RESEARCH PAPER

Microwave-Assisted Green and Efficient Synthesis of Benzimidazole Derivatives using Ni,S-Doped Tio₂ as a Reusable Heterogeneous Nano-catalyst

Akshay Patil[1], Dr.Brajadulal Ghosh[2]

[1*,2]Department of Chemistry, School of Science, Sandip University, Nashik

ABSTRACT

A green and efficient protocol has been developed for the synthesis of benzimidazole derivatives using 1% (Ni,S) doped in TiO2 as a reusable heterogeneous nanocatalyst under microwave irradiation. The present method is based on the condensation of o-phenylenediamine with various aromatic aldehydes to give the corresponding benzimidazole derivatives in excellent yields in a short reaction time. Microwave irradiation can accelerate the reaction rate significantly compared to conventional heating methods, resulting in better efficiency and lower energy consumption. The synthesized nanocatalyst was characterized by standard analytical techniques including XRD, SEM and XPS which confirmed the successful doping and high surface activity. The catalytic system shows great advantages of being practically simple, high yielding, less by-products formation and ease of recovery and reusability of the catalyst over several cycles without significant loss of activity. In addition, the broad substrate scope shows the usefulness of this protocol for different substituted aldehydes. The present method is a sustainable and environmentally benign protocol for the rapid synthesis of biologically important benzimidazole derivatives in good yields, in accordance with the principles of green chemistry.

Keywords: Benzimidazole derivatives, microwave-assisted synthesis, Ni,S-doped TiO_2, heterogeneous nanocatalyst, green chemistry, reusable catalyst, heterocyclic compounds, catalyst reusability.

How to cite this article: Patil A, Ghosh B, Microwave-Assisted Green and Efficient Synthesis of Benzimidazole Derivatives using Ni,S-Doped Tio₂ as A Reusable Heterogeneous Nano-Catalyst. Int J Drug Deliv Technol. . 2026;16(26s):809-817. Doi: 10.25258/ijddt.16.26s.86.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

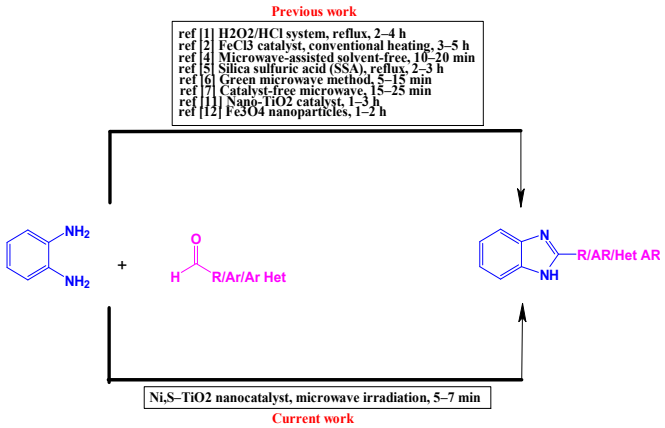
Nitrogen-containing heterocyclic compounds represent a basic class of organic molecules that are of interest to medicinal chemistry, materials science and pharmaceutical research. Among them, benzimidazole derivatives have come to prominence as a significant scaffold owing to their broad spectrum of biological and pharmacological activities such as antimicrobial, antiviral, anticancer, anti-inflammatory and antifungal [1–3]. The benzimidazole nucleus is structurally related to naturally occurring purine bases and thus exhibits strong affinity toward a variety of biological targets. Therefore, benzimidazole based compounds have been widely used in the development of therapeutic agents such as proton pump inhibitors, antihypertensive drugs and antiviral drugs [4-6]. Such important applications have led to a continuous interest in the development of efficient and sustainable methods for the synthesis of benzimidazole derivatives. Benzimidazole derivatives have been synthesized traditionally by the condensation reaction of o-phenylenediamine with aldehydes, carboxylic acids or their derivatives in the presence of strong mineral acids or oxidizing agents [7–9]. Although effective, these methods often suffer from some drawbacks such as harsh reaction conditions, long reaction times, low selectivity of the product, and the use of hazardous reagents and solvents [10,11]. Furthermore, the homogeneous catalytic systems usually cause problems of catalyst recovery and recyclability which can lead to increased waste generation and environmental concerns. These limitations point to the need to develop more environmentally benign, efficient and economically feasible synthetic methodologies.

The increasing importance of sustainable chemistry in recent years has led to the application of the principles of green chemistry which aim at minimizing waste, energy consumption and the use of benign reagents and catalysts [12–14]. In this context, microwave-assisted organic synthesis has emerged as a powerful tool as an alternative to the conventional heating methods. Microwave irradiation has several advantages such as rapid and uniform heating, shorter reaction times, higher yields and better reaction selectivity [15–17]. Microwave energy can interact directly with polar molecules and reaction intermediates, resulting in effective energy transfer and, therefore, the acceleration of chemical transformations. Thus microwave-assisted synthesis has emerged as a powerful tool for rapid construction of heterocyclic frameworks. In the meantime, heterogeneous nanocatalysis has emerged as a promising technique in modern organic synthesis. Nanocatalysts have unique properties such as high surface area-to-volume ratio, higher number of active sites and higher catalytic efficiency as compared to their bulk counterparts [18-20]. Moreover, the heterogeneous nanocatalysts can be easily separated from the reaction mixture and reused, which make them highly attractive for sustainable and industrial applications. Titanium dioxide (TiOn) has been the most studied among various nanomaterials owing to its good chemical stability, low toxicity, economy and wide-ranging catalytic properties [21–23].

Many efforts have been performed to modify TiO2 by doping transition metals and non-metals for further improving its catalytic performance. These modifications can alter the electronic structure, enhance the charge transfer properties, and increase the number of active sites on the catalyst surface [24–26]. Especially, the doping of transition metals such as nickel (Ni) has been proven to improve catalytic activity by allowing electron transfer processes, while non-metal doping with sulfur (S) can improve surface characteristics and catalytic efficiency [27–29]

It is expected that the co-doping of Ni and S will have a synergistic effect that will significantly improve the catalytic efficiency of TiO2, making it a highly efficient nanocatalyst for organic transformations. However, the application of Ni,S-doped TiO2 nanocatalysts in the synthesis of benzimidazole derivatives is still scarce, especially under microwave-assisted conditions. The combination of microwave irradiation with a highly active and reusable nanocatalyst provides a promising strategy for the development of rapid, efficient and environmentally friendly synthetic protocols.

