

A Review: Synthesis of Benzimidazole derivatives by using Various Nanoparticles as a Catalyst

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Abstract: Heterocyclic compounds are used and put to use more frequently in medical chemistry because they are a part of the structure of many biological components. One of the heterocyclic compounds, benzimidazole, has been extensively employed in drug manufacturing and medicinal chemistry because of its structural resemblance to naturally occurring nucleotides like the adenine base of DNA and a component of vitamin B12. This work summarises the synthesis of benzimidazole derivatives using transition metal nanoparticles as a catalyst.

Keywords: Benzimidazole, Nanoparticles, Medicinal Chemistry, and O-Phenylenediamine.

I. INTRODUCTION

Since Woolley proposed in 1944 that benzimidazole can behave as purines to stimulate a number of biological processes [1], the medicinal potential of the benzimidazole nucleus has received widespread recognition. A few years later, Brink discovered that this molecule and certain of its derivatives, including 5,6-dimethylbenzimidazole, exhibit properties resembling those of vitamin B12 [2,3]. This substance has only recently been developed due to the presence of the benzimidazole nucleus in many bioactive medications, including antihypertensive, anti-inflammatory, antiviral, analgesic, anticancer, proton pump inhibitor, anticonvulsant, antifungal, anticoagulant, antihistamine, antiparasitic, and antiulcer agents [4-11]. As a result, over the past 10 years there has been a significant increase in research into the synthesis of bioactive compounds from benzimidazole.

Many benzimidazole compounds have been created for their pharmacological properties, according to the literature review. Following this paradigm, this paper summarises the most recent research on methods to fully avoid or drastically cut back on the use of hazardous solvents used to produce benzimidazoles. It is also highlighted how many benzimidazole derivatives with diverse pharmacological activity can be described using a substitution model. The wide range of bioactivities that benzimidazoles and their derivatives display as well as the significance of these compounds for synthetic reasons have drawn a lot of attention to the development of libraries of these chemicals. benzimidazole compounds with excellent biological activity and stability were produced by replacing them [12,13]. Omeoprazole and other synthetic benzimidazole compounds with electron-donating groups are effective antiulcer drugs [14,15]. The ability of benzimidazole compounds to treat conditions including hypertension and ischemia-reperfusion injury has been demonstrated, however [16].

Ophenylenediamine interacts with carboxylic acids or their derivatives, in accordance with past manufacturing processes mentioned in the literature [17,18]. Monoacyl derivatives of o-phenylenediamine are transformed into the appropriate benzimidazole in order to stop oxidation at a temperature higher than the melting point of the original molecule [19]. It follows that aldehydes rather than carboxylic acids were used to make the 2- and 1,2-substituted benzimidazoles. Due to their slow reaction times, high temperatures, and use of hazardous solvents, these synthetic approaches, however, highlighted a number of difficulties. [20 The usage of non-renewable, insufficiently ecological, and selective catalysts is also widespread. Serious concerns for the environment and the general public's health are raised by the use of hazardous solvents and the production of a sizable volume of industrial waste.

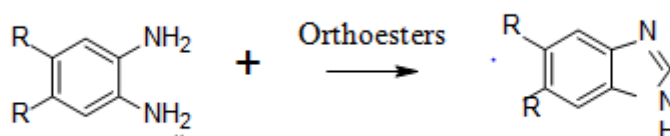
The pharmaceutical industry has recently been motivated by green chemistry theories that advocate the use of eco-friendly solvents [23,24], waste reduction through selective reaction methods, and recyclable reagents [25-40]. Researchers and business have been working very hard to create a new synthetic method in response to this issue. The study of prospective drugs has advanced tremendously. The value of using catalysts has increased. It has been found that the production of benzimidazole derivatives is more environmentally friendly when Lewis acids are used as efficient catalysts in various transformations. The first example of the synthesis of these substances is the straightforward synthesis of benzimidazole derivatives at room temperature using o-phenylenediamines and orthoesters (Scheme 1) [41]. 403, 392 from 37 catalysts in 2023.

Benzimidazoles and their derivatives have undergone extensive research due to the vast spectrum of bioactivities and importance for synthetic processes. Beginning in the early 1990s, fluorine, propylene, tetrahydroquinoline, and cyclized molecules were introduced to produce benzimidazole derivatives with exceptional biological activity and stability. [12,13]. Omeoprazole and other synthetic benzimidazole compounds containing electron-donating groups have been shown to be effective antiulcer drugs [14,15]. Yet, studies have demonstrated the efficacy of benzimidazole compounds in the treatment of ischemia-reperfusion damage and hypertension. [16] Ophenylenediamine interacts with carboxylic acids or their derivatives, as demonstrated by early synthesis techniques that have been recorded in the literature [17,18]. Monoacyl derivatives of o-phenylenediamine are transformed into the appropriate benzimidazole in order to prevent oxidation at a temperature higher than the melting point of the starting compounds [19]. Later, aldehydes rather than carboxylic acids were used to synthesise 2- and 1,2-substituted benzimidazoles. Due to slow reaction times, high temperatures, and the use of hazardous solvents, these synthetic techniques have, however, shown a number of problems [20–22]. Yet, the use of non-renewable, insufficiently green, and selective catalysts is pervasive. There are significant environmental and public health concerns raised by the use of hazardous solvents and the production of a significant volume of industrial waste.

