



WASTE CURD WATER CATALYSED SYNTHESIS OF BENZIMIDAZOLE DERIVATIVES: A GREEN APPROACH

Swapnil J. Wagh^{*a}, Dinesh N. Navale^b, Prasanna B. Ranade^b, Santosh W. Zote^c, and Dnyaneshwar K. Kulal^d

^aDepartment of Chemistry, Nanasaheb Y. N. Chavan, Arts, Science & Commerce College Chalisgaon, Dist Jalgaon Maharashtra, India.

^bDepartment of Chemistry, Vivekanand Education Society's College of Arts, Science and Commerce (Autonomous), Sindhi Society, Chembur, Mumbai, India.

^cDepartment of Chemistry, PTVA's Sathaye College (Autonomous), Dixit Road, Vile Parle (East), Mumbai, India.

^dDepartment of Chemistry, Ramnarain Ruia Autonomous College, L. N. Road, Matunga, Mumbai, India.

*Corresponding author Email: dr.swapnilwagh11@gmail.com

ABSTRACT:

An effective and novel green approach developed for preparation of 2- substituted benzimidazole. The benzimidazole derivatives prepared by condensation of 2,3-Diamino benzene and substituted benzaldehydes using waste curd water (WCW) under normal reaction condition. The waste curd water has shown its dual action as a solvent and biocatalyst also in the synthesis of Benzimidazole derivatives. This novel synthesis method produced benzimidazole derivatives with short reaction time and good yield of 76-85%. Our protocol is economical, more efficient and environmentally benign than conventional protocols for benzimidazole synthesis.

KEY WORDS:

2,3-Diamino benzene, 2-substituted Benzimidazole, waste curd water (WCW), Green synthesis, Benzaldehyde, biocatalyst.

INTRODUCTION:

In recent decades, scientists have been engrossed towards development of novel heterocyclic compounds as it showed remarkable applications in agricultural, industrial, pharmaceutical, medicinal and material chemistry fields.ⁱ The wide range of heterocyclic compounds with distinct structural features have been utilized in different beneficial determinations.ⁱⁱ Among these heterocycles, benzimidazole is one of the most important example of nitrogen containing heterocycle which has been well known for its biologically activities such as anti-HIV, anti-

cancer, anti-inflammatory, anti-bacterial, anti-fungal, anti-histaminic, anti-oxidant and anti-coagulant agents.^{iii-viii}

Hence, molecular skeleton containing benzimidazole ring showed huge applications^{ix-x} and in that perspective development of benzimidazole derivatives by using novel synthetic methods made challenges for synthetic organic chemists. Generally, synthesis of benzimidazole achieved by acid catalyzed condensation of 2,3-diamino benzene and benzaldehyde.^{xi} Many reports for synthesis of 2- substituted benzimidazole using different acids such as citric acid^{xii}, acetic acid,^{xiii} B.S.A.,^{xiv} lactic acid^{xv} etc. Along with acid catalyzed conditions, synthesis of 2-substituted benzimidazole achieved by metal catalysed,^{xvi} nanoparticle catalyzed,^{xvii} Microwave assisted,^{xviii} mortar-pestle operated,^{xix} ionic liquids,^{xx} DES catalyzed^{xxi} methodologies were reported. The wide ranges of homogenous as well as heterogenous catalysts were screened for synthesis of benzimidazole derivatives. But now days, only synthesis of heterocyclic compound is not sufficient and chemists are credited for development of heterocycles using Green synthesis approach.^{xxii} With this interest our group reported eco-friendly tamarind juice catalyzed synthesis of coumarin derivatives^{xxiii} and in continuation of green synthesis approach, we focused on development of benzimidazole derivative with the use of simple, efficient and environmentally benign catalyst. Herein we reported synthesis of 2-substituted benzimidazole by reaction of 2,3-diamino benzene and benzaldehyde derivatives using waste curd water (wcw) as biocatalyst at room temperature.

