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SYNTHETIC APPROACHES OF BENZIMIDAZOLE DERIVATIVES: A REVIEW

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ABSTRACT

Benzimidazole is considered a privileged moiety for the development of molecules with therapeutic potential. Over the years several drugs viz: albendazole, pantoprazole, astemizole, telmisartan, thiabendazole, and benomyl have been developed by optimizing benzimidazole-based structures. Given the various pharmacological implications of benzimidazoles, it encourages to explore new synthetic protocols for benzimidazoles. The review presented here highlights exclusively the recent synthetic approaches to prepare benzimidazole derivatives. Numerous search engines like Science Direct, Semantic Scholar, Scopus, PubMed, and Google Scholar were utilized to collect the data. It was found that benzimidazoles were synthesized in an eco-friendly manner by employing a green reaction medium or reagent with improved yields and efficiency. Various precursors such as o-phenylene diamines, 2-nitroaniline, aniline, o-anilinic amidines, and o-aminoaryl ketone were utilized to obtain the benzimidazole. This work will provide support to synthesize numerous benzimidazole compounds in a convenient and eco-friendly manner.

Keywords: Benzimidazole, Synthesis, O-Phenylene Diamines, Aromatic Aldehydes, Green Chemistry

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INTRODUCTION

The benzimidazole ring system forms when a benzene ring is fused to imidazole rings. A benzimidazole is comprised of an imino hydrogen and a tertiary nitrogen. Benzimidazoles contain a relatively strong acidic and weakly basic group.[1] A variety of drugs have been developed by optimizing benzimidazole-based structures. Benzimidazoles are the most widely studied drugs as antihelmintics. Benzimidazole carbamates such as mebendazole, albendazole, fenbendazole and flubendazole are established as antihelmintics. Having a broad spectrum of antiparasitic activity, they have a low level of toxicity and can be used effectively to treat intestinal helminth infections.[2] Benzimidazoles have also been utilized as proton pump inhibitors and H_2 receptor antagonists. Pentoprazole, omeprazole, rabeprazole, lansoprazole, astemizole, and mizolastine are indicated for the treatment and prevention of recurrent duodenal ulcers, gastric ulcers, and Zollinger-Ellison syndrome.[3,4] Research efforts for the development of antihypertensives lead to non-peptidic benzimidazole angiotensin II-AT_1 antagonists such as telmisartan and candesartan.[5] Benzimidazoles are a clinically effective class, used in the treatment of systemic fungal infections. Some benzimidazole-containing compounds such as benomyl, carbendazim, and thiabendazole were shown to have very potent antifungal activity.[6,7] In view of various pharmacological implications of benzimidazole derivatives as mentioned earlier, it inspires us to investigate new synthetic protocols for benzimidazoles. Over the years several papers have been published which reveal numerous synthetic methods and pharmacological aspects of benzimidazole derivatives.[8,9,10,11,12] The review presented here highlights exclusively in describing diverse synthetic methods of benzimidazole reported, employing green reaction medium or novel reagent with improved efficiency. This review systematically classified the synthesis of benzimidazoles from Various precursors such as o-phenylene diamines (OPD), aniline, 2-nitroaniline, o-anilinic amidines, o-aminoaryl ketone, etc.

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Synthetic Methodologies for Benzimidazoles

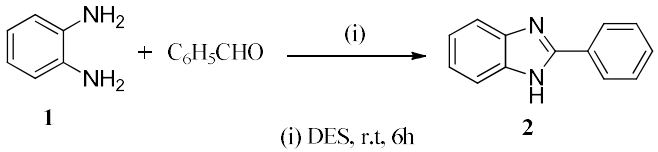
As can be seen from the review of the literature on the synthesis of benzimidazole, Hoebrecker *et al.* are the first to have synthesized this compound in the year 1872 by conducting a reduction of 2-nitro-4-methyl acetanilide.[13]

From o-phenylene Diamines

Benzimidazoles are generally prepared by reaction between 1,2-diamino benzenes with carboxylic acids or their derivatives under Philip's condition.[14] Various methods have been reported mentioning the use of aldehydes in the preparation of benzimidazoles.

By Reaction with Aldehydes

Saibuna *et al.* synthesized benzimidazole by using Deep Eutectic Solvents (Scheme-1). Seven deep eutectic solvents (DESs) were tested during the trial run, and DES 1 displayed the best conversion (comprising of zirconium oxychloride octahydrate and urea at a ratio of 1:5). In addition to being efficient, the method has exciting features such as easy catalyst preparation, humble reaction process, high yield, and recyclability of catalysts (Scheme-1).[15] Sustainable preparation of benzimidazoles, was reported using DES, choline chloride (ChCl): Urea. Compounds were prepared from OPD in the company of various aldehydes. DES was used together as a reaction medium and reagent, resulting in improved yields and improved efficiency.[16]