Business has recently been stimulated by green chemistry theories that advocate the use of eco-friendly solvents [23,24], waste reduction through selective reaction techniques, and recyclable reagents [25-40]. Researchers and business have been working extremely hard on novel synthetic techniques as a result of this conundrum. 2.1. Because the search for better and more useful methods for the synthesis of benzimidazoles continues to be a primary research focus, catalysis is used in the synthesis of benzimidazoles. The justification is that developing novel synthetic methods for producing potentially therapeutic compounds has become a prominent topic of study. The value of using catalysts has increased. It has been found that the production of benzimidazole derivatives is more environmentally friendly when Lewis acids are used as efficient catalysts in various transformations. A simple procedure can be used to make benzimidazole derivatives using orthoesters and o-phenylenediamines (Scheme 1) [41]. There is proof that the catalysts $ZrOCl_2$, $TiCl_4$, $SnCl_4$, $5H_2O$, and $HfCl_4$ are efficient. Regarding the latter, o-phenylenediamine has been used to create substituted benzimidazoles.

1) Scheme 1

By microwave irradiating $ZrOCl_2 \cdot 8H_2O$ at room temperature, Reddy et al. (2008) described a straightforward, effective, and one-pot technique for producing 2-substituted benzimidazole utilising orthophenylenediamine and orthoesters such orthoformate, orthoacetate, and orthovalerate. [25]

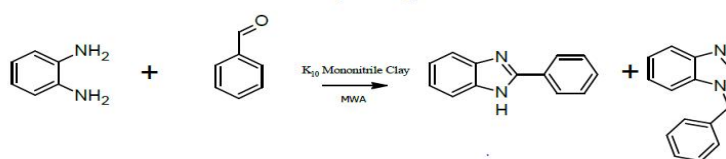


2) Scheme 2

In 2007, Kumar et al. used ceric (IV) ammonium nitrate, certain aldehydes, and ortho phenyl diamines to make specific benzimidazoles (CAN). This method is beneficial and appealing to organic chemists since it generates natural chemicals in high yields below reaction times with a quick reaction time. [26]

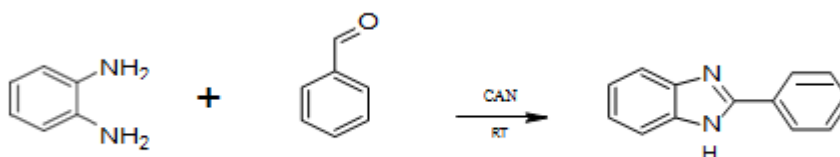
Scheme 3

Javanshir et al. (2010) claim that under grinding and solvent-free circumstances at room temperature, novel 2'-aminobenzimidazolomethylnaphthol derivatives were generated through the catalysis of L-proline in the presence of 2-aminobenzimidazole, 2-naphthol, and aromatic aldehydes. [27] In the absence of a solvent and using fragrant aldehydes, Perumal et al. (2004) describe a series of techniques for the rapid and efficient synthesis of 2-aryl-1-aryl methyl-1H-1,3-benzimidazoles. N-alkylated compounds are occasionally produced by the processes. [28]



Scheme 4

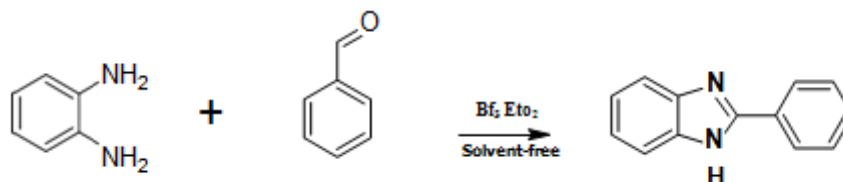
Kidwai et al. (2010) described the efficaciously catalysed synthesis of benzimidazole derivatives in PEG the usage of o-phenylenediamine and aldehydes as catalysts.



