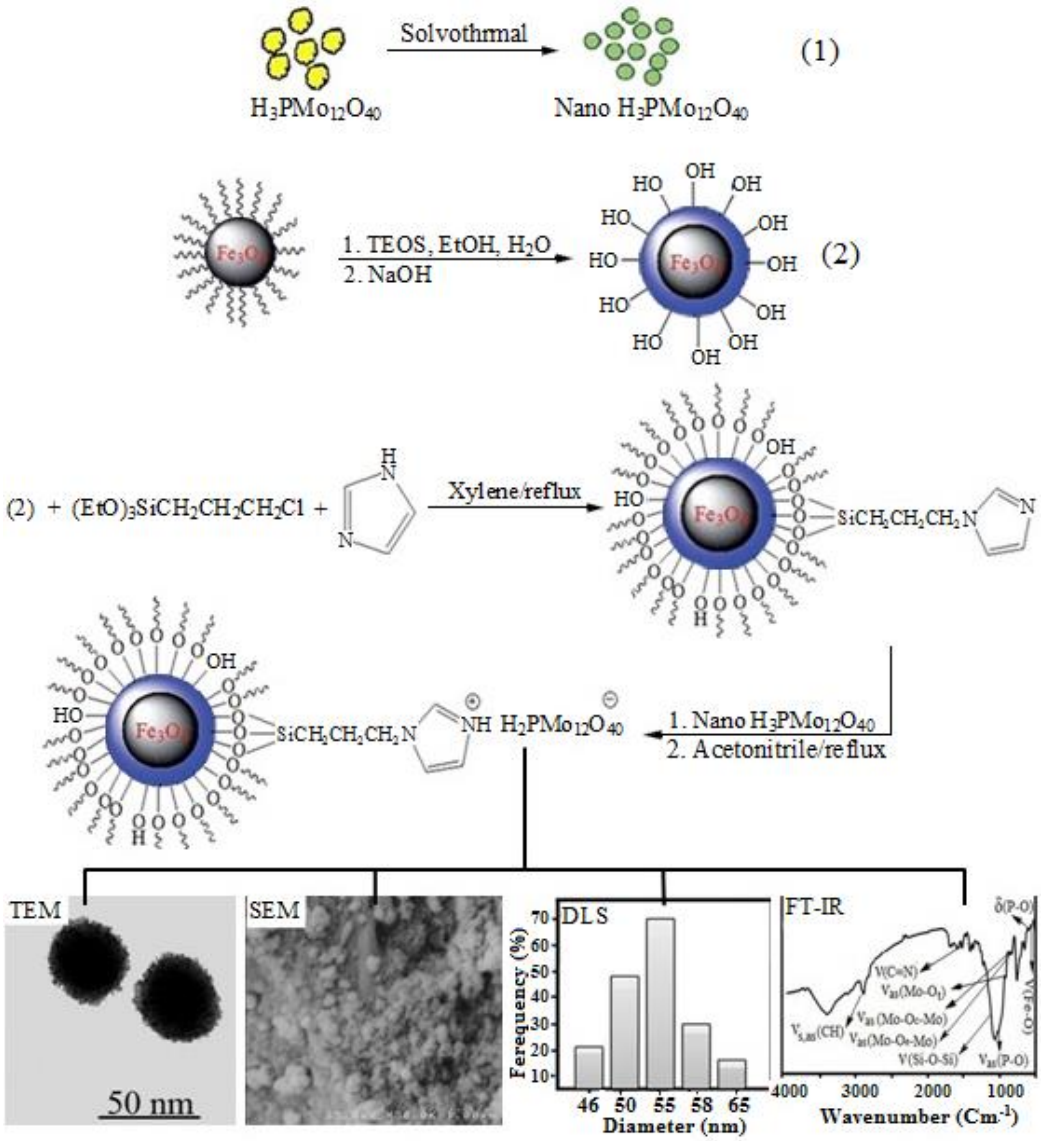


Fig.1 Process for preparation of immobilization of $H_3PMo_{12}O_{40}$ nanoparticles (PMA^n) on imidazole functionalized Fe_3O_4@SiO_2 nanoparticle. [30]

Then to optimize the reaction conditions in terms of solvent, temperature and amount of catalyst, a model reaction was performed by the condensation of benzil (1 mmol), benzaldehyde (1 mmol), aniline (1 mmol) and ammonium acetate (1 mmol) under solvent free conditions at

different temperatures with variant amounts of catalyst Fe_3O_4@SiO_2-Imid-PMA^n and the observations are as follows: in the absence of catalyst at 110 °C formation of product was not observed even after 12 h (Table 1, entry 1). To improve the yield of the product the above reaction was tested with 0.01, 0.02, 0.03 and 0.04 g catalyst at 110 °C (Table 1, entry 2-5) and observed the maximum yield (92%) in shorter reaction time (1.5 h) with 0.03 g catalyst. Further increasing of catalyst loading does not affect the yield (Table 1, entry 5). The effect of temperature was studied by carrying out the model reaction at different temperatures under solvent free (room temperature, 60 ^{o}Cand 100 ^{o}C) (Table 2, entries 6-8) and the best result was obtained at 110 ^{o}C (Table 2, entry5). Increasing the temperature to 120 °C has no effect in the yield of product (Table 1, entry 9). As it was shown in Table 1, solvent free condition at 110 ^{o}C with 0.03 g catalyst is obviously the best choice for these reactions (Table 1, entry 4).

The use of other solvents such as MeOH, EtOH, CH_3CN, CH_2Cl_2, $PhCH_3$ and H_2O afforded the desired product in lower yields (Table 1, entries 10-16).

During the past two decades many investigations have established the critical role of microwave irradiation in the rate acceleration of diverse chemical reactions. [31] Considering this fact, we decided to examine our methodology under microwave irradiation. Therefore, the reaction was repeated under solvent free conditions in microwave irradiation with different amounts of catalyst (Table 1, entries 17-19) and observed the maximum yield (94%) in shorter reaction time (10 min) with 0.03g catalyst (Table 1, entries 18).

