

# *A Bioactive Imidazole Synthesis with an Eco-Friendly Approach*

Khan Shoyeab Mutalib, Kadu Sumera Mustaq and Sheikh Aliza Ajaz

Department of Chemistry

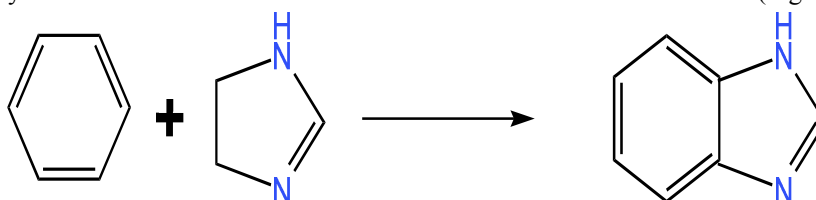
Anjuman Islam Janjira Degree College of Science, Murud- Raigad, Maharashtra, India

**Abstract:** A special and expanding area of chemistry is green chemistry. Chemical synthesis occurs more frequently every day in our environment. Toxins are bad for our health and the environment, yet chemistry has advanced as medicines have been created to solve our concerns. If you want to lower the risk associated with a system, change the cause rather than the consequence. Green chemistry is a strategy for reducing the production and usage of dangerous compounds by improving chemical industrial processes. A sustainable method for manufacturing benzimidazole derivatives is by green synthesis of benzimidazole. By avoiding the use of risky chemicals, harmful solvents, and excessive energy inputs, this artificial approach lessens the impact of the process on the environment. The process makes use of natural or renewable resources, such as plant extracts or biological waste, as catalysts or reagents to manufacture high-yield and high-purity benzimidazole derivatives. By the use of green chemistry, benzimidazole derivatives are finding new and unheard-of applications in a range of fields, such as medicine, materials science, and agriculture. Moreover, it provides a viable and environmentally responsible substitute for traditional synthesis techniques.

**Keywords:** Benzimidazole, green synthesis, eco-friendly

## I. INTRODUCTION

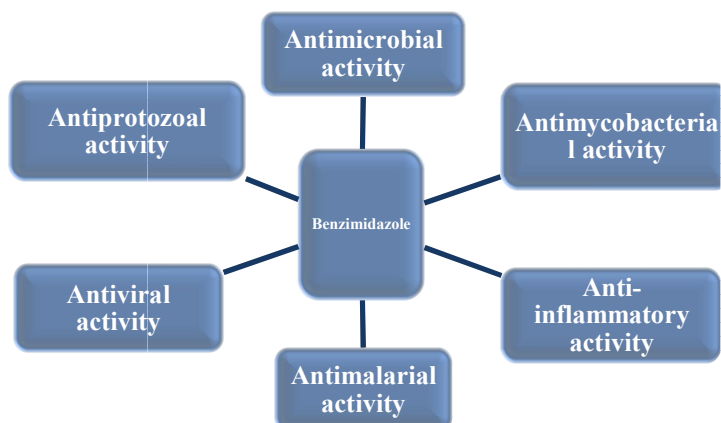
The heterocyclic aromatic chemical benzimidazole is thought to have strong pharmacological activity and the potential to be physiologically active. It has a unique structure in medicinal chemistry and is a significant pharmacophore. <sup>[1]</sup> This compound is bicyclic in nature which Consists of the fusion of benzene and imidazole (Fig.1).[2]



**Fig 1: Structure of Benzimidazole.**

It has a significant impact on medical science and a variety of therapeutic benefits, including anti-ulcer[3], anti-hypertensive[4], analgesic[5], anti-inflammatory[6], anti-viral[7], anti-fungal[8], anti-cancer[9], and anti-bacterial[10] properties.