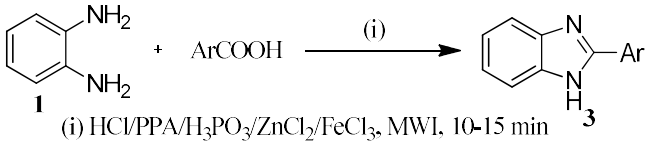
Scheme-1

Benzimidazoles were synthesized in an environmentally friendly manner using mortar and pestle grinding using acetic acid as a catalyst. By this mechanochemical procedure, aldehyde and OPD were condensed and then cyclized, resulting in benzimidazoles with 97% yields.[17] Under mild conditions, OPD reacted with aldehydes using a catalytic amount of H_2SO_4@HTC to obtain benzimidazole derivatives.[18] By using Bronsted acid/base assisted titanocene dichloride, benzimidazole was specifically prepared from OPD and benzaldehyde.[19] Phosphosulfonic acid (PSA) was reported as a catalyst for the synthesis of benzimidazoles consisting of OPD under ambient temperature with various aromatic aldehydes in the presence of ethanol. Moreover, the PSA can be recycled 6 times without any decrease in activity.[20] Sulfonic acid-functionalized mesoporous silica-based nanoporous carbon (CMK-5-SO_3H) were evaluated for the preparation of benzimidazoles from aldehydes and OPD under ambient condition using water as a solvent. CMK-5-SO_3H was found to be a more hydrophobic and water-resistant catalyst.[21] Numerous 2-substituted benzimidazoles were obtained from OPD and substituted aldehydes in the company of weakly acidic NH_4Cl catalyst and ethanol as a solvent at room temperature. The synthetic protocol was ecofriendly, and simple and resulted in superior yield.[22] A practical process for the synthesis of benzimidazoles by joining OPD with aldehydes using $TiCl_3OTf$ in the company of ethanol at room temperature was reported.[23] A new ionic liquid anchored on silica-coated magnetic cobalt-ferrite ($CoFe_2O_4$@SiO_2@PAF-IL) nanoparticles, was used to synthesize benzimidazole. The method offers several advantages, including excellent yields, solvent-free conditions and environment-friendly, short reaction times, and easy preparation.[24] In the presence of atmospheric air, magnetic nano-Fe_3O_4 was used to catalyze the preparation of benzimidazoles by reacting the OPD with aryl aldehydes with 85-97% yields.[25] The preparation of analog 2-aryl-1-arylmethylbenzimidazoles has been explored with cobalt manganese oxide nanocatalyst ($CoMnO_2$ NPs) as a highly efficient green catalyst under a solvent-free environment. Shorter reaction times, simple experimental procedures, high yields, non-toxic catalyst, reusability of catalyst, and solvent-free environment are some of the major benefits of this method.[26] Benzimidazole was obtained from OPD under a solvent-free environment using nano-Ni (II)/Y zeolite catalyst described by Mobinikhaledi *et al*.[27] This method is characterized by low catalyst loadings, easy purification, and environmental friendliness. To prepare benzimidazoles under a solvent-free set-up, a green and effective trifluoroacetate-bonded polyethylene graphene oxide composite was used. The OPD and aromatic aldehydes were used under solvent-free set-up at 75°C with the composite. The catalyst has

several desirable properties, including cost-effectiveness, ease of handling and storage, durability, recoverability, environmental friendliness, and nonmetallic nature.[28] Employing ionogel under solvent-free conditions, a systematic approach was established for the preparation of benzimidazoles. Ionogel proved to be highly suitable for the catalytic preparation of benzimidazoles. Moreover, the ionogel was able to be recycled to produce benzimidazoles.[29] Novel benzimidazoles were prepared by combining various salicylaldehydes with OPD using 3,3-(butane-1,4-diyl)bis(1,2-dimethyl-1H-imidazole-3-ium)Br in a one-pot reaction in the absence of solvents or oxidants.[30] Yadav and his group synthesized an effective sulfonated cobalt ferrite solid acid catalyst (CFNP@SO_3H). Through OPD condensation with numerous aliphatic, aromatic, and heterocyclic aldehydes, 2-substituted benzimidazole derivatives were synthesized. Excellent metrics such as high RME value, lower E factor, 100 % carbon efficiency, and 90.65 % atom economy values are some noticeable characteristics. Additionally, the catalyst can be regained with the help of simple magnet and can be reused seven times without significant sacrifice of productivity.[31] An effective and simple method for the preparation of 2-arylbenzimidazoles from OPD and aryl aldehydes using solid catalyst Ag_2CO_3/Celite, in ethanol at 70°C has been reported. It is characterized by excellent yields, short reaction time, and simplicity.[32] In the presence of ethanol, zirconocene dichloride (Cp_2ZrCl_2) was proven to be an excellent catalyst for the preparation of various benzimidazoles using OPD and aromatic aldehydes.[33] Using the cobalt (II) assisted on mesoporous silica-type substance (Co/SBA-15), a one-pot preparation of benzimidazole derivatives was accomplished by condensation of OPD with aromatic aldehydes under gentle conditions. It was viable to recycle the catalyst seven times with outstanding longevity and without significant loss of activity.[34] The condensation of OPD and aryl aldehydes in 1: 2 molar ratio was made using triphenyl bismuth bisperfluorooctanesulfonate [$Ph_3Bi(OSO_2C_8F17)2$] by Wang *et al*.[35] for the preparation of 1,2-disubstituted benzimidazoles in presence of THF at ambient temperature.