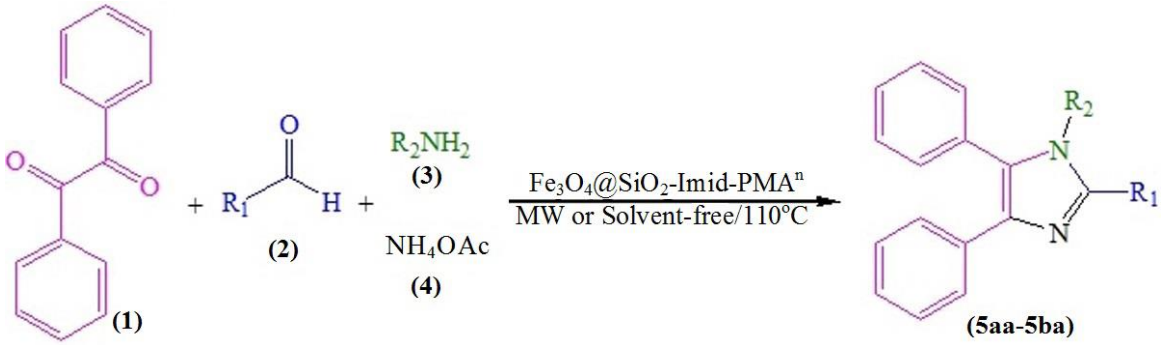
Table 1 Condensation of benzil, benzaldehyde, aniline and ammonium acetate under different conditions.[a]

Entry	Solvent/catalyst amount (g)	Conditions	Time (h)	Yield[b] (%)
1	Solvent-free/None	110^{o}C	12	-
2	Solvent-free/0.01	110^{o}C	2	24
3	Solvent-free/0.02	110^{o}C	2	82
4	Solvent-free/0.03	110^{o}C	1.5	92
5	Solvent-free/0.04	110^{o}C	1.5	91
6	Solvent-free/0.03	rt	4	17
7	Solvent-free/0.03	60^{o}C	4	53
8	Solvent-free/0.03	100^{o}C	2	85
9	Solvent-free/0.03	120^{o}C	1.5	92
10	MeOH/0.03	Reflux	4	57
11	EtOH/0.03	Reflux	4	65
12	CH_3CN/0.03	Reflux	4	51

13	CH_2Cl_2/0.03	Reflux	4	23
14	$CHCl_3$/0.03	Reflux	4	29
15	$PhCH_3$/0.03	Reflux	4	15
16	H_2O/0.03	Reflux	4	48
17	Solvent-free/0.02	MW(100W)	15 min	88
18	Solvent-free/0.03	MW(100W)	10 min	94
19	Solvent-free/0.04	MW(100W)	10 min	94

[a]Conditions: benzil (1mmol), benzaldehyde (1mmol), aniline (1mmol) and ammonium acetate (1 mmol).
[b]Yields refer to isolated pure product.

Then, the scope and efficiency of the process was explored under the optimized conditions. For this purpose, a broad range of structurally diverse aromatic aldehydes as well as amines (aliphatic or aromatic) was successfully condensed with benzil and ammonium acetate under solvent free conditions at 110 °C or under microwave conditions (Scheme 2**)** and the results are displayed in Table 2. As be seen the yields were good to excellent without preparation of any side products and the reaction times are very low. Aromatic aldehydes bearing such functional groups as nitro, chloro, bromo, methyl, or methoxy were able to affect the imidazole synthesis. We have also observed that the electronic effect on the aldehydes had influence on the yield and time of reaction conditions: that is, aryl aldehydes with electron-withdrawing groups reacted rapidly (Table 2, entries 4, 5, 12-15, 22, 27), while substitution of electron-rich groups on the benzene ring decrease the reactivity (Table 2, 3, 7-10, 16, 17, 23-26). Also, the substrate scope of the reaction was evaluated using another primary amine i.e. benzyl amine. Both aromatic and aliphatic primary amines have been successfully subjected to this method (Table 2). Beside this, our methodology has been used successfully for heteroaromatic aldehydes, and corresponding imidazoles were obtained in excellent yields and without any byproduct (Table 2, entries 11, 18, 19). Also, microwave irradiation has shown better yields and especially reaction times.
All the products obtained were fully characterized by ^{1}H NMR and ^{13}C NMR spectroscopy and by comparison of their physical and spectral data with those of authentic samples.



Scheme 2 Synthesis of 1,2,4,5-tetrasubstituted imidazoles via a one-pot four component condensation reaction in the presence of Fe_3O_4@SiO_2-Imid-PMA^n catalyst.

Table 2 Synthesis of 1,2,4,5-tetrasubstituted imidazoles via a one-pot four component condensation reaction in the presence of Fe_3O_4@SiO_2-Imid-PMA^n catalyst.