Trifluoroacetic acid (TFA) changed into added as an efficient catalyst for the selective synthesis of 2-aryl-1-aryl methyl-1H-1,3. [30]

Scheme 5

Using ophenylenediamine and aldehydes as a catalyst, TiCl₄ is used to produce differently substituted benzimidazoles without the need for a solvent. Aliphatic, fragrant, and unsaturated aldehydes can all benefit from this technique. [31]



Scheme 6

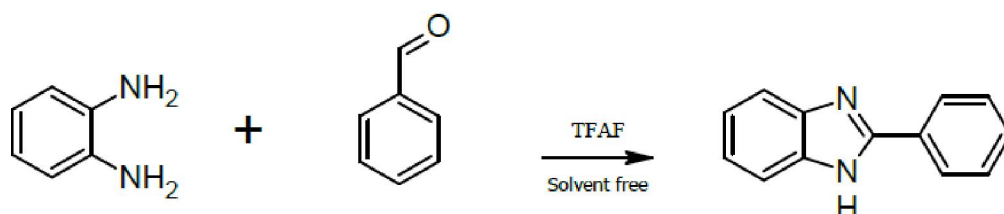
Joshi et al. (2010) described onepot multistep benzimidazole synthesis operations using a unique catalytic approach. [32]

Scheme 7

In solvent-free conditions, Nagawade et al. (2006) produced variably substituted benzimidazoles in excellent yields from *o*-phenylenediamine and aldehydes using BF₃OEt₂ as a catalyst. With replaced *o*-, the mechanism operates similarly [33]

Scheme 8

Patil et al. (2010) produced certain benzimidazoles derivatives making use of phenylenediamine and aldehydes with a catalytic amount of zinc acetate at room temperature. The yield from the response is very good. [34]



Scheme 9

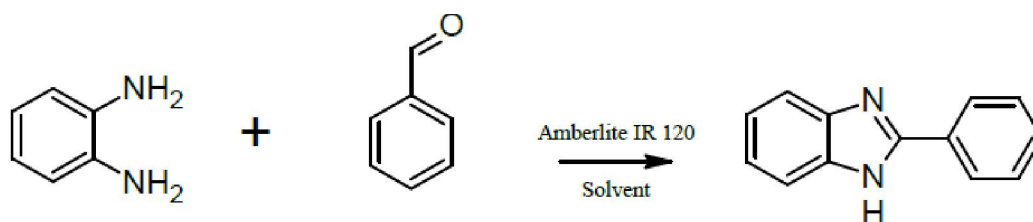
Pure required products by using solid support such as silica gel/ neutral alumina/fly ash under are carried microwave-assisted solvent less conditions.[36]

Scheme 10

Dowex 50W is made from a wide range of substituted *o*-phenylenediamines and aromatic aldehydes (as a catalyst in an aqueous media). [37]

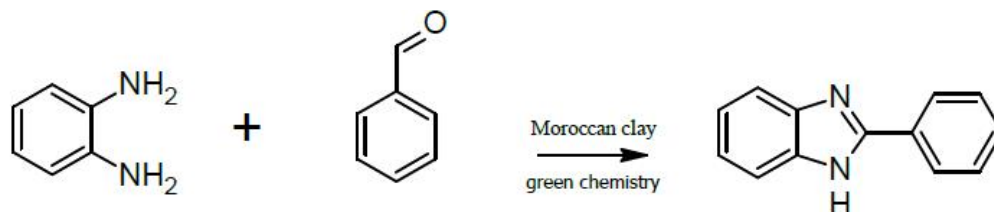
Scheme 11

O-phenylenediamine with different aldehydes is efficiently catalysed by Amberlite IR-120 under solvent-free conditions and microwave irradiation within the time frame of three to five minutes. [38]



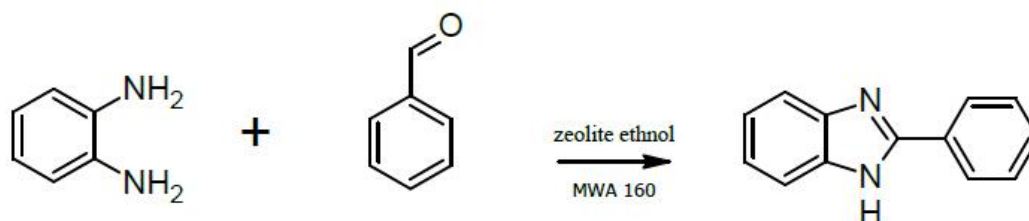
Scheme 12

The heterogeneous reaction conditions offer a relatively simple, clean, affordable, and selective technique for the synthesis of benzimidazole derivatives. [39]



Scheme 13

created 2-aryl-benzimidazoles through the condensation of different aryl aldehydes and o-phenylenediamine. Scheme 13: By reacting anthranilic acid and benzaldehyde in a microwave environment, Mohan et al.



Scheme 14

In 2009, a series of substituted orthophenyldiamine were produced by utilizing formaldehyde or another aromatic aldehyde and the appropriate amines. Instead of using the traditional method, microwave irradiation technology increased pace and yields. [44]

Scheme 15

Produced 2-aryl-benzimidazoles by condensing o-phenylenediamine with distinctive aryl aldehydes. The catalyst for the reaction is 1,3-dibromo 5,5-dimethyl hydantoin (DBH), which operates effectively in the absence of any organic solvent or below solvent-loose conditions while being heated and microwave-irradiated in high yields. [45].

II. CONCLUSION

In this we have reviewed the various methods for the synthesis of the benzimidazole derivatives. It can be worked on the various microwave and sonication methods.

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