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ARTICLE

Synthesis of substituted pyrimidine using $ZnFe_2O_4$ nanocatalyst via one pot multi-component reaction ultrasonic irradiation

Pravin Chavan[1] | **Sachin Bangale**[2] | **Dattatraya Pansare**[3] | **Rohini Shelke**[4] | **Shivaji Jadhav**[5] | **Shrikrushna Tupare**[6] | **Dhanraj Kamble**[7] | **Megha Rai**[8]

[1]Department of Chemistry, Doshi Vakil College, Raigad, India

[2]Department of Chemistry, G. M. Vedak College of Science Tala, Raigad, India

[3]Department of Chemistry, Deogiri College, Aurangabad, India

[4]Department of Chemistry, Sadguru Gadage Maharaj College Karad, Satara, India

[5]Department of Chemistry, Tarai College of Arts and Science, Aurangabad, India

[6]Department of Chemistry, K.E.S. Anandibhai Pradhan Science College, Raigad, India

[7]Department of Chemistry, S. B. College of Science, Aurangabad, India

[8]Department of Chemistry, Dr. Rafiq Zakaria College for Women, Aurangabad, India

Correspondence
Pravin Chavan, Department of Chemistry, Doshi Vakil College, Goregaon, Raigad, Maharashtra, India.
Email: chemistryp141286@gmail.com
Dattatraya Pansare, Department of Chemistry, Deogiri College, Aurangabad-431005, Maharashtra, India.
Email: dnpansare74@gmail.com

Abstract

A highly efficient, eco-friendly, recyclable heterogeneous $ZnFe_2O_4$ nano-catalyzed synthesis of 2-amino-4-substituted 1,4-dihydrobenzo[4,5]imidazo [1,2-a]pyrimidine-3-carbonitrile **(4a-j)** derivatives via one pot multicomponent reaction of benzimidazole (**1**), substituted aromatic aldehyde (**2a-j**) and malononitrile (**3**) under ultrasonic irradiations. Significance of this synthetic approach is short reaction time, easy handling, simplicity, efficiency, high yield, and recoverable catalyst.

1 | INTRODUCTION

Multi-component reactions (MCRs) are efficient and powerful protocols for the rapid synthesis of highly selective products and organic components, as well as multiple and diverse new bonds have been created in highly efficient and atom-economical manner through one pot synthesis. Thus it saved time, energy and evaded multistep purification of various intermediates.[1] Benzo[4,5]imidazo [1,2-a]pyrimidines have recently attracted attention as important fused nitrogen heterocyclic scaffords in the field of drugs and pharmaceuticals. These heterocycles have been widely used as Antifungal,[2] hepatoprotective,[3] antihypertensive,[4] antitumour,[5] and cardiotonic agent.[6]

Pyrimidine ring is one of the most important class of heterocyclic compounds found in many natural products.

It is found in vitamins such as thiamine (a), folic acid (b) and in medicinal scaffold such as antifungal flu cytosine (c), antibacterial brodimoprim (d), and antipsychotic drug risperidone (e) (Figure 1).[7–10]

Based on the importance of these compounds, various catalyst have been reported for synthesis of benzo[4,5] imidazo[1,2-a]pyrimidines including MgO, C_5H_5N, Me_2NH, Et_3N, N_2H_4,*p*-TSA, NH_4OAc, and $InCl_3$.[11–21] However, some of the reported synthetic methods have several disadvantages such as low yields, hazardous solvent, long reaction time, high temperature reactions, expensive, and large amount of catalyst. Due to these facts, it is important to find an efficient, milder, faster, and more eco-friendly protocols with excellent yields for the synthesis of benzo[4,5]imidazo[1,2-a]pyrimidines.

Recently, nanoparticles of mixed metal oxide ($ZnFe_2O_4$) have been broadly used in modern organic synthesis. Some examples of synthesized compounds by using ($ZnFe_2O_4$) nanocatalyst are 2,3-dihydroquinazolin-4(1H)ones[22] and pyrano[2,3-d]pyrimidines[23] derivatives. $ZnFe_2O_4$ is one of the economically efficient, insoluble in organic solvents, easily recover, easy to separate, having low surface area, heterogeneous, and economically cheap nanocatalyst.[24–29] Use of $ZnFe_2O_4$ nanocatalyst in organic synthesis resulted in several benefits such as yield improvement, time reduction, commercially efficient, suitable experimental procedure to work up and recovery of catalyst etc.

