



One Pot Synthesis, Characterization of Benzothiazole/ Benzimidazole Tethered Imidazole derivatives Using Clay As Catalyst

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ABSTRACT

A Green approach for benzothiazole/benzimidazole tethered imidazole derivative synthesis utilizing brick derived clay as a catalyst. Brick clay catalyst used in this synthesis has shown excellent catalytic activity by increasing efficiency, reducing the reaction time and most importantly it is reusable for further reaction runs. These derivatives were synthesized by four component condensation reaction that involve benzil, aldehyde, 2-aminobenzimidazole/2-amino-6-nitrobenzothiazole and ammonium acetate. The clay catalyst is characterized by FT-IR while the synthesized derivatives were characterized by FT-IR, ¹H NMR and ¹³C NMR. Brick clay is a cheap, non-hazardous catalyst and can be reused up to many reaction runs with good to excellent yields.

Keywords: Imidazole, Benzothiazole, Benzimidazole, Clay catalyst, Green synthesis.

INTRODUCTION

The development of economical and environmentally viable catalyst has a great importance in the field of organic synthesis and is extensively needed for industrial processes. In recent years heterogeneous catalysts have attracted huge interest due to their magnificent properties in organic synthesis. Heterogeneous catalyst exhibits excellent catalytic activity with ability of easy separation from the synthesized product and reusability. Current reports on the heterogeneous catalysts have highlighted their tremendous arena of modifications and applications on the new fronts of organic synthesis. The magnetic nanophotocatalyst

WO₃ZnO/Fe₃O₄ developed for the synthesis of benzimidazole derivatives¹. The nanocomposite W-ZnO@NH₂-CBB successfully used as a photocatalyst for the photochemical synthesis of benzimidazoles induced by UV-Visible light². The magnetic catalyst H₃PW₁₂O₄₀@Fe₃O₄/EN-MIL-101 used for synthesis of indazole phthalazine-triones³. A nanoporous basic catalyst developed by grafting amine on UiO-66 and used for the synthesis of 2-Aminothiophenes⁴. The mesoporous catalyst Nb-Zr/KIT-6 successfully used for benzylpyrazolyl coumarins synthesis⁵. The synthesis of 3-substituted indoles were reported by using H₅PW₁₀V₂O₄₀@VO_x/SBA-15-NH₂ as a catalyst⁶. Heterogeneous catalysts exhibit properties like low toxicity, recyclability, easy



separation, great diversity at structural level and stability at high temperatures⁷⁻¹⁰.

The clay material forms an important part of heterogeneous catalysts due their vast availability and interesting catalytic properties. In recent times, these are heavily explored for their catalytic potential in organic synthesis¹¹. The naturally occurring clays are mostly acidic in nature and exhibit high surface area. The clay catalysts found their prominent applications in the field of refining of petroleum and transformation of bio-ethanol into hydrocarbons^{12,13}. The need for cheap, non-toxic and reusable catalysts is very high in industrial processes. Red brick clay which is easily available and non-hazardous is a perfect catalytic material^{14,15}. Red brick clay is composed of mainly SiO₂ (12.36%), Fe₂O₃ (5.28%) and Al₂O₃ (5.23%). The red brick clay has been used as an efficient catalyst in many reactions and it also showed selective 1,4-butanediol dehydration with an excellent yield^{16,17}. The photo-catalytic oxidative degradation of dyes like malachite green (MG) is efficiently catalyzed by iron and zinc supported on red brick nanocomposites^{18,19}.

Nitrogen containing heterocyclic moieties has a huge importance in organic synthesis²⁰. Imidazole moiety has significance in synthetic and medicinal fields due to its crucial role as building blocks in products of natural origin²¹. Imidazole derivatives attracted significant attention by their prominent biological activities that include antihypertensive, antimicrobial and anticancer²²⁻²⁵. Benzimidazole is a crucial moiety in the field of medicinal chemistry owing to a wide variety of pharmacological and biological activities, which include anticancer, antimicrobial and anti-inflammatory²⁶⁻²⁹. Benzothiazole is another prominent moiety which possesses a broad range of biological activities. The benzothiazole derivatives incorporating imidazole moiety exhibited tremendous antifungal activity. Benzothiazole derivatives were also known for their anticancer activity. The magnificent activities of these moieties inspired us to synthesize the imidazole derivatives with benzimidazole and benzothiazole. The benzimidazole/benzothiazole tethered imidazole derivatives definitely provide leads for further drug development.^{30,31}

