

Green and Efficient Synthesis of 2-phenyl-1H-benzimidazole Using Recycled Steel Slag as a Novel and Readily Removable Catalyst

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Abstract. This paper reports the efficient synthesis of 2-phenyl-1H-benzimidazole using recycled steel slag as a green and novel catalyst. Steel slag is a waste by-product from the steel refining process. It contains iron and copper species that act as Lewis acids to catalyze the reaction between phenylacetaldehyde and o-phenylenediamine. The transformation was carried out in a 9:1 ethanol–water mixture at 80 °C open to air. The reaction yielded 2-phenyl-1H-benzimidazole in 89% yield within 30 minutes. The use of steel slag as catalyst has several advantages, including low cost, mild reaction conditions, and easy removal from the reaction mixture via filtration. Overall, this method provides an efficient and sustainable methodology to synthesize 2-phenyl-1H-benzimidazole and other benzimidazole derivatives, which is a class of compound that is widely applicable in medicinal chemistry and materials science.

Keywords: Green chemistry, Catalysis, Organic Chemistry

1. Introduction

Benzimidazole derivatives are a privileged class of heterocyclic compounds with broad applications in medicinal chemistry [1-4], agrochemicals [5-6], and materials science [7-8]. Among them, 1H-benzimidazole (1) has attracted particular attention from the organic chemistry community [9]. There are many marketed drugs that contain 1H-benzimidazole motif showing various medical activities (Figure 1).

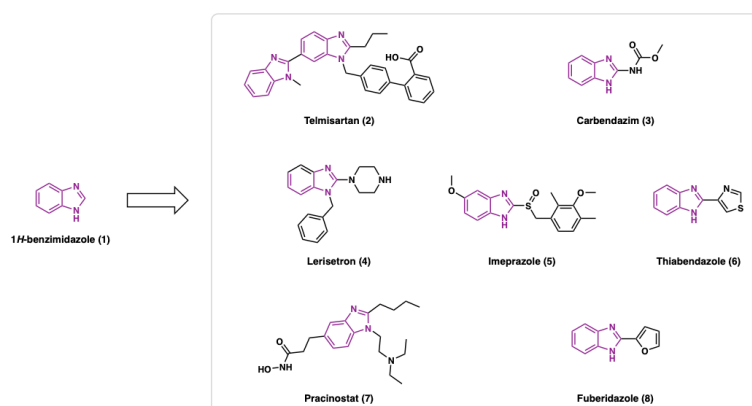


Figure 1. Examples of marketed drugs with 1H-benzimidazole (1) motif.

Among the marketed drugs, Telmisartan (2) is an angiotensin II receptor blocker used to treat hypertension and exhibits partial PPAR- γ agonism, and it is used to treat cardiovascular diseases [10]. Carbendazim (3) and Fuberidazole (8) are widely used fungicide [11]. Lerisetron (4) is used for managing chemotherapy-induced nausea by blocking serotonin signaling [12]. Omeprazole (5) is a proton pump inhibitor that treats acid reflux by covalently inhibiting the H⁺/K⁺-ATPase in gastric parietal cells [13-14]. Thiabendazole (6) is an antifungal anthelmintic drug [15] and Pracinostat (7) is an histone deacetylase (HDAC) inhibitor under clinical development for breast cancer [16]. Overall, these benzimidazole-based drugs exhibit a wide range of different biological activities and highlight the benzimidazole scaffold's versatility across therapeutic and agrochemical domains.

There have been many reports on synthetic methods for benzimidazole derivatives [9]. However, most conditions often involve harsh reaction conditions including strong acids [17] and oxidants [18], prolonged reaction times, elevated reaction temperatures or the use of toxic or expensive catalysts, such as Pd [19], In(OTf)₃ [20], Zn(OTf)₂ [21], Cu-Fe [22], or Pd-Cu [23]. These limitations underscore the need for more sustainable, environmentally friendly and green synthetic methodologies. In recent years, the development of green chemistry approaches has become an important area of research in organic synthesis [24-25], with a particular focus on discovering efficient, recyclable, and low-cost catalyst systems [26]. Steel slag, a byproduct of steel production, is typically considered industrial waste. However, it contains significant amounts of transition metals such as iron and copper, which are known to act as effective Lewis acid catalysts. The valorization of steel slag not only offers a sustainable pathway for waste utilization but also aligns with circular economy principles by converting waste into value-added materials.

In this study, we report a novel and efficient protocol for synthesizing 2-phenyl-1H-benzimidazole using recycled steel slag as a heterogeneous catalyst. The reaction proceeded under mild conditions in an ethanol–water mixture and afforded high yields of the target compound. The catalyst can be easily separated by filtration and reused. This work demonstrates the potential of industrial byproducts as practical catalysts in organic synthesis. The methodology offered an environmentally friendly alternative to conventional methods.

2. Methods

Steel slag was recycled and purchased from Ansteel Iron and Steel Group Corporation in Anshan, Liaoning, China. Organic reagents and solvents were purchased from Sigma Aldrich. The reactions were monitored by thin-layer chromatography on Merck silica gel plates and by Agilent 6475 Triple

Quadrupole LC/MS. ¹H NMR was recorded on MR400 Agilent Technology NMR spectrometer using DMSO-d₆ as solvent.