By Reaction With Carboxylic Acid

2-Arylbenzimidazoles were synthesized via microwave irradiation (MWI) and without using solvent under ambient temperature with catalytic amounts of acids as mentioned in (Scheme-2). Benzimidazoles and their structural analogs can be easily synthesized using this simple and practical green synthetic procedure.[36]



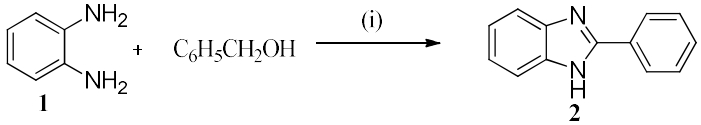
(i) HCl/PPA/H_3PO_3/$ZnCl_2$/$FeCl_3$, MWI, 10-15 min

Scheme-2

Wen *et al.*[37] developed a method for cyclization of OPD with carboxylic acids to synthesize benzimidazole using propylphosphonic anhydride (T3P) under microwave irradiation. As a one-pot procedure, the reaction times were fast, the workup was simple, and the yields were excellent. The synthesis of benzimidazoles using microwave-assisted conditions was reported by Niknam *et al.* varieties of carboxylic acids are used for synthesizing benzimidazole.[38] By reacting substituted o-phenylenediamine with diverse heterocyclic carboxylic acids, 2-substituted benzimidazolyl heterocycles have been synthesized using $POCl_3$ as a solvent as well as a catalyst.[39] The reported reactions have the advantages of quick reaction time, good yields, and ease of operation.

By Reaction with Alcohol

Using rutile-supported catalysts, OPD and benzyl alcohol were reacted at 100°C to yield 2-phenylbenzimidazole with high yields of 88%. Under mild reaction conditions, titanium-supported iridium catalysts Ir (2Wt %) /JRC-TiO_4 (0.01 mmol) showed excellent activity (Scheme-3). An interesting finding was that titania supports significantly affected the low-temperature activeness of iridium catalysts. [40]



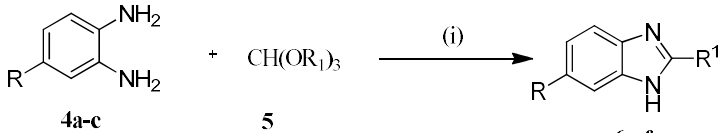
(i) Ir (2Wt %)/JRC-TIO_4 (0.010 mmol as Ir), Mesitylene, Under Ar, 120 ^{0}C, 18h

Scheme-3

Xu *et al.*[41] reported the Pd/C promoted oxidative condensation of OPD with benzyl alcohols under the aqueous condition to give the corresponding 2-arylbenzimidazoles in 43-90% yield. Iridium-supported solid catalysts displayed outstanding results under mild conditions in the dehydrogenative preparation of 2-phenylbenzimidazole from substituted benzyl alcohol and OPD. Among the tested catalysts, the titania-supported iridium has been proved highly efficient catalyst at temperatures of 120 °C.[42] A method for efficiently oxidizing alcohols and producing benzimidazoles from OPD with ceric ammonium nitrate $\{(NH4)_2Ce(NO_3)_6\}$ and PEG1000–ionic liquid-immobilized 2,2,6,6-tetramethylpiperidine-1-oxyl (Imim-PEG1000-TEMPO) was reported by Wang and co-workers. Using this scheme provided exceptional activity and selectivity, resulting in high yields for the target products.[43] A highly efficient catalyst, TEMPO-PEG4000-NHC-Cu(II) [2,2,6,6-tetramethyl piperidine-1-oxyl] (5 mol %), t-BuONa in water was utilized for oxidative preparation of benzimidazoles from alcohols. Further, these reactions can be performed in water with good yields.[44]

By Reaction with Orthoester

Using sulfonated rice husk ash as a solid acid catalyst, a simple process was reported for the preparation of benzimidazoles 6a-f from OPD and orthoesters 5 (Scheme-4). After a very brief reaction period, high yields of the products are obtained, and the catalyst can be recycled without losing its catalytic nature up to five times.[45]



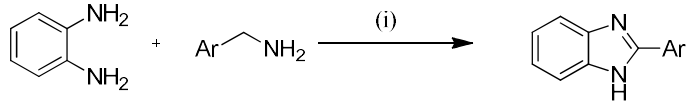
4a-c **5** **6a-f**

(i) RHA-SO_3H, 60 °C; R = H, NO_2, Me; R_1 = H, Me

Scheme-4

By Reaction with Benzylamine

Zinc complexes containing a neutral iminopyrrole-morpholino ligand were synthesized and subsequently used as a catalyst to create a wide variety of benzimidazole derivatives 8a-g (Scheme-5) by aerobic oxidation of different benzylamines 7a-g with OPD 1.[46]



1 **7a-g** **8a-g**

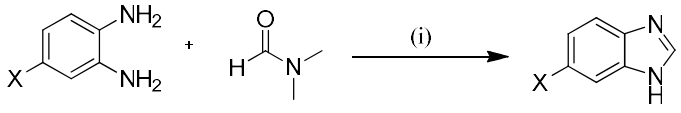
(I) zinc complexes supported iminopyrrole-morpholine ligand

Ar = C_6H_5, 2-ClC_6H_4, 4-ClC_6H_4, 2-FC_6H_4, 4-FC_6H_4, 3-$OCH_3C_6H_4$, 4-$OCH_3C_6H_4$

Scheme-5

By Reaction with N-Substituted Amides

An efficient one-pot protocol has been developed by Nale *et al.*[47] for the preparation of various benzimidazole derivatives 11a-d by using various o-phenylenediamines 9a-d and N,N-dimethylformamides 10 in a zinc-catalyzed cyclization process employing poly methylhydrosiloxane, the compounds were synthesized in reasonable yields. (Scheme-6).