With reference to above literature survey, in continuation to our previous research work of pharmaceutical moieties,[30–36] we have focused on synthesis of imidazo [1,2-*a*]pyrimidine-3-carbonitrile derivatives **(4a-j)** using efficient and heterogeneous Zinc Ferrite ($ZnFe_2O_4$) as nanocatalyzed one-pot three-component condensation reaction of benzimidazole (**1**) and malononitrile **(3)** with substituted aromatic aldehyde **(2a-j)** in methanol under ultrasonic irradiations. Author has selected normal spinel catalyst $ZnFe_2O_4$ for present synthesis because ammonia molecule preferred to adsorbed on the surface of Zn atom of spinal zinc ferrite and it is used to removal of ammonia.[37] Zinc Ferrite ($ZnFe_2O_4$) proves its vital role as nanocatalyst in present organic synthesis.

2 | RESULT AND DISCUSSION

2.1 | Catalyst characterization

2.1.1 | XRD analysis-

The crystalline size (d) was determined by Scherrer's formula-

$$d = \frac{0.9\lambda}{\beta\cos\theta}$$

The XRD pattern of the $ZnFe_2O_4$ particles (Figure 2) calcined at 180, 300, 500, 800, and 1000°C temperature. Series of diffraction peaks at 20° were assigned different to planes (111), (311), (400), (422), and (511). According to the (311) diffraction pattern of $ZnFe_2O_4$ crystal, the particle size of $ZnFe_2O_4$ can be calculated from the full width at half-maximum using the Scherrer's equation. Obviously, the particle size of $ZnFe_2O_4$ changes as the *Tc* controlled fewer than 180, 300, 500, 800, and 1000°C, the order is 22, 22, 25, 32, and 32 nm, respectively. These indicate that the crystallinity of $ZnFe_2O_4$ accelerated as the *Tc* above 500°C.