"The design of chemical products and processes that minimise or count the use and manufacture of harmful compounds," is how Paul Anastas and John Warner described green chemistry in 1990. Environmental challenges and concerns that mortal society encounters frequently include ozone depletion, air pollution, climate change, soil and water pollution, acid rain, the depletion of natural resources, and the build-up of hazardous waste. Green Chemistry is based on twelve principles. The 12 principles of green chemistry were first presented by Paul T. Anastas and John C. Warner in their 1998 book, Green Chemistry Theory, and Practice. The California Green Chemistry Scientific Advisory



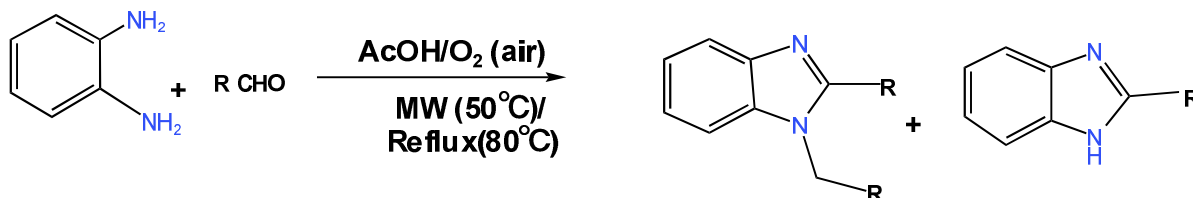
Council counts both people as members. The 12 principles are, in essence.

1. Encourage garbage rather than treating or gathering it.
2. Include in the finished product all the equipment utilised during the manufacturing process.
3. Employ synthetic methods that produce compounds that are either not harmful to people or the environment or only mildly so.
4. Create chemical goods that are efficient but less harmful.
5. Where feasible, avoid using cleaning agents and supplemental materials.
6. Employ energy-efficient procedures at room temperature and pressure to cut costs and harm to the environment.
7. Make use of sustainable raw materials as feedstocks.
8. Reuse chemical blockers and intervenors to cut back on or count waste.
9. Choose catalysts that carry out a single reaction several times alternatively than lower effective reagents.
10. Employ compounds that easily degrade into harmless substances in the environment.
11. Improve the reasoning behind real-time monitoring to cut down on harmful drugs.
12. Employ chemicals that pose little risk of mishap, explosion, or fire.<sup>[11]</sup>



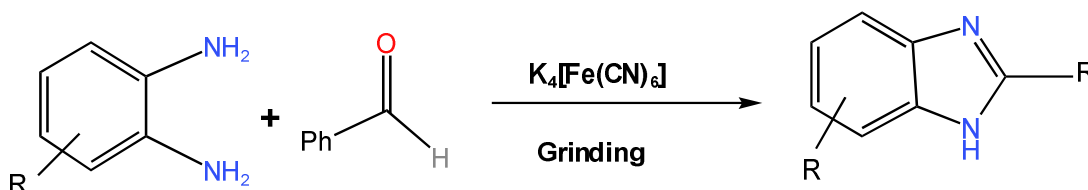
### Green Synthesis of Benzimidazole

In 2010, Davood Azarifar and colleagues used a microwave oven to condense o-phenyline diamine to create benzimidazoles. They came to the conclusion that the benefits of this system include a gentle, manipulable process, eco-friendly and green characteristics that avoid harmful detergents, quicker response times, and high product yields.<sup>[12]</sup>



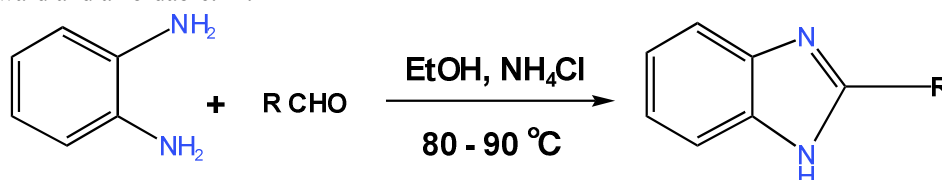
**Fig 1: Microwave-assisted benzimidazole synthesis from OPD by Davood A et al**