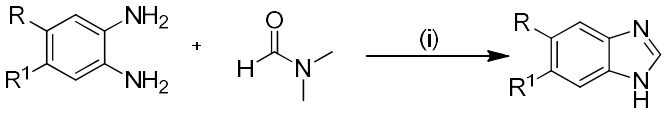


9a-d **10** **11a-d**

(i) $Zn(OAc)_2.2H_2O$, PHMS, 120 °C, 18 h; X = OH, OMe, Me, Cl

Scheme-6

1,2-arylenediamines 12a-h and N,N-dimethylformamide 13 (Scheme-7) were employed in an acidic medium, for the synthesis of benzimidazoles 14a-h in an efficient, rapid, and inexpensive manner.[48]



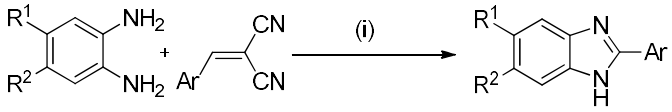
12a-h **13** **14a-h**

(i) 70 % HCl, 100 °C, 1 h; R = H or Me; R_1 = NO_2, Br, Me, Cl

Scheme-7

By Reaction with Arylidene Malononitrile

A fast, highly efficient, and environmentally helpful synthetic protocol for the construction of 2-aryl benzimidazoles 17a-j has been mentioned by Habibi *et al*.[49] Under aqueous media, phenylenediamine derivatives 15a-d were converted to high-yielding 2-aryl benzimidazole derivatives (Scheme-8).



15 **16** **17a-j**

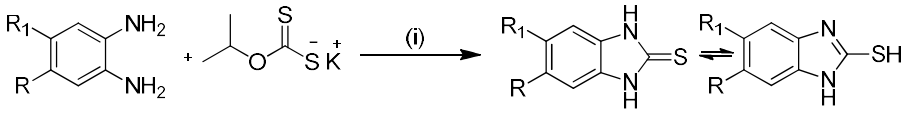
(i) H_2O, 75 °C, 20 min

R_1, R_2 = H or Me; Ar = C_6H_5, 2-ClC_6H_4, 4-ClC_6H_4, 3-$NO_2C_6H_4$, 4-$NO_2C_6H_4$, 3-$OCH_3C_6H_4$, 4-$OCH_3C_6H_4$, 4-$CH_3C_6H_4$, 4-BrC_6H_4, 2-SH C_6H_4

Scheme-8

By Reaction with Isopropyl Xanthate

Several benzimidazole-2-thiol derivatives 20a-e have been synthesized using an easy, green, efficient, and simple procedure. The proposed method makes use of the reaction of corresponding aromatic amines with potassium isopropyl xanthate 19 under conventional heating and ultrasonic irradiation as catalysts (Scheme-9). This protocol offers several advantages, including the use of water and glycerol as green solvents, simplicity, short reaction times, and high yield.[50]



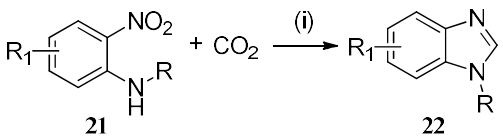
18a-e **19** **20a-e**

(i) $CuSO_4$ (10 mol %), H_2O/Glycerol, 90 °C; R_1 = H, Cl, Me; R = H or Me

Scheme-9

From 2-Nitroaniline

In the company of atmospheric CO_2, Pd/C catalyst, and $PhSiH_3$ as a reducing agent benzimidazole 22 was synthesized from o-nitroaniline 21 (Scheme-10). The compound TBD (1,5,7-triazabicyclo [4.4.0] dec-5-jan) was chosen as an alkali, as it facilitates the insertion of CO_2. By reducing the nitro group followed by cyclizing the amine using CO_2 as a carbon source, benzimidazoles were synthesized. Furthermore, the catalyst was utilized five times lacking any considerable reduction in yield.[51]



21 **22**

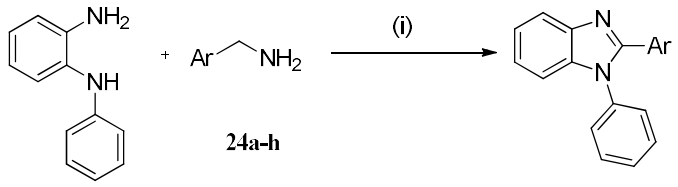
(i)Pd/C, $PhSiH_3$ (ii) TBD, 70 0C, 15 h

Scheme-10

From o-Arylene Diamines

Oxidative C-H transformation of primary aliphatic amines is achieved using a biocompatible $CuBr_2$ electron transfer reconciler and organocatalyst like topaquinone to furnish 1,2-disubstituted benzimidazoles 25a-h

(Scheme-11). During this one-pot process, ambient air was used, and equimolar amounts of each precursor were used.[52]



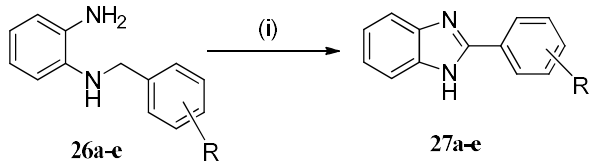
23 **24a-h** **25a-h**

(i) $CuBr_2$ / 1_{ox}, air, MeOH, 45 °C

Ar = C_6H_5, 4-ClC_6H_4, 4-$NH_2C_6H_4$, 4-BrC_6H_4, 4-MeC_6H_4, 4-$CF_3C_6H_4$, 4-$CH_3C_6H_4$, 2-thenyl

Scheme-11

Benzimidazole derivatives 27a-e were prepared by ligand-free copper bromide catalyzed oxidation and subsequent cyclization of 1,2-diamine 26a-e (Scheme-12).[53]

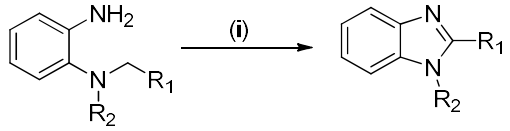


26a-e **27a-e**

(i) CuBr, K_2CO_3, DMSO, 120 °C; R = 2-Cl, 4-Cl, 4-Me, 4-OMe, 4-NO_2

Scheme-12

Iridium-promoted acceptorless cross dehydrogenative conjoining of tertiary amines 28a-i was developed by sun xiang *et al*.[54] Several benzimidazoles 29a-i were prepared by a C–H activation mechanism involving iridium (Scheme-13).