In this paper we report a microwave assisted green and efficient synthesis of benzimidazole derivatives in the presence of Ni,S-doped TiO2 as a reusable heterogeneous nano-catalyst. The developed methodology presents several important advantages such as much shorter reaction times, high yields of product, operational simplicity, and. excellent catalyst recyclability. Moreover, the protocol exhibits a broad substrate scope and uses less hazardous reagents, and thus is in good agreement with the principles of green chemistry. The present work emphasizes the potential of Ni,S-doped TiO2 as an efficient nanocatalyst and also provides a sustainable protocol for the synthesis of biologically important benzimidazole derivatives



Scheme 1 Greener approach for the synthesis of Imidazole derivatives

Corresponding Author: Akshay Patil, akshay06121991@gmail.com

In the present study a green and efficient protocol was developed for the synthesis of benzimidazole derivatives using 1% (Ni,S) doped TiO2 nanocatalyst under microwave irradiation. The reaction is a condensation of o-phenylenediamine with various aromatic and heteroaromatic aldehydes. The microwave-assisted synthesis has been extensively described to increase the reaction rate and yield in comparison with the conventional heating methods. However, the combination of the present work with doped nanocatalysts for the synthesis of benzimidazoles remains relatively unexplored, thus justifying this work.

To optimize the reaction conditions, the condensation of o-phenylenediamine with 4-chlorobenzaldehyde was selected as a model reaction. Initially, the reaction was carried out at room temperature under stirring, but no product formation was observed even after 2 h. When the reaction temperature was increased to 80–90 °C under conventional heating, only a low yield of the desired product was obtained after prolonged reaction time, indicating the limitations of traditional methods. The reaction was then performed under microwave irradiation without a catalyst, however only trace amounts of the product were observed. This clearly indicates the importance of the catalyst for the reaction. A remarkable improvement was observed when the reaction was performed under microwave conditions in the presence of 1%(Ni,S) doped in TiO2 nanocatalyst (5 mg) giving 72% yield in 10 minutes. This better efficiency of microwave conditions can be explained by rapid and uniform heating which speeds up molecular interactions and reaction kinetics.

Further optimization was performed by varying the catalyst loading. The catalyst amount was varied from 5 mg to 15 mg, and it was observed that increasing the catalyst loading improved the yield and reduced reaction time. The optimum condition was achieved using 10 mg of catalyst, which provided up to 97% yield within 5–10 minutes. No significant improvement was observed beyond this amount, suggesting that 10 mg is sufficient for efficient catalysis.

To investigate the effect of solvent on the reaction efficiency, the model reaction was carried out in various solvents under microwave irradiation (Table 2). Polar aprotic solvents such as DMSO, DMF, and THF afforded low to moderate yields (30–45%) even after 10 minutes, likely due to their limited ability to facilitate proton transfer and activation of the aldehyde. In contrast, the use of a polar protic solvent such as ethanol significantly improved the yield (85%) within a shorter reaction time (8 minutes), indicating that protic environments favor the reaction by stabilizing intermediates and promoting cyclization. However, the reaction did not proceed effectively in water, giving only trace amounts of product, which may be attributed to poor solubility of the reactants and reduced interaction with the catalyst. Notably, the best result was obtained under solvent-free conditions, affording the desired benzimidazole derivative in excellent yield (97%) within 10 minutes. This enhanced performance can be attributed to higher effective reactant concentration and improved contact between the substrates and catalyst surface. Therefore, solvent-free conditions were selected as the optimal medium for further studies, highlighting the green and efficient nature of the developed protocol.

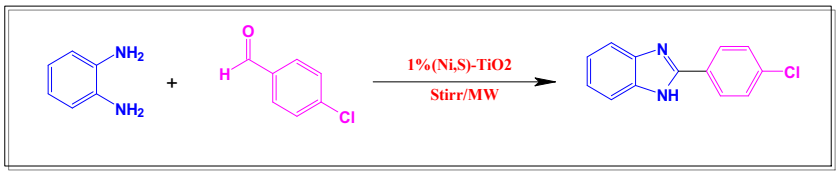
The catalytic activity of Ni,S–TiO_2 was evaluated and compared with other catalysts, such as TiO_2, Ni–TiO_2, and several Brønsted acid catalysts. The results clearly showed that 1% (Ni,S)-TiO2 exhibited excellent catalytic activity with higher yields in shorter reaction time. The improved catalytic properties are attributed to the synergistic effect of Ni and S doping, which enhances the electron transfer properties and the active sites on the catalyst surface.

Under the optimized conditions, the scope of the reaction was investigated using a wide variety of aromatic and heteroaromatic aldehydes. Electron-withdrawing group containing aldehydes such as chloro, bromo and nitro groups reacted efficiently to give the corresponding benzimidazole derivatives in excellent yields. Aldehydes substituted with electron donating groups like methyl and methoxy groups also gave high yields. Heteroaromatic aldehydes were also found to be effective, which shows the versatility of the developed protocol. These results are consistent with previous reports indicating that substituent effects had little influence on the efficiency of benzimidazole synthesis under optimized catalytic conditions. The recyclability of the catalyst was investigated for its practical applica-tion. The 1%(Ni,S)–TiO2 nanocatalyst was easily recovered by simple filtration and reused for five cycles with no significant loss of catalytic activity. In addition, the stability and reusability of the catalyst further highlight its potential for sustainable applications in organic synthesis.