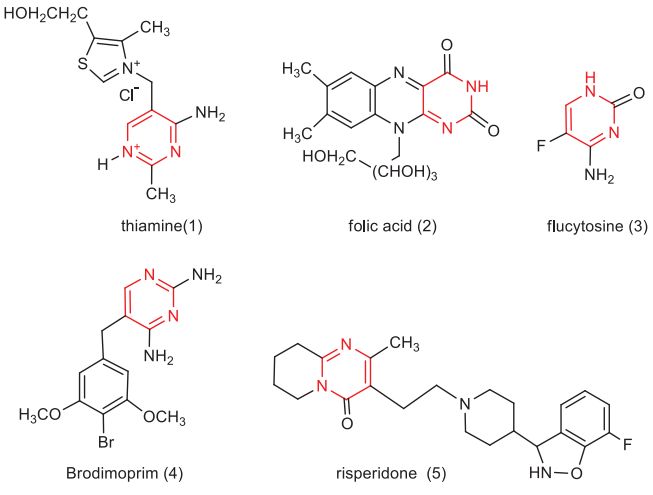


FIGURE 1 Fused pyrimido heterocyclic drugs

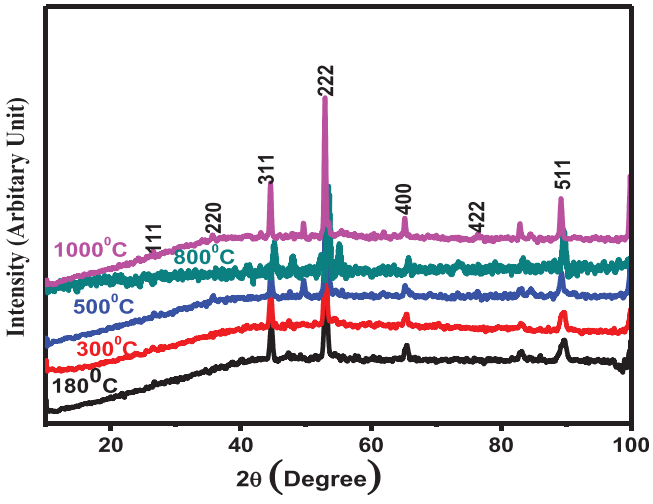


FIGURE 2 XRD pattern of calcinied mixed precursor at various temp

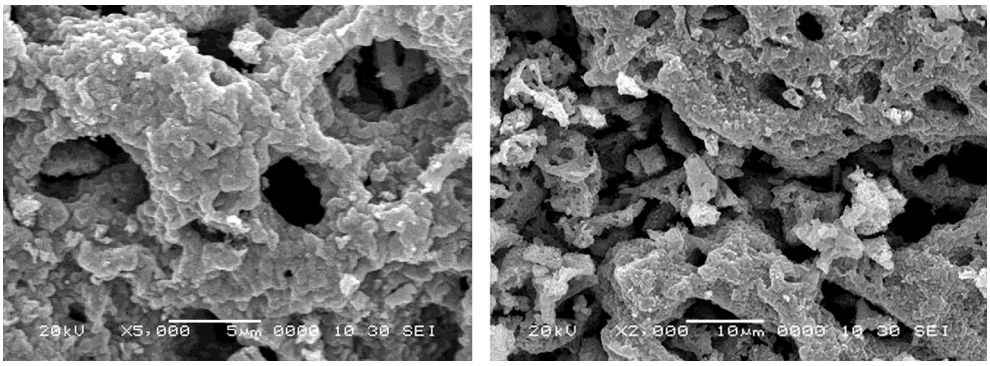


FIGURE 3 SEM images of $ZnFe_2O_4$ (1) low resolution and (2) high resolution

2.1.2 | SEM analysis-

Morphological study of $ZnFe_2O_4$ nanocatalyst was carried out with the help of SEM technique represented in Figure 3.

SEM analysis clearly indicates that the particle sizes are irregular with nano size range. Some nanoparticles agglomerations containing very fine particle, the shape of particles are not defined porous nature, small, and large core approximately (5 μm). Porous size of particles is a favorable to a gas sensing application.

2.1.3 | TG-DTA analysis

Differential thermal analysis (DTA) was performed at heating rate of 10 K/min to investigate the thermal properties of $ZnFe_2O_4$. Figure 4 indicates dehydration, decomposition, and denitration of given materials. The following reactions clearly matched with Figure 4.

$$2C_2NH_5O_2 + (9/2)O_2 \rightarrow N_2\uparrow + 4CO_2\uparrow + 5H_2O\uparrow$$

$$Zn(NO_3)_3 + Fe(NO_3)_3 + 4C_2H_5NO_2 \rightarrow ZnFe_2O_4 + 8CO_2\uparrow + 10H_2O\uparrow + 5N_2\uparrow$$

$ZnFe_2O_4$ powder stable at about 800°C temperature.[38,39]

The synthesized $ZnFe_2O_4$ have efficiency to play the role of Nanocatalyst so it was used in the synthesis of 2-Amino-4-substituted 1,4-dihydrobenzo[4,5]imidazo [1,2-a]pyrimidine-3-carbonitrile **(4a-j)** derivatives. Initially, reaction model of (2-aminobenzimidazole **(1),** 4-chlorobenzaldehyde **(2a)** and malononitrile (**3**) was chosen to optimize the reaction conditions at 70°C. Optimization results of reaction scheme such as different solvents, various catalysts, yield and reaction time are shown in Table 1.

Conversion of reaction was studied with reference to amount of catalyst, Scheme 1 reaction was carried out with or without catalyst. In the absence of catalyst,

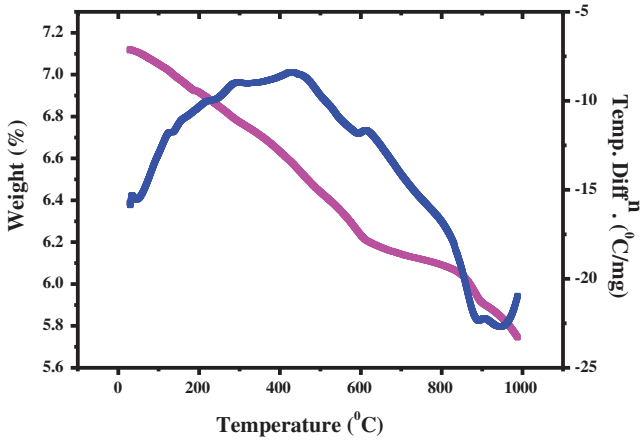


FIGURE 4 TG-DTA curve of mixed precursor

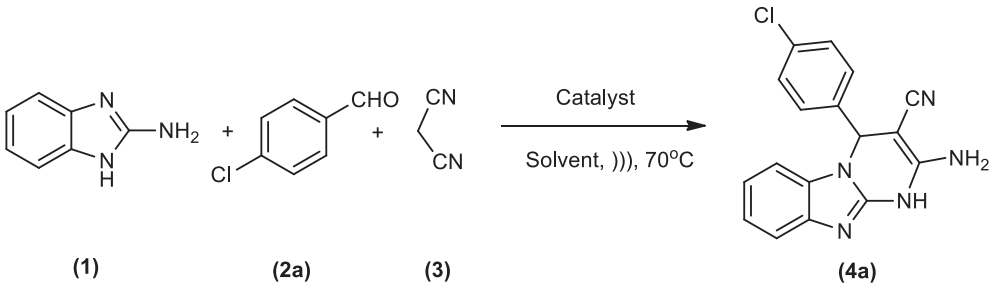
product transformation was not observed which despite of long reaction time and amount of product (Table 1, entry 1) formed was meager. Therefore, we focused on the search for suitable catalyst. With the help of Selected Lewis acid catalysts- $FeCl_3$, $AlCl_3$, $CuSO_4.5H_2O$, and $ZnFe_2O_4$, nanoparticles carried out present reaction which resulted moderate (74%, 68%, 66%, and 94%) yields. Among these (Table 1, entries 2-5), $ZnFe_2O_4$ nanoparticle was selected as catalyst in present work giving good yield and easy recovery, within shorter reaction time (Table 1, entry 5). Similar, examination of different solvents such as MeOH, DCE, ACN, and EtOH (Table 1, entries 5-8) were done by using model reaction under ultrasonic irradiations. We found MeOH as a suitable solvent for our particular organic synthesis of substituted pyrimidine due to its uniform solubility, excellent yield and short reaction time (Table 1, entry 5).