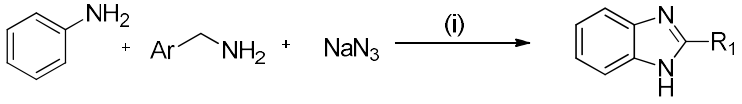
28a-i **29a-i**

(i) $[Ir(cod)Cl]_2$ (5 mol %), CF_3CH_2OH, reflux; R_1 = H, Me, C_2H_5, Ph; R_2 = Me, C_2H_5, C_3H_7

Scheme-13

From Aniline and its Derivatives

In the company of copper (II)-catalyzed TBHP at moderate temperatures, the cross-conjoining of aniline 30 and primary aliphatic amines 31a-g in the presence of sodium azide resulted in the formation of benzimidazole 32a-g. The multicomponent reaction includes a cascade of C-H transformation, transamination, ortho-selective amination, and subsequent cyclization (Scheme-14).[55]



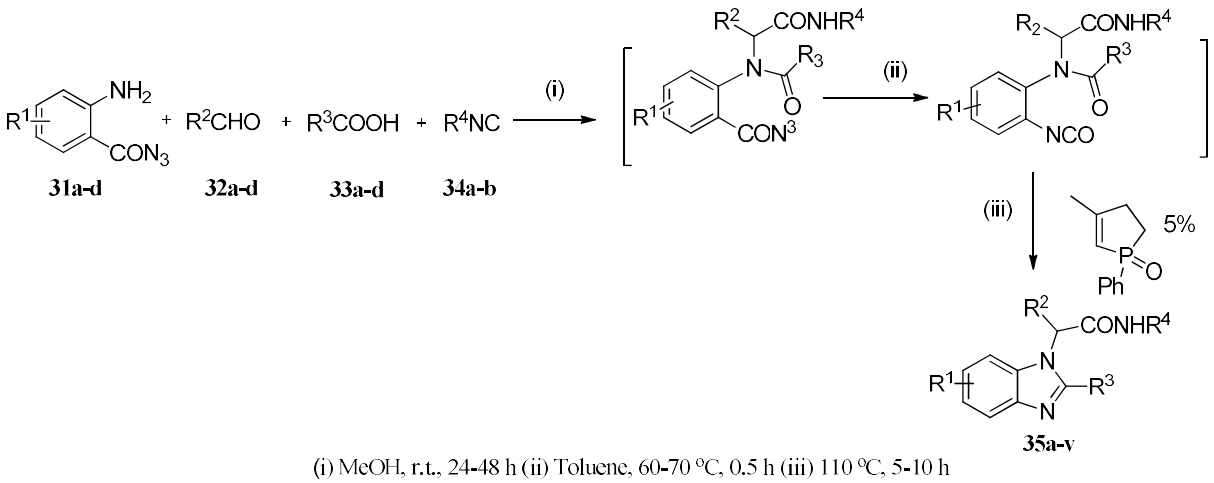
30 **31a-g** **32a-g**

(i) 10 mol % $Cu(OAc)_2$, AcOH, TBHP, DMSO, 80 °C

R = Ph, 2-MeC_6H_4, 4-MeC_6H_4, 2-$OMeC_6H_4$, 4-ClC_6H_4, 4-ClC_6H_4, 4-FC_6H_4

Scheme-14

Effortless and single-pot preparation of benzimidazole derivatives through a successive Ugi condensation and catalytic aza-Wittig was reported by Yan *et al*.[56] Benzimidazoles 35a-v were produced by combining 2-aminobenzoyl azide 31a-d, aldehyde 32a-d, acid 33a-d, and isocyanide 34a-b in reasonable to good yields in the company of a catalytic amount of phospholene oxide (Scheme-15).



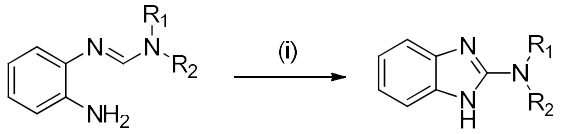
(i) MeOH, r.t., 24-48 h (ii) Toluene, 60-70 °C, 0.5 h (iii) 110 °C, 5-10 h

R_1 = 5-CH_3, 4-Cl, 5-CH_3, H; R_2 = 3-BrC_6H_4, 4-$CH_3OC_6H_4$, 4-ClC_6H_4, n-Pr;R_3 = 4-$CF_3OC_6H_4$, Ph, 3-IC_6H_4, CH_3; R_4 = t-Bu, c-C_6H_{11}

Scheme-15

From o-anilinic Amidines

Benzimidazoles 37a-c were synthesized using equimolecular amounts of o-aniline amidines 36a-c and $Ru(byp)_3Cl_2$ photocatalyst was synthesized under neat conditions by ring opening and ring-closing intramolecular hetero-cyclization reaction (Scheme-16).[57]

