Heterocyclic Letters
Vol. 15| No.3|611-620|May-July|2025
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

NANO Gd_2O_3 IS AN EFFECTIVE CATALYST FOR THE SYNTHESIS OF BENZIMIDAZOLE DERIVATIVES UNDER MILD CONDITIONS

Sanjog G. Mumbaikar [a], Vishvanath D. Patil [b]*, Vaishnav D. Gharat [c] Tulshidas S. Waghmare [d], Suraj A. Patil [e]

Organic Chemistry Research Laboratory, Department Of Chemistry, C. K. Thakur A.C.S. College New Panvel, Raigad, Maharashtra, INDIA
vishvanathpatil148@gmail.com / mumbaikarsanjog@gmail.com

.

ABSTRACT:
Nano Gd_2O_3 catalyst was used to develop an efficient, green, and simple approach for synthesizing benzimidazole derivatives via the reaction of aldehyde with ortho phenyl diamine. This reusable Nano catalyst effectively catalysed the synthesis of benzimidazole derivatives. Chloroform solvent in reactions is used. It is environmentally benign, and multi-component. The reaction proceed with room temperature in extremely short periods of time. The catalyst and some chosen derivatives were characterized using a variety of techniques, including IR, NMR, XRD, SEM and TEM.

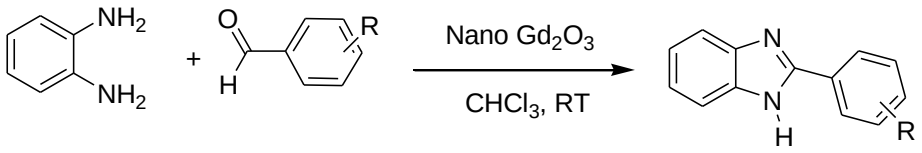
KEY WORDS: Benzimidazole, Gd_2O_3 , Mild condition.

INTRODUCTION:

There is a high demand for the creation of straightforward, effective, safe for the environment, and profitable chemical processes or techniques for commonly used organic molecules[I]. For the manufacture of numerous pharmaceutical compounds with anti-helmintic[II], anti-psychotic[III], and antifungal[IV] properties, benzoimidazoles are crucial pharmacophores. Because of benzimidazoles are biologically active and therefore significant chemical compounds for commence, a number of synthetic routes have been established to produce them. It involves the use of ammonium chloride[V], lithium bromide[VI], copper (II) hydroxide[VII], zirconyl (IV) nitrate[VIII], amberlite IR-120, and ultrasonic sound[IX], Under ultrasound irradiation, a new sodium iodide and ammonium molybdate co-catalytic system is also employed to synthesize 2-benzimidazoles using hydrogen peroxide[X]. Sulfanilic acid supported by polymers is employed as a heterogeneous catalyst in the synthesis of derivatives of benzimidazoles[XI]. Benzimidazoles were synthesized using ionic liquids, including [Bmim]PF6 under reflux[XII] and 3-methyl-1-(3-sulfopropyl)-imidazoliumtrifluoro acetate under ultra Sonication were employed to create benzimidazoles[XIII]. There are numerous procedures that use nanocatalysts to synthesize benzimidazoles. These include Nano-$Fe3O_4/O_2$[XIV]. Supported by SBA-15 Cobalt Nanocatalysts[XV], $Fe_3O_4@SiO_2$/collagen[XVI], On nanosilica, $FeCl_3$ is

supported[XVII], CuO nano-particles[XVIII] and Mixed metal oxide nanocrystals that are mesoporous[XIX]. However, all of these procedures have shortcomings, including the need for harsh reaction conditions, the use of costly, moisture-sensitive reagents, a challenging work-up process, and low yields.

Accordingly, the current study describes a straightforward, effective synthetic approach for the synthesis of 2-phenyl benzimidazoles using Nanocrystalline Gd_2O_3 as a nano-catalyst (Scheme).



R= H, Cl, NO_2, OH, OCH_3,etc.