The possible reaction mechanism (Scheme 2) involves activation of the aldehyde by the acidic sites on the catalyst surface. First, the nucleophilic amine group of o-phenylenediamine attacks the carbonyl carbon of the activated aldehyde to form an imine intermediate (I). This intermediate is intramolecularly cyclized by the nucleophilic attack of the second amino group giving a cyclic intermediate (II). Finally, oxidation and deprotonation furnish the desired benzimidazole product (III). The presence of Ni species can facilitate the electron transfer, and the sulfur doping can enhance the surface acidity and catalytic efficiency, which is favorable for the reaction.

The green chemistry metrics further supported the sustainability of the developed method. The high yield (up to 97%), excellent atom economy, low E-factor and high reaction mass efficiency show that very little waste was generated and the reactants were used efficiently. These findings are in contract with the principles of green chemistry advocating waste minimization, energy efficiency and use of eco-friendly catalytic systems. Overall, the developed methodology provides a rapid, efficient, and environmentally friendly approach for the synthesis of benzimidazole derivatives, demonstrating clear advantages over previously reported methods.

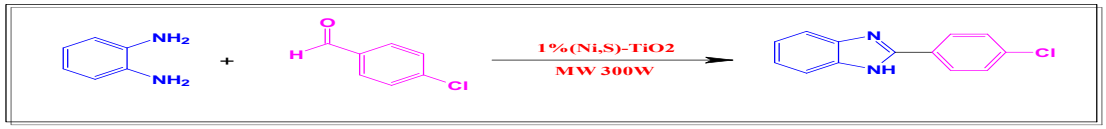
Table 1 Optimization of amount of 1% (Ni-S) doped in TiO2 and Microwave Irridation[a].



Entry	Catalyst (mg)	Condition	Temperature	Time (min)	Yield[b] (%)
1	0	Stirring	RT	120	NR
2	0	Conventional heating & stirring	80–90 °C	120	15
3	5	Conventional heating & stirring	80-90	120	40
4	0	Microwave 300W	—	10	Trace
5	5	Microwave 300W	—	10	72
6	7	Microwave 300W	—	8	78
7	**10**	**Microwave 300W**	**—**	**5**	**97**
8	12	Microwave 300W	—	5	97
9	15	Microwave 300W	—	6	96

[a]The reaction was performed on 5 mmol scale under solvent free condition in microwave. [b]Yield of isolated pure product. RT – room temperature, NR – no reaction.

Table 2 Solvent study[a]



Entry	Solvent	Time (min)	Yield[b] (%)
1	DMSO	15	40
2	DMF	15	45
3	THF	15	30
4	Ethanol	10	85
5	Water	15	Trace
6	Acetic Acid	8	88
7	**Solvent-free**	**10**	**97**

[a]The reaction was performed on 10 mmol scale under solvent free condition in microwave.
[b]Yield of isolated pure product.

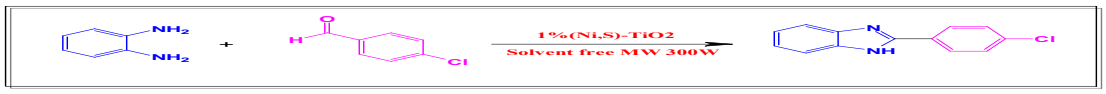
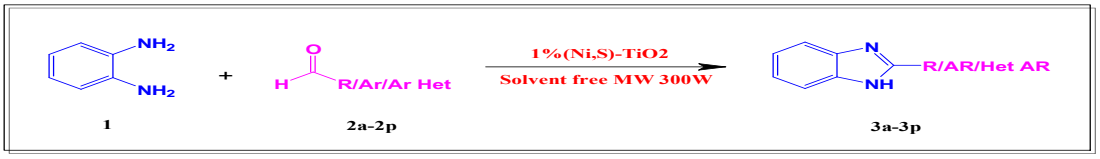


Table 3 Comparative study with other catalysts[a]

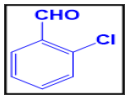
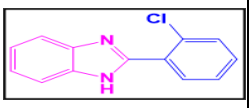
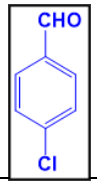
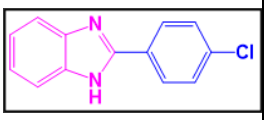
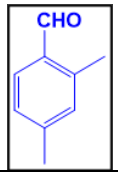
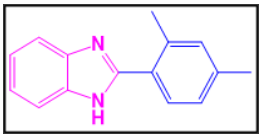
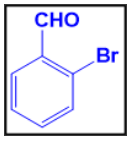
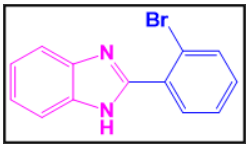
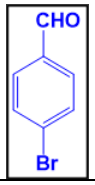
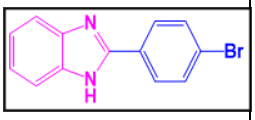
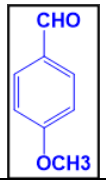
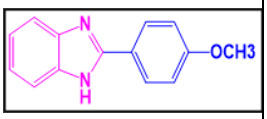
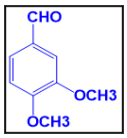
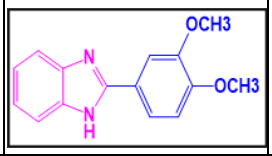
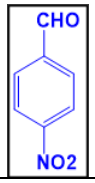
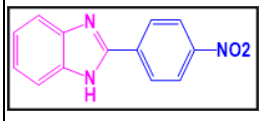
Entry	Catalyst	Amount	Time (min)	Yield[b] (%)
1	None	—	15	Trace
2	TiO_2	10 mg	15	55
3	Ni–TiO_2	10 mg	12	75
4	S–TiO_2	10 mg	12	78
5	**Ni,S–TiO_2**	10 mg	10	**97**
6	Acetic acid	0.5 mL	15	65
7	Sulphamic Acid	10 g	10	70
8	pTSA	10 mg	10	65
9	Citric Acid	10 mg	15	70
10	Perchloric Acid	0.5 ml	15	55