Also differential percentage of molar concentrations (5, 10, 15, and 20 mol%) of catalyst ($ZnFe_2O_4$ nanoparticles) were studied at 70°C temperature, under ultrasonic irradiations. Amongst these various amount of catalyst (Table 1, entries 9-11), 10 mol% (Table 1, entry 5) $ZnFe_2O_4$ nanoparticles catalyst was observed suitable, as

TABLE 1 Optimizations of solvents and catalysts in the synthesis (2-amino-4-substituted 1,4-dihydrobenzo[4,5]imidazo[1,2-a] pyrimidine-3-carbonitrile)

Entry	Solvent	Catalyst (mol%)	Time (min)	Yields %
1	Neat	None	180	25
2	MeOH	$FeCl_3$ (10)	120	74
3	MeOH	$AlCl_3$ (10)	180	68
4	MeOH	$CuSO_4.5H_2O$(10)	180	66
5	**MeOH**	**$ZnFe_2O_4$(10)**	**90**	**96**
6	DCE	$ZnFe_2O_4$(10)	120	76
7	CAN	$ZnFe_2O_4$(10)	120	80
8	EtOH	$ZnFe_2O_4$ (10)	90	85
9	MeOH	$ZnFe_2O_4$ (5)	96	76
10	MeOH	$ZnFe_2O_4$ (15)	90	95
11	MeOH	$ZnFe_2O_4$ (20)	90	95

Note: Reaction conditions: benzimidazole (**1**) (1 mmol), 4-chloro benzaldehyde **(2a)** (1 mmol), malononitrile (**3**) (1 mmol), 8 mL solvent and 70°C temperature under ultrasonic irradiations. The bold value shows best result.



SCHEME 1 Model reaction- synthesis of 2-amino-4-substituted 1,4-dihydrobenzo[4,5]imidazolo[1,2-a]pyrimidine-3-carbonitrile (**4a**) catalyzed by $ZnFe_2O_4$ under ultrasonic irradiations

it recurred higher yield, short reaction time, and catalyst recovery at 70°C under ultrasonic irradiations. We also studied the reaction scheme for various temperatures but we observed that given reaction scheme produced several biproduct formation at higher temperature and found various spot on TLC. $ZnFe_2O_4$ is also plays vital role in rate of reaction so we finalized 70°C as reaction temperature. After increasing the amount of catalyst, no improvement was observed in reaction results.

After fixing protocol for synthesis of series of reaction, benzimidazole (1 mmol), malononitrile (1 mmol) were treated with substituted aromatic aldehydes (1 mmol) in presence of $ZnFe_2O_4$ (10 mol%) as a catalyst.

In continuation to our present research work, we have also studied the effect of electron withdrawing, electron releasing and halogen groups at different positions in aromatic ring of various aldehydes in the synthesis of 2-amino-4-substituted 1,4-dihydrobenzo[4,5]imidazo [1,2-a]pyrimidine-3-carbonitrile illustrated in Table 2.

Aldehyde bearing electron withdrawing groups decreased the reaction time with slightly increased the percentage of yields and electron releasing groups increased the reaction times with no outstanding effect on the percentage of yields due to ultrasonic effect. Consequently, this protocol gives the desired products in good yields and in relatively short reaction times (Table 2).