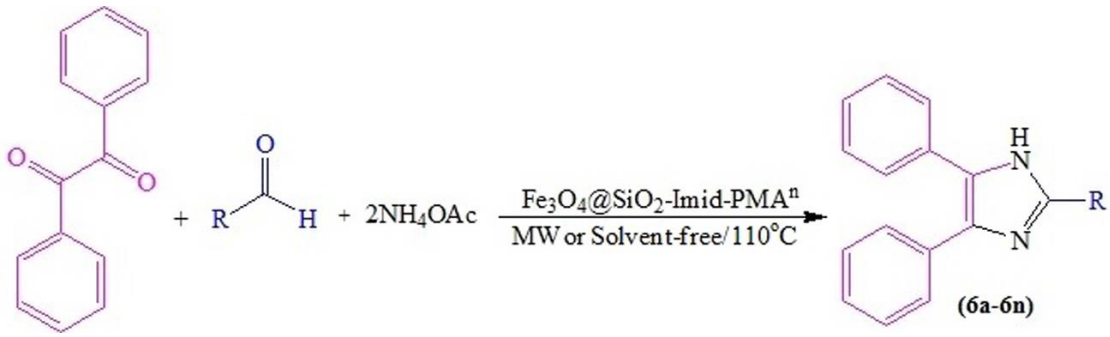
Entry	R_1	R_2	Product	Time (min) (MW)/(110 °C)	Yield (%)[b] (MW)/(110 °C)	Mp. (◦C) (Lit.)[c] Ref.
1	C_6H_5	C_6H_5	**5aa**	10/90	95/92	217-219 (218)[32]
2	4-CH_3-C_6H_4	C_6H_5	**5ab**	15/120	91/89	190-191 (189)[32]
3	4-OH-C_6H_4	C_6H_5	**5ac**	20/150	89/86	281-282 (280-281)[33]
4	4-Cl-C_6H_4	C_6H_5	**5ad**	8/75	97/94	162-164 (160-163)[34]
5	4-Br-C_6H_4	C_6H_5	**5ae**	10/75	96/92	210-212 (207-211)[34]
6	C_6H_5	$C_6H_5CH_2$	**5af**	8/75	95/90	159-161 (158-160)[32]
7	4-CH_3-C_6H_4	$C_6H_5CH_2$	**5ag**	15/90	92/88	164-166 (165-166)[32]
8	3-CH_3O-C_6H_4	$C_6H_5CH_2$	**5ah**	20/150	90/86	129-131
9	4-CH_3O-C_6H_4	$C_6H_5CH_2$	**5ai**	20/150	89/83	156-158 (157-160)[35]
10	4-HO-C_6H_4	$C_6H_5CH_2$	**5aj**	17/150	90/87	136-138 (134-135)[36]
11	2-furyl	$C_6H_5CH_2$	**5ak**	7/75	94/93	157 (156-157)[36]
12	4-Cl-C_6H_4	$C_6H_5CH_2$	**5al**	10/60	95/90	147-149 (146-148)[32]
13	4-NO_2-C_6H_4	4-CH_3-C_6H_4	**5am**	5/50	97/91	221
14	3-NO_2-C_6H_4	4-CH_3-C_6H_4	**5an**	10/75	95/94	150-152 (149-151)[37]
15	4-CN-C_6H_4	4-CH_3-C_6H_4	**5ao**	5/60	93/89	202-203 (198-201)[38]
16	4-CH_3-C_6H_4	4-CH_3-C_6H_4	**5ap**	12/90	90/85	190-192
17	3-HO-C_6H_4	4-CH_3-C_6H_4	**5aq**	15/90	89/84	233-235 (235-237)[38]
18	2-thienyl	4-CH_3-C_6H_4	**5ar**	8/75	93/87	201-203 (199-202)[38]
19	3-indolyl	4-CH_3-C_6H_4	**5as**	18/180	88/85	219-221 (218-220)[38]
20	C_6H_5	CH_3	**5at**	12/120	87/84	145-147 (144-145)[32]
21	4-CH_3-C_6H_4	CH_3	**5au**	15/150	86/85	209-211
22	4-Br-C_6H_4	CH_3	**5av**	12/150	88/83	202-204
23	4-CH_3-C_6H_4	cyclohexyl	**5aw**	20/180	86/81	161-163 (164)[36]
24	4-CH_3-C_6H_4	*iso*-C_4H_9	**5ax**	15/150	90/84	153-154 (151-153)[36]
25	4-CH_3O-C_6H_4	n-Pr-NH_2	**5ay**	15/120	88/81	79-81 (76-80)[39]
26	4-CH_3-C_6H_4	n-Pr-NH_2	**5az**	12/120	90/85	82-84 (78-83)[39]
27	4-Cl-C_6H_4	n-Pr-NH_2	**5ba**	10/90	94/90	88 (85-87)[39]

[a]Reaction conditions: benzil (1 mmol), aldehyde (1 mmol), primary amine (1 mmol) and ammonium acetate (1 mmol) in the presence of Fe_3O_4@SiO_2-Imid-PMA[n] catalyst at 110°C and/or under Microwave Irradiation.
[b]Isolated yield.
[c]Melting points reported in the parenthesis refer to the literature melting points.

In order to explore the applicability of this method, the same reaction conditions were used for synthesis of 2,4,5-trisubstituted imidazoles via a one-pot, cyclo-condensation of benzil (1 mmol), aldehyde (1 mmol) and ammonium acetate (3 mmol) under solvent-free classical heating conditions and using microwave irradiation are given in Table 2.

A wide range of aldehydes containing electron-withdrawing and electron-donating groups were investigated. Aldehydes containing electron-withdrawing groups such as, chloro, bromo and nitro underwent condensation in short reaction times with excellent isolated yields with both of conditions (Scheme 2 and Table 3, entries 2-8). Aldehydes containing electron-donating groups such as methyl, methoxy and hydroxyl required longer reaction time. (Table 2, 9-14). Using microwave irradiation gave comparable yields of products but with shorter reaction time, compared to conventional heating.

A mechanism for the catalytic activity of Fe_3O_4@SiO_2 -Imid-PMA[n] in the synthesis of imidazole derivatives is shown in Scheme 4. [44] After the protonation of the carbonyl group of the aryl aldehyde and the nucleophilic attack of the nitrogen atoms of ammonia, obtained from NH_4OAc, and aniline to it, intermediate **(I)** is formed. In the presence of Fe_3O_4@SiO_2 -Imid-PMA[n], intermediate **(I)** condenses with benzil to form intermediate **(II)** which in turn forms tetrasubstituted imidazoles by dehydration.