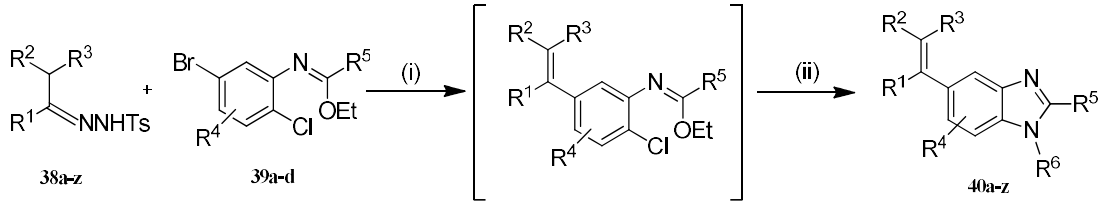


(i) $Ru(byp)_3Cl_2$, blue LED, r.t.; R_1 = H or ipr R_2 = ipr

Scheme-16

From N-tosylhydrazones

By using a palladium catalyst, a one-pot reaction among N-tosylhydrazones 38a-z, N-(dihalophenyl)-imidates 39a-d, and amines was devised by Naret *et al*.[58] This reaction occurs by Barluenga cross-coupling and *N*-arylation succeeded by cycloaddition to obtain benzimidazole derivatives 40a-z (Scheme-17). By palladium-catalyzed reaction, two C-N bonds and one C-C bond were obtained.



(i) $Pd_2(dba)_3CHCl_3$, LiO-t-Bu (ii) R_6NH_2; R^1, R^2, R^3, R^5, R^6 = alkyl, aryl; R^4 = Me, F

Scheme-17

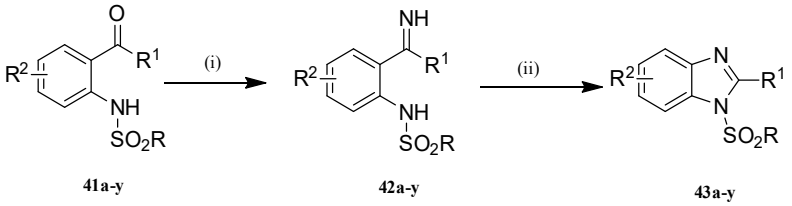
From O-aminoaryl Ketone

o-Aminoaryl N-H ketimines 42a-y have been rearranged by the Beckmann-type reaction by Zhang *et al.*[59] to prepare N-Ts benzimidazoles 43a-y. By reacting ammonia with the corresponding ketones 41a-y, the ketimine derivatives were easily prepared, and (diacetoxyiodo) benzene acted as an effective oxidant, leading to the formation of desired benzimidazole (Scheme-18).

CONCLUSION

In recent times, various protocols have been reported for the successful preparation of benzimidazole and its derivatives. In many methods, the benzimidazole nucleus is prepared mostly by using OPD as a precursor. OPD was condensed with aldehyde/ carboxylic acid/ alcohol/ Orthoester/ benzylamine/N-

substituted amide/ arylidene malononitrile. In a few instances, benzimidazole is also prepared by employing 2-nitroaniline/ aniline/o-anilinic amidines as a starting material. Several novel catalysts such as H_2SO_4@HTC, SBA-15-Ph-PrSO_3H, sulfonated cobalt ferrite solid acid catalyst, CMK-5-SO_3H, phospho sulfonic acid, titanium-supported iridium catalysts, etc. have been employed during the preparation.



41a-y **42a-y** **43a-y**

(i) NH_3 (ii) PhI $(OAc)_2$, MeOH, r.t., 1-6 h; R_2 = H, 5-Me, 5-NO_2, 7-OMe, 5-Cl; R_1 = Me, C_2H_5, Ph

Scheme-18

The recently reported methods have several advantages over the traditional method, those are shorter reaction time, simple experimental procedures, high yields, non-toxic catalyst, reusability of catalyst, and solvent-free conditions.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

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REFERENCES

1. P.N. Preston, *The Chemistry of Heterocyclic Compounds, Benzimdazoles and Cogeneric Tricyclic Compounds*; John Wiley & Sons, Vol. 40, (2009).
2. Q.A. McKellar and E.W. Scott,_*Journal of Veterinary Pharmacology and Therapeutics*, **13(3)**, 223(1990), https://doi.org/10.1111/j.1365-2885.1990.tb00773.x
3. A. Patil, S. Ganguly and S. Surana, *Rasayan Journal of Chemistry*, **1(3)**, 447(2008).
4. M. Gaba and C. Mohan, *Medicinal Chemistry Research*, **25(2)**, 173(2016), https://doi.org/10.1007/s00044-015-1495-5
5. K.V. Vyas and M. Ghate, *Mini-Reviews in Medicinal Chemistry*, **10(14)**, 1366(2010), https://doi.org/10.2174/138955710793564151
6. M. Iman, T. Peroomian, A. Davood, M. Amini, S. Sardari and P. Azerang, *Pharmaceutical Chemistry Journal*, **10(49)**, 687(2016), https://doi.org/10.1007/s11094-016-1354-9
7. B. Gadhiya, M. Rajput, A. Bapodra and K. Ladva, *Rasayan Journal of Chemistry*, **9(3)**, 355(2016).
8. Y.T. Lee, Y.J. Tan, C.E. Oon, *Acta Pharmaceutica Sinica B*,**13(2)**, 478 (2023), https://doi.org/10.1016/j.apsb.2022.09.010