3. General procedure for the synthesis of 2-phenyl-1H-benzimidazole.

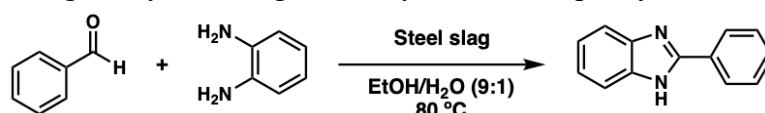
To a stirred solution of benzaldehyde (48.0 mg, 0.400 mmol) and recycled steel slug (14.4 mg, 30 wt%) in 9:1 EtOH:H₂O (5.0 mL), was added o-phenylenediamine (55.9 mg, 0.516 mmol) in one portion. The reaction was stirred at 80 °C for 30 minutes open to air. The reaction was cooled down to room temperature. The reaction was filtered over celite. The filtrate was evaporated in vacuo, and the residue was purified by silica chromatography eluting with 0-100% EtOAc in heptane.

4. Results

To optimize the reaction conditions for the synthesis of 2-phenyl-1H-benzimidazole, we investigated the effect of recycled steel slag catalyst loading. Reactions were carried out using benzaldehyde (1 equiv) and o-phenylenediamine (1.3 equiv) in a 9:1 ethanol–water mixture at 80 °C. The yields were determined after purification by silica chromatography (Table 1).

In the absence of any catalyst, the reaction proceeded slowly with moderate yields. The reaction reached 75% yield after 60 minutes (entry 1) and 56% after 30 minutes (entry 2). These two control experiments indicated a slow background reaction. When 10 wt% steel slag was added, the reaction rate improved significantly, affording 83% yield after 60 minutes (entry 3) and 70% after 30 minutes (entry 4). Increasing the catalyst loading to 30 wt% further improved the yield to 85% within 30 minutes (entry 5). The optimal result was obtained with 50 wt% steel slag, which delivered 89% yield in 30 minutes (entry 6). Product was confirmed by comparing with authentic sample (LCMS and ¹H NMR).

Table 1. Steel slag catalyst loading for the synthesis of 2-phenyl-1H-benzimidazole.^a



Entry	Steel Slag (weight %)	Time (min)	Yield (%) ^b
1	0	60	75
2	0	30	56
3	10	60	83
4	10	30	70
5	30	30	85
6	50	30	89

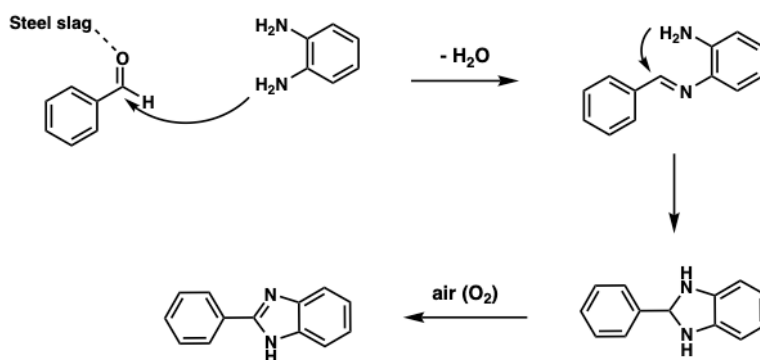
^aReaction condition: Benzaldehyde (1 equiv), o-phenylenediamine (1.3 equiv), 9:1 EtOH:H₂O, 80 °C. ^bIsolated yields.

5. Discussion

The results demonstrate the catalytic efficiency of recycled steel slag in promoting the synthesis of 2-phenyl-1H-benzimidazole. In the absence of catalyst, the condensation between benzaldehyde and o-phenylenediamine proceeded slowly, highlighting the need for a catalyst to enhance reaction

efficiency. The introduction of steel slag significantly accelerated the reaction, with yields increasing in tandem with catalyst loading.

At 10 wt% loading (entry 4), steel slag provided notable improvement over the background reaction (entry 2). Higher loadings of 30 wt% (entry 5) and 50 wt% (entry 6) further enhanced the yield within a shorter reaction time, with the highest yield (89%) achieved at 50 wt% in just 30 minutes. This trend suggests that the active metals, such as iron and copper, in steel slag function effectively as catalysts, which can facilitate imine formation and subsequent cyclization under mild and aerobic conditions.



Scheme 1. Proposed mechanism for synthesis of 2-phenyl-1H-benzimidazole

A proposed mechanism for the transformation is described in Scheme 1. The syntheses commenced with Steel slag coordinating with benzaldehyde as a Lewis acid. Then, the benzaldehyde was prone to react with o-phenylenediamine in a condensation reaction with the loss of 1 equivalence of water. As the imine formed, intramolecular attack from the diamine cyclized to form a dihydrobenzimidazole, which can be easily oxidized in air to yield desired 2-phenyl-1H-benzimidazole.

In addition, the reaction is heterogeneous, and steel slag can be easily removed by filtration. The catalysts may be recycled for future use. These features of steel slag catalysts align with green chemistry principles. In summary, these results highlight steel slag as a low-cost, sustainable, and efficient catalyst for benzimidazole synthesis.

6. Conclusion

In summary, we have developed a green and efficient methodology to synthesize 2-phenyl-1H-benzimidazole using recycled steel slag as catalyst. Steel slag significantly shortened the reaction time and improved yield under mild conditions. Optimal results were achieved with 50 wt% catalyst loading of steel slag, affording 89% yield of 2-phenyl-1H-benzimidazole in 30 minutes. This work not only demonstrates the utility of steel slag in organic synthesis, but also offers a sustainable approach to recycle and reuse industrial waste. The ease of catalyst separation and its potential reusability further support its application in environmentally friendly chemical processes.

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