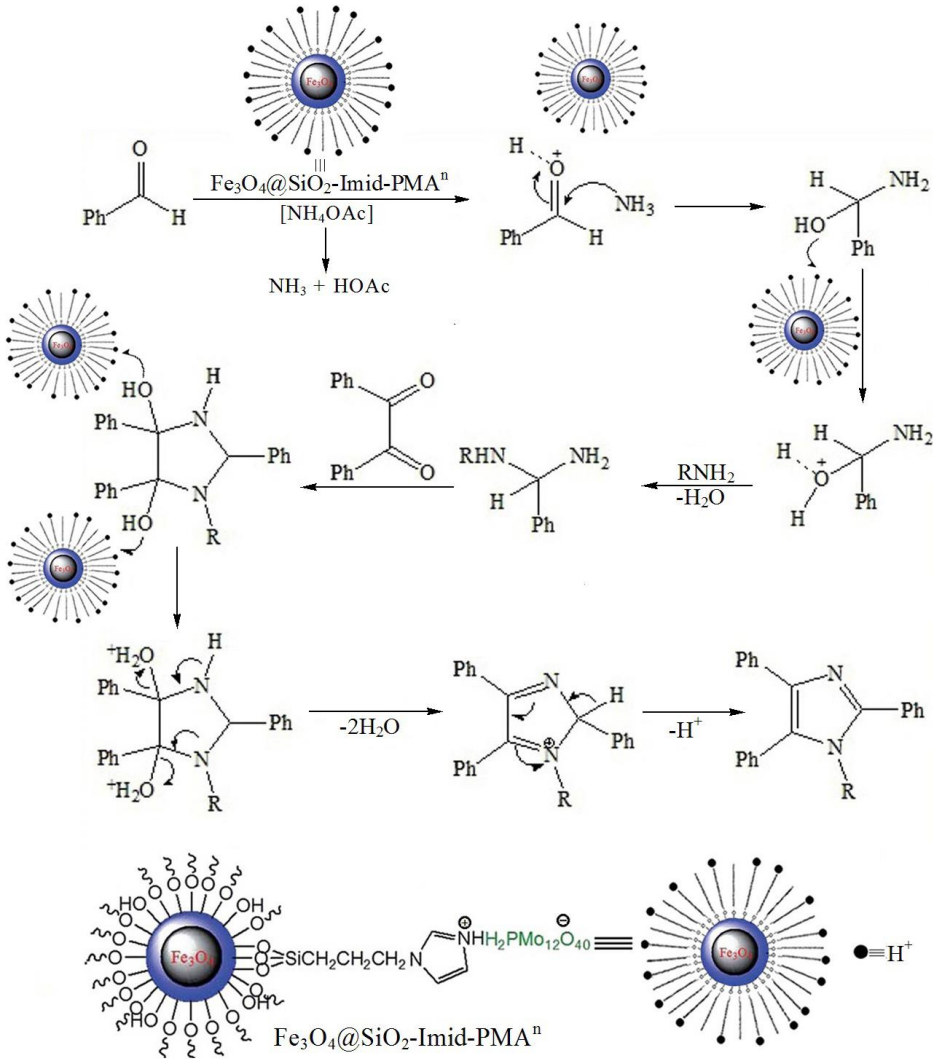


Scheme 2 Synthesis of 2,4,5-trisubstituted imidazole derivatives catalyzed by Fe_3O_4@SiO_2-Imid-PMA[n] catalyst.

Table 3 Synthesis of 2,4,5-trisubstituted imidazole derivatives catalyzed by Fe_3O_4@SiO_2-Imid-PMA^n catalyst.

Entry	R	Product	Time (min) (MW)/(110 °C)	Yield (%)[b] (MW)/(110 °C)	Mp. (◦C) (Lit.)[c] Ref.
1	C_6H_5	**6a**	10/75	94/88	273-274 (272-273)[18]
2	4-Cl-C_6H_4	**6b**	5/60	96/89	261-262 (262-263)[18]
3	2-Cl-C_6H_4	**6c**	8/75	91/87	198-200 (199-201)[40]
4	3-NO_2-C_6H_4	**6d**	8/75	93/86	264-266 (265-267)[18]
5	4-NO_2-C_6H_4	**6e**	5/60	97/94	237-239 (239-242)[41]
6	2,4-$Cl_2C_6H_3$	**6f**	5/75	95/91	174-175 (172-173)[41]
7	4-Br-C_6H_4	**6g**	10/80	89/85	262-264 (261-263)[41]
8	2-Br-C_6H_4	**6h**	8/75	90/83	203-204 (201-202)[41]
9	4-CH_3-C_6H_4	**6i**	15/90	88/87	227-228 (226-227)[18]
10	4-Me_2N-C_6H_4	**6j**	18/120	87/81	256-258 (255-256)[42]
11	4-CH_3O-C_6H_4	**6k**	15/120	89/86	226-228 (227-228)[42]
12	4-HO-C_6H_4	**6l**	18/150	84/79	254-256 (256-257)[18]
13	3,5-$(MeO)_2C_6H_3$	**6m**	20/180	82/76	257-258 (255-256)[42]
14	2-HO-C_6H_4	**6n**	20/180	80/73	207-209 (209-211)[43]

[a]Reaction conditions: benzil (1 mmol), aldehyde (1 mmol) and ammonium acetate (3 mmol) in the presence of Fe_3O_4@SiO_2 -Imid-PMA^n catalyst (0.03 g) at 110 °C and/or under Microwave Irradiation.
[b]Isolated yield.
[c]Melting points reported in the parenthesis refer to the literature melting points.



Scheme 4 Probable mechanism for the formation of tetrasubstituted imidazoles using Fe_3O_4@SiO_2-Imid-PMA^n as catalyst.

