*Section A -Research paper*

# LEVERAGING CATALYST IN THE PREPARATION OF 2-BENZIMIDAZOLE DERIVATIVES: A COMPREHENSIVE STUDY

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## Abstract

The scaffold benzimidazole plays an emerging role in the synthesis of significant biological active compounds. The term "Green Chemistry" is the advancement in the field of chemistry to synthesize compounds by adopting new eco-friendly strategies. By using gentler reagents and more environmentally friendly synthetic techniques, these green approaches reduce environmental contamination and the risk to human health. Further, these synthetic processes are included solvent-free reactions, uses of different catalysts, water as a solvent, ionic liquids, microwave-assisted synthesis, etc. In this review, we concentrate on the various catalysts used in the production of derivatives of 2-substituted benzimidazoles.

**Keywords:** Benzimidazole, Green chemistry, eco-friendly, catalyst, microwave, ionic liquid

## Introduction

Benzimidazole is a very important fused heterocyclic compound containing Benzene and imidazole rings. This motif is also known as 1, 3-benzothiazoles and benzimidazoles. This pharmacophore is frequently found in a variety of natural products for instance in Vitamin B as well as therapeutically active synthetic compounds [1]. Benzimidazole and its synthetic analog show an extensive spectrum of biological and pharmacological activities such as analgesic[2], anti-inflammatory[2], antioxidant[3], antianxiety[4], antifungal[5], anti-hypertensive[6], anthelmintic[7], antiviral[8], topoisomerase inhibitors[9], anticancer[10] and anti-convulsant activities[11]. On account of their interesting therapeutic activities, researchers have paid great attention to the synthetic patterns of benzimidazole derivatives. Ortho-phenylenediamine (OPDA) is the main precursor used in the synthesis of benzimidazole. Most commonly OPDA is condensed with alkyl or aryl carboxylic acid and alkyl or aryl aldehydes in the presence of different reaction conditions. The literary works show many synthetic procedures have been reported in order to create benzimidazoles, for instance, synthesis in the presence of strong acids and high temperatures, microwave methods, solvent-free synthesis, ionic liquids, and the use of different catalysts nowadays, the incorporation of different catalysts is the most favored approach for the synthesis of benzimidazole. This review article's objective is to highlight the catalytical routes of 2-substituted benzimidazoles in the past decades.

## Synthetic Routes

### Through the condensation of OPDA with various aldehydes

A variety of benzimidazoles has been synthesized with the condensation of OPDA with a variety of benzaldehydes. Due to the abundance of available aldehydes, this approach has been widely applied. But it is widely recognized that a direct fusion of o-aryl diamines and aldehydes produces a complicated combination of side products so it is not an adequate synthetic technique. So, researchers endeavor on the most efficient methods utilizing different catalysts in different reaction conditions. The fusion of OPDA with substituted benzaldehydes in the vicinity of catalysts is shown in Fig. 1. A variety of catalysts, reactants, and reactions conditions for the creation of monosubstituted or disubstituted benzimidazoles from OPDA and a variety of substituted benzaldehydes are shown in Table 1 along with the references [12-69].

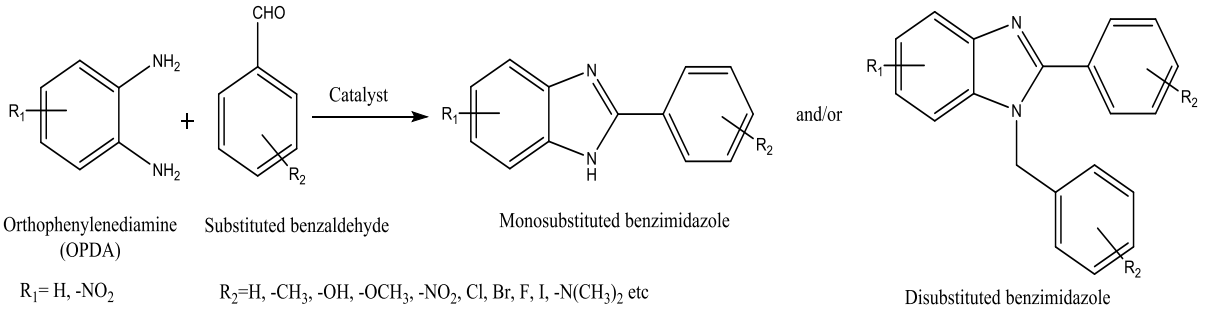


**Figure 1**

**Table 1.** Synthesis of benzimidazoles by different researchers using different catalyst

| S. No. | Reactants | Catalyst | Reaction conditions | Reference |
|---|---|---|---|---|
| 1 | OPDA and Aryl aldehyde (1:1) | Ceric ammonium nitrate | Polyethylene glycol solvent,50℃ | [12] |
| 2 | OPDA and Aryl aldehyde (1:1) | $ZnO.H_2O_2$ | Room temperature (RT) | [13] |
| 3 | OPDA and Aryl aldehyde (1:2) | $AcOH/O_2$ | Microwave 50℃ or reflux | [14] |
| 4 | Substituted OPDA and aryl aldehyde (1:1) | $NH_4Cl$ | Chloroform solvent, RT | [15] |
| 5 | OPDA and Aryl aldehyde (1:1) | Yttrium (III) chloride | Acetonitrile, RT | [16] |
| 6 | OPDA and Aryl aldehyde (1:1) | surfactant-modified Moroccan Ghassoulite clay | Methanol, RT, 30-45 minutes | [17] |
| 7 | OPDA and Aryl aldehyde (1:1) | Animal Bone Meal (ABM) | Toluene, 110℃ | [18] |
| 8 | Substituted OPDA and Aryl aldehyde (1:1) | Lead peroxide | Solvent-free, Room Temperature | [19] |
| 9 | Substituted OPDA and Aryl aldehyde (1:2) | Trifluoroacetic acid (TFA) | H2O/ethanol :1/2 | [20] |
| 10 | Substituted OPDA and Aryl aldehyde (1:1) | potassium ferrocyanide complex | Solvent-free, Grinding | [21] |
| 11 | OPDA and Aryl aldehyde | magnetic nano-$Fe_3O_4$ | Atmospheric oxygen, | [22] |