9. M. Nardi, N.C. Cano, S. Simeonov, R. Bence, A. Kurutos, R. Scarpelli, D. Wunderlin, A. Procopio, *Catalysts*, **13(2)**, 392 (2023), https://doi.org/10.3390/catal13020392
10. P.N. Preston, *Chemical Review*, **74(3)**, 279(1974), https://doi.org/10.1021/cr60289a001
11. M. Faheem, A. Rathaur, A. Pandey, V. Kumar Singh, and A.K. Tiwari, *Chemistry Select*, **5(13)**, 3981(2020), https://doi.org/10.1002/slct.201904832
12. H. Hernández-López, C.J. Tejada-Rodríguez, S. Leyva-Ramos. *Mini-Reviews in Medicinal Chemistry*, **22(9)**,1268 (2022), https://doi.org/10.2174/1389557522666220104150051
13. K.P. Barot, S. Nikolova, I. Ivanov and M.D. Ghate, *Mini-Reviews in Medicinal Chemistry*, **13(10)**, 1421(2013), https://doi.org/10.2174/13895575113139990072
14. Z. Wang Phillips-ladenburg, benzimidazole synthesis. In *Comprehensive Organic Name Reactions and Reagents*; John Wiley & Sons, Inc. (2010), https://doi.org/10.1002/9780470638859.conrr496
15. M. Shaibuna, K. Hiba, A.M. Shebitha, M.J.K. Kuniyil and K. Sreekumar, *Current research in green and sustainable chemistry*, **5**, 100285(2022), https://doi.org/10.1016/j.crgsc.2022.100285
16. M.L. Di Gioia, R. Cassano, P.Costanzo, N. Herrera Cano, L. Maiuolo, M. Nardi, F.P. Nicoletta, M. Oliverio and A. Procopio, *Molecules*, **24(16)**, 2885(2019), https://doi.org/10.3390/molecules24162885
17. P. Zhang, C. Liu, L. Yu, H. Hou, W. Sun, F. Ke, *Green Chemistry Letter Review*, **14(4)**, 612(2021). https://doi.org/10.1080/17518253.2021.1991483
18. S. Belkharchach, H. Ighachane, A. Rochdi, M. Ait Ali and H.B. Lazrek, *Organic Preparations and Procedures International*, **53(3)**, 268(2021), https://doi.org/10.1080/00304948.2021.1873066
19. M. Zhuang, L. Tu, Y. Wu, Y. Jian, Y. Wang, W. Zhang, H. Sun and Z. Gao, *Molecular Catalysis,* **524***,* 112181(2022), https://doi.org/10.1016/j.mcat.2022.112181
20. S. Rezayati, M. Mehmannavaz, E. Salehi, S. Haghi, R. Hajinasiri and S. Afshari Sharif Abad, *Journal of Science Islamic Republic Iran*, **27(1)**, 51(2016).
21. D. Zareyee, S.R. Tuyehdarvary, L. Allahgholipour, Z. Hossaini and M.A. Khalilzadeh, *Synlett*, **27(08)**, 1251(2016), https://doi.org/10.1055/s-0035-1561354
22. S.R. Rithe, R.S. Jagtap and S.S. Ubarhande, *Rasayan Journal of Chemistry*, **8(2)**, 213(2015).
23. J. Azizian, P. Torabi and J. Noei, *Tetrahedron Letter*, **57(2)**, 185(2016), https://doi.org/10.1016/j.tetlet.2015.11.092
24. M.A. Bodaghifard and S. Shafi, *Journal of the Iranian Chemical Society*, **18(3)**, 677(2021), https://doi.org/10.1007/s13738-020-02055-1
25. M.A. Zolfigol, V. Khakyzadeh, A.R. Moosavi-Zare, A. Zare and P. Arghavani-Hadi, Z. Mohammadi and M.H. Beyzavi, *South African Journal of Chemistry*, **65(1)**, 280(2015).
26. H. Ahmadian, H. Veisi, C. Karami, A. Sedrpoushan, M. Nouri, F. Jamshidi and I. Alavioon, *Appllied Organometalic Chemistry*, **29(5)**, 266(2015), https://doi.org/10.1002/aoc.3283
27. A. Mobinikhaledi, M. Zendehdel, F. Goudarzi and G.R. Bardajee, *Synthesis and Reactivity in Inorganic Metal organic Nano-Metal Chemistry*, **46(10)**, 1526(2016), https://doi.org/10.1080/15533174.2015.1137020
28. E. Rostami and S.M. Haghayeghi, *Iranian Journal of Catalysis*, **11(1)**, 37(2021).
29. P. Sharma and M. Gupta, *Journal of Chemical Sciences*, **128(1)**, 1(2016), https://doi.org/10.1007/s12039-015-1000-1
30. M. Nikpassand and D. Pirdelzendeh, *Dyes and Pigments*, **130**, 314(2016), https://doi.org/10.1016/j.dyepig.2016.03.038
31. P. Yadav, P. Kakati, P. Singh and S.K. Awasthi, *Applied Catalysis A: General*, **612**, 118005(2021), https://doi.org/10.1016/j.apcata.2021.118005
32. E. Soleimani, M.M. Khodaei, H. Yazdani, P. Saei and J.Z. Reza, *Journal of the Iranian Chemical Society*, **12(7)**, 1281(2015), https://doi.org/10.1007/s13738-015-0592-1
33. S. Karhale, K. Patil, C. Bhenki, G. Rashinkar and V. Helavi, *Research on Chemical Intermediates*, **42**, 7257(2016), https://doi.org/10.1007/s11164-016-2534-7
34. F. Rajabi, S. De and R. Luque, *Catalysis Letters*, **145(8)**, 1566(2015), https://doi.org/10.1007/s10562-015-1546-z
35. P. Wang, J. Wang, C.T. Au, R. Qiu, X. Xu and S.F. Yin, *Advanced Synthesis and Catalysis*, **358(8)**, 1302(2016), https://doi.org/10.1002/adsc.201500998