Fe_3O_4@SiO_2-Imid-PMA^n magnetic catalyst dispersed in solvent can be easily separated by external magnetic field within several minutes without the need for a filtration step, and then can be readily re-dispersed with slight shake, indicating directly that the nanoparticles possess magnetic properties. Such magnetic separation performance makes the nanoparticles more effective and convenient in application. The reusability and recovery of the catalyst are important issues, especially when the reactions use solid catalysts. For the recycling study, the reusability of Fe_3O_4@SiO_2-Imid-PMA^n catalysts were investigated in the synthesis of 1,2,4,5-tetrasubstituted imidazoles and in the synthesis of 2,4,5-trisubstituted imidazoles under solvent-free at 110 ^oC and using microwave irradiation (Fig. 2A). In order to confirm the reusability and

stability of this magnetic nanocatalyst it was recovered by a magnetic field and the remaining solid was washed with ethyl acetate (3×10 mL), dried and the catalyst reused for subsequent reactions for at least 6 times without any activation process (Fig. 2A, a, b, c, d).

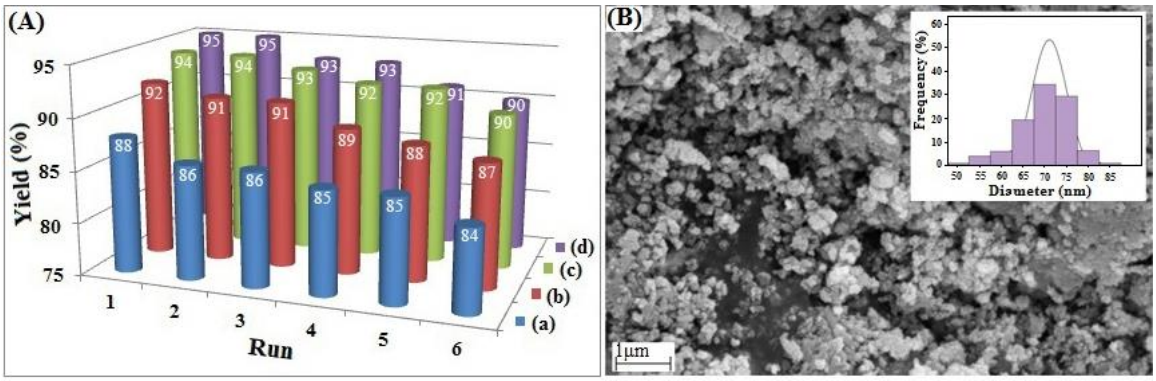


Fig. 2 (A) Recyclability of Fe_3O_4@SiO_2-Imid-PMA^n in the synthesis of 1,2,4,5-tetrasubstituted imidazoles **(b,d)** and in the synthesis of 2,4,5-trisubstituted imidazoles **(a,c)**. **(B)** SEM and DLS images of Fe_3O_4@SiO_2-imid-PMA^n nanoparticles after six reaction cycles.

[a]Reaction conditions: benzil (1 mmol), benzaldehyde (1 mmol), ammonium acetate (3 mmol), Fe_3O_4@SiO_2- Imid-PMA^n (0.04 g) under solvent-free at 110^{o}C.

[b]Reaction conditions: benzil (1 mmol), benzaldehyde (1 mmol), aniline (1 mmol), ammonium acetate (1 mmol), Fe_3O_4@SiO_2- Imid-PMA^n (0.04 g) under solvent-free at 110 ^{o}C.

[c]Reaction conditions: benzil (1 mmol), benzaldehyde (1 mmol), ammonium acetate (3 mmol), Fe_3O_4@SiO_2- Imid-PMA^n (0.03 g) under Microwave Irradiation.

[d]Reaction conditions: benzil (1 mmol), benzaldehyde (1 mmol), aniline (1 mmol), ammonium acetate (1 mmol), Fe_3O_4@SiO_2- Imid-PMA^n (0.03 g) under Microwave Irradiation.

SEM and DLS images of the catalyst after the six recycle in the synthesis of 1,2,4,5-tetraphenylimidazole (**5aa**) under solvent-free conditions at 110 ^{o}C have been represented in Fig. 2B. As shown in Fig. 2B, Fe_3O_4@SiO_2-imid-PMA^n nanoparticles had an average diameter of 75 nm, were of uniform size, and showed good dispersity. Additionally, the hydrodynamic diameter of catalyst was investigated by DLS technique (Fig. 2B). This size distribution is centered at a value of 70 nm. Generally, the size of catalysts will be increased after each cycle and leaching of $H_3PMo_{12}O_{40}$ and increasing of catalyst size lead to decreases the yield.

To determine the exact species responsible for the observed reactions and to measure the extent of PMA^n leaching after the reactions, we have used the hot filtration test. [45] For this aim, we have studied the condensation of benzil, benzaldehyde, aniline and ammonium acetate in the presence of Fe_3O_4@SiO_2- Imid-PMA^n catalyst under solvent free conditions at 110 ^{o}C. Then we carried out a 'hot filtration' test; when the reaction was half done, Fe_3O_4@SiO_2- Imid-PMA^n nanoparticles were removed in situ at the reaction temperature, and the reactants were allowed to

undergo further reaction in the solution. We confirmed that there was too small conversion of the reactants in the absence of the nanoparticles. These results indicate that there was little active PMA^n species in the solution phase.

The amounts of the nano heteropolyacid leaching into solution for the reaction benzil, benzaldehyde, aniline and ammonium acetate under solvent free conditions at 110°C was detected by checking the molybdenum (Mo) loading amount before and after each reaction cycle through ICP. The amount of Mo leaching after the first run was determined by ICP analysis to be only 0.47%, and after 6 repeated recycling was 3.92%. Therefore, the analysis of the reaction mixture by the ICP technique showed the leaching of $H_3PMo_{12}O_{40}$ was negligible.

Additionally, the size and surface area of catalysts after each reaction cycle for the synthesis of 1,2,4,5-tetraphenylimidazole (**5aa**), was investigated by DLS and nitrogen physisorption method (BET) respectively and results are provided in Table 4. As shown, the size of catalysts will be increased after each cycle. Generally, leaching of PMA, increase of catalyst size and decrease of surface area led to a decrease in the yield of reaction.