| | | | | |
|---|---|---|---|---|
| | (1:1) | | 85℃ | |
| 12 | OPDA and Aryl aldehyde (1:2) | Amberlite IR-120 | Microwave, 160 W, 3-5 minutes | [23] |
| 13 | OPDA and Aryl aldehyde (1:1) | $NaHSO_4$-$SiO_2$ | Ethanol, reflux (8 Hours) | [24] |
| 14 | Substituted OPDA and aryl aldehyde (1:1) | Silica boron sulfonic acid (SBSA) | Water (10 ml), Room Temperature | [25] |
| 15 | Substituted OPDA and aryl aldehyde (1:1) | $H_5IO_6$-$SiO_2$ | Acetonitrile, Room Temperature | [26] |
| 16 | OPDA and Aryl aldehyde (1:1) | zirconyl nitrate | Reflux 2-5 h | [27] |
| 17 | OPDA and Aryl aldehyde (1:1) | lanthanum chloride ($LaCl_3$) | Acetonitrile, Room Temperature | [28] |
| 18 | OPDA and Aryl aldehyde (1:2) | Copper (II) hydroxide | Methanol, RT | [29] |
| 19 | OPDA and Aryl aldehyde (1:1) | PVP-trifluoromethanesulfonic acid | Solvent-free, RT | [30] |
| 20 | Substituted OPDA and aryl aldehyde (1:2) | DBSA | $I_2$, $H_2O$, RT, Stir | [31] |
| 21 | OPDA and Aryl aldehyde (1:1) | $ZnCl_2$. $SiO_2$ | Solvent-free | [32] |
| 22 | OPDA and Aryl aldehyde (1:1) | Boric acid | Water, RT | [33] |
| 23 | OPDA and Aryl aldehyde (1:1) | $NH_4Cl$ | Ethanol, 80-90℃ | [34] |
| 24 | OPDA and Aryl aldehyde (1:1) | Zinc triflate | Ethanol, reflux 8h | [35] |
| 25 | OPDA and Aryl aldehyde (1:1) | Dioxane dibromide | Acetonitrile, 30-60 minutes, RT | [36] |
| 26 | OPDA and Aryl aldehyde (1:2) | Silica gel G | Grinding, RT, 30-50 minutes | [37] |
| 27 | OPDA and Aryl aldehyde (1:1) | hydroxyapatite core@shell γ-$Fe_2O_3$ nanoparticles | Water or solvent-free, 80℃ | [38] |
| 28 | OPDA and Aryl aldehyde (1:1) | zeolite AIMCM-41 | Solvent-free, Microwave | [39] |
| 29 | OPDA and Aryl aldehyde (1:1) | Co/SBA-15 | Solvent-free, reflux | [40] |
| 30 | OPDA and Aryl aldehyde (1:2) | Cobalt manganese oxide | Solvent-free, 80℃ | [41] |
| 31 | OPDA and Aryl aldehyde (1:2) | $FeCl_3/Al_2O_3$ | Methanol | [42] |
| 32 | OPDA and Aryl aldehyde (1:1) | $RuO_2$-$MnO_3$ | Ethanol, reflux | [43] |
| 33 | OPDA and Aryl aldehyde (1:1) | Ionic liquid [B mim]$PF_6$ | Water, reflux | [44] |
| 34 | OPDA and Aryl aldehyde (1:1) | $NaHSO_4$-$SiO_2$ | Solvent-free | [45] |
| 35 | OPDA and Aryl aldehyde (1:1) | 5-sulfosalicylic acid | Ethanol, reflux | [46] |
| 36 | OPDA and Aryl aldehyde (1:1) | Resins (Amberlyt, Tulsion and Indion) | Ethanol, 80-90℃ | [47] |
| 37 | OPDA and Aryl aldehyde (1:1) | $Fe_3O_4$NPs | Solvent-free, reflux | [48] |

| | | | | |
|---|---|---|---|---|
| 38 | OPDA and Aryl aldehyde (1:1) | $Cu(OTf)_2$ | Water, reflux | [49] |
| 39 | OPDA and Aryl aldehyde (1:1) | $ZrOCl_2.8H_2O$ | Acetonitrile, RT, 15 minutes | [50] |
| 40 | OPDA and Aryl aldehyde (1:1) | Cu-bentonite | DMF, Reflux | [51] |
| 41 | OPDA and Aryl aldehyde (1:1) | Oxalic acid | Microwave | [52] |
| 42 | OPDA and Aryl aldehyde (1:1) | Cu-doped ZnO | DCM, RT, Sonication | [53] |
| 43 | OPDA and Aryl aldehyde (1:1) | Tribromo melamine (TBM) | Ethanol, RT | [54] |
| 44 | OPDA and Aryl aldehyde (1:1) | modified montmorillonite clay | Toluene, RT, 3h | [55] |
| 45 | OPDA and Aryl aldehyde (1:1) | $Zn(NH_2SO_3)_2$ | Ethanol, 80℃ | [56] |
| 46 | OPDA and Aryl aldehyde (1:1) | $Au/TiO_2$, 25℃ | $CHCl_3$: MeOH (3:1) | [57] |
| 47 | Substituted OPDA and Aryl aldehyde (1:1) | Nano-$SnCl_4/SiO_2$ | Reflux | [58] |
| 48 | OPDA and Aryl aldehyde (1:1) | Nano-$ZrO_2$ | 60℃, 3 hr | [59] |
| 49 | OPDA and Aryl aldehyde (1:2) | $SnO_2$ nanoparticle | Ethanol, RT | [60] |
| 50 | OPDA and Aryl aldehyde (1:1) | $Zn/NaHSO_3$ | Heat, 60 minutes | [61] |
| 51 | OPDA and Aryl aldehyde (1:1) | $BF_3.OEt_2$ | 30 minutes, RT | [62] |
| 52 | Substituted OPDA and Aryl aldehyde (1:1) | $NH_4Cl$ or $Na_2S_2O_5$ | Ethanol, reflux | [63] |
| 53 | OPDA and Aryl aldehyde (1:2) | Water extract from onion | Ethanol/water, 12-18 hr | [64] |
| 54 | OPDA and Aryl aldehyde (1:1) | Photocatalyst (BTT-TPA-COF) | 2hr | [65] |
| 55 | OPDA and Aryl aldehyde (1:1) | Camphor sulfonic acid (organo-catalyst) | Ethanol: water (1:1), RT, 1-2 h | [66] |
| 56 | OPDA and Aryl aldehyde (1:1) | $Al_2O_3$/CuI/PANI | Ethanol, RT | [67] |
| 57 | Substituted OPDA and Aryl aldehyde (1:1) | Lewis catalyst $Er(OTf)_3$ | Microwave | [68] |
| 58 | OPDA and Aryl aldehyde (1:1) | $Fe_2O_3.SiO_2$-$NH_2$-COOH/$IRMOF_3$-Gly, Arg or Lys | 30 minutes | [69] |

**Through the condensation of OPDA with various aryl-carboxylic acids**

Various 2-arybenzimidazoles can be produced effectively by reacting (4-methyl-1, 2-phenylenediamine) with a variety of aromatic carboxylic acids with the aid of a zeolite (Fig. 2) [70].

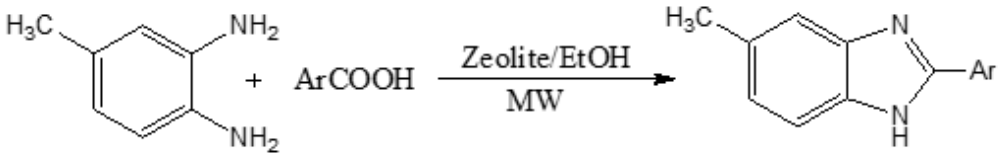


**Figure 2**

Employing $BF_3OEt_2$ as a trigger, 4-methoxy-1, 2-phenylenediamine was reacted with various aromatic carboxylic acids to create a library of 2-substituted-benzimidazoles in Fig. 3 [71].

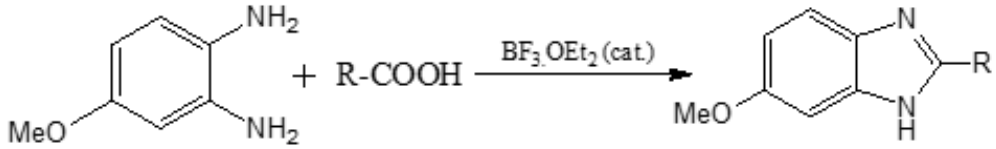


**Figure 3**

$SiO_2/H_2SO_4$ was used as a catalyst to create a variety of benzimidazole derivatives in a microwave oven (Fig. 4) [72].