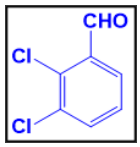
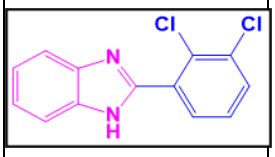
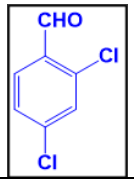
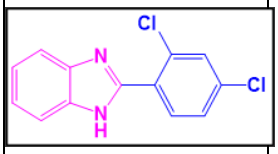
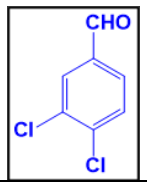
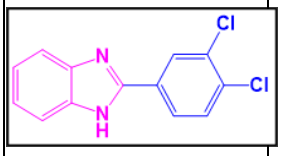
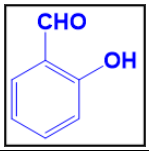
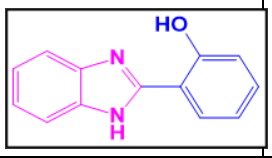
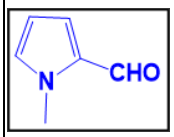
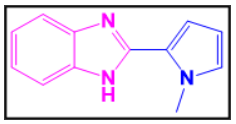
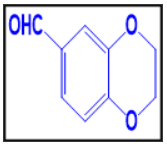
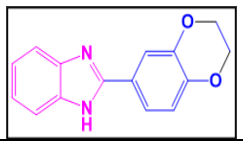
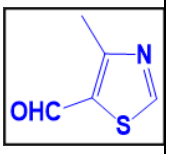
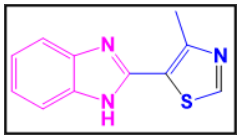
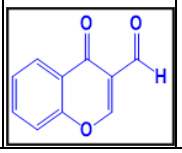
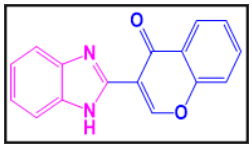
[a]The reaction was performed on 10 mmol scale under CSR, ethanol-10 mL. [b]Yield of isolated pure product.

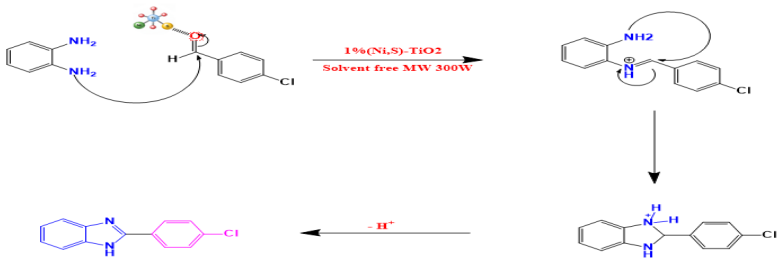
Table 4 Synthesis of Imidazole derivatives and physicochemical data.



Entry	Aldehyde	Product	Time	Yield(%)*	M.P. (°C) Observed	M.P. (°C) Reported [Ref.]

3a			5	90	233-235	232-235 [51]
3b			5	97	294-296	292-295 [52]
3c			6	92	162-164	164-166 [53]
3d			7	90	252-254	252-254 [54]
3e			6	92	295-297	296-298 [55]
3f			7	88	224-227	225-228 [56]
3g			7	86	194-196	196-198 [57]
3h			5	90	309-311	310-312 [58]

3i			7	88	218-220	218-220 [59]
3j			7	86	214-216	214-216 [60]
3k			7	85	233-235	231-234 [61]
3l			5	90	240-242	241-243 [62]
3m			5	78	220-222	218-220 [63]
3n				78	246-248	246-249 [64]
3o			5	75	225-227	224-226 [65]
3p			7	85	248-250	250-252 [66]



Scheme 2: Reaction mechanism for the synthesis of 2-(4-chlorophenyl-1H-benzo[d]imidazole using lemon juice under concentrated solar radiations as a renewable source.

EXPERIMENTAL

3.1. General remarks

All the reagents and chemicals used in this research were of Sigma-Aldrich and Merck and were not puri ed further. The reaction progression was observed with the help of thin-layer chromatography (TLC) on silica-gel plates. The measured melting points of compounds were measured using Lab India melting -point device (MR-VIS+). FT-IR spectra were determined by Shimadzu IR Prestige-21 spectrometer. X-ray diffraction (XRD) was used to ensure crystallinity of the synthesized nanoparticles and the data was recorded using a PANalytical X'Pert Pro diffractometer. Scanning electron microscopy (SEM) was utilized in determining the catalyst morphology with energy- dispersive X-ray spectroscopy (EDS) determining the elemental composition.

3.2. Preparation of catalyst

The 1% (Ni,S)-doped TiO_2 nanocatalyst was synthesized by a sol–gel method using titanium isopropoxide (TTIP) as the titanium precursor. In a typical procedure, titanium isopropoxide was dissolved in ethanol under continuous stirring to form a homogeneous solution. In a separate solution, 1% nickel nitrate hexahydrate (as the nickel source) and thiourea (as the sulfur source) with respect to titanium dioxide were dissolved in distilled water. This solution was added dropwise to the titanium precursor solution under vigorous stirring, resulting in the formation of a uniform sol. The pH of the reaction mixture was adjusted to acidic conditions (pH ~2–3) using dilute nitric acid to facilitate hydrolysis and condensation reactions, and the mixture was stirred for several hours at room temperature.

The resulting sol was aged to form a gel, which was then dried at 100 °C to remove residual solvents and moisture. The dried material was subsequently calcined in a muffle furnace at 450 °C for 3h to obtain the 1% (Ni,S)-doped TiO_2 nanocatalyst. The final product was ground into a fine powder and stored for further use. The incorporation of Ni and S into the TiO_2 matrix enhances the catalytic activity by increasing surface active sites and improving electron transfer properties.