Run	Mean article size [a] (nm)		Surface area [b] (m^2 g^{-1})	
	MW method	Thermal method	MW method	Thermal method
1	56	58	422	420
2	60	61	415	400
3	62	65	399	391
4	62	65	390	389
5	63	68	381	370
6	68	70	376	357

[a] By DLS.
[b] By BET.

Conclusion

In conclusion, an extremely efficient method has been developed for the synthesis of biologically active three and tetrasubstituted imidazoles via condensation of benzil with various aromatic aldehydes, a primary amine and ammonium acetate using Fe_3O_4@SiO_2-Imid-PMA^n as a recyclable nanocatalyst under solvent-free conditions and microwave irradiation. This method is bestowed with several unique merits, such as cleaner reaction profiles, high reaction rates and excellent yields, simple experimental and work-up procedures, no side reactions and use of recyclable and environmentally benign nature of catalyst, and thus significantly contributes to

the practice of green chemistry. In addition, the excellent catalytic performance and the easy preparation, thermal stability and separation of the catalyst by external magnetic field make it a good heterogeneous system and a useful alternative to other heterogeneous catalysts.

Selected data

(Table 2, **5aa**) **1,2,4,5-Tetraphenylimidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 7.20-7.45 (m, 20H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 124.1, 124.5, 125.1, 126.9, 128.3, 129.1, 130.3, 130.6, 132.9, 134.3, 136.8, 139.0, 139.2, 139.5, 139.8, 140.1, 144.6; FT-IR (KBr, Cm^{-1}) = 1446, 1477, 1493, 1604; Anal. Calcd. for $C_{27}H_{20}N_2$: C, 87.07; H, 5.41; N, 7.52%. Found: C, 87.12; H, 5.37; N, 7.57%.

(Table 2, **5ab**) **1,4,5-Triphenyl-2-*p*-tolyl-1*H*-imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.26 (s, 3H), 7.08 (d, *J*= 8.0 Hz, 2H), 7.16-7.18 (m, 1H), 7.22-7.25 (m, 6H), 7.26-7.28 (m, 5H), 7.31-7.32 (m, 3H), 7.50 (d, *J*= 8.0 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.5, 127.2, 128.4, 128.9, 129.0, 129.2, 129.50, 129.58, 129.6, 129.9, 131.3, 131.9, 132.0, 135.3, 137.60, 137.63, 138.6, 147.0; FT-IR (KBr, Cm^{-1}) = 691, 765, 827, 1347, 1492, 1601, 2931, 3024, 3052; Anal. Calcd. for $C_{28}H_{22}N_2$: C, 87.01; H, 5.74; N, 7.25%. Found: C, 86.96; H, 5.68; N, 7.29%.

(Table 2, **5ac**) **4-(1,4,5-Triphenyl-1*H*-imidazol-2-yl)phenol**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 6.64 (d, *J*= 9.0 Hz, 2H), 7.18-7.24 (m, 9H), 7.27-7.28 (m, 3H), 7.30-7.32 (m, 3H), 7.47-7.49 (d, *J*= 7.0 Hz, 2H), 9.60 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 115.8, 122.1, 127.1, 127.2, 128.9, 129.1, 129.3, 129.6, 129.9, 130.6, 131.4, 131.5, 132.0, 135.5, 137.3, 137.7, 147.3, 158.4; Anal. Calcd. for $C_{27}H_{20}N_2O$: C, 83.48; H, 5.19; N, 7.21%. Found: C, 83.41; H, 5.25; N, 7.18%.

(Table 2, **5ad**) **2-(4-Chlorophenyl)-1,4,5-triphenyl-1*H*-imidazole**

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.08 (d, *J*= 6.9 Hz, 2H), 7.15 (d, *J*= 6.9 Hz, 2H), 7.26-7.33 (m, 11H), 7.42 (d, *J*= 7.8 Hz, 2H), 7.63 (d, *J*= 8.7 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$/DMSO-d_6) δ: 127.4, 127.9, 128.6, 128.7, 128.8, 129.1, 129.7, 130.4, 130.7, 131.5, 136.9, 145.9; FT-IR (KBr, Cm^{-1}) = 693, 764, 835, 1081, 1407, 1493, 1595, 2913, 3108; Anal. Calcd. for $C_{27}H_{19}N_2Cl$: C, 79.70; H, 4.71; N, 6.88%. Found: C, 79.61; H, 4.67; N, 6.93%.

(Table 2, **5ae**) **2-(4-bromophenyl)-1,4,5-triphenyl-1*H*-imidazole**

^{1}H NMR, 500 MHz (DMSO-d_6) δ: 7.16–7.33 (m, 15H), 7.48 (d, *J*= 7.08 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$/DMSO-d_6) δ: 122.7, 127.2, 127.4, 129.0, 129.3, 129.5, 129.7, 130.4, 131.0, 131.9, 132.0, 132.4, 135.1, 137.2, 137.9, 145.8.

(Table 2, **5af**) **1-Benzyl-2-(phenyl)-4,5-diphenyl-1*H*-imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 5.12 (s, 2H), 6.76–6.82 (d, *J*= 7.8 Hz, 2H), 7.18-7.41 (m, 14H), 7.55-7.65 (m, 4H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 48.2, 126.0, 126.4, 126.9, 127.3, 128.2, 128.5, 128.6, 128.7, 128.9, 129.1, 130.5, 130.8, 131.0, 132.7, 134.1, 137.3, 137.9,148.1; FTIR (KBr, Cm^{-1}) = 695, 763, 1352, 1494, 1523, 1603, 3028, 3067; Anal. Calcd. for $C_{28}H_{22}N_2$: C, 87.01; H, 5.74; N, 7.25%. Found: C, 87.09; H, 5.66; N, 7.19%.

(Table 2, **5ag**) **1-Benzyl-2-(4-methylphenyl)-4,5-diphenyl-1*H*-imidazole**

^{1}HNMR (500 MHz, DMSO-d_6) δ: 2.33 (s, 3H), 5.14 (s, 2H), 7.13-7.16 (m, 2H), 7.18-7.21 (m, 2H), 7.24-7.29 (m 4H), 7.32-7.35 (m, 3H), 7.39-7.44 (m, 6H), 7.54 (d, *J*= 8.0 Hz, 2H).