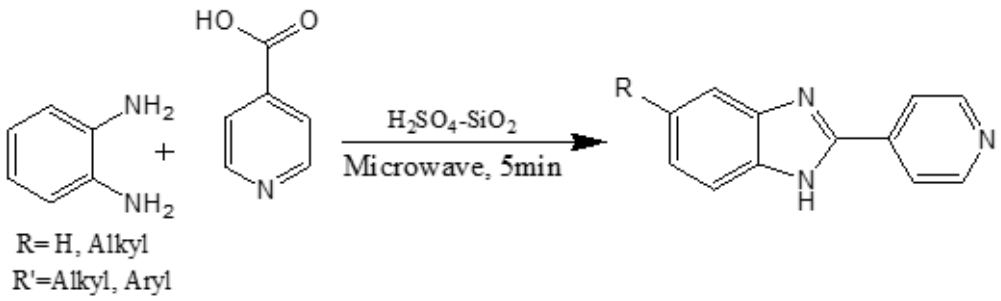


**Figure 4**

A collection of 2-aryl benzimidazoles were efficiently created (Fig. 5) by reacting substituted o-phenylene diamines and different carboxylic acids using Borane-THF [73].

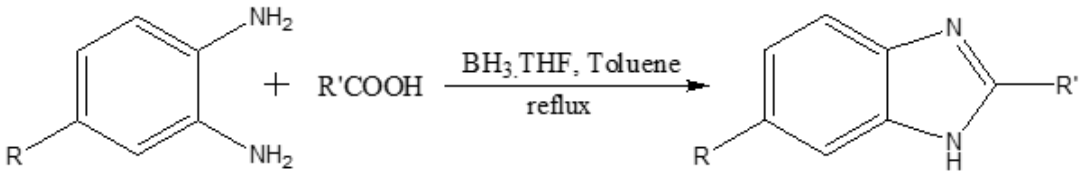


**Figure 5**

Five different benzimidazole analogues were prepared by reacting 2-substituted benzimidazoles with different amines by adopting both conventional and microwave methods (Fig. 6) [74].

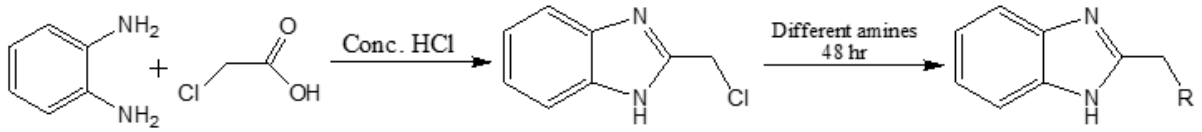


**Figure 6**

The formation of disubstituted benzimidazole compounds (Fig. 7) from aromatic amines and benzoic acid in two stages was made easy, quick, and efficient by employing sodium acetate and producing reaction products in an excellent yield [75].

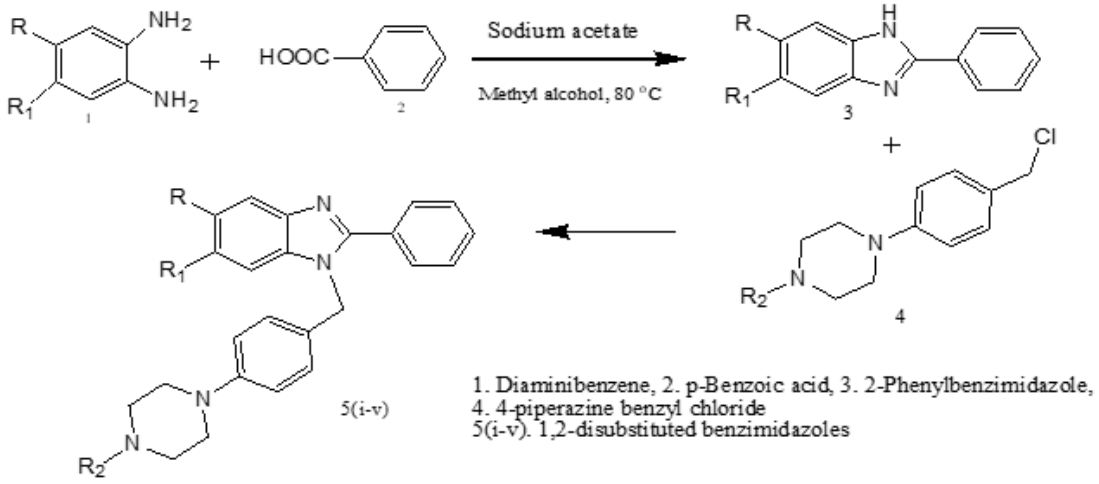


**Figure 7**

## Miscellaneous methods

A number of benzimidazoles, benzoxazoles, and oxazolo [4, 5-b] pyridines (Fig. 8) were produced under the sans solvent, silica sulfuric acid was used to produce [76].

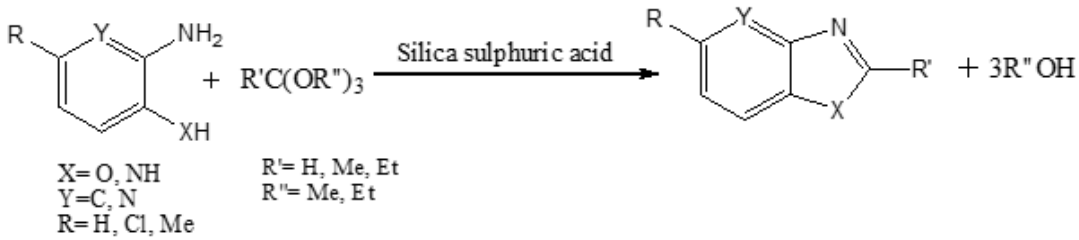


**Figure 8**

A new and efficient one-pot synthetic method was developed for the synthesis of various N-substituted 2-hetero-benzimidazoles from o-haloarcarbodimides and N- or O-nucleophiles (Fig. 9) [77].

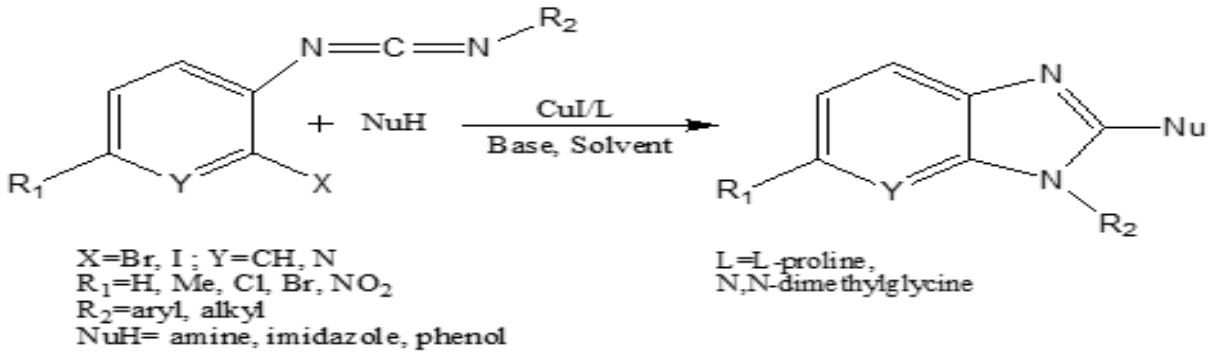


**Figure 9**

A sustainable approach was presented for the creation of novel benzimidazoles from 1, 2-phenylenediamines and ortho-esters using magnetically recoverable $Fe_3O_4$ nanoparticles (Fig. 10) [78].