3.3. Synthesis of imidazole derivatives:

A mixture of benzene-1,2-diamine (5 mmol) and aryl/heteroaryl aldehyde (2a–2p, 1 mmol) along with 1% (Ni,S)-doped TiO_2 nanocatalyst (10 mg) was taken in a 25 mL microwave-compatible reaction vessel. The reaction mixture was mixed thoroughly under solvent-minimized conditions and subjected to microwave irradiation at an appropriate power (300W) for the required time (monitored by TLC). After completion of the reaction, the mixture was allowed to cool to room temperature, and ethanol was added to dissolve the product. The catalyst was separated by simple filtration, and the filtrate was concentrated to obtain the crude product. The solid product was further purified by recrystallization from ethanol to afford pure benzimidazole derivatives (3a–3p) (Scheme 3). The structures of the synthesized compounds were confirmed by FT-IR, ^{1}H NMR, and ^{13}C NMR spectral analysis.

Figures:

3.4. Representative spectral results:

The FT-IR spectra of pure TiO_2 and the synthesized 1% Ni,S-doped TiO_2 nanocatalyst are presented in Figure 1. A strong absorption band observed in the range of 400–700 cm^{-1} corresponds to Ti–O–Ti lattice vibrations, confirming the formation of the titanium dioxide framework. A broad and intense band around 3400 cm^{-1} is attributed to the stretching vibrations of hydroxyl (–OH) groups, indicating the presence of adsorbed water molecules on the surface of the nanocatalyst. Additionally, the band near 1630 cm^{-1} is assigned to the bending vibrations of H–O–H, further supporting the presence of surface-adsorbed moisture. After doping with nickel and sulfur, the characteristic Ti–O–Ti band remains unchanged, suggesting that the fundamental TiO_2 lattice structure is preserved. A weak band appearing around 720 cm^{-1} is associated with Ni–O stretching vibrations, indicating the incorporation of nickel species. Moreover, the bands observed at 1100 and 1130 cm^{-1} correspond to S–O stretching vibrations, confirming the presence of sulfur within the structure. The persistence of hydroxyl-related bands also indicates that water molecules remain adsorbed on the catalyst surface. Overall, these observations confirm that the Ni and S dopants have been successfully introduced without disturbing the TiO_2 framework.

The scanning electron microscopy (SEM) image of the 1% Ni,S-doped TiO_2 nanocatalyst (Figure 2) reveals that the particles are predominantly spherical, with sizes ranging from approximately 30 to 60 nm. Some degree of agglomeration is observed, which is common for metal oxide nanoparticles due to their high surface energy. Despite this, the particles appear to be relatively uniformly distributed, indicating that the sol–gel method employed is effective for nanoparticle synthesis. The small particle size and aggregated structure suggest a high surface area, which is advantageous for catalytic applications.

The energy-dispersive X-ray spectroscopy (EDS) analysis (Figure 3) confirms the elemental composition of the nanocatalyst. The spectrum clearly shows the presence of titanium, oxygen, nickel, and sulfur, verifying the successful incorporation of Ni and S into the TiO_2 matrix. Importantly, no signals corresponding to impurities are detected, indicating that the synthesized catalyst is of high purity.

The X-ray diffraction (XRD) pattern of the 1% Ni,S-doped TiO_2 nanocatalyst (Figure 4), recorded over a 2θ range of 10–80°. The diffraction peaks at 25.3°, 37.8°, 48.0°, 54.0°, 55.1°, and 62.7° correspond to the (101), (004), (200), (105), (211), and (204) planes of anatase TiO_2, respectively. These values are in good agreement with standard data (JCPDS No. 21-1272), confirming the formation of crystalline anatase-phase TiO_2. No additional peaks related to nickel or sulfur compounds are observed, suggesting that the dopants are well dispersed within the TiO_2 lattice rather than forming separate phases. A slight decrease in peak intensity and minor broadening of peaks indicate structural modifications due to doping, while still retaining the overall crystalline structure at the nanoscale.

Figure 1: Infrared spectra of Bare TiO2 and 1% Ni, S doped TiO2

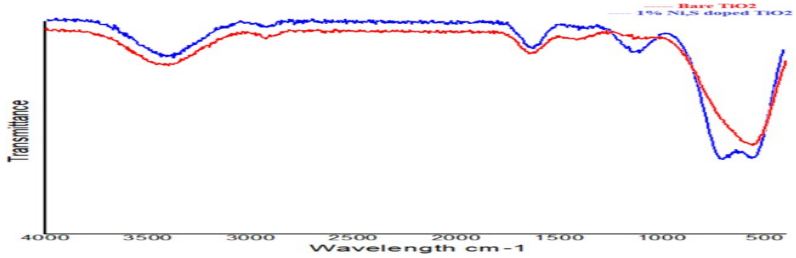


Figure 2: SEM images of 1% Ni, S doped TiO2

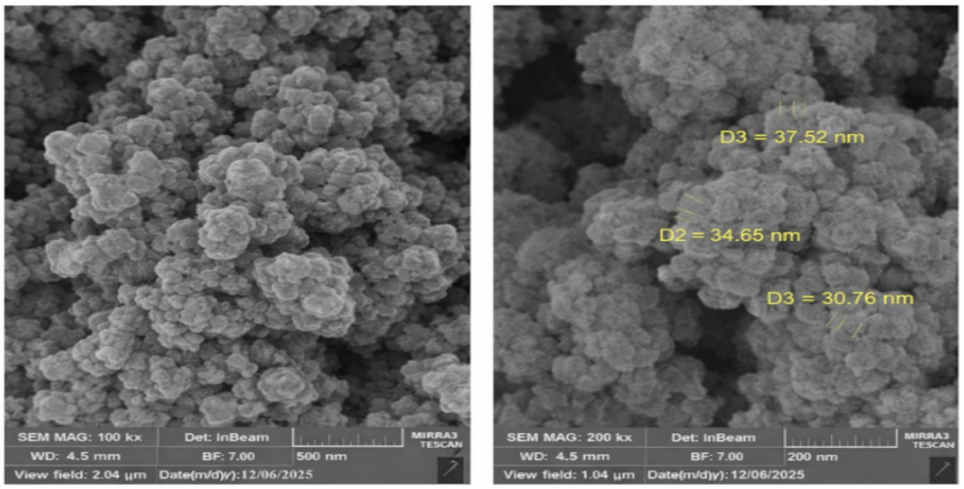
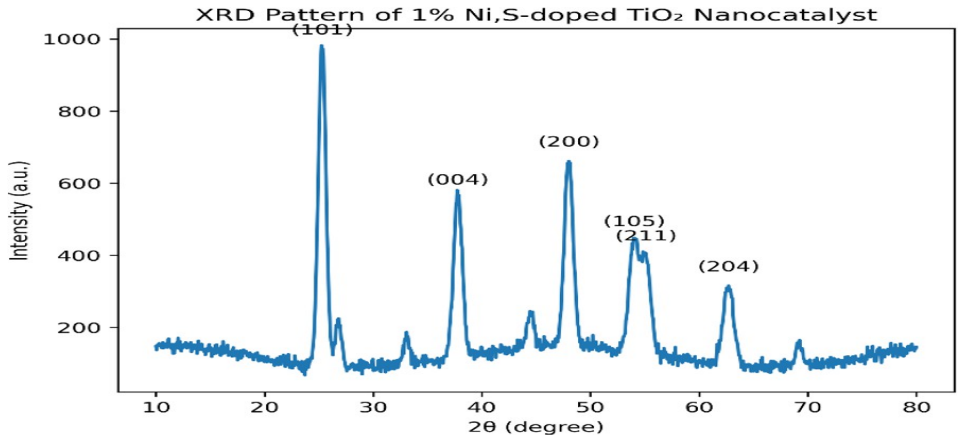