Over the years, researchers have introduced wide variety of catalyst for the synthesis

of imidazole derivatives. Reports have revealed that zeolite³², p-dodecylbenzenesulfonic acid (DBSA)³³, DABCO³⁴, HNO₃@ nano-SiO₂³⁵, L-proline³⁶, HClO₄-SiO₂³⁷, PEG-400³⁸, MgAl₂O₄³⁹, nano TiCl₄-SiO₂⁴⁰, nano-crystalline sulfated zirconia⁴¹, NH₄Fe(SO₄)₂·KOH⁴², Phenoxy Spacer⁴³, nanocrystalline silica supported tin oxide (SiO₂:SnO₂)⁴⁴, Sodium lauryl sulfate⁴⁵, Cu@ imine/Fe₃O₄ magnetic nanoparticles⁴⁶, sulfamic acid functionalized hollow magnetic spheres⁴⁷ have significantly improved the efficiency but environmental aspects remain overlooked. The novelty of this work lies in the fact that we have reported a greener catalyst in the form of brick derived clay which is very economical due to easy availability with simple workup and we have successfully utilized it for the synthesis of benzothiazole/benzimidazole tethered imidazole derivatives with very good efficiency. The synthesized benzothiazole/benzimidazole tethered imidazole derivatives can provide important leads for further drug development. Brick derived clay proved itself as a promising catalyst in this synthesis with additional benefits of its cheapness, easy availability with simple workup, reusability and most importantly it is environmentally favorable material as compared to other alternatives.

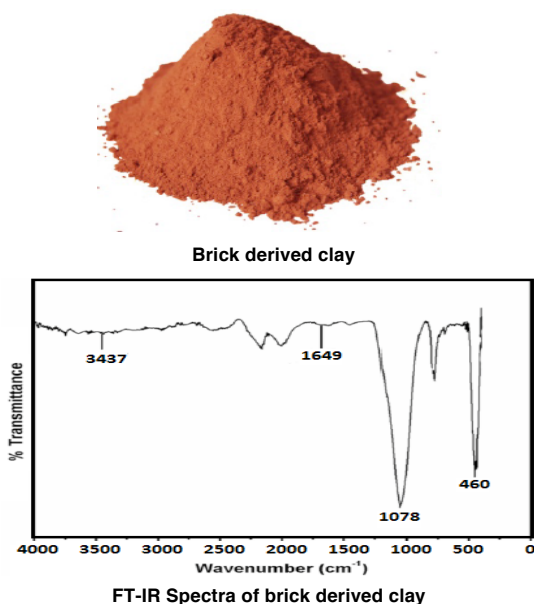
Herein, we report inexpensive, reusable and non-toxic brick derived catalyst for the synthesis of benzothiazole/benzimidazole tethered imidazole derivatives by one pot condensation reaction with terrific yields.

MATERIAL AND METHODS

The reagents used in this research work were obtained from Sigma Aldrich, Merck and Loba-chemie. The brick derived clay material used in this synthesis was obtained by grinding the red brick to fine powder. The reaction progress was monitored using TLC Silica gel 60 aluminum plates (Merck). Melting points of all the derivatives were observed in thermal apparatus for melting point. FT-IR spectra were recorded by using Bruker FT-IR spectrophotometer. JEOL JNM-ECX500 spectrometer was used for ¹HNMR and ¹³CNMR analysis of derivatives.

Synthesis of brick derived clay catalyst

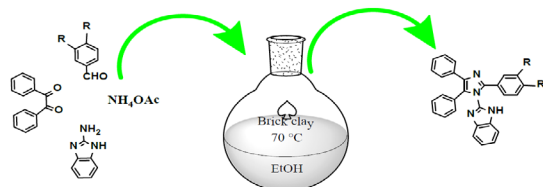
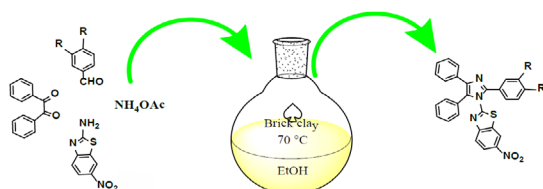
The clay material was obtained by grinding the brick to fine powder. This grinded powder is then heated in the oven for 24 h at 120°C to make it moisture free.



Synthesis of benzothiazole/benzimidazole tethered imidazole derivatives

General procedure

All the four components namely benzil, 2-aminobenzimidazole/2-amino-6-nitrobenzothiazole, selected aldehyde, ammonium acetate were taken in one millimolar quantity along with brick derived clay catalyst (50 mg) in ethanol and refluxed for 45-60 min at 70°C. The progression of the reaction is observed by thin layer chromatography (Ethyl acetate-n-hexane 2:3). When the reaction reaches its completion the product filtered for separating the catalyst and cooled at room temperature. The recrystallization has done with ethanol and product obtained with optimum purity.