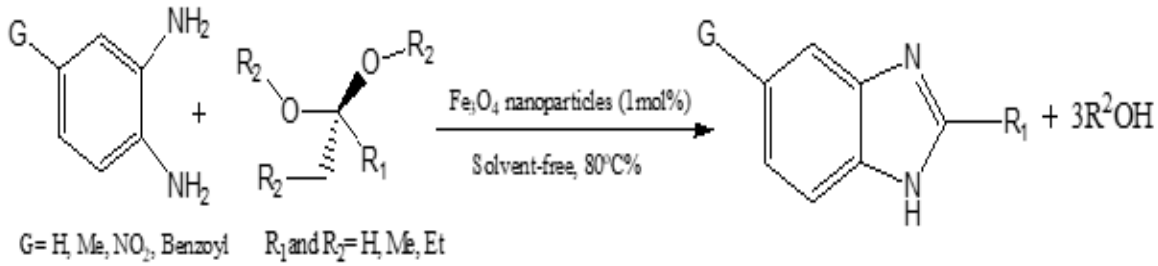


**Figure 10**

A simple technique for creating the benzimidazole ring system was devised (Fig. 11) through a carbon-nitrogen cross-coupling reaction involving $K_2CO_3$ [79].

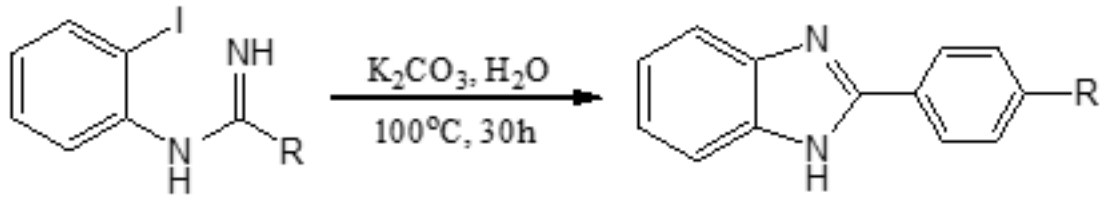


**Figure 11**

The condensation of orthoester and 1,2-phenylenediamine by using ionic fluid, 1-butyl imidazolium bisulfate, led to the development of a sustainable and effective process for the synthesis of benzimidazoles (Fig. 12) [80].

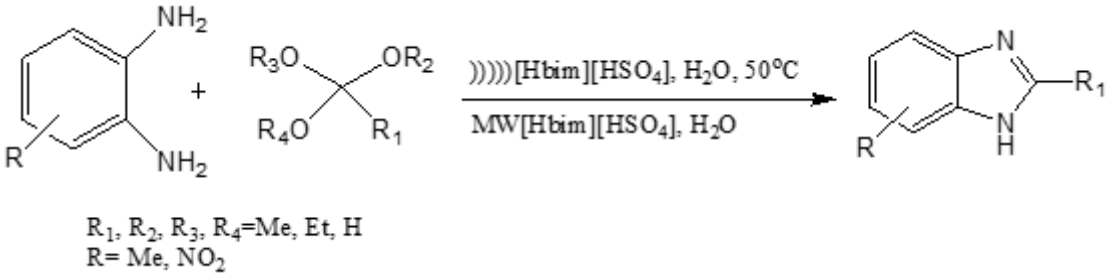


**Figure 12**

The direct synthesis of benzimidazoles (Figure 13) was reported from 2-nitroaniline and ethanol over Cu-Pd/(Mg)γ-$Al_2O_3$ heterogeneous catalyst [81].

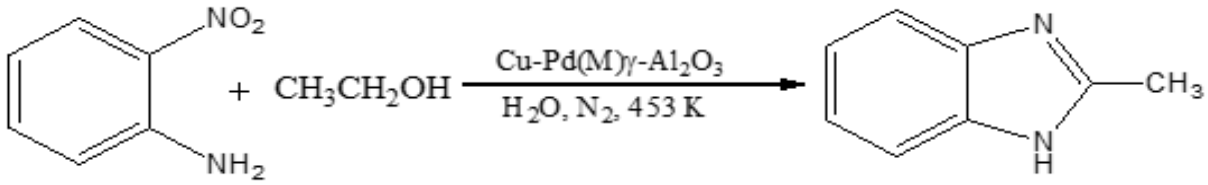


**Figure 13**

As a result of the condensation of citronellal from kaffir lime oil and 1,2-phenylenediamine, many benzimidazole derivatives were created shown in Fig. 14 [82].

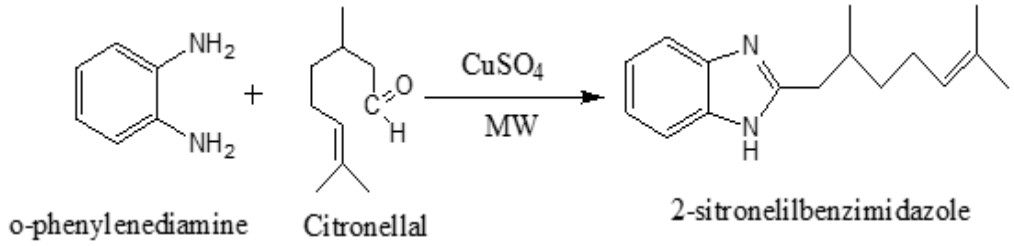


**Figure 14**

Different Benzimidazoles were created by consolidating o-nitroaniline with several aromatic aldehydes (Fig. 15) and a tiny amount of sodium dithionite at ambient temperature [83].

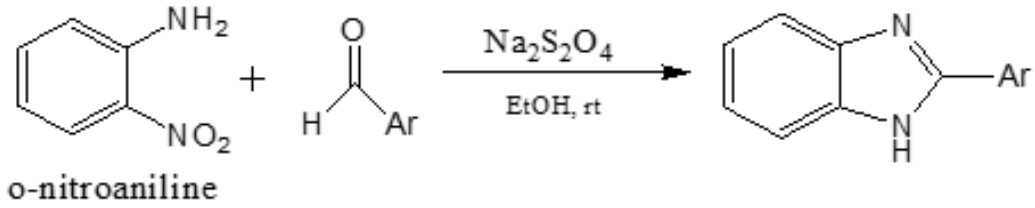


**Figure 15**

A polystyrene heterogeneous [PS-Zn (II)-SALTETA] catalyst has been both created and generated. Further, this catalyst was successfully utilized to synthesize benzimidazoles in the presence of dimethylamine borane (DMAB) (Fig. 16) [84].

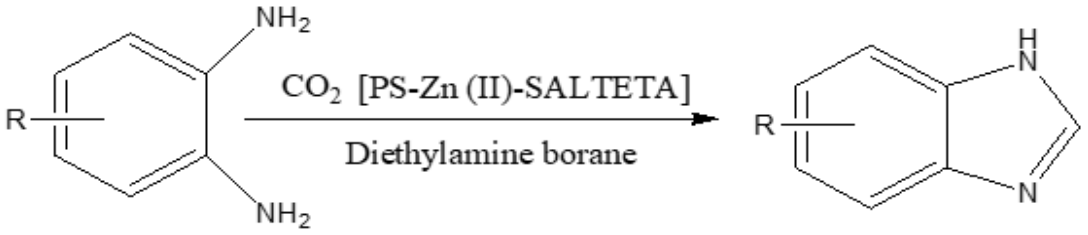


**Figure 16**

The green manufacturing of 2-phenyl-1H-benzo[d]imidazole via catalytic hydrogenation fusion of 2-nitroaniline with benzaldehyde using N-doped carbon nanotubes (Co@NC900) was developed (Fig. 17) [85]

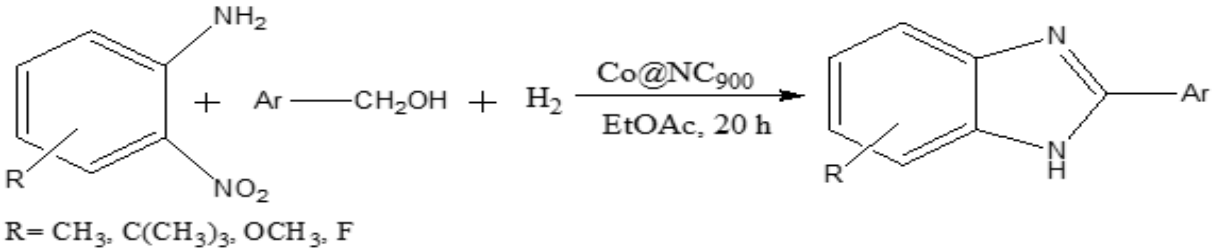


**Figure 17**

A collection of benzimidazoles with 1, 2 substitutions were synthesized by iron-catalyzed acceptor-less dehydrogenation coupling of primary alcohols with o-phenylenediamines (Fig. 18) [86].