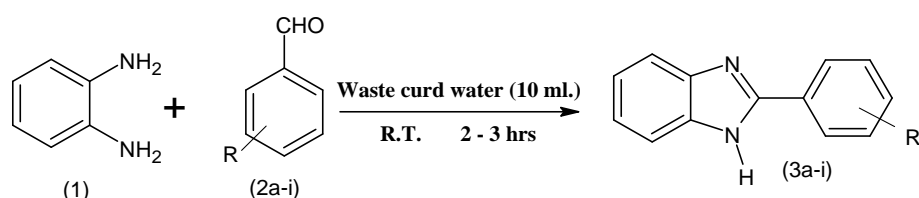
EXPERIMENTAL SECTION:

The chemicals were purchased from Loba Chemie and Sigma Aldrich companies and used as it is without further purification. The waste curd water (wcw) was prepared as per reported procedure.^{xxiv} The reaction progress monitored by thin layer chromatography using silica gel. All the melting points were taken in open glass capillaries and are uncorrected.

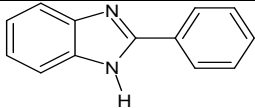
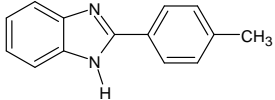
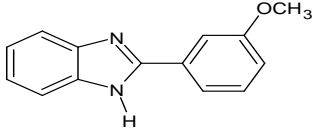
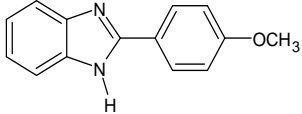
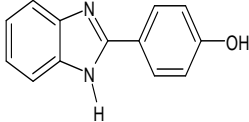
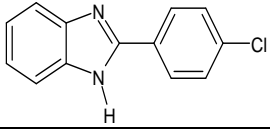
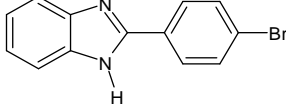
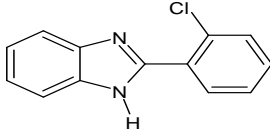
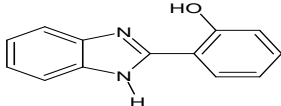
GENERAL PROCEDURE:

Preparation of 2- substituted benzimidazole (Scheme-1):

To the 50 ml. round bottom flask, benzaldehyde (1 mmol) (**2a**), 2, 3-diaminobenzene (1 mmol) (**1**) and 10 ml of catalyst (wcw) was added. The reaction mixture was stirred at room temperature for 2-3 hrs. The progress of reaction monitored by using TLC. On the completion of reaction which confirmed on TLC, the reaction mixture was poured into ice cold water under stirring solid product was get separate out. The separated product was filtered, washed with water and on drying it offered crude solid product. The solid product was purified with recrystallization process. The pure products were yielded. The melting points of all the synthesized compounds (**3a-i**) were matches with reported literature values.^{xxv- xxvii}



Scheme-1: Synthesis of 2-Substituted Benzimidazole derivatives

Entry	R-	Product ^a	Time (Hrs.)	Yield ^b (%)	Melting Points (°C)	
					Observed	Reported ^{xxv}
3a	-H		2	83	289-290	288-290
3b	4-Methyl		1.5	84	260-261	261-263
3c	3-Methoxy		2.5	76	206-207	205-206
3d	4-Methoxy		2	82	229-230	229-231
3e	4-Hydroxy		1.4	81	254-255	254-256
3f	4-Chloro		1.2	85	290-291	291-293
3g	4-Bromo		1	84	251-253	250-252
3h	2-Chloro		2.8	80	232-233	232-234
3i	2-Hydroxy		3	77	239-240	240-242

a All synthesized products are well-known and their melting point values were matches with reported literature values.

b Yields refer to pure isolated products.

Table-1: Condensation reactions of 1,2-Diamino benzene with various derivatives of aldehyde

RESULT AND DISCUSSION:

We have been reported, preparation of 2-phenyl-1H-1, 3- benzimidazoles (3a-i) derivatives using novel waste curd water (wcw) as a biocatalyst. In our preliminary study, we monitored a model reaction of 2,3 Diaminobenzene (1) and benzaldehyde (2a) in presence of catalyst w.c.w. , it was found that the reaction could be finished with use of 5 ml. Waste Curd water at room temp. Under stirring condition. With the success in model reaction for screening of catalyst we moved for the optimal catalyst loading study and we carried out same reaction with variation of catalyst loading amount from 0 to 20 ml. In that, it was observed that