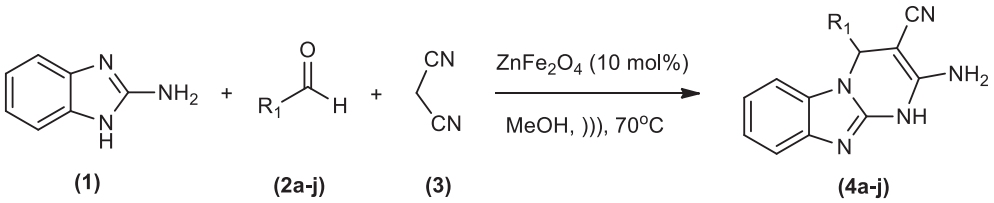
Step **I**- in reaction, intermediate (**5**) occurred via Knoevenagel condensation between malononitrile (**3**) and aromatic aldehyde (**2a-j**) in the presence of heterogeneous $ZnFe_2O_4$ nanocatalyst. In step **II**- immediate Michael addition adduct (**6**) occurred from 2-aminobenzimidazole (**1**) intermediate (**5**) and finally, 2-amino-4-substituted-1,-4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-3-carbonitrile **(4a-j)** was formed from intramolecular cyclisation of Michael adduct (**6**) (Scheme 3). After completion of individual reaction, reaction mixture was cooled at room temperature following addition of 7 mL of ethyl acetate to this mixture. The reaction mixture as filtered using G1 sinter funnel and $ZnFe_2O_4$ nanocatalyst was covered washing with double distilled water, dried and used for other suitable purposes. The products were purified by column

TABLE 2 $ZnFe_2O_4$ nanocatalyzed multi-component synthesis of 2-amino-4-substituted-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-3-carbonitrile (**4a-j**)

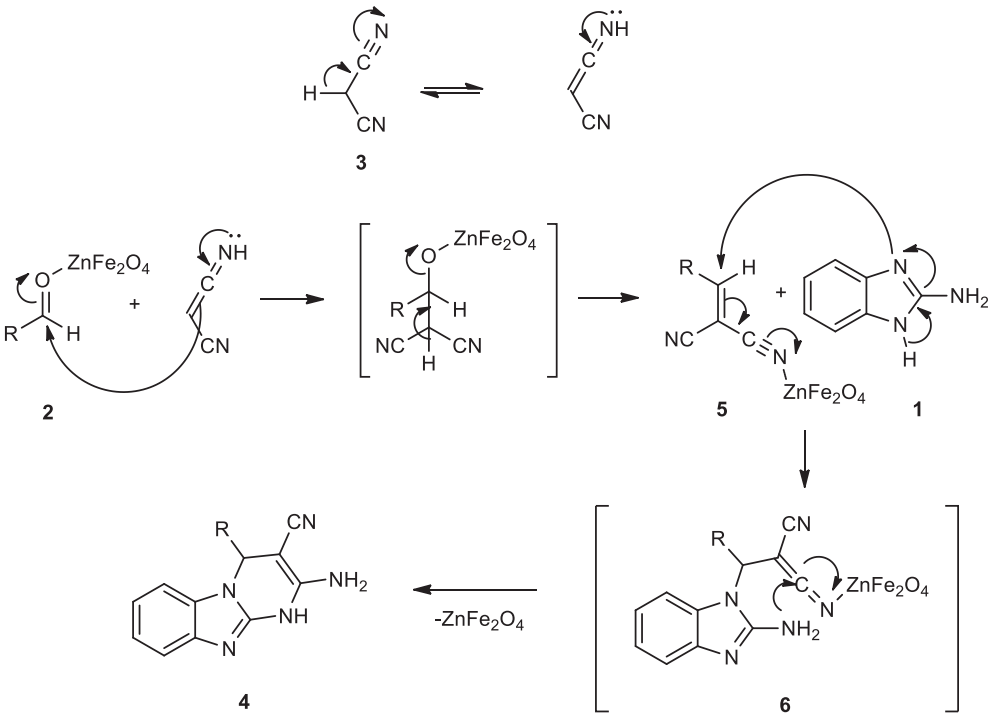
				Yield (%)		M.P. (°C)	
Entry	**R^1**	**Product**	**Time (min)**	**Found**	**Reported (ref.)**	**Found**	**Reported (ref.)**
1	4-Cl-C_6H_4	4a	75	96	93[27]	232-235	238[27]
2	3-Br-C_6H_4	4b	82	93	89[27]	240-243	240[27]
3	4-F-C_6H_4	4c	89	94	91[27]	265-267	270[27]
4	4-MeO-C_6H_4	4d	81	92	86[29]	205–208	-
5	4-HO-C_6H_4	4e	79	89	80[29]	210–213	215[29]
6	4-Me-C_6H_4	4f	84	92	88[29]	222-225	-
7	4-CN-C_6H_4	4g	74	96	92[29]	218–220	215[29]
8	2,4- $(Cl)_2C_6H_3$	4h	79	95	-	236–239	-
9	2-OH-4-$MeOC_6H_3$	4i	88	93	-	216–218	-
10	4-NO_2-C_6H_4	4j	77	95	-	224–227	-

Note: Reaction conditions- benzimidazole (**1**) (1 mmol), aromatic aldehyde **(2a-j)** (1 mmol), malononitrile (**3**) (1 mmol), $ZnFe_2O_4$ (10 mol%) catalyst and methanol (8 mL) at 70°C under ultrasonic irradiations.