By treating 1, 2-diamine with aldehydes and employing the essence match complex  $K_4[Fe(CN)_6]$  as catalysis, Kabeer A. Shaikh et al. (2012) successfully synthesised Benzimidazoles in high yields. Via the environmentally friendly, moderate, and cost-effective technique of oxidising the carbon-nitrogen bond, the system was operated without the use of any solvents.<sup>[13]</sup>



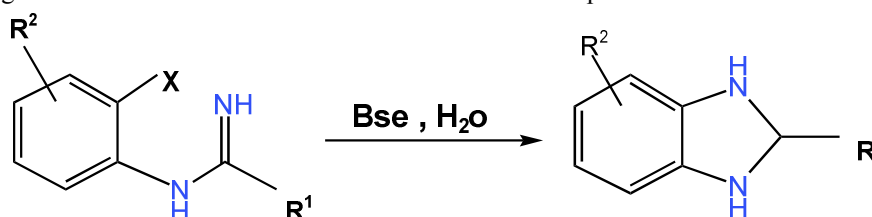
**Fig 2: B.N.B. Vaidehi et al synthesis of benzimidazole from OPD in the presence of ring closure agents,**

M. Rekha and colleagues investigated the catalytic activity of alumina, zirconia, manganese oxide/alumina, and manganese oxide/zirconia in the condensation reaction between o-phenylenediamine and an aldehyde or a ketone to synthesise, respectively, 2-substituted benzimidazoles and 1, 5-disubstituted benzodiazepines, and discovered that it was straightforward and affordable.<sup>[14]</sup>



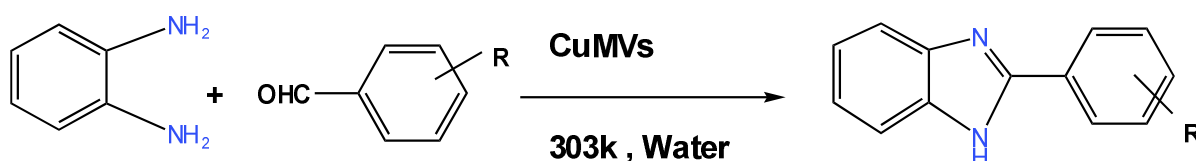
**Fig 3: Benzimidazole synthesis from OPD in the presence of a green catalyst**

The research of Chunxia Chen et al. The intermolecular cyclization of N-(2-iodoaryl) benzamidine produces benzimidazole derivatives in moderate to high yields and is a simple technique for the synthesis of the benzimidazole ring system through a carbon-nitrogen cross-coupling reaction in the presence of  $K_2CO_3$  in water at 100 °C for 30 h. Amazingly, the process only uses water and doesn't employ any additional reagents or catalysts, making the technology incredibly advantageous from both an economic and environmental standpoint.<sup>[15]</sup>



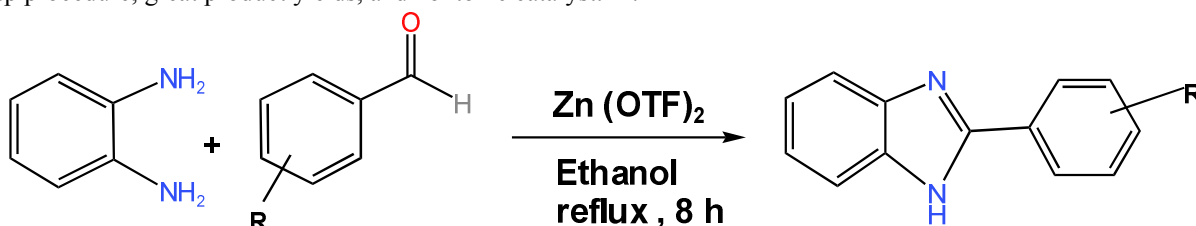
**Fig 4: Chunxia Chen et al solvent/reagent-free synthesis of benzimidazole from N-(2-haloaryl) benzamidine,**

2018 K. Kantharaju et al. By using water extract of papaya bark ash (WEPBA) as a green catalyst and reacting substituted Ophenylenediamine with various substituted benzoyl chlorides at room temperature, a quicker, more ecologically friendly method has been created to make 2-substituted benzimidazole. The overall environmental and financial benefits of this strategy are numerous. high output.<sup>[16]</sup>