I. EXPERIMENTAL:-

1. Materials and Methods

All of the necessary compounds were analytical grade (AR) and didn't require any additional purification. A Varian Mercury plus 500 MHz NMR spectrometer was used to record the synthesized benzoimidazole ^{1}HNMR spectra. Using Tetramethylsilane (TMS, δ=0) as an internal standard, the values of all the chemical shifts were expressed in terms of δ and expressed as parts per million. Every IR spectrum was captured using KBr pellets on a Perkin Elmer FT-IR spectrometer. Every synthetic benzoimidazole was recognized by matching its melting point data with reliable information found in the literature. A selection of benzoimidazoles spectrum data was acquired.

2. General procedure for synthesis of 2-phenyl benzimidazoles

Nano Gd_2O_3 (0.029 g, 0.08 mmol) was added to a solution of o-phenylenediamine (0.108 g, 1 mmol) and aromatic aldehyde (1 mmol) diluted in $CHCl_3$ (4 ml) to create a reaction mixture. At room temperature, the reaction mixture was magnetically agitated, and TLC was used to monitor the reaction's progress. It was diluted with $CHCl_3$ (3 x 5 ml) and filtered to separate the catalyst once the reaction was finished (as shown by TLC). The reduced pressure procedure was used to further concentrate all extracts after they had been dried over anhydrous Na_2SO_4. Column chromatography was used to further purify the crude product (with a 10:2 eluting solution consisting of pet ether and ethyl acetate and silica gel 60 to 120 grit).$CHCl_3$ was used to repeatedly wash and dry the isolated catalyst. There are other uses for it.

3. Synthesis and characterization of Nano crystalline Gd_2O_3

Gadolinium nitrate hexahydrate (0.45 gm.) was used as a source of metal ions in the synthesis of nano gadolinium oxide, and a predicted quantity of glycine (0.075 gm) and L-ascorbic acid (0.17gm) were added with the least amount of deionized water (5 ml) possible. After the surplus water transparent solution is removed, it is heated on a hot plate to 80 degrees Celsius to homogenize it and create a gel developed. After the water gel is removed, it is ingested, and for two to three seconds, brownish gasses are released. Ultimately, a cement-colored powder is created, which is then heated to 600 degrees Celsius for 240 minutes in a muffle furnace to eliminate carbonaceous material. The resulting fine Gd_2O_3 nanoparticles range in size from 18 nm to 35 nm.

II. Nanomaterial characterization:-

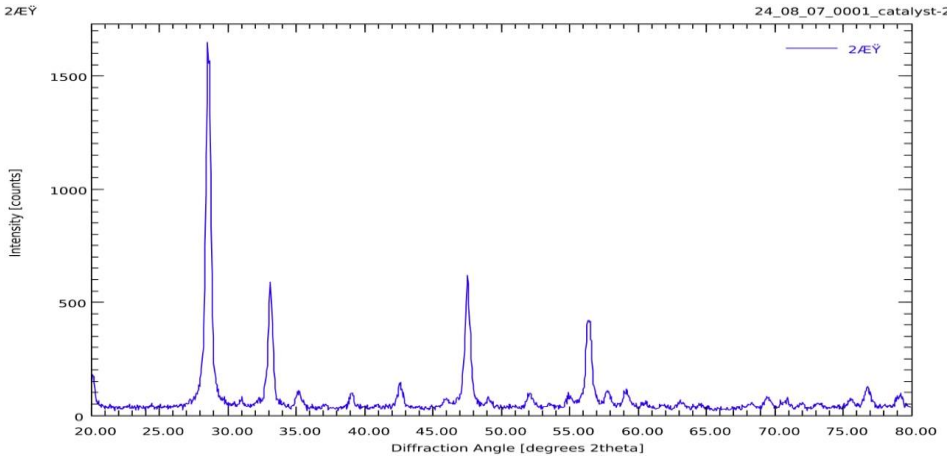