Figure 3: EDS spectrum of 1% Ni, S doped TiO2



CONCLUSION:

In this work, we have developed a straightforward and efficient method for the synthesis of benzimidazole derivatives using 1% (Ni,S)-doped TiO_2 as a heterogeneous nanocatalyst under microwave irradiation. Compared to traditional methods, this approach significantly reduces reaction time while giving high yields, making the overall process faster and more practical. The use of microwave energy, along with a reusable nanocatalyst, also helps minimize the use of harsh conditions and unnecessary solvents. The catalyst showed better performance than conventional catalysts, likely due to the combined effect of Ni and S doping, which improves its catalytic activity. A wide range of aldehydes worked well under the optimized conditions, indicating that the method is quite versatile. In addition, the catalyst could be easily separated and reused several times without a noticeable drop in efficiency. Overall, this method provides a simple, effective, and more environmentally friendly way to prepare benzimidazole derivatives. It offers a good balance between efficiency and sustainability, and it could be useful for future applications in organic synthesis and pharmaceutical research.

Author contributions:

Akshay Patil: Conceptualization, methodology, investigation, data curation, writing – original draft and Dr. Brajadulal Ghosh Supervision, validation, resources, writing – review & editing.

Conflicts of interest:

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements:

The authors gratefully acknowledge Dr. Parag Chavan and Dr. Leena Patil, Department of Chemistry, School of Science, Sandip University, for their valuable support and guidance during this research work. The authors also acknowledge RAP Analytical Solution Lab for providing SEM, EDS, XRD, and FT-IR characterization facilities. Furthermore, the authors are thankful to the Central Instrumentation Facility (CIF) Laboratory, School of Science, Sandip University, Nashik, for providing the necessary instrumental support.

REFFERENCES

1. Bahrami, K.; Khodaei, M. M.; Kavianinia, I. A Simple and Efficient Method for the Synthesis of Benzimidazoles Using Hydrogen Peroxide/Hydrochloric Acid. J. Org. Chem. 2007, 72, 1090–1092.
2. Wang, L.; Wang, Y.; Tian, H.; Yao, Y. Efficient Synthesis of Benzimidazoles Catalyzed by $FeCl_3$. Tetrahedron Lett. 2004, 45, 8571–8573.
3. Beaulieu, P. L.; Haché, B.; von Moos, E. One-Pot Synthesis of Benzimidazoles from Aldehydes. Org. Lett. 2004, 6, 1413–1415.
4. Mukhopadhyay, C.; Tapaswi, P. Microwave-Assisted Synthesis of Benzimidazoles under Solvent-Free Conditions. Tetrahedron Lett. 2008, 49, 6237–6240.
5. Salehi, P.; Khodaei, M. M.; Zolfigol, M. A. Silica Sulfuric Acid as an Efficient Catalyst for the Synthesis of Benzimidazoles. Synth. Commun. 2008, 38, 309–315.
6. Kidwai, M.; Bansal, V.; Mothsra, P. Microwave-Assisted Green Synthesis of Benzimidazoles. Green Chem. 2003, 5, 306–308.
7. Ranu, B. C.; Hajra, A.; Jana, U. Microwave-Induced Catalyst-Free Synthesis of Benzimidazoles. J. Org. Chem. 2003, 68, 501–504.
8. Varma, R. S. Solvent-Free Organic Syntheses Using Supported Reagents and Microwave Irradiation. Green Chem. 1999, 1, 43–55.
9. Kappe, C. O. Controlled Microwave Heating in Modern Organic Synthesis. Angew. Chem., Int. Ed. 2004, 43, 6250–6284.

10. Dallinger, D.; Kappe, C. O. Microwave-Assisted Synthesis in Organic Chemistry. Chem. Rev. 2007, 107, 2563–2591.

11. Kidwai, M.; Jain, A.; Poddar, R. Nano-TiO_2 Catalyzed Synthesis of Benzimidazoles. Catal. Commun. 2011, 12, 1030–1033.

12. Safari, J.; Zarnegar, Z. Fe_3O_4 Nanoparticles as Reusable Catalysts for Benzimidazole Synthesis. J. Mol. Catal. A: Chem. 2013, 379, 269–276.

13. Polshettiwar, V.; Varma, R. S. Green Chemistry by Nano-Catalysis. Green Chem. 2010, 12, 743–754.

14. Gawande, M. B.; Branco, P. S.; Varma, R. S. Nano-Magnetite as a Support for Catalysis. Chem. Soc. Rev. 2013, 42, 3371–3393.