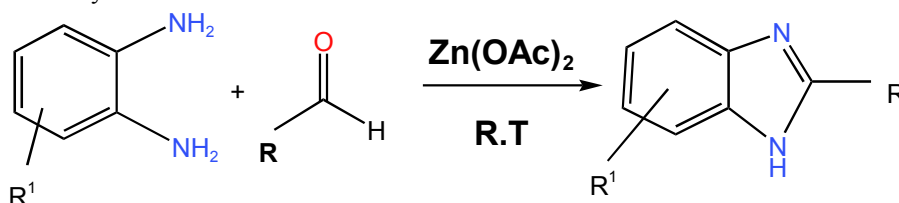
**Fig 5 : Benzimidazole is made from OPD utilising a green solvent and a green catalyst,**

Ramineni Srinivasulu et al. synthesise 2-substituted benzimidazole derivatives from o-phenylenediamine and substituted aldehydes in ethanol solvent at reflux temperature using zinc triflate as an efficient catalyst. They deduced that zinc triflate had been created to serve as a trustworthy catalyst for the synthesis of benzimidazole from aldehydes and o-phenylenediamine. The use of this inexpensive and easily accessible catalyst is what gives this process its usefulness, environmental friendliness, and economic allure. Other advantages of the current strategy are the simple setup procedure, great product yields, and nontoxic catalyst.<sup>[17]</sup>



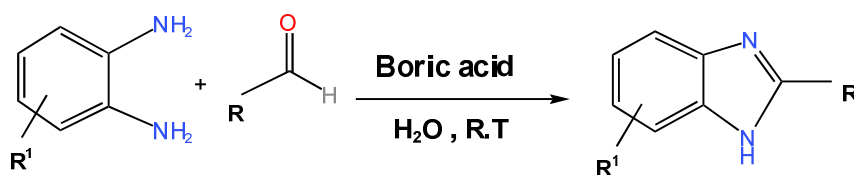
**Fig 6: Ramineni Srinivasulu et al efficient green catalyst-based synthesis of benzimidazole from OPD**

By utilising a catalytic quantity of zinc acetate and reacting modified o-phenylene diamine with aldehyde derivatives at room temperature, Vishvanath D. Patil et al. were able to create excellent yields of benzimidazole derivatives. An appealing aspect of this approach is the excellent selectivity in mild, neutral, and solvent-free conditions with a readily available, affordable catalyst.<sup>[18]</sup>



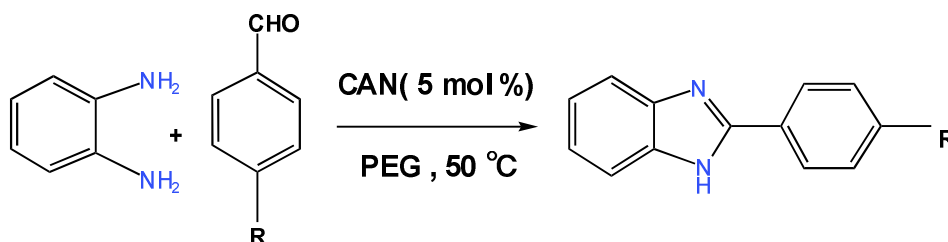
**Fig 8: Benzimidazole is made from OPD using an effective green catalyst by Vishvanath D. Patil et al.,**

With the help of aldehydes, boric acid, and water at room temperature, Zahed Karimi-Jaberi et al. were able to produce 2-Substituted in a single pot. The process was convenient and proved to be eco-friendly, and the products were isolated with high yields.<sup>[19]</sup>

