SYNTHETIC APPROACHES TOWARDS BENZIMIDAZOLES:
A REVIEW

Rameshwar R. Magar
Department of Chemistry,
Sant Dnyaneshwar Mahavidyalaya Soegaon,
Dist. Aurangabad. (Maharashtra), 431120, India
Corresponding author- rrmagar@gmail.com

ABSTRACT
The synthesis of benzimidazole heterocycles has attracted the interest of organic chemist because of its biological and medicinal properties. Benzimidazole can be synthesized by the reaction of O-phenylenediamine and aldehyde. The synthesis of this moiety from easily available chemicals is advantageous due to its enormous use in chemistry. This review focuses on recent developments for the synthesis of Benzimidazoles. The present review describes the systematic survey for the methods of synthesis of this scaffold using different strategies.

KEYWORDS
O-phenylenediamine, Aldehyde, Benzimidazole
INTRODUCTION

Heterocyclic chemistry is an important branch of organic chemistry. Heterocyclic compound plays a crucial role in our biological system and the important part of chemical sciences. The nitrogen containing heterocyclic compounds display significant role in medicinal and synthetic chemistry. Benzimidazole is important heterocyclic compounds because of its wide range of biological and pharmacological activities. Benzimidazole derivatives have found to possess enormous therapeutic application such as antiparasitic [1], anti-inflammatory [2, 3], antiviral [4], anthepatitis [5], antitumor [6], as agonist [7], anticancer [8, 9], antimicrobial [10], antiprotozoal [11], antibacterial [12] and anthelmintic [13]. In addition, Benzimidazole derivatives exhibit significant activity against several viruses including influenza [14], HIV [15] and human cytomegalovirus (HCMV) [16].

Thus, considering the importance of Benzimidazole derivatives several synthetic routes have been reported to prepare these biologically important heterocycles. The present review focuses the reported protocol for the synthesis of Benzimidazole derivatives.

LITERATURE REVIEW ON SYNTHESIS OF BENZIMIDAZOLE DERIVATIVES

S. S. Dhar et al [17] have reported the synthesis of Benzimidazole by the reaction of o-phenylenediamine and aromatic acid/aldehyde using VO (acac)₂ catalyst under microwave irradiation with 80-90 % yield.(Scheme-1)

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\text{NH}_2\cdot\text{Ar-CHO} \xrightarrow{\text{VO(acac)}_2, \text{MW}} \text{Ar-N=N-N} \]

Scheme-1

M. Kalhor et al [18] have reported transition metal nitrate M (NO₃)₂. 6H₂O (M = Mn, Fe, Co, Ni, Cu) as catalyst for the synthesis of Benzimidazole by the reaction of o-phenylenediamine and aromatic aldehyde in ethanol at room temperature condition for 12 min. with 50-92 % yield.(Scheme-2)
R. Shelkar and Co-worker [19] have described Nano CeO$_2$ catalyst for the synthesis of Benzimidazole by the condensation of o-phenylenediamine and aromatic aldehyde in aqueous medium at room temperature condition gives 96% yield. (Scheme-3)

A. Maleki et al [20] have used Chitosan supported Fe$_3$O$_4$ nanoparticle a magnetically recyclable heterogeneous Nano catalyst for the synthesis of Benzimidazole by the condensation of o-phenylenediamine and aromatic aldehyde in ethanol at room temperature with 85-96% yield. (Scheme-4)

H. Naeimi and Z. Babaei [21] have reported the synthesis of Benzimidazole by the reaction of o-phenylenediamine and aromatic aldehyde in H$_2$O/ EtOH using MnO$_2$ nanoparticle as catalyst under ultrasonic condition gives 85% yield. (Scheme-5)
S. G. Patil and Co-worker [22] have developed the process of synthesis of Benzimidazole using sulfonated graphene oxide catalyst by the condensation of o-phenylenediamine and aromatic aldehyde under solvent free condition at room temperature with 67-89 % yield. (Scheme-6)

S. R. Mendes et al [23] have reported Ce (NO₃)₃. 6H₂O catalyst for the synthesis of Benzimidazole by the reaction of o-phenylenediamine and aromatic aldehyde in DMF stirred at 80 °C gives 97 % yield. (Scheme-7)

K. S. Bharathi and co-worker [24] have reported the synthesis of Benzimidazole by the reaction of o-phenylenediamine and aromatic aldehyde using Ni-MCM-41 catalyst in glycerol stirred at 90 °C for 4 h with 66-93 % yield. (Scheme-8)
A. P. Tayade and R. P. Pawar [25] have described Sodium hypophosphite catalyst for the synthesis of Benzimidazole by the condensation of o-phenylenediamine and aromatic aldehyde under microwave irradiation condition gives 80% yield. (Scheme-9)

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\begin{align*}
\text{NH}_2 & \quad \text{NH}_2 \\
\text{NH}_2 & \quad \text{RCHO} \\
& \quad \text{SHP, MW} \\
& \quad \text{5 Min.}
\end{align*}
\]

Scheme-9

CONCLUSION

In summary, this review covers reported strategies for the synthesis of Benzimidazole. In recent years using greener protocol by employing Microwave assisted technology, sonochemical condition, using solvent free condition, heterogeneous catalysis and green solvent especially water as solvent have made access to this important heterocyclic compound.

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