SCHEME 2 Synthesis of 2-amino-4-substituted 1,4-dihydrobenzo[4,5]imidazo [1,2-a]pyrimidine-3-carbonitrile (**4a-j**) catalyzed by $ZnFe_2O_4$ under ultrasonic irradiations



SCHEME 3 Mechanism for the synthesis of 2-amino-4-substituted-1,4-dihydrobenzo [4,5]imidazo[1,2-a]pyrimidine-3-carbonitrile **(4a-j)** is outlined in Scheme **2**. These products formed by multistep reaction in one pot



chromatography. The synthesized series of compounds were characterized by FTIR, ^{1}H NMR, ^{13}C NMR, analysis. Advantages of present method were efficiency, high percentage of yields, shorter reaction time, simplicity and easy work-up.

3 | CONCLUSION

Present research work concludes, an highly efficient, synthesis of 2-amino-4-substituted 1,4-dihydrobenzo[4,5] imidazo[1,2-a]pyrimidine-3-carbonitrile (**4a-j**) via one pot three component condensation reaction of benzimidazole (**1**), malononitrile (**3**) and aromatic aldehyde (**2a-j**) using heterogeneous $ZnFe_2O_4$ nanoparticles catalyst at 70°C under ultrasonic irradiation. Some nanoparticles agglomerations containing very fine particle, the shape of particles are not defined porous nature and small and large core approximately (5 μm). Outcome of this synthetic protocol are reduced reaction time, one time chemical addition, easy handling, simplicity, efficiency, high yield, and recoverable catalyst.

4 | EXPERIMENTAL

4.1 | General experimental information

All A.R. Grade chemicals were used. They were purchased from Sigma-Aldrich and Avra Chemicals. Ultrasonication irradiator was performed (230 V AC, 50 Hz, liquid holding capacity of bath, 5.5 L) at temperature 70°C. Water condenser fixed with round bottom flasks having reaction ingredients were suspended at center of the ultrasonication bath up to the completion of reaction. ^{1}H NMR spectra were recorded on a Bruker-400 MHz NMR and ^{13}C NMR spectra were recorded on 100 MHz ^{13}C NMR. The IR spectra were reported on a Perkin-Elmer FT-IR Spectrometer Melting points were measured manually by open capillary. TLC was carried out on aluminum sheets (precoated with 0.2 mm layer of silica gel). All reagents were commercially available. TG-DTA analysis, XRD spectra was recorded by Bruker AXS D8 Advance X-ray diffractometer. SEM images were obtained on S-4800 Type-II, HITACHI Japan.

4.2 | Preparation of $ZnFe_2O_4$ nanoparticles

$ZnFe_2O_4$ nanoparticle was prepared by combustion method. In this preparation, urea was used as fuel. Initially, zinc nitrates, iron nitrates and urea are taken in appropriate size beaker using stoichiometric amount (1:1:4) and dissolved until clear solution was obtained. This clear solution was evaporated (80°C) using hot plate and thick gel was obtained, again on increasing temperature (180°C) of hot plate thick gel, nanocrystalline powder was formed. Finally, the synthesized powder was sintered at 300, 500, 800, and 1000°C temperature for 4 hours. $ZnFe_2O_4$ nanoparticle was characterized by the X-ray diffraction (XRD) patterns were recorded on (Bruker AXS D8 Advance X-ray diffractometer) using monochromatic Cu-Kα radiation[38] (wavelength $\lambda = 1.5406$ Å), SEM and TG-DTA methods.

4.3 | General procedure for synthesis of 2-amino-4-(R)-1,2-dihydroxybenzo[4,5] imidazo[1,2-a]pyrimidine-3-carbonitrile derivatives (4a-j)

A round bottom flask was charged with benzimidazole (**1**) (1 mmol), aromatic aldehyde **(2a-j)** (1 mmol), malononitrile (**3**) (1 mmol), and $ZnFe_2O_4$ (10 mol%) catalyst in methanol (8 mL). The mixture was irradiated in ultrasonic bath at (70°C). The reaction condition was assessed by TLC plate using ethyl acetate and cyclohexane (7:3) as solvent. After the completion of reaction, add 4 mL of methanol in reaction mixture, dissolved total catalyst in methanol and evaporated the solvent using high pressure vacuum pump. Finally, the product was purified by recrystallization techniques using ethanol to afford the pure products.