N,N-dimethyl-4-(1-(6-nitrobenzo[d]thiazol-2-yl)-4,5-diphenyl-1H-imidazol-2-yl)aniline (HP-1)

yellow solid; yield 89% ; m.p. 210-213°C; IR(ν max, cm^{-1}) : 3025 (=C-H), 1648 (C=C, imidazole), 1540(C=N, imidazole); ^1H NMR (400 MHz, $\text{DMSO}-d_6$) 8.01-8.67(*d*, 3H, Ar-H), 6.70-7.6 (*d*, 4H, Ar-H), 7.27-7.40 (*d*, 10H, Ar-H), 3.04 (s, 6H, C-H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) 172, 158, 157, 153, 144, 141, 138, 135, 133, 131.8, 130, 126, 125, 123, 122, 121, 120, 119, 117, 112, 111, 110, 49, 48, 42, 40, 39, 38, 37.

2-(2-(3,4-dimethoxyphenyl)-4,5-diphenyl-1H-imidazol-1-yl)-6-nitrobenzo[d]thiazole (HP-2)

Pale yellow solid; yield 86% ; m.p. 196-199°C; IR(ν max, cm^{-1}) : 3030 (=C-H), 1674 (C=C, imidazole), 1583(C=N, imidazole); ^1H NMR (400 MHz, $\text{DMSO}-d_6$) 8.01-8.06(*d*, 3H, benzothiazole), 7.5-7.9 (*d*, 10H, C-H), 7.01-7.04 (*d*, 3H, C-H), 3.8 (*d*, 6H, O-CH₃); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) 196, 192, 172, 171, 156, 149, 142, 138, 137, 136, 135, 132, 131, 130, 129, 128, 127, 125, 123, 115, 112, 109, 98, 95, 58, 56, 42, 40, 38.

4-(1-(1H-benzo[d]imidazol-2-yl)-4,5-diphenyl-1H-imidazol-2-yl)-N,N-dimethylaniline (HP-3)

White solid; yield 88%; m.p. 205-208°C; IR(ν max, cm^{-1}) : 3248(NH) 3015 (=C-H), 1675 (C=C, imidazole), 1533(C=N, imidazole); ^1H NMR (400 MHz, $\text{DMSO}-d_6$) 9.4-7.9(*d*, 4H, Ar-H), 6.7-7 (*d*, 4H, Ar-H, Benzimidazole), 7.6-7.9 (t, 10H, C-H), 6.02 (*d*, 1H, N-H), 3.04 (s, 6H, N-CH₃); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) 196, 194, 193, 192, 190, 188, 185, 172, 170, 156, 154, 146, 139, 137, 133, 132, 131, 130, 128, 126, 125, 120, 112, 44, 42, 41, 40, 39, 38, 21.

2-(2-(3,4-dimethoxyphenyl)-4,5-diphenyl-1H-imidazol-1-yl)-1H-benzo[d]imidazole (HP-4)

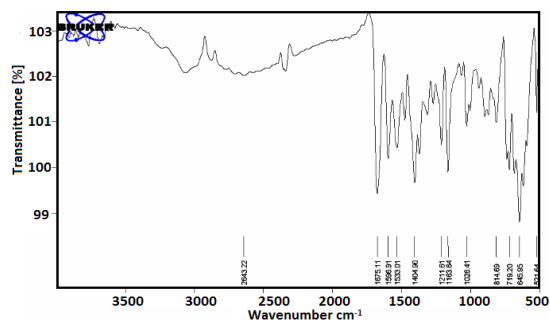
White solid; yield 84%; m.p. 215-218°C; IR(ν max, cm^{-1}) : 3090 (=C-H), 1673 (C=C, imidazole), 1508(C=N, imidazole); ^1H NMR (400 MHz, $\text{DMSO}-d_6$) 9.7-7.9 (*d*, 10H, Ar-H), 7.1-7.3 (*d*, 4H, Benzimidazole), 7.01-7.04 (*d*, 3H, C-H), 6.02 (*d*, 1H, N-H), 3.7 (*d*, 6H, O-CH₃); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) 194, 193, 191, 174, 170, 156, 154, 153, 149, 146, 139, 138, 136, 134, 133, 129, 128, 126, 119, 118, 117, 113, 112, 110, 56, 54, 42, 40, 39, 22.