36. R. Wang, X. Lu, X. Yu, L. Shi and Y. Sun, *Journal of Molecular Catalysis A:Chemical*, **266(1)**, 198(2007), https://doi.org/10.1016/j.molcata.2006.04.071
37. X. Wen, J. El Bakali, R. Deprez-Poulain and B. Deprez, *Tetrahedron Letters*, **53(19)**, 2440(2012), https://doi.org/10.1016/j.tetlet.2012.03.007
38. K. Niknam and A. Fatehi-Raviz, *Journal of the Iranian Chemical Society*, **4(4)**, 438(2007), https://doi.org/10.1007/BF03247230
39. V.K.A. Kalalbandi and J. Seetharamappa, *Synthetic Communications*, **46(7)**, 626(2016), https://doi.org/10.1080/00397911.2016.1160412
40. K. Wada, H. Yu and Q. Feng, *Chinese Chemical Letters*, **31(3)**, 605(2020), https://doi.org/10.1016/j.cclet.2019.05.054
41. C. Xu, Z.Q. Xiao, H.M. Li, X. Han, Z.Q. Wang, W.J. Fu, B.M. Ji X.Q. Hao and M.P. Song, *Synfacts*, **12(2)**, 216(2016), https://doi.org/10.1055/s-0035-1561136
42. K. Wada, K. Tateyama, H. Miura, S. Hosokawa and R. Abe, *Catalysis Science and Technology*, **6**, 1677(2016), https://doi.org/10.1039/C5CY01601K
43. Z.G. Wang, Y.G. Xia, Y. Jin and M. Lu, *Applied Organometallic Chemistry*, **29(2)**, 109(2015), https://doi.org/10.1002/aoc.3253
44. Z. Wang, X. Cao, Y. Yang and M. Lu, *Synthetic Communications*, **45(12)**, 1476(2015), https://doi.org/10.1080/00397911.2015.1017053
45. F. Shirini, M. Mamaghani and M. Seddighi, *Research on Chemical Intermediates*, **41(8)**, 5611(2015), https://doi.org/10.1007/s11164-014-1685-7
46. K. Bano, D.A. Kisan and T.K. Panda, *European Journal of Inorganic Chemistry*, **2022(10)**, e202200023(2022), https://doi.org/10.1002/ejic.202200023
47. D.B. Nale and B.M. Bhanage, *Synlett*, **26(20)**, 2835(2015), https://doi.org/10.1055/s-0035-1560319
48. P.P. Kattimani, R.R. Kamble, G.Y Meti, *RSC Advances*, **5(37)**, 29447(2015), https://doi.org/10.1039/C5RA00021A
49. A. Habibi, Y. Valizadeh, M. Mollazadeh and A.Alizadeh, *International Journal of Organic Chemistry,* **05(04)**, 256(2015), https://doi.org/10.4236/ijoc.2015.54025
50. R. Ranjbar-Karimi, A. Talebizadeh and L. Amiri-Zirtol, *Organic Chemistry Research*, **2(1)**, 64(2016), https://doi.org/10.22036/org.chem..2016.13579
51. V.V. Phatake and B.M. Bhanage, *Tetrahedron Letters*, **68**, 152940(2021), https://doi.org/10.1016/j.tetlet.2021.152940
52. K.M.H. Nguyen and M. Largeron, *Chemistry-A Europian Journal*, **21(36)**, 12606(2015), https://doi.org/10.1002/chem.201502487
53. B. Mirza and M. Zeeb, *Synthetic Communication*, **45(4)**, 524(2015), https://doi.org/10.1080/00397911.2014.971971
54. X. Sun, X.H. Lv, L.M. Ye, Y. Hu, Y.Y. Chen, X.J. Zhang and M. Yan, *Organic and Biomolecular Chemistry,* **13(27)**, 7381(2015), https://doi.org/10.1039/C5OB00904A
55. D. Mahesh, P. Sadhu and T. Punniyamurthy, *The Journal of Organic Chemistry*, **81(8)**, 3227(2016), https://doi.org/10.1021/acs.joc.6b00186
56. Y.M. Yan, Y. Rao and M.W. Ding, *The Journal of Organic Chemistry*, **81(3)**, 1263(2016), https://doi.org/10.1021/acs.joc.5b02575
57. I.R. Siddiqui, F. Ibad, A. Ibad, M. A. Waseem and G. Watal, *Tetrahedron Letters*, **57(1)**, 5(2016), https://doi.org/10.1016/j.tetlet.2015.10.042
58. T. Naret, P. Retailleau, J. Bignon, J.D. Brion, M. Alami and A. Hamze, *Advanced Synthesis and Catalysis*, **358(11)**, 1833(2016), https://doi.org/10.1002/adsc.201600173
59. X. Zhang, R. Huang, J. Marrot, V. Coeffard and Y. Xiong, *Tetrahedron*, **71(4)**, 700(2015), https://doi.org/10.1016/j.tet.2014.11.066

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