4.3.1 | 2-Amino-4-(4-chlorophenyl)-1,4-dihydrobenzo[4,5]imidazolo[1,2-a] pyrimidine-3-carbonitrile(4a)

Yield 94%; yellow solid; M.P. 232-235°C. FT IR (KBr cm^{-1}): 3254, 2933, 2187, 1675, ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.62 (s, 1H, NH), 7.63 (d,1H, Ar), 7.43-7.40 (m, 2H, Ar), 7.32 (d, 2H, Ar), 7.24 (d, 1H, Ar), 7.18 (d, 2H, Ar), 6.89 (s, 2H, NH_2), 5.27 (s, 1H, CH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 151.60, 149.39, 144.1, 135.3, 131.3, 131.0, 129.1, 128.1, 123.1, 121.9, 120.0, 119.0, 116.1, 113.1, 62.0, 55.4.

4.3.2 | 2-Amino-4-(3-bromophenyl)-1,4-dihydrobenzo[4,5]imidazolo[1,2-a] pyrimidine-3-carbonitrile(4b)

Yield 90%; yellow solids; M.P. 240-243°C. 3278, 2939, 2189, 1683, ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.61 (s, 1H, NH), 7.58 (d, 1H, Ar), 7.51 (d, 2H, Ar), 7.29(t, 3H, Ar),

7.15 (t, 1H, Ar), 6.89 (t, 1H, Ar), 6.88 (s, 2H, NH_2), 5.27 (s, 1H, CH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.0, 149.1, 144.0, 141.1, 131.6, 130.5, 130.1, 129.0, 123.2, 122.0, 120.0, 119.1, 116.1, 112.3, 61.6, 53.0.

4.3.3 | 2-Amino-4-(4-fluorophenyl)-1,4-dihydrobenzo[4,5]imidazolo[1,2-a] pyrimidine-3-carbonitrile(4c)

Yield 92%; yellow solid; M. P. 265-267°C, 3279, 2940, 2182, 1691, ^1H NMR (400 MHz, DMSO-d_6) δ 8.26 (s, 1H, NH), 7.59 (d, 1H, Ar), 7.21-7.18 (m, 5H, Ar), 7.10 (t, 1H, Ar), 7.00 (t, 1H, Ar), 6.78 (s, 2H, NH_2), 5.33 (s, 1H, CH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.2, 160.1 (C-F), 152.0, 148.9, 144.1, 135.5, 131.0, 130.2, 123.3, 122.1, 119.8, 119.1, 116.8, 115.1, 112.7, 60.2, 54.6.

4.3.4 | 2-amino-4-(4-methoxyphenyl)-1,4-dihydrobenzo[4,5]imidazolo[1,2-a] pyrimidine-3-carbonitrile(4d)

yellow solid; Yield 90%; M. P. 205-208°C, 3268, 2936, 2186, 1684, 1196, ^1H NMR (400 MHz, DMSO-d_6) δ 8.51 (s, 1H, NH), 7.94 (d, 2H, Ar), 7.65 (t, 1H, Ar), 7.20-7.15 (m, 1H Ar), 7.10 (t, 1H, Ar), 7.00 (t, 1H, Ar), 6.91(d, 2H, Ar), 6.79 (s, 2H, NH_2), 5.16 (s, 1H,CH), 3.40 (s, 3H CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ 161.0, 151.3, 149.2, 144.1, 133.5, 133.4, 129.4, 127.3, 124.1, 123.2, 120.1, 115.6, 115.0, 113.9, 64.1, 63.0, 52.7, 14.3.

4.3.5 | 2-amino-4-(4-hydroxyphenyl)-1,4-dihydroxybenzo[4,5]imidazo[1,2-a] pyrimidine-3-carbonitrile(4e)

white solid, Yield 88%; M. P. 210-213°C, FTIR (KBr cm^{-1}): 3298, 3246, 2931,2185, 1674, ^1H NMR 400 MHz, DMSO-d_6) δ 8.22 (s, 1H, NH), 7.59 (d, 1H, Ar), 7.21-7.18 (m, 5H, Ar), 7.10 (t, 1H, Ar), 7.00 (t, 1H, Ar), 6.78 (s, 2H, NH_2), 5.33 (s, 1H, OH), 5.10(s, 1H, CH), ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.1, 152.1, 148.8, 143.0, 135.1, 130.9, 130.1, 123.3, 123.5, 120.2, 119.1, 116.9, 116.1, 113.1, 112.6, 60.3, 55.7.