RESULTS AND DISCUSSION

In our investigation, the brick derived

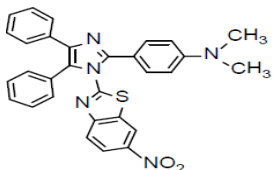
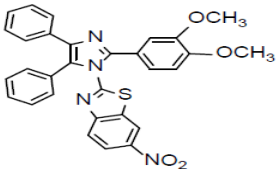
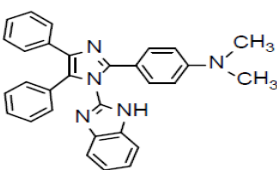
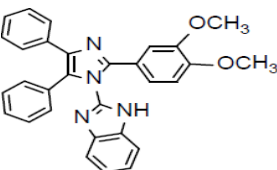
clay has emerged as a promising catalyst for the synthesis of benzothiazole/benzimidazole tethered imidazole derivatives. The work up is straight forward without any hectic procedure. All the four component reactions were carried out at 70°C and reached completion point within 45 to 60 min with very high efficiency. The yield of imidazole derivatives mainly depends on the functional group associated with aldehyde. An aldehyde with electron-withdrawing groups yields more in comparison to aldehyde with electron-donor groups. The FT-IR spectrum of the products showed characteristic vibrational bands of imidazole moiety at 1596 cm⁻¹ for C=N and 1675 cm⁻¹ for C=C groups.

The catalyst has exhibited excellent efficiency in all the reactions and the product yield of various derivatives of benzothiazole/benzimidazole tethered imidazole were 84–89% as shown in Table 1.



FT-IR spectra of HP-3

Table 1: Showing synthesized benzothiazole/benzimidazole tethered imidazole derivatives with reaction time and yield

	Product	Time(min)	Yield %
HP-1		52	89
	N,N-dimethyl-4-(1-(6-nitrobenzo[d]thiazol-2-yl)-4,5-diphenyl-1H-imidazol-2-yl)aniline		
HP-2		46	86
	2-(2-(3,4-dimethoxyphenyl)-4,5-diphenyl-1H-imidazol-1-yl)-6-nitrobenzo[d]thiazole		
HP-3		56	88
	4-(1-(1H-benzo[d]imidazol-2-yl)-4,5-diphenyl-1H-imidazol-2-yl)-N,N-dimethylaniline		
HP-4		48	84
	2-(2-(3,4-dimethoxyphenyl)-4,5-diphenyl-1H-imidazol-1-yl)-1H-benzo[d]imidazole		

The quantity of catalyst which results in highest efficiency is tested by carrying out a sequence of reactions with similar reaction conditions but varied amount of the catalyst starting from 10 mg. We have found that yield of the product

significantly enhanced from 62 to 89% when we increased the amount of catalyst from 10 to 50 mg. The product yield does not change by further increase in the amount of catalyst. So for the further synthesis the amount of catalyst is fixed to 50 mg.

Table 2: Showing efficiency of the brick derived clay catalyst at different amount.

Weight of catalyst (mg)	Reaction time (min)	Yield (%)
10	45	62
20	45	74
30	45	81
40	45	85
50	45	89

Reaction conditions; Substrate: Benzil, Aldehydes, Amines and Ammonium acetate, reaction temperature: 70°C, solvent: ethanol

The recovered catalyst is recycled with ethanol and ready for reuse in the next reaction run. The reused catalyst showed excellent efficiency without any appreciable loss in it. The efficiency of brick derived clay catalyst after successive reaction runs tabulated in Table 3.

Table 3: Showing Efficiency of brick derived clay catalyst after successive reaction runs

Reaction Runs	% Yield
1 st	89
2 nd	88
3 rd	85
4 th	84
5 th	82

We have compared the efficiency of the brick derived clay catalyst with other reported catalysts that are predominantly used in the synthesis of imidazole derivatives like Zeolite, DABCO, HNO₃@ nano-SiO₂ and data tabulated in Table 4.

Table 4: Showing comparison of the brick derived clay catalyst with other reported catalysts for imidazole derivatives synthesis

Catalysts	Solvent– Temperature	Reaction Time	Product Yield%
Zeolite ³²	Ethanol 100°C	85 min	87
DABCO ³⁴	t-BuOH 70°C	13–14 h	81
HNO ₃ @ nano-SiO ₂ ³⁵	solvent-free 100°C	3.5 h	90
Brick derived clay	Ethanol 70°C	45-60 min	89

This work is primarily focused to enhance the greenness in the synthesis of imidazole derivatives. We have reported novel benzothiazole/benzimidazole tethered imidazole derivatives synthesized by utilizing brick derived clay catalyst. This catalyst is very economical and environmentally benign.

CONCLUSION

The brick derived clay used in this work qualifies itself on both the fronts, economically as well as environmentally. The yield of products clearly highlights the effectiveness of this catalyst for the synthesis of benzothiazole/benzimidazole tethered imidazole derivatives. This catalyst proves its efficiency by minimizing both the reaction time and waste material. It has delivered excellent yield of the product, moreover this catalyst shows reusability as an important edge over others. Therefore, the brick derived clay can act as a promising candidate for synthesis of benzothiazole / benzimidazole tethered imidazole derivatives with minimal impact on the environment.

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