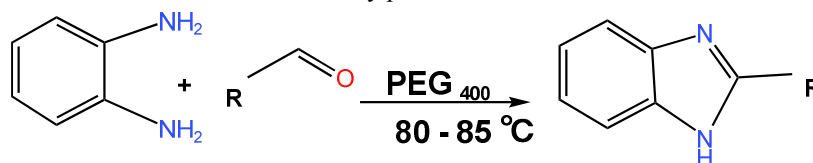


**Fig 9: benzimidazole Synthesis from OPD by using efficient green catalyst by Zahed Karimi-Jaberi et al .,**

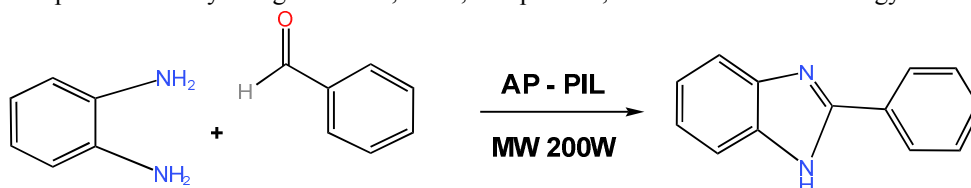
Mazahir Kidwai and colleagues created benzimidazole derivatives using o-phenylenediamine and aldehydes as starting materials and ceric ammonium nitrate (CAN) as a catalyst in PEG as the solvent. This technology offers a fresh method for the efficient and low-catalyst-loading mixing of benzimidazoles. It is appealing for large assiduity activities due to the recovery and successful reutilization of the detergent as well as the simple setup and cleaning tasks of this sustainable system.<sup>[20]</sup>



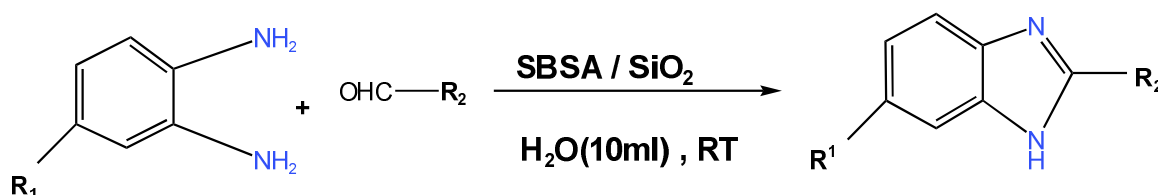
**Fig 10: Benzimidazole is made from OPD using a green solvents and green catalyst by Mazaahir Kidwai et al.,** By employing the environmentally friendly solvent PEG400 to combine o-phenylenediamine with a number of aldehydes, Mita D. Khunt et al. were able to successfully produce the benzimidazole.<sup>[21]</sup>



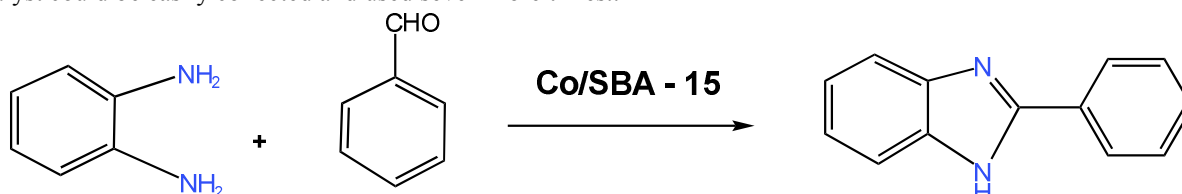
**Fig 11: Benzimidazole is made from OPD utilising an effective green solvent by Mita D. Khunt et al.,** R.Azzallou et al. (2011) described a quick and simple procedure for producing 2-aryl benzimidazole from o-phenylenediamine and aldehyde utilising microwave irradiation and a tiny quantity of newly developed Moroccan clay catalyst that has been modified with a surfactant. For the synthesis of benzimidazole derivatives, the heterogeneous reaction condition provides a very straightforward, clean, inexpensive, and selective methodology.<sup>[22]</sup>



**Fig. 12: Al-PILC-catalyzed 2-substituted benzimidazole synthesis with microwave radiation.** By condensing phenylenediamine with different aryl aldehydes, M. Forouzani et al. (2012) created 2-aryl-benzimidazole. 1,3-dibromo5,5-dimethyl hydantoin (DBH) catalyses a more ecologically friendly approach that operates effectively in high yields without the use of organic solvothermal conditions or microwave irradiation..<sup>[23]</sup>