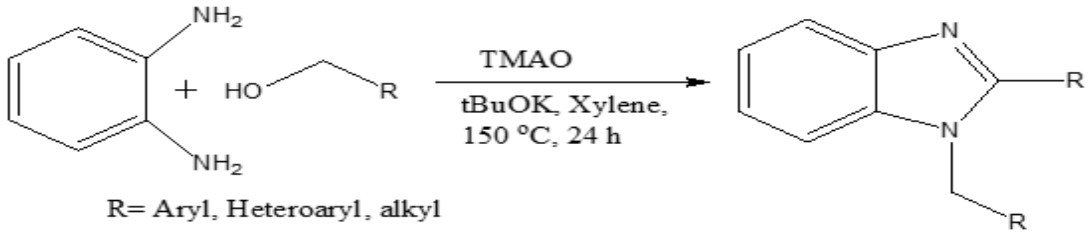


**Figure 18**

A copper-catalyzed domino C-N cross-coupling, one pot, and facile method was introduced to produce 2-arylamino benzimidazole derivatives from thiourea (Fig. 19) [87].

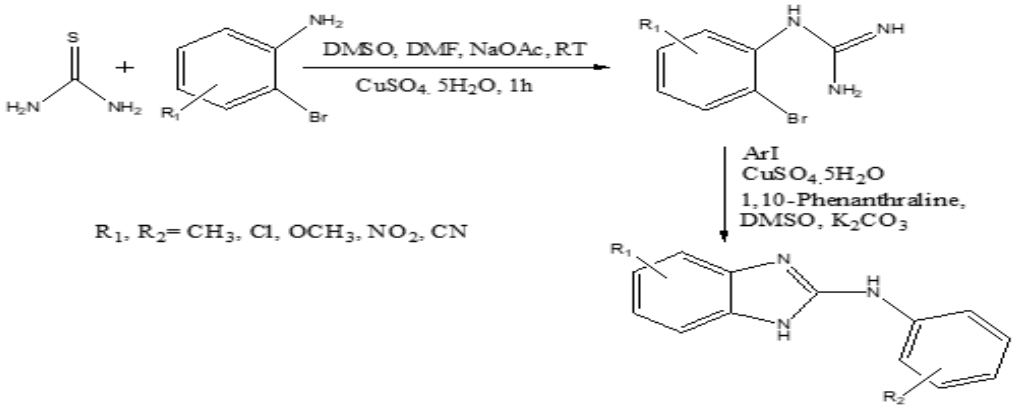


**Figure 19**

In Fig. 20, N-substituted o-phenylenediamines, terminal alkynes, and sulfonyl azides were used to create 1, 2-disubstituted benzimidazoles by a copper-catalyzed three-component coupling synthesis [88].

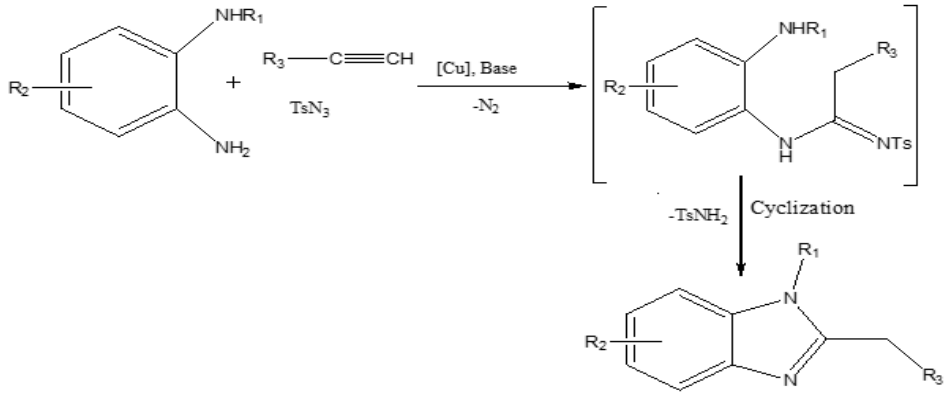


**Figure 20**

Cucurbit [6] uril-supported magnetic nanoparticles ($Fe_3O_4$-CB[6]) were produced and used for the first time in the manufacturing of variety of 2-substituted benzimidazoles as a very effective, inexpensive, and environmentally friendly catalyst (Fig. 21) [89].

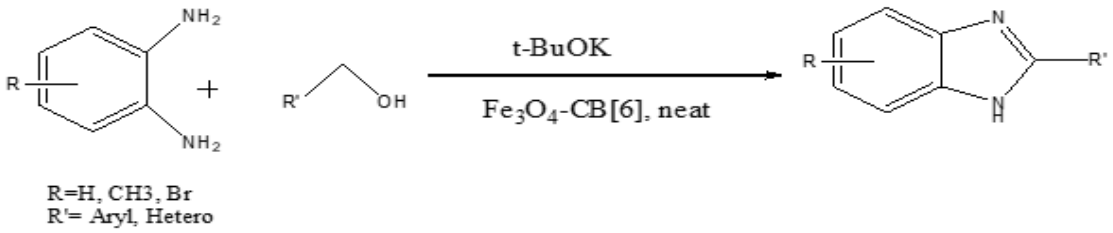


**Figure 21**

A nanocomposite of Pt@MIL-101 (Fe) was prepared and used sequentially in a one-pot reaction that uses light to combine alcohols with o-phenylenediamines to create benzimidazoles (Fig. 22) [90].

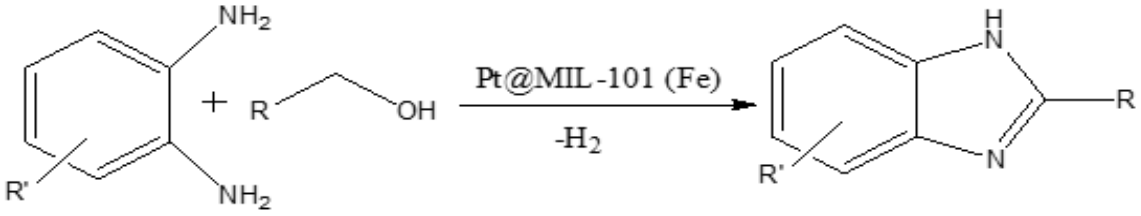


**Figure 22**

## Conclusion

Green chemistry attains the goal of today and enlightens the future of organic synthesis with a precious scheme based on surrounding protection. This review concludes that there is a huge variety of valuable catalysts has been utilized when creating physiologically energetic benzimidazole derivatives. Since then, researchers have been fascinated with designing new synthetic techniques for benzimidazole having zero harm to individuals and the environment.