(Table 2, **5ah**) **1-Benzyl-2-(3-methoxyphenyl)-4,5-diphenyl-1*H*-imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 3.68 (s, 3H), 5.16 (s, 2H), 6.79 (d, *J*= 7.5 Hz, 2H), 7.15-7.19 (m, 4H), 7.20-7.21 (m, 5H), 7.30-7-31 (m, 3H), 7.40-7.41 (m, 3H), 7.46-7.47 (m, 2H); ^{13}CNMR (125 MHz, DMSO-d_6) δ: 48.6, 55.9, 114.6, 115.6, 121.7, 126.4, 127.0, 127.1, 128.0, 128.9, 129.4, 129.74, 129.78, 130.5, 131.1, 131.4, 131.7, 132.8, 135.4, 137.7, 138.2, 147.7, 160.0; FT-IR (KBr, Cm^{-1}) = 691, 1214, 1479, 1574, 1606, 2897, 3021.

(Table 2, **5ai**) **1-Benzyl-2-(4-methoxyphenyl)-4,5-diphenyl-1*H*-imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 3.77 (s, 3H), 5.13 (s, 2H), 6.76 (d, *J*= 7.0 Hz, 2H), 6.90 (d, *J*= 9.0 Hz, 2H), 7.13-7.21 (m, 6H), 7.26-7.28 (m, 2H), 7.38-7.39 (m, 3H), 7.46 (d, *J*= 7.0 Hz, 2H), 7.58 (d, *J*= 9.0 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 48.5, 56.0, 114.9, 124.0, 126.4, 126.9, 127.0, 128.0, 128.9, 129.3, 129.6, 129.7, 130.6, 130.8, 131.6, 131.7, 135.5, 137.5, 138.3, 147.9, 160.5; Anal. Calcd. for $C_{29}H_{24}N_2O$: C, 83.63; H, 5.81; N, 6.73%. Found: C, 83.65; H, 5.87; N, 6.70%.

(Table 2, **5aj**)**1-Benzyl-2-(4-hydroxyphenyl)-4,5-diphenyl-1*H*-imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 5.12 (s, 2H), 6.71–7.35 (m, 17H), 7.45-7.52 (d, J = 7.5 Hz, 2H), 9.65 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 47.6, 115.3, 121.5, 125.6, 126.0, 127.1, 128.1, 128.5, 128.8,

128.9, 129.6, 130.0, 130.8, 134.7, 136.5, 137.5, 147.5, 158.0; FT-IR (KBr, Cm^{-1}) = 1487, 1557, 1607, 2930; Anal. Calcd. for $C_{28}H_{22}N_2O$: C, 83.56; H, 5.51; N, 6.96%. Found: C, 83.49; H, 5.47; N, 6.89%.

(Table 2, **5al**) **1-Benzyl-2-(4-chlorophenyl)-4,5-diphenyl-1*H*-imidazole.**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 5.16 (s, 2H), 6.75 (d, *J*= 7.0 Hz, 2H), 7.13-7.20 (m, 6H), 7.29-7.30 (m, 2H), 7.40-7.41 (m, 3H), 7.45-7.50 (m, 4H), 7.68 (d, *J*= 8.0 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 48.6, 126.5, 127.0, 127.2, 128.1, 128.9, 129.4, 129.5, 129.8, 130.5, 131.0, 131.3, 131.4, 131.6, 134.4, 135.2, 137.9, 146.7; FT-IR (KBr, Cm^{-1}) = 693, 754, 1031, 1447, 1496, 1602, 2904, 3106; Anal. Calcd. for $C_{28}H_{21}ClN_2$: C, 79.84; H, 5.03; N, 6.66%. Found: C, 79.87; H, 5.11; N, 6.60%.

(Table 2, **5am**) **2-(4-Nitrophenyl)-4,5-diphenyl-1-*p*-tolyl-1*H*-imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.28 (s, 3H), 7.15-7.20 (m, 5H), 7.24-7.27 (m, 4H), 7.31-7.32 (m, 3H), 7.50 (d, *J*= 7.5 Hz, 2H), 7.63 (d, *J*= 8.5 Hz, 2H), 8.14 (d, *J*= 9.0 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.5, 124.3, 127.2, 127.6, 129.0, 129.1, 129.3, 129.5, 129.6, 130.7, 130.8, 131.9, 133.7, 134.5, 134.8, 137.3, 138.7, 139.5, 144.7, 147.5.

(Table 2, **5an**) **2-(3-Nitrophenyl)-4,5-diphenyl-1-*p*-tolyl-1*H*-imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.26 (s, 3H), 7.32-7.39 (m, 6H), 7.54-7.56 (m, 8H), 7.77 (t, *J*= 7.7 Hz, 1H), 8.20 (d, *J*= 8.0 Hz, 1H), 8.52 (d, *J*= 7.5 Hz, 1H), 8.95 (s, 1H).

(Table 2, **5ao**) **4-(4,5-Diphenyl-1-*p*-tolyl-1*H*-imidazol-2-yl)benzonitrile**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.24 (s, 3H), 7.08-7.49 (m, 14H), 6.68 (d, *J*= 7.5 Hz, 2H), 7.95 (d, *J*= 7.5 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.4, 111.3, 115.2, 121.0, 127.12, 127.18, 128.7, 129.1, 129.36, 129.39, 130.1, 130.3, 131.1, 131.4, 132.0, 137.2, 138.7, 143.9, 147.5, 153.33, 153.66.