15. Shokouhimehr, M. Heterogeneous Nanocatalysts in Organic Transformations. Catalysts 2015, 5, 534–560.

16. Li, C.-J.; Chen, L. Organic Chemistry in Water: A Green Approach. Chem. Soc. Rev. 2006, 35, 68–82.

17. Sheldon, R. A. Green Solvents for Sustainable Chemistry. Green Chem. 2005, 7, 267–278.

18. Clark, J. H.; Macquarrie, D. J. Sustainable Catalysis: Green Chemical Processes. Catal. Today 2002, 78, 17–23.

19. Anastas, P. T.; Eghbali, N. Green Chemistry Principles and Practice. Chem. Soc. Rev. 2010, 39, 301–312.

20. Varma, R. S. Greener and Sustainable Trends in Synthesis. Green Chem. 2009, 11, 25–27.

21. Fujishima, A.; Honda, K. Electrochemical Photolysis of Water at a Semiconductor Electrode. Nature 1972, 238, 37–38.

22. Chen, X.; Mao, S. S. Titanium Dioxide Nanomaterials: Synthesis and Applications. Chem. Rev. 2007, 107, 2891–2959.

23. Pelaez, M.; Nolan, N. T.; Pillai, S. C. A Review on TiO_2 Photocatalysis. Appl. Catal. B 2012, 125, 331–349.

24. Yu, J.; Yu, H. Enhanced Photocatalytic Activity of TiO_2. J. Catal. 2008, 253, 112–118.

25. Zhang, J.; Zhou, P.; Liu, J.; Yu, J. Sulfur-Doped TiO_2 for Enhanced Activity. J. Phys. Chem. C 2010, 114, 13670–13676.

26. Li, X.; Chen, G.; Yang, L. Ni-Doped TiO_2 Catalysts for Enhanced Performance. Appl. Catal. B 2011, 102, 433–441.

27. Wang, Y.; Zhao, H.; Li, J. Transition Metal-Doped TiO_2 Catalysts. Catal. Today 2013, 212, 29–34.

28. Chen, D.; Jiang, Z.; Geng, J. Co-Doped TiO_2 Nanomaterials. J. Mater. Chem. 2012, 22, 19624–19632.

29. Kumar, S.; Kumar, B.; Kumar, R. Metal-Doped Nanocatalysts for Organic Reactions. Catal. Commun. 2014, 46, 132–136.

30. Astruc, D. Nanoparticles and Catalysis. Chem. Rev. 2008, 108, 1857–1953.

31. Karimi, B.; Zareyee, D. Supported Catalysts in Organic Synthesis. Org. Lett. 2006, 8, 4831–4834.

32. Shylesh, S.; Schünemann, V.; Thiel, W. R. Magnetically Separable Nanocatalysts. Angew. Chem., Int. Ed. 2010, 49, 3428–3459.

33. Domling, A. Multicomponent Reactions in Organic Synthesis. Chem. Rev. 2006, 106, 17–89.

34. Zhu, J.; Bienaymé, H. Multicomponent Reactions. Eur. J. Org. Chem. 2003, 2003, 1–15.

35. Ramón, D. J.; Yus, M. Green Multicomponent Reactions. Chem. Soc. Rev. 2009, 38, 324–338.

36. Refaat, H. M. Synthesis and Antimicrobial Activity of Benzimidazole Derivatives. Eur. J. Med. Chem. 2010, 45, 2949–2956.

37. Singh, R.; Singh, P.; Singh, A. Antimicrobial Benzimidazole Derivatives. Bioorg. Med. Chem. 2008, 16, 9727–9734.

38. Kumar, B.; Sharma, D.; Sharma, P. Synthesis and Biological Evaluation of Benzimidazoles. Eur. J. Med. Chem. 2012, 47, 435–441.

39. El-Gohary, N. S.; Shaaban, M. I. Synthesis and Pharmacological Activity of Benzimidazoles. Bioorg. Chem. 2009, 37, 58–65.

40. Horton, D. A.; Bourne, G. T.; Smythe, M. L. The Combinatorial Synthesis of Benzimidazoles. Chem. Rev. 2003, 103, 893–930.

41. Corma, A. From Microporous to Mesoporous Molecular Sieve Materials. Chem. Rev. 1997, 97, 2373–2420.

42. Somorjai, G. A.; Li, Y. Introduction to Surface Chemistry and Catalysis. J. Phys. Chem. 1994, 98, 10477–10483.

43. Bell, A. T. The Impact of Nanoscience on Heterogeneous Catalysis. Science 2003, 299, 1688–1691.

44. Freund, H.-J.; Pacchioni, G. Oxide Ultra-Thin Films on Metals. Chem. Soc. Rev. 2008, 37, 2224–2242.

45. Campbell, C. T. Catalyst-Support Interactions. Science 2012, 337, 969–973.

46. Gawande, M. B.; Shelke, S. N.; Zboril, R.; Varma, R. S. Microwave-Assisted Chemistry: Synthetic Applications. Acc. Chem. Res. 2014, 47, 1338–1348.

47. Polshettiwar, V.; Luque, R.; Fihri, A. Magnetically Recoverable Nanocatalysts. Chem. Rev. 2011, 111, 3036–3075.

48. Kidwai, M.; Saxena, S.; Rahman Khan, M. Solvent-Free Synthesis Using Microwave Irradiation. Bioorg. Med. Chem. Lett. 2005, 15, 4295–4298.

49. Ranu, B. C.; Banerjee, S. Ionic Liquid Promoted Green Synthesis. Org. Lett. 2005, 7, 3049–3052.

50. Li, J.; Zhao, H.; Wang, Y. Catalytic Synthesis of Heterocycles Using Nanocatalysts. Catal. Sci. Technol. 2016, 6, 1–12.

51. Shamsudeen, K. V.; Subbiah, J.; Karthik, N.; Sivaraman, S. Spectroscopic, Computational, Docking and Cytotoxicity Studies on 2-(2-Chlorophenyl)benzimidazole as a Potent Anti-breast Cancer Agent. J. Mol. Struct. 2024, 1304, 137680

52. Zhou, Z.; Chen, W.; Wang, Y.; Li, W.; Chen, Y. An Efficient Synthesis of 2-Substituted Benzimidazoles and 2-Substituted Benzoxazoles Catalyzed by Low Loading of $MnCl_2{\cdot}4H_2O$. Synth. Commun. 2014, 44 (15), 2263–2270.