## References

1. Kankate RS, Gide PS, Belsare. Microwave-assisted synthesis, antifungal evaluation and molecular docking of benzimidazole derivatives. Der Pharma Chemica. 2014; 6(6): 396-405.
2. Gaba M, Gaba P, Uppal D. Benzimidazole derivatives: search for GI-friendly anti-inflammatory analgesic agents. Acta Pharma. Sin. B. 2013; 5(4): 337-342.
3. Mentese E, Yilmaz F, Bekircan O. Synthesis and antioxidant activities of some new tri-heterocyclic compounds containing benzimidazole, thiophene, and 1, 2, 4-triazole rings. J Enzyme Inhib. Med Chem. 2015; 30(3): 435-441.
4. Gollapali NR, Karumudi BS, Kondeti TN. Green Synthesis & Biological Evaluation of Novel Benzimidazole Derivatives as Antianxiety Agents. J. basic appl. Res. 2016; 2(3): 221-225.
5. Nandha B, Nargund LVG, Nargund SL. Design and synthesis of some new imidazole and 1, 2, 4-triazole substituted fluoro-benzimidazoles for antitubercular and antifungal activity. Der Pharma Chemica. 2013; 5(6): 317-327.
6. Khan MT, Razi MT, Jan SU. Synthesis, characterization, and antihypertensive activity of 2-phenyl substituted benzimidazoles. Pak. J. Pharm. Sci. 2018; 31(3): 1067-1074.
7. Navarro AM, Torres BN, Campos AH. Anthelmintic activity of benzimidazole derivatives against *Toxocara canis* second-stage larvae and *Hymenolepis nana* adults. Acta Tropica. 2009; 109: 232-235.
8. Sharma D, Narasimhan B, Kumar P. Synthesis, the antimicrobial and antiviral activity of substituted benzimidazoles. J Enzyme Inhib Med Chem. 2009; 24(5): 1161-1168.
9. Swiatkiewicz KB, Olasik EM. New benzimidazole derivatives as Topoisomerase I inhibitors-Synthesis and Fluorometric analysis. Acta Pol. Pharm. 2013; 70(3): 451-458.

10. Nofal ZM, Soliman EA, El-Karim SAB. Novel benzimidazole derivatives as expected anticancer agents. Acta Pol. Pharm. 2011; 68(4): 519-534.
11. Bhrigu B, Siddiqui N, Pathak D. Anticonvulsant evaluation of some newer benzimidazole derivatives: Design and synthesis. Acta Pol. Pharm. 2012; 69(1): 53-62.
12. Kidwai M, Jahan A, Bhatnagar D. Polyethylene glycol: A recyclable solvent system for the synthesis of benzimidazole derivatives using CAN as catalyst. J. Chem. Sci. 2010; 122 (4): 607-612.
13. Meshram GA and Patil V. Efficient synthesis of benzimidazole and quinoxaline derivatives with $ZnO.H_2O_2$ under mild conditions. Int. J. Chem. Sci. 2010; 8(1): 119-131.
14. Azarifar D, Pirhayati M, Maleki B. Acetic acid-promoted condensation of *o*-phenylenediamine with aldehydes into 2-aryl-1-(arylmethyl)-1*H*-benzimidazoles under microwave irradiation. J. Serb. Chem. Soc. 2010; 75(9): 1181-1189.
15. Nannapaneni DT, Gupta AV, Reddy MI. Synthesis, Characterization, and Biological Evaluation of Benzimidazole Derivatives as Potential Anxiolytics. J Young Pharm. 2010; 2(3): 273-279.
16. Subrahmanyam CS, Narayanan S. Yttrium (iii) chloride: a mild and efficient catalyst for the synthesis of benzimidazoles. Int. J. Appl. Biol. Pharm. 2010; 1(2): 689-794.
17. Azzallou R, Mamouni R, Riadi Y. A Mild and Efficient one-pot Synthesis of 2-substituted Benzimidazoles through a New Surfactant-modified Moroccan Clay Catalyst. Rev. Chim., 2010; 61(12):1155-1157.
18. Riadi Y, Mamouni R, Azzalou R. An efficient and reusable heterogeneous catalyst Animal Bone Meal for facile synthesis of benzimidazoles, benzoxazoles, and benzothiazoles. Tetrahedron Lett, 2011; 52: 3492-3495.
19. Patil VD, Patil J, Rege P. Mild and efficient synthesis of benzimidazole Using lead peroxide under solvent-free Conditions. Synth. Commun., 2011; 41: 58-62.
20. Mohammadizadeh MR, Taghavi SZ. Trifluoroacetic Acid as an Efficient Catalyst for the Room Temperature Synthesis of 2-Aryl-1-arylmethyl-1*H*-1,3-benzimidazoles in Aqueous Media. E. J. Chem., 2011; 8(1): 101-106.
21. Shaikh KA, Patil VA. An efficient solvent-free synthesis of imidazolines and benzimidazoles using $K_4[Fe(CN)_6]$ catalysis. Org. Commun., 2012; 5(1): 12-17.
22. Zolfigol MA, Khakyzadeh V, Moosavi-Zare AR. Nano-$Fe_3O_4/O_2$: Green, magnetic and Reusable Catalytic System for the Synthesis of Benzimidazoles. Afr. J. Chem., 2012; 65: 280-285.
23. Pasha MA, Nizam A. Amberlite IR-120 catalyzed, microwave-assisted rapid synthesis of 2-aryl-benzimidazoles. J. Saudi Chem. Soc., 2012; 16: 237-240.
24. Kumar KR, Satyanarayana PVV, Reddy BS. $NaHSO_4$-$SiO_2$ promoted synthesis of Benzimidazole derivatives. Arch. Appl. Sci. Res., 2012; 4(3): 1517-1521.
25. Sajjadifar S, Mirshokraie SA, Javaherneshan N. SBSA as a New and Efficient Catalyst for the One-Pot Green Synthesis of Benzimidazole Derivatives at Room Temperature. Am. J. Org. Chem., 2012; 2(2), 1-6.
26. Sontakke VA, Ghosh S, Lawande PP. A Simple, Efficient Synthesis of 2-Aryl Benzimidazoles Using Silica Supported Periodic Acid Catalyst and Evaluation of Anticancer Activity. Org. Chem., 2013; 1-7.
27. Gorepatil PB, mane YD, Ingle VS. Zirconyl (IV) Nitrate as Efficient and Reusable Solid Lewis Acid Catalyst for the Synthesis of Benzimidazole Derivatives. J. Chem., 2013; 1-7.