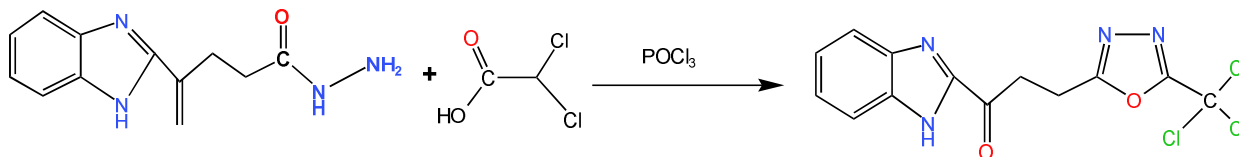


**Fig. 13: Benzimidazole can be made utilising a novel, effective catalyst called SBSA.** F. Rajabi et al. (2015) used cobalt(II) supported on mesoporous silica type material to synthesise benzimidazole from o-phenylenediamine and benzaldehyde under mild conditions. After the reaction was finished, the supported cobalt catalyst could be easily collected and used seven more times..<sup>[24]</sup>



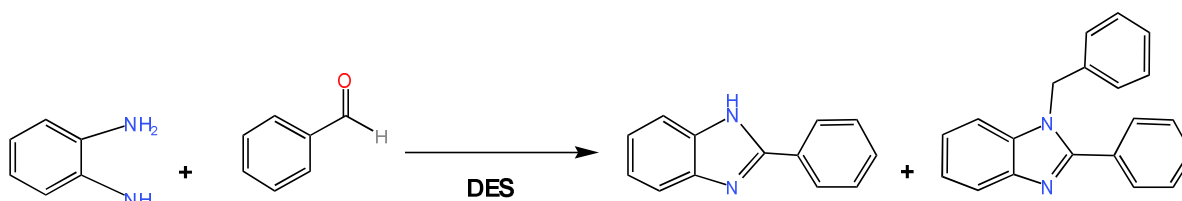
**Fig. 14: Synthesis of using Co/SBA-15 as a catalyst to produce benzimidazole from o-phenylenediamine and benzaldehyde.**

The synthesis of 1-(1H-benzimidazole-2-yl)-3-[5-(trichloromethyl)-1,3,4-oxadiazol-2-yl] was described by M. Rashid et al. in 2012. By reacting with trichloroacetic acid under microwave irradiation, 4-(1H-benzimidazole-2-yl)-4-oxobutane hydrazide can be converted into propane-1-one in a good yield.<sup>[25]</sup>



**Fig 15: Synthesis of benzimidazole when exposed to microwave energy.**

Di Gioia, M.L., et al., 2019. Starting with o-phenylenediamine in the presence of benzaldehyde, a green 2-substituted benzimidazole is synthesised. DES (ChCl: urea DES) is also added. Between 600C and 800C, the reaction mixture was left on a magnetic stirrer while being checked by TLC. Derivatives of the benzimidazole are produced. Without the need of an external solvent, using deep eutectic solvent as the reaction medium and reagent offers benefits for both yields and reaction setup.<sup>[26]</sup>



**Fig 16: Using an active eutectic solvent, green synthesis of favoured benzimidazole scaffolds.**

## II. CONCLUSION

Obtaining benzimidazole derivatives using an environmentally friendly process and chemicals is known as "green synthesis" of benzimidazole. Compared to conventional synthetic methods, this strategy has a number of benefits, such as the use of renewable starting materials, a decrease in waste production, and a reduction in energy usage. Additionally, a number of methods, including catalyst-free, microwave-assisted, and ultrasound-assisted synthesis, can be used to produce benzimidazole in an environmentally friendly manner. These techniques have been proven to be successful, economical, and capable of producing large quantities of the required output. Consequently, building sustainable and environmentally friendly synthetic methods for creating important organic molecules is made possible by the green synthesis of benzimidazole.

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