reaction gave highest yield of 83% product with 10 ml. of wcw loading. Also in order to investigate optimal temperature condition, the similar model reaction was carried out at 10° C, R.T., 100° C conditions but it was observed that, product yield seen maximum for the room temp. condition. So, Waste curd water containing lactic acid can efficiently catalyze a one-pot synthesis of 2-substituted benzimidazole via condensation of 2, 3-Diaino benzene with benzaldehyde derivatives using 10 ml. of waste curd water under stirring at r.t. for 2-3 hrs. (Scheme- 1). With this optimal reaction conditions, which synthesized the desired 2-substituted benzimidazole derivatives (3a-i) with good yields of 78 -85% yield. Thus, we have developed a new protocol for the preparation of 2- substituted benzimidazole in presence of waste curd water as novel, efficient and greener catalyst with short reaction time and high yields.

CONCLUSION:

In conclusion, we have been report the development of green and proficient protocol for the development of 2-substituted benzimidazole derivatives using waste curd water as a greener solvent cum biocatalyst under normal temperature condition. This novel protocol involves development of benzimidazole derivatives with easy work-up, short reaction time and good yield of products. Thus, environmentally benign, cheap, readily available Waste curd water (wcv) catalyst efficiently produced 2-substituted benzimidazole derivatives using green approach. The utilization of bio waste curd water proved to be as an attractive strategy for the development of some other heterocyclic motifs in future.

ACKNOWLEDGEMENT:

The author Swapnil wagh is thankful to the Management and Principal of Nanasaheb Y. N. Chavan Arts, Science and Commerce College Chalisgaon, Dist.-Jalgaon (MS) India, for their constant encouragement and providing the necessary laboratory facilities for this work.

REFERENCES:

- i.** Al-Mulla A. A review: biological importance of heterocyclic compounds. *Der Pharma Chemica*. 2017; **13**;141-147.
- ii.** Mermer A, Keles T, Sirin Y. Recent studies of nitrogen containing heterocyclic compounds as novel antiviral agents: A review. *Bioorganic Chemistry*. 2021 Sep.
- iii.** Rashid M. Design, synthesis and ADMET prediction of bis-benzimidazole as anticancer agent. *Bioorganic chemistry*. 2020 Mar 1; 96: 103576.
- iv.** Miller JF, Turner EM, Gudmundsson KS, Jenkinson S, Spaltenstein A, Thomson M, Wheelan P. Novel N-substituted benzimidazole CXCR4 antagonists as potential anti-HIV agents. *Bioorganic & medicinal chemistry letters*; 2010, **20**:2125-8.
- v.** Singh N, Pandurangan A, Rana K, Anand P, Ahamad A, Tiwari AK. Benzimidazole: A short review of their antimicrobial activities. *International current pharmaceutical journal*. 2012,**5**:110-118.
- vi.** Keri RS, Hiremathad A, Budagumpi S, Nagaraja BM. Comprehensive review in current developments of benzimidazole-based medicinal chemistry. *Chemical biology & drug design*. 2015, **86**, 19-65.
- vii.** Vasava MS, Bhoi MN, Rathwa SK, Jethava DJ, Acharya PT, Patel DB, Patel HD. Benzimidazole: A milestone in the field of medicinal chemistry. *Mini reviews in medicinal chemistry*. 2020, **20**, 532-565.