4.3.6 | 2-Amino-4-(4-methylphenyl)-1,4-dihydrobenzo[4,5]imidazolo[1,2-a] pyrimidine-3-carbonitrile(4f)

yellow solid; Yield 85%; M.P. 230-233°C. FTIR (KBr cm^{-1}): 3284, 2954, 2183, 1677, ^1H NMR (400 MHz, DMSO-d_6) δ 8.56 (s, 1H, NH), 7.62 (d,1H, Ar), 7.43 (d, 1H, Ar), 7.31 (d, 1H, Ar), 7.26-7.14 (m, 3H, Ar), 7.10 (t, 1H, Ar), 6.92 (s, 2H, NH_2), 5.27 (s, 1H, CH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 151.6, 149.4, 144.1, 135.3, 131.4, 131.2, 129.1, 128.3, 123.2, 121.8, 120.2, 119.1, 116.0, 113.1, 62.0, 55.5, 17.6.

4.3.7 | 2-amino-4-(4-cynophenyl)-1,4-dihydroxybenzo[4,5]imidazo[1,2-a] pyrimidine-3-carbonitrile(4g)

white solid, Yield 96%; M. P. 218-220°C, FTIR (KBr cm^{-1}): 3310, 3266, 2973,2191, 1685, ^1H NMR 400 MHz, DMSO-d_6) δ 8.82 (s, 1H, NH), 7.81 (d, 1H, Ar), 7.71-7.48 (m, 4H, Ar), 7.32 (t, 1H, Ar), 7.22 (t, 1H, Ar), 7.05 (t, 1H, Ar), 6.85 (s, 2H, NH_2), 5.10(s, 1H, CH), ^{13}C NMR (100 MHz, DMSO-d_6): δ 162.1, 155.5, 150.8, 147.1, 140.1, 136.9, 131.1, 125.1, 123.1, 120.4, 118.1, 117.9, 116.1, 113.5, 112.6, 60.3, 54.6.

4.3.8 | 2-amino-4-(2,4-dichlorophenyl)-1,4-dihydroxybenzo[4,5]imidazo[1,2-a] pyrimidine-3-carbonitrile(4h)

white solid, Yield 95%; M. P. 236-239°C, FTIR (KBr cm^{-1}): 3297, 3250, 2953,2151, 1646, ^1H NMR 400 MHz, DMSO-d_6) δ 8.61 (s, 1H, NH), 7.50 (s, 1H, Ar), 7.36-7.41 (m, 2H, Ar), 7.15 (m, 2H, Ar), 6.95 (m, 2H, Ar), 6.72 (s, 2H, NH_2), 5.07(s, 1H, CH), ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.2, 152.4, 148.1, 147.1, 139.1, 136.8, 130.1, 122.3, 123.2, 121.4, 117.9, 117.8, 117.1, 112.8, 111.9, 59.8, 54.7.

4.3.9 | 2-amino-4-(2-hydroxy,4-methoxyphenyl)-1,4-dihydroxybenzo[4,5] imidazo[1,2-a]pyrimidine-3-carbonitrile(4i)

Yellow solid, Yield 93%; M. P. 216-218°C, FTIR (KBr cm^{-1}): 3267, 3226, 2948, 2161, 1639, ^1H NMR 400 MHz, DMSO-d_6) δ 8.58 (s, 1H, NH), 7.60 (s, 1H, Ar), 7.31-7.39 (m, 2H, Ar), 7.14 (m, 2H, Ar), 6.78 (m, 2H, Ar), 6.69 (s, 2H, NH_2), 5.06(s, 1H, CH), ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.2, 151.4, 149.1, 146.1, 138.1, 134.8, 134.1, 121.3, 123.1, 120.4, 118.0, 117.6, 117.0, 112.1, 111.1, 59.6, 55.4.

4.3.10 | 2-amino-4-(4-nitrophenyl)-1,4-dihydroxybenzo[4,5]imidazo[1,2-a] pyrimidine-3-carbonitrile(4j)

yellow solid, Yield 95%; M. P. 224-227°C, FTIR (KBr cm^{-1}): 3305, 3259, 2987, 2189, 1675, ^1H NMR 400 MHz, DMSO-d_6) δ 8.76 (s, 1H, NH), 7.71-7.48 (m, 4H, Ar),

7.34-7.22 (t, 4H, Ar), 6.81 (s, 2H, NH_2), 5.09 (s, 1H, CH), ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.1, 156.5, 161.8, 149.1, 141.1, 137.9, 133.1, 126.1, 124.1, 120.4, 119.1, 118.9, 116.1, 113.6, 119.6, 61.3, 54.7.

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CONFLICT OF INTEREST

The authors confirm that, this article content has no conflict of interest.

ORCID

Pravin Chavan https://orcid.org/0000-0002-1232-9343
Dattatraya Pansare https://orcid.org/0000-0002-0419-3538
Rohini Shelke https://orcid.org/0000-0002-2053-4785

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