An Efficient Nio–Zro₂ Catalyzed Synthesis Of 2-Aryl-1-Arylmethyl-1H-Benzimidazole Derivatives

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***Abstract*— Nickel oxide (NiO) supported on zirconium oxide (ZrO_2) was successfully synthesized for a soul–gel method and evaluated as an efficient heterogeneous catalyst for the preparation of 2-aryl-1-arylmethyl-1H-benzimidazoles. NiO–ZrO_2 catalytic system was investigated in the condensation reaction of benzaldehydes with o-phenylenediamine in ethanol at reflux conditions. This protocol shows excellent efficiency, affording the desired benzimidazole derivatives in good to high yields with short reaction times. The prepared catalytic system shows non-toxic, clean, green and easy separation from the reaction mixture. Furthermore, the NiO–ZrO_2 catalyst exhibited remarkable reusability and could be recycled up to four consecutive cycles without loss of catalytic activity.**

***Index Terms*— NiO-ZrO_2 catalyst, 2-Aryl-1-arylmethyl-1H-benzimidazole, Sol-Gel method.**

I. INTRODUCTION

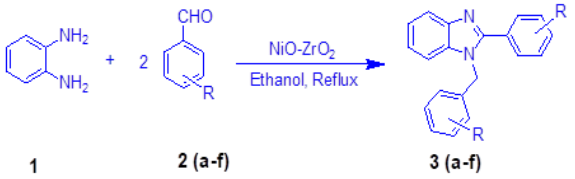
Heterocyclic compounds importance class of organic molecules that play a vital role in medicinal chemistry, materials science, and agrochemical applications. Among these, nitrogen-containing heterocycles are particularly significant due to their wide range of biological activities. The benzimidazole moiety is importance in medicinal chemistry due to its presence in biologically relevant molecules. Benzimidazole derivatives are structural component of Vitamin B12 and biologically significant structure such as purine and caffeine. The growing interest in benzimidazole core frameworks is importance for various biological and pharmacological activities. In benzimidazole shows the strong binding affinity towards a broad range of enzymes and protein receptors, these heterocyclic systems are widely recognized as "privileged scaffolds" in modern drug discovery and design [1-7].

Various methods have been reported for the synthesis of 2-aryl-1-arylmethyl-1H-benzimidazole using the condensation reaction of benzaldehyde with o-phenylenediamine. These include the use of K-10 clay under microwave irradiation [8], silica–sulfuric acid [9], L-proline [10], ferric perchlorate [11], p-toluenesulfonic acid [12], Dowex-50 [13], benzyl methylimidazolium hydrogen sulfate [14], diamine hydrochloride [15], Amberlite IR-120 [16], sodium dodecyl sulfate [17], mesoporous metal oxides [18], Indion 190 resin [19], SDS–water systems [20], nano-In_2O_3 [21], and metal hydrogen sulfates [$M(HSO_4)_n$] [22]. However, these methods suffer from certain limitations, including the use of volatile organic solvents, expensive reagents, high catalyst loadings, multi-step procedures, prolonged reaction times, and harsh reaction conditions.

Catalysts are broadly classified into two main categories: homogeneous and heterogeneous catalysts. Homogeneous catalysts exist in the same phase as the reactants, typically in the liquid phase, and include systems such as Lewis's acids, ionic liquids, and metal salts. Although homogeneous catalysis often provides high activity and selectivity, it suffers from several drawbacks, including toxicity, difficulty in separation, challenges in handling, and lack of reusability. In contrast, heterogeneous catalysts operate in a different phase than the reactants, commonly as solid catalysts in contact with liquid or gaseous reactants. Examples include metal oxides, zeolites, and mixed metal oxide systems such as NiO–ZrO_2. Heterogeneous catalysts offer significant advantages, including low toxicity, ease of handling, simple separation from reaction mixtures, and excellent reusability, making them more

suitable for environmentally benign and sustainable green chemical processes [23, 24]. In continuation our previous work on the NiO-ZrO_2 catalyzed synthesis of polyhydroquinoline derivatives [25].

In the present study focuses on an efficient NiO–ZrO_2 catalyzed synthesis of 2-aryl-1-arylmethyl-1H-benzimidazole derivatives. This method aims to provide a simple, high-yielding, and sustainable approach under mild reaction conditions, highlighting the potential of NiO–ZrO_2 as an effective catalyst in heterocyclic synthesis (Scheme 1).



Scheme 1

II. RESULTS AND DISCUSSION

In model reaction, 2 mmol of benzaldehyde and 1 mmol o-phenylenediammine in study the effect of solvents in NiO-ZrO_2 catalyst. We have study the model reaction in various solvents such as methanol, acetone, acetonitrile which give moderate yields of the desired product. We also tested ethanol as solvent it's exhibited well to excellent yields under same condition Table 1 (entry 4). Therefore, we have chosen ethanol as solvent for the synthesis of different derivatives.