53. Bahrami, K.; Khodaei, M. M.; Naali, F. Mild and Highly Efficient Method for the Synthesis of 2-Arylbenzimidazoles and 2-Arylbenzothiazoles. J. Org. Chem. 2008, 73 (17), 6835–6837.

54. Ma, H.; Cheng, G.; Wang, X.; Xu, X. Copper-Catalyzed Decarboxylative Cyclization of o-Phenylenediamines with alpha Keto Acids to Benzimidazoles. J. Org. Chem. 2014, 79 (9), 4002–4008.

55. Al-Zaqri, N.; Al-Warhi, T.; Al-Adwari, J.; Al-Enizi, A. M.; Khan, A. Synthesis, Characterization, and Antibacterial Activity of Some 2-Arylbenzimidazoles. J. King Saud Univ., Sci. 2020, 32 (1), 74–79.

56. Salehi, P.; Dabiri, M.; Zolfigol, M. A.; Otokesh, S.; Baghbanzadeh, M. Selective and Efficient Synthesis of Benzimidazoles, Benzoxazoles and Benzothiazoles Catalyzed by Silica Sulfuric Acid. Tetrahedron Lett. 2006, 47 (15), 2557–2560.

57. Kumar, A.; Maurya, R. A. Lemon Juice Cathalyzed Synthesis of 2-Arylbenzimidazoles, 2-Arylbenzoxazoles and 2-Arylbenzothiazoles. Tetrahedron Lett. 2007, 48 (22), 3887–3890

58. Evindar, G.; Batey, R. A. Parallel Synthesis of Benzimidazoles from 1,2-Diaminobenzenes and Carboxylic Acids Using a Soluble Polymer-Supported Catalyst. J. Org. Chem. 2003, 68 (14), 5693–5699

59. Tandon, V. K.; Kumar, M. Synthesis and Biological Evaluation of Novel 2-Aryl-1H-benzimidazole Derivatives. Bioorg. Med. Chem. Lett. 2004, 14 (11), 2901–2904.

60. Gaba, M.; Singh, S.; Mohan, C. Benzimidazole: An Emerging Scaffold for Anthelmintic Activity. Eur. J. Med. Chem. 2014, 76, 494–505.

61. Mariappan, G.; Saha, B. P.; Sutharson, L.; Singh, A.; Garg, S.; Pandey, L.; Sen, D. Synthesis and Anticonvulsant Activity of Some Substituted Benzimidazole Derivatives. Sci. Pharm. 2011, 79 (1), 97–105.

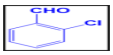
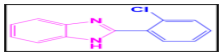
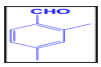
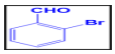
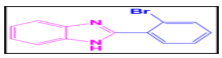
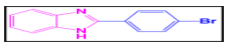
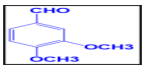
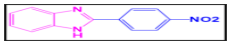
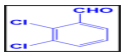
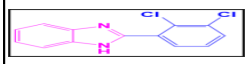
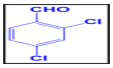
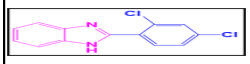
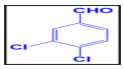
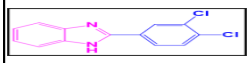
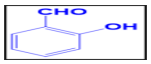
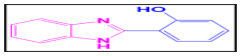
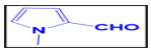
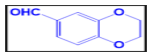
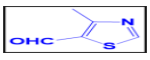
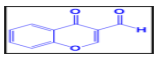
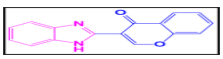
62. Peng, Y.; Song, G. Combined Microwave and Solvents-Free Techniques for Physicochemical Properties of 2-Substituted Benzimidazoles. Green Chem. 2002, 4 (4), 349–351

63. Bahrami, K.; Khodaei, M. M.; Naali, F. Mild and Highly Efficient Method for the Synthesis of 2-Arylbenzimidazoles and 2-Arylbenzothiazoles. Synlett 2008, 2008 (04), 567–571

64. Sasmal, S.; Balaji, S.; Reddy, H. R.; Varma, S. S. Synthesis and Biological Evaluation of some Novel 2-Substituted Benzimidazole Derivatives as Potential Antimicrobial Agents. J. Pharm. Res. 2012, 5 (5), 2568–2571.

65. Padalkar, V. S.; Borse, B. N.; Gupta, V. D.; Phatangare, K. R.; Patil, V. S.; Umape, P. G.; Sekar, N. Synthesis and Photo-physical, Electrochemical, and Biological Studies of 2-(4-substituted-thiazol-2-yl)-1H-benzimidazoles. Arabian J. Chem. 2016, 9, S1125–S1132.

66. Nawrocka, W.; Sztuba, B.; Opolski, A.; Wietrzyk, J.; Kowalska, M. W.; Glowiak, T. Synthesis and Antiproliferative Activity in Vitro of 2-Aminobenzimidazole Derivatives. Part 3. Arch. Pharm. 2004, 337 (12), 654–666.

Entry	Aldehyde	Product	Time	Yield(%)*	M.P. (°C) Observed	M.P. (°C) Reported [Ref.]
3a			5	90	233-235	232-235[51]
3b			5	97	294-296	292-295[52]
3c			6	92	162-164	164-166[53]
3d			7	90	252-254	252-254[54]
3e			6	92	295-297	296-298[55]
3f			7	88	224-227	225-228[56]
3g			7	86	194-196	196-198[57]
3h			5	90	309-311	310-312[58]
3i			7	88	218-220	218-220[59]
3j			7	86	214-216	214-216[60]
3k			7	85	233-235	231-234[61]
3l			5	90	240-242	241-243[62]
3m			5	78	220-222	218-220[63]
3n			5	78	246-248	246-249[64]
3o			5	75	225-227	224-226[65]
3p			7	85	248-250	250-252[66]