(Table 2, **5ap**) **4,5-Diphenyl-1,2-dip-tolyl-1*H*-imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.25 (s, 3H), 2.26 (s, 3H), 7.08-7.10 (m, 6H), 7.15-7.17 (m, 1H), 7.21-7.23 (m, 4H), 7.24-7.30 (m, 5H), 7.47-7.49 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.4, 21.5, 127.2, 128.6, 128.9, 129.0, 129.1, 129.2, 129.3, 129.5, 130.4, 131.4, 132.0, 135.0, 135.4, 137.5, 138.5, 138.8, 147.0.

(Table 2, **5aq**) **3-(4,5-Diphenyl-1-*p*-tolyl-1*H*-imidazol-2-yl)phenol**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.26 (s, 3H), 6.68-6.70 (m, 2H), 6.97-7.31 (m, 14H), 7.47 (d, *J*= 7.5 Hz, 2H), 9.48 (s, 1H).

(Table 2, **5ar**) **4,5-Diphenyl-2-(thiophen-2-yl)-1-*p*-tolyl-1*H*-imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.31 (s, 3H), 6.51 (d, *J*= 3.5 Hz, 1H), 6.62 (t, *J*= 4.5 Hz, 1H), 7.18-7.29 (m, 12H), 7.47-7.50 (m, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.6, 126.1, 127.1, 127.3, 127.9, 128.3, 129.0, 129.3, 129.6, 130.8, 130.9, 131.9, 132.1, 133.8, 134.4, 134.9, 137.6, 139.9, 142.3.

(Table 2, **5as**) **3-(4,5-Diphenyl-1-*p*-tolyl-1*H*-imidazol-2-yl)-1*H*-indole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.32 (s, 3H), 6.24 (s, 1H), 7.17-7.39 (m, 15H), 7.58 (d, *J*= 7.5 Hz, 2H), 8.59 (d, *J*= 8.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.6, 106.6, 112.3, 120.7, 122.7, 122.9, 124.2, 126.9, 127.0, 129.0, 129.3, 129.7, 130.3, 130.8, 131.7, 132.0, 135.4, 135.8, 136.3, 137.0, 139.3, 144.4.

(Table 2, **5at**) **1-Methyl-2,4,5-triphenyl- 1*H*-imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 3.58 (s, 3H), 7.38-7.40 (m, 3H), 7.43-7.45 (m, 2H), 7.58-7.60 (m, 5H), 7.72-7.73 (m, 3H), 7.94-7.96 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 34.8, 124.5, 127.6, 128.4, 128.6, 129.4, 129.6, 129.7, 129.8, 130.0, 130.2, 130.8, 131.1, 131.8, 132.6, 145.5.

(Table 2, **5au**) **1-Methyl-4,5-diphenyl-2-*p*-tolyl-1*H*-imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.45 (s, 3H), 3.56 (s, 3H), 7.23-7.38 (m, 5H), 7.44-7.47 (m, 3H), 7.50-7.55 (m, 4H), 7.58-7.60 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 21.9, 34.7, 128.5, 129.6, 129.7, 130.2, 130.5, 130.7, 131.0, 131.72, 131.77, 145.6.

(Table 2, **5av**) **2-(4-Bromophenyl)-1-methyl-4,5-diphenyl-1*H*-imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 3.47 (s, 3H), 7.15 (t, *J*= 7.2 Hz, 1H), 7.21 (t, *J*= 7.2 Hz, 2H), 7.43-7.45 (m, 4H), 7.50-7.53 (m, 3H), 7.72-7.77 (m, 4H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 33.9, 122.9, 127.1, 128.9, 129.6, 129.9, 130.7, 131.44, 131.49, 131.5, 131.7, 132.4, 135.5, 137.5, 146.6.

(Table 2, **5az**) **2-(4-methylphenyl)-4,5-diphenyl-1-propyl-1*H*- imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.52 (t, *J*= 7.4 Hz, 3H), 1.30 (m, *J*= 7.4 Hz, 2H), 2.50 (s, 3H), 3.80 (t, *J*= 7.6 Hz, 2H), 7.12-7.35 (m, 12H), 7.50 (d, *J*= 8 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 11.3, 22, 24.2, 53.4, 121.1, 122.9, 124, 125.3. 126.2, 127, 127.9, 128.8, 130.2, 130.9, 133, 142.4, 156.2; FTIR (KBr, Cm^{-1}) = 1492, 1622, 3026; Anal. Calcd. for $C_{25}H_{24}N_2$: C, 85.19; H, 6.86; N, 7.95%; Found: C, 85.24; H, 6.95; N, 7.89%.

(Table 2, **5ba**) **2-(4-Chlorophenyl)-4,5-diphenyl-1-propyl-1*H*-imidazole**

^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.51 (t, *J*= 7.6 Hz, 3H), 1.34 (m, *J*= 7.6 Hz, 2H), 3.81 (t, *J*= 8.4 Hz, 2H), 7.15-7.30 (m, 12H), 7.34 (d, *J*= 8.4 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 11.0, 23.5, 46.3, 126.5, 126.6, 128.5, 129.2, 129.4, 129.6, 130.5, 130.6, 130.8, 131.2, 133.3, 134.9, 136.1, 146.9; FTIR (KBr, Cm^{-1}) = 1009, 1487, 1644, 3021; Anal. Calcd for $C_{24}H_{22}ClN_2$: C, 77.30; H, 5.68; N, 7.51%. Found: C, 77.27; H, 5.65; N, 7.56%.

(Table 3, **6k**) **2-(4-Methoxyphenyl)-4,5-diphenyl-1*H*-imidazole**

^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.83 (s, 3H), 6.98 (d, *J*= 7.6 Hz, 2H), 7.18-7.68 (m, 10H), 7.82 (d, *J*= 7.6 Hz, 2H), 9.14 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 160.1, 146.0, 128.5, 127.7, 126.6, 122.7, 114.2, 110.0, 55.3; Anal. Calcd. For $C_{22}H_{18}N_2O$: C, 80.96; H, 5.56; N, 8.58%; Found: C, 80.81; H, 5.71; N, 8.69%.

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