28. Venkateswarlu Y, Kumar SR, Leelavathi P. Facile and efficient one-pot synthesis of benzimidazoles using lanthanum chloride. Org. Med. Chem. Lett., 2013; 3(7): 1-8.
29. Chari MA, Mosaa ZA, Shobha D. Synthesis of Multi-functionalised 2-Substituted Benzimidazoles Using Copper (II) Hydroxide as Efficient Solid Catalyst. Int. j. Org. chem. 2013; 3: 243-250.
30. Karami C, Ghodrati K, Izadi M, et al, 2013. A fast procedure for the preparation of benzimidazole derivatives using polymer supported with trifluoromethanesulfonic acid as novel and reusable catalyst. J. Chil. Chem. Soc., 58(3), 1914-1917.
31. Kumar V, Khandare DG, Chatterjee A. DBSA mediated chemo-selective synthesis of 2-substituted benzimidazoles in aqueous media. Tetrahedron Lett. 2013; 54: 5505-5509.
32. Tushar M, Kaneria DM, Kapse GK. A Mild and Efficient Synthesis of Benzimidazole by Using Zinc Chloride under Solvent Free Condition. IJPSR. 2013; 2(1): 90-98.
33. Herari MRP, Ashori M. Boric Acid Catalyzed Convenient Synthesis of Benzimidazoles in Aqueous Media. J. chem., 2013; 1-5.
34. Kathivelan D, Yuvaraj P, Babu K. A green synthesis of benzimidazoles. Indian J. chem., 2013; 52B: 1152-1156.
35. Srinivasulu R, Kumar KR, Satyanarayana PVV. Facile and Efficient Method for Synthesis of Benzimidazole Derivatives Catalyzed by Zinc Triflate. Green Sustain. Chem., 2014; 4: 33-37.
36. Birajdar SS, Hatnapure GD, Keche AP. Synthesis of 2-substituted-1*H*-Benzo[d]imidazoles through Oxidative cyclization of O-phenylenediamine and substituted aldehydes using Dioxane dibromide. Res. J. Pharm. Biol. Chem. Sci., 2014; 5(1): 487-493.
37. Samanta S, Guha C, Mallik AK. An efficient and Eco-friendly synthesis of 2-aryl-benzimidazoles using silica gel as catalyst. Eur. Chem. Bull. 2014; 3(4): 396-399.
38. Nezhad ER, Karimian S. Synthesis of benzimidazole derivatives using Ni2+ supported on hydroxy-apatite core @ shell $\gamma$-$Fe_2O_3$ nanoparticles both under solvent and solvent-free conditions. Iranian J. Catal. 2015; 5(4): 305-309.
39. Katkar SS, Kategaonkar AH. Synthesis of benzimidazole derivatives catalysed by in/AlMCM-41as a heterogeneous catalyst. Org. Chem. 2015; 11(12): 415-419.
40. Rajabi F, Sudipta D, Luque R. An Efficient and Green Synthesis of Benzimidazole Derivatives using SBA-15 Supported Cobalt Nano-catalysts. Catal. Lett. 2015; 145: 1566-1570.
41. Ahmadian H, Veisi H, Karami C. Cobalt manganese oxide nanoparticles as recyclable catalyst for efficient synthesis of 2-aryl-1-arylmethyl-1H-1,3-benzimidazoles under solvent-free conditions. Appl. Organometal. Chem. 2015: 1-4.
42. Monreal I, Torres-Pacheco LJ, Oropeza-Guzman MT. *In-situ* Fe electro-oxidation to Improve the Synthesis of Mono and Disubstituted Benzimidazoles. Int. J. Electrochem. Sci. 2015; 10: 6743-6753.
43. Vidhate KN, Waghmare RA. An efficient and ecofriendly $RuO_2$-$MoO_3$ solid heterogeneous catalyst for the synthesis of benzimidazole from aldehydes. Adv. Appl. Sci. Res. 2015; 6(6): 167-170.
44. Bhavsar A, Makone S, Shirodkar S. Synthesis of Benzimidazole and Benzothiazole Derivatives by Using Ionic Liquids. Int. J. Adv. Res. Sci. Eng. Technol. 2016; 3(8): 2485-2487.

45. Raju GN, Sai KB, Naveen K. Green Synthesis & Biological Evaluation of Novel Benzimidazole Derivatives as Antianxiety Agents. J. Basic Appl. Res. 2016; 2(3): 221-225.
46. Bhenki C, Karhale S, Helavi V. 5-sulfosalicylic acid as an efficient organo-catalyst for environmentally benign synthesis of 2-substituted benzimidazoles. Iran. J. Catal. 2016; 6(5): 409-413.
47. Bahule BB, Mhaske CB, Kalaskar SB. A mild and efficient method for the preparation of substituted Benzimidazole derivatives from o-phenylene diamine and various aromatic aldehydes catalysed by cation exchange resins. Res. J. chem. Sci. 2017; 7(3): 40-43.
48. Cahyana AH, Ardiansah B, Asrianti NA. $Fe_3O_4$ Nanoparticles: An Efficient and Recyclable Catalyst for Benzimidazoles Synthesis. AIP Conf. Proc. 2018; 020061-1-6.
49. Kagne R, Kalalawe V, Munde D. An efficient synthesis of Benzimidazole derivatives by using Metal triflate catalyst in an aqueous media. Int. J. Chem. Tech. Res. 2017; 10(6): 1145-1149.
50. Kulkarni MA, Pahade NV, Pawar SP. A simple and convenient one pot synthesis of 2-arylBenzimidazole derivatives using zirconium oxychloride as a Catalyst. Heterocyclic Lett., 2017; 7(1): 99-103.
51. Mestari A, Ejjoummany A, Rakhila Y. Cu-bentonite as an efficient and recyclable material catalyst for the synthesis of benzimidazoles, benzoxazoles and benzothiazoles. J. Mater. Environ. Sci., 2017; 8(S): 4816-4823.
52. Tripathi JP, Kasana VK. Microwave Assisted Synthesis of Benzimidazoles catalysed by Oxalic Acid. Int. J. Appl. Sci. Eng. Tech., 2018; 6(III): 94-99.
53. Nagtilak MC, Labade SN, Sawant SS. Synthesis and Characterization of Fine Powdered Cu-Doped ZnO and their catalytic Application for Ultrasound-Mediated Synthesis of Substituted Benzimidazole and their Antimicrobial Activity. Int. J. Chem. Phys. Sci., 2018; 7: 34-43.
54. Shirkhani P, Seifournia H, Mirzajanzadeh E. Tribromo melamine (TBM) as an efficient and inexpensive catalyst for the one-pot synthesis of benzimidazoles and benzoxazole derivatives. Asian J. Green Chem., 2018; 2: 160-170.
55. Borah SJ, Das DK. Modified Montmorillonite: An Active Heterogeneous Catalyst for the Synthesis of Benzimidazoles. J. Chem. Pharm. Res., 2018; 10(7): 118-123.
56. Mathapati SR, Jadhav AH, Swami MB. Zinc sulfamate catalysed efficient selective synthesis of Benzimidazole derivatives under ambient conditions. Lett. Org. Chem., 2019; 16: 740-749.
57. Tzani MA, Gabriel C, Lykakis IN. Selective Synthesis of Benzimidazoles from o-Phenylenediamine and Aldehydes Promoted by Supported Gold Nanoparticles. Nano-mater., 2020; 10: 1-17.
58. Zamani L, Faghih Z, Zomorodian K. Nano-$SnCl_4.SiO_2$, an efficient catalyst for the synthesis of benzimidazole derivatives as antifungal and cytotoxic agents. 2019, 14(6), 496-503.
59. Tentu NR, Suliman YA, Faheem A, Fadwa A, Naushad A, Nalla KR, MV Basaveswara Rao, Cheedarala RK, G. Rajasekhar Reddy, Tentu MN. Reusable Nano-zirconia-catalyzed synthesis of benzimidazoles and their antibacterial and antifungal activities. Molecules. 2021, 26, 4219, 1-14.