- viii.** Kumar BV, Vaidya SD, Kumar RV, Bhirud SB, Mane RB. Synthesis and anti-bacterial activity of some novel 2-(6-fluorochroman-2-yl)-1-alkyl/acyl/aroyl-1H-benzimidazoles. *European journal of medicinal chemistry*, 2006; **41**; 599-604.
- ix.** Marinescu M, editor. *Chemistry and applications of benzimidazole and its derivatives*. BoD–Books on Demand; 2019 Oct 2.
- x.** Hashem HE, El Bakri Y. An overview on novel synthetic approaches and medicinal applications of benzimidazole compounds. *Arabian Journal of Chemistry*. 2021; **14**; 410-418.
- xi.** Rao NS, Ratnam CV.; Reaction between o-phenylenediamine and aromatic aldehydes, *Current science*, 1955, **24**; 299-301.
- xii.** Singh N, Arya P, Tripathi PK, Negi DS. Synthesis, Characterization and Antibacterial Activity of Two Novel Benzimidazole Compounds from Citric Acid. *Journal of Applicable Chemistry*. 2018; **7**; 52-58.
- xiii.** Benincori T, Sannicolo F. New benzimidazole synthesis. *Journal of heterocyclic chemistry*. 1988, **25**, 1029-1033.
- xiv.** Sajjadifar S, Mirshokraie SA, Javaherneshan N, Louie O. SBSA as a New and efficient catalyst for the one-pot green synthesis of benzimidazole derivatives at room temperature. *American Journal of Organic Chemistry*. 2012; **2**, 1-6.
- xv.** Yu ZY, Zhou J, Fang QS, Chen L, Song ZB. Chemoselective synthesis of 1, 2-disubstituted benzimidazoles in lactic acid without additive. *Chemical Papers*. 2016; **70**; 1293-1298.
- xvi.** Peng J, Ye M, Zong C, Hu F, Feng L, Wang X, Wang Y, Chen C. Copper-catalyzed intramolecular C–N bond formation: A straightforward synthesis of benzimidazole derivatives in water. *The Journal of organic chemistry*, 2011 **76**; 716-719.
- xvii.** Mohammadi R. Magnetic copper ferrite nanoparticles catalyzed synthesis of benzimidazole, benzoxazole and benzothiazole derivatives. *Journal of Synthetic Chemistry*. 2022; **23** ; 22-26.
- xviii.** Sharma P, Reddy TS, Kumar NP, Senwar KR, Bhargava SK, Shankaraiah N. Conventional and microwave-assisted synthesis of new 1H-benzimidazole-thiazolidinedione derivatives: A potential anticancer scaffold. *European journal of medicinal chemistry*. 2017,**138**;234-245.
- xix.** Zhang P, Liu C, Yu L, Hou H, Sun W, Ke F. Synthesis of benzimidazole by mortar–pestle grinding method. *Green Chemistry Letters and Reviews*, 2021 ;**14** ;612-9.
- xx.** Zhang M, Zang H, Ma B, Zhang X, Xie R, Cheng B. Green Synthesis of 5-Hydroxymethylfurfural from Chitosan Biomass Catalyzed by Benzimidazole-Based Ionic Liquids. *ChemistrySelect*. 2017; **32**; 10323-8.
- xxi.** Di Gioia ML, Cassano R, Costanzo P, Herrera Cano N, Maiuolo L, Nardi M, Nicoletta FP, Oliverio M, Procopio A. Green synthesis of privileged benzimidazole scaffolds using active deep eutectic solvent. *Molecules*; 2019; **16**, 2885.
- xxii.** Brahmachari G. Green synthetic approaches for biologically relevant heterocycles: Advanced synthetic techniques- An overview., *Green Synthetic Approaches for Biologically Relevant Heterocycles*, 2021, **1**; 1-8.
- xxiii.** Dinesh N. Navale , Prasanna B. Ranade , Santosh W. Zote , Dnyaneshwar K. Kulal and Swapnil J. Wagh, Eco-Friendly One Pot Synthesis of Coumarin Derivatives by Pechmann Condensation using Tamarind Juice as a Biocatalyst, *International Journal of Innovative Science and Research Technology*, 2023, **8**, 1917-1920.
- xxiv.** Rajput J, Koli S, Mohite B, Bendre R, Patil S, Patil V. A green tactic for the synthesis of classical 3, 3-bisindolylmethanes in waste curd water. *SN Applied Sciences*, 2019; **1**, 1-8.

- xxv.** Naeimi H, Alishahi N., Highly Efficient and Facile Method for Synthesis of 2-Substituted Benzimidazoles via Reductive Cyclization of O-Nitroaniline and Aryl Aldehydes.; Organic Chemistry International, 2012.
- xxvi.** Xiangming H, Huiqiang M, Yulu W. p-TsOH catalyzed synthesis of 2-arylsubstituted benzimidazoles. Arkivoc. 2007; **13**; 150-4.
- xxvii.** R. R. Nagawade and D. B. Shinde, "TiCl₄ promoted synthesis of benzimidazole derivatives," Indian Journal of Chemistry B, 2007, **46**, 349–351.

Received on July 14, 2023.