Table 1 Effect of solvent on the synthesis of 2-aryl-1-arylmethyl-1H-benzimidazole[a]

Entry	Solvent	Time (min.)	Yield (%) [b]
1	Methanol (CH_3-OH)	150	89
2	Acetone (CH_3-CO-CH_3)	145	90
3	Acetonitrile (CH_3CN)	160	87
4	Ethanol (CH_3CH_2OH)	130	95
aReaction condition: benzaldehyde (2 mmol), o-phenylenediammine (1 mmol), catalyst (0.03 g) in refluxed. bIsolated yields.			

After study the solvent system, we have focused the effect of catalyst loading in model reaction. In the without catalyst, no any product formation observed, confirming the essential role of the NiO-ZrO_2 catalytic system. The reaction was then performed with varying amounts of catalyst such as 0.01 g and 0.02 g which shows lower yield and longer reaction times in model reaction. catalyst loading increasing from 0.03 g, 0.04 g and 0.05 g gave improved the yields and times affording good to excellent results. However, no notable improvement in the catalytic loading. Therefore 0.03 g of catalyst was selected as the optimal amount for carrying out the reaction Table 2 (entry 4).

Table 2 Effect of catalyst loading on the synthesis of 2-aryl-1-arylmethyl-1H-benzimidazole[a]

Entry	Catalyst	Time (min.)	Yield (%) [b]
1	No catalyst	190	-
2	0.01 g	160	90
3	0.02 g	150	91
4	0.03 g	130	95
5	0.04 g	130	95
6	0.05 g	130	95
aReaction condition: benzaldehyde (2 mmol), o-phenylenediamine (1 mmol), catalyst in ethanol refluxed. bIsolated yields.			

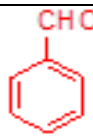
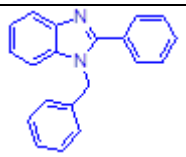
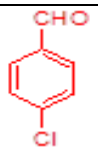
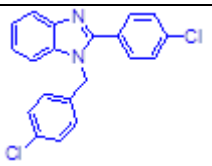
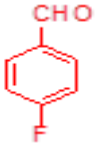
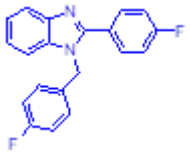
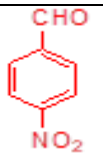
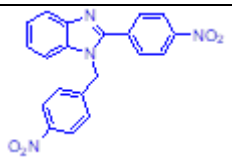
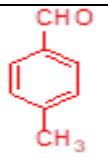
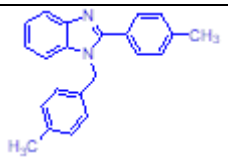
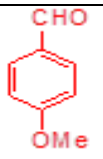
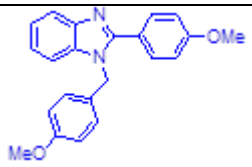
The model reaction was further studied using both conventional and non-conventional methods. The non-conventional approaches such as ultrasonication method resulted in longer reaction times and lower yields of product Table 3 (entry 1). In contrast, the microwave-assisted method significantly reduced the reaction time; however, it afforded comparatively lower yields than the conventional method. Overall, the conventional reflux condition provided the best balance of reaction time and yield Table 3 (entry 3). Therefore, the conventional method was selected as the most suitable approach for the synthesis of 2-aryl-1-arylmethyl-1H-benzimidazole.

Table 3 Comparison of conventional and non-conventional methods for the synthesis of 2-aryl-1-arylmethyl-1H-benzimidazole[a]

Entry	Condition	Time (min.)	Yield (%) [b]
1	Ultrasonication (non-conventional)	150	87
2	Microwave irradiation (non-conventional)	19	88
3	NiO-ZrO2 (Conventional)	130	95
aReaction condition: benzaldehyde (2 mmol), o-phenylenediamine (1 mmol), catalyst (0.03 g), in ethanol (15 mL) at refluxed. bIsolated yields.			

A variety of different benzaldehydes such as electron-withdrawing and electron-donating substituents were studies for the synthesis of 2-aryl-1-arylmethyl-1H-benzimidazoles. All derivatives reacted efficiently in the presence of the NiO–ZrO_2 catalytic system, it's showing the desired products in good to excellent yields, demonstrating the scope and importance of the catalyst Table 4.

Table 4 synthesis of 2-aryl-1-arylmethyl-1H-benzimidazoles using NiO-ZrO_2 catalyst[a].

Entry	Aldehyde	Products	Time (min.)	Yields (%) [b]	M.P. (°C)
3a			130	95	132-134
3b			135	94	134-136
3c			160	90	113-115
3d			170	89	193-195
3e			140	91	129-131
3f			150	90	129-131

[a]Reaction condition: aldehydes (2 mmol), o-phenylenediamine (1 mmol), catalyst (0.03 g), in ethanol (15 mL) at refluxed. bIsolated yields.

Industrial and economical applicability, the recyclability and reusability of the catalyst were investigated. After completion of the reaction, the NiO–ZrO_2 catalyst was easily recovered by simple filtration method it was washed with n-hexane to remove any organic residues, and dried in an oven at 80 °C for 1 h before reuse in the next catalytic cycle. The catalyst reused at least four consecutive cycles without any significant loss in catalytic activity.

Table 5 Recyclability and reusability of NiO–ZrO_2 catalyst[a].

Run	Fresh	1	2	3	4
Yield (%) [b]	95	94	94	93	92

aReaction condition: benzaldehyde (2 mmol), o-phenylenediammine (1 mmol), catalyst (0.03 g), in ethanol (15 mL) at refluxed. byield after consecutive cycles.

III. EXPERIMENTAL

3.1 Characterization Techniques

All chemicals were purchased from Merck and Fluka and used without further purification. Melting points were determined using open capillaries and are uncorrected. ^{1}H NMR spectra were recorded on a 300 MHz FT-NMR spectrometer using $CDCl_3$ as the solvent. FT-IR spectra were recorded on a JASCO FT-IR 4100 spectrometer (Japan) using KBr discs.

3.2 Synthesis of NiO-ZrO_2 catalytic materials

The NiO–ZrO_2 catalytic material was prepared via the simple sol–gel method. Nickel (II) chloride hexahydrate [Ni $(H_2O)_6$] Cl_2 (0.31 g) and zirconium (IV) oxychloride octahydrate ($ZrOCl_2$. $8H_2O$) (2.7 g) were dissolved in double-distilled water under continuous stirring to form a uniform solution. Ammonium hydroxide (NH_4OH) was slowly added to the solution, leading to the formation of a white precipitate. The mixture was further stirred at room temperature for 5 h to complete the precipitation process. The resulting solid was collected by filtration and dried at 110 °C for 10 h to obtain a powder precursor. The dried material was then calcined at 500 °C for 2 h, to from NiO–ZrO_2 catalytic material.

3.3 General procedure for the synthesis of 2-aryl-1-arylmethyl-1H-benzimidazoles using NiO-ZrO_2 catalyst. 3 (a-f)

A reaction procedure of aldehyde (2 mmol), o-phenylenediamine (1 mmol), and NiO–ZrO_2 heterogeneous catalyst (0.03 g) in ethanol (15 mL) was refluxed for the appropriate time Table 4. Time to time check the reaction by using thin-layer chromatography (TLC) techniques using solvent system of petroleum ether: ethyl acetate (7:3) as the mobile phase. In the reaction completed, the mixture was cooled and the catalyst was recovered by simple filtration for reuse in next cycles. The filtrate was then poured onto crushed ice, resulting in precipitation of the crude product, which was collected by filtration. The obtained solid was further purified by recrystallization from ethanol to afford the pure product 3 (a-f).

3.4 Spectroscopic Data of Representative Compounds

1-benzyl-2-phenyl-1H-benzo[d]imidazole (3a): ^{1}H NMR ($CDCl_3$, 300MHz) δ: 5.44 (s, 2H), 6.24-8.16 (m, 14H); IR (KBr, cm^{-1}): 3060, 1598, 1485, 1396, 730.

1-(4-chlorobenzyl)-2-(4-chlorophenyl)-1H-benzo[d]imidazole (3b): ^{1}H NMR ($CDCl_3$, 300MHz) δ: 5.46 (s, 2H), 7.01-7.94 (m, 12H); IR (KBr, cm^{-1}): 3054, 1605, 1435, 828, 740.

1-(4-fluorobenzyl)-2-(4-fluorophenyl)-1H-benzo[d]imidazole (3c): ^{1}H NMR ($CDCl_3$, 300MHz) δ: 5.42 (s, 2H), 6.94-7.63 (m, 12). IR (KBr, cm^{-1}): 3072, 1595, 1492, 1400, 745.

VI. CONCLUSION

In conclusion, NiO-ZrO_2 catalytic system was successfully synthesized by using Sol-Gel method and effectively applied for the synthesis of 2-aryl-1-arylmethyl-1H-benzimidazoles. In NiO-ZrO2 catalytic system exhibited clean, non-toxic, reusability up to the four cycles without loss of activity. These finding suggest that the NiO-ZrO2 system is promising and sustainable catalyst for the synthesis of biologically important benzimidazole derivatives.

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