60. Effat SP, Seyed MV, Mehdi H. D. Facile and benign synthesis of mono- and Di-substituted benzimidazoles by using $SnO_2$ nanoparticles catalyst. J Nanostructure, 2021; 11(2): 286-296.
61. Hridoydip RD, Suvodip M and Pranab G. One pot reductive synthesis of benzimidazole derivatives from 2-nitroaniline and aromatic aldehydes using $Zn/NaHSO_3$ in water medium. Progress in chemical and biochemical research. 2021; 4(1): 57-67.
62. Rohit V, Chitra G, Ali Mohd G, Sanjay S and PK Singh. Synthesis, characterization and potent antimicrobial and antifungal activity of 2-substituted benzimidazole derivatives. Indian Journal of Chemistry. 2021; 60B: 148-151.
63. Lotfi MA, Hind RA, Fahad MA, Sabri M, Sridevi C, Suliman AM, Hamdoon AM. A facile approach synthesis of benzoylaryl benzimidazole as potential α-amylase and α-glucosidase inhibitor with antioxidant activity. Bioorganic chemistry. 2021; 114: 1-12.
64. Kaliyan Prabakaran, Selvaraj Loganthan and Muthu Seenivasa Perumal. Water extract of onion catalyst: An economical green route for the synthesis of 2-substituted and 1,2-disubstituted benzimidazole derivatives with high selectivity. Journal of Heterocyclic Chemistry. 2021, 58(1): 340-349.
65. Bincai L, Ying C, Yubao Z and Jianqiang H. Benzotrithiophene and triphenylamine based covalent organic frameworks as heterogeneous photocatalysts for benzimidazole synthesis. Journal of Catalysis. 2021; 402: 52-60.
66. Gurpreet Kaur, Radha Moudgil, Mussarat Shamim, Vivek Kumar Gupta, Bubun Banerjee. Camphor sulphonic acid catalysed a simple, facile and general method for the synthesis of 2-arylbenzothiazoles, 2-arylbenzimidazoles and 3H-spiro[benzo[d]thiazole-2,3'-indolin]-2'-ones at room temperature. Synthetic communications 2021; 51(7): 1100-1120.
67. Sahil K, Garima R, Sunita H, Ramesh C. $Al_2O_3$/CuI/PANI nanocomposite catalyzed green synthesis of biologically active 2-substituted benzimidazole derivatives. Dalton Transactions, 2021; 50: 7750-7758.
68. Monica N, Sonia Bonacci, Natividad HC, Manuela O and Antonio P. The highly efficient synthesis of 1,2-disubstituted benzimidazoles using microwave irradiation. Molecules 2022; 27(1751): 1-9.
69. Yang L, Chen L, Guo J, Cun Li & Tianming J. Core-shell magnetic microspheres as heterogeneous catalyst for synthesis of benzimidazole, Journal of Coordination Chemistry, 2022; 75(1-2): 280-292.
70. Mobinikhaledi A, Zendehdel M, Jamshidi FH. Zeolite-catalyzed synthesis of substituted benzimidazoles under solvent-free condition and microwave irradiation. Synthesis and reactivity in Inorganic, metal-organic and nano-metal chemistry. 2007; 37: 175-177.
71. Sharma MC, Kohli DV, Sharma S. Synthesis and antihypertensive activity of some new benzimidazole derivatives of 4'-(6-methoxy-2-substituted-benzimidazole-1-ylmethyl)-biphenyl-2-carboxylic acid in the presences of $BF_3 \cdot OEt_2$. Der Pharm. Sin., 2010; 1(1): 104-115.
72. Baltork IM, Moghadam M, Tangestaninejad S. Silica Sulfuric Acid Catalysed Synthesis of Benzoxazoles, Benzimidazoles and Oxazolo[4,5-b]pyridines Under Heterogeneous and Solvent-Free Conditions. J. Iran. Chem. Soc., 2008; 5: S65-S70.

73. Cui W, Kargbo RB, Hashemi ZS. Efficient One-Pot Synthesis of 2-Substituted Benzimidazoles from Tri-acyloxyborane Intermediates. Syn. Lett., 2012; 23: 247-250.
74. Guruswamy B, Arul R. A micro-wave assisted synthesis of benzimidazole derivatives using solid support. Der Pharm. Chem., 2011; 3(6): 483-486.
75. Sravanthi A, Chetan SH, Subrahmanyam EVS. Synthesis of 1, 2 disubstituted benzimidazoles using sodium acetate as catalyst. Int. Res. J. Pharm., 2019; 10(3): 181-184.
76. Baltork M, Moghadam M, Tangestaninejad S, Mirkhani V, Zolfigol MA and Hojati SF. Silica sulphuric acid catalysed synthesis of Benzoxazoles, Benzimidazoles and Oxazolo [4,5-b]pyridines under Heterogeneous and solvent-free conditions. Journal of the Iranian Chemical Society. 2008; 5(10): S65-S70.
77. Lv X, Bao W. Copper-Catalyzed Cascade Addition/Cyclization: An Efficient and Versatile Synthesis of N-Substituted 2-Heterobenzimidazoles. J. Org. Chem., 2009; 74(15), 5618-5621.
78. Karami B, Nikoseresht S, Khodabakhshi S. Novel Approach to Benzimidazoles Using Fe3O4 Nanoparticles as a Magnetically Recoverable Catalyst. Chi. J. Catal., 2012; 33(2): 298-301.
79. Chen C, Chen C, Li B. Aqueous Synthesis of 1-*H*-2-Substituted Benzimidazoles via Transition-Metal-Free Intramolecular Amination of Aryl Iodides. Mol., 2012; 17: 12506-12520.
80. Devkate CG, Warad KD, Bhalerao MB. Green and Efficient Synthesis of Benzimidazole Derivatives and their Antibacterial Screening. J. Chem. Pharm. Res., 2017; 9(8): 209-213.
81. Feng F, Deng Y, Cheng Z. Heterogeneous Catalytic Synthesis of 2-Methylbenzimidazole from 2-Nitroaniline and Ethanol over Mg Modified Cu-Pd/-$Al_2O_3$. Catalysts. 2018; 9(8): 1-11.
82. Rahmawati LM, Warsito, Iftitah ED. Study of Citronellal Condensation Reactions with 1,2-phenylenediamine by $CuSO_4$ Catalyst under Microwave Irradiation. Material Science and Engineering. 2019; 546: 1-9.
83. Naeimi H, Alishahi N. Highly Efficient and Facile Method for Synthesis of 2-Substituted Benzimidazoles via Reductive Cyclization of O-Nitroaniline and Aryl Aldehydes. Org. Chem. Int., 2012; 498521: 1-5.
84. Imdadul HB, Biswas S, Md Sarikul Islam, Riyajuddin SK, Sarkar P, Ghosh K and SK Manirul Islam. Catalytic synthesis of benzimidazoles and organic carbamates using a polymer supported zinc catalyst through $CO_2$ fixation. **New** J. Chem. 2019; 43**:** 14643-14652.
85. Chuncheng L, Weihao W, Xueting W and Jinzhu C. H2 activation with Co nanoparticles encapsulated in N-doped carbon nanotubes for green synthesis of benzimidazoles. Chem. Sus. Chem. 2020; 13: 1-13.
86. Putta RR, Chun S, Lee SB, Oh D, Hong S. Iron-catalyzed acceptorless dehydrogenative coupling of alcohols with aromatic diamines: Selective synthesis of 1,2-disubstituted benzimidazoles. Frontiers in Chemistry. 2020; 8(429): 1-8.
87. Baddapati SNM, Tamminana R, Gollapudi RK, Nurbasha S, Assal ME, Alduhaish O, Siddiqui MRH, Bollikolla HB, Adil SF. Copper-promoted one-pot approach: synthesis of benzimidazoles. Molecules. 2020; 5(1788): 1-13.

88. Weiguang Y, Yu Z, Zitong Z, Li l, Liao C and Hui L. Preparation of 1,2-substituted benzimidazoles via a copper-catalyzed three-component coupling reaction. RSC advances. 2021; 11: 8701-8707.
89. Shruti V, Shelly K, Richa S and Devendra DP. Cucurbit [6]uril-supported Fe3O4 magnetic nanoparticles catalyzed green and sustainable synthesis of 2-substituted benzimidazoles via acceptorless dehydrogenative coupling. ACS Omega. 2022; 7: 9754-9764.
90. Yuhuan Q, Mingming H, Zhengxin D and Zhaohui L. Pt@MIL-101 (Fe) for efficient visible light-initiated coproduction of benzimidazoles and hydrogen from the reaction between o-phenylenediamines and alcohols. Journal of Catalysis. 2022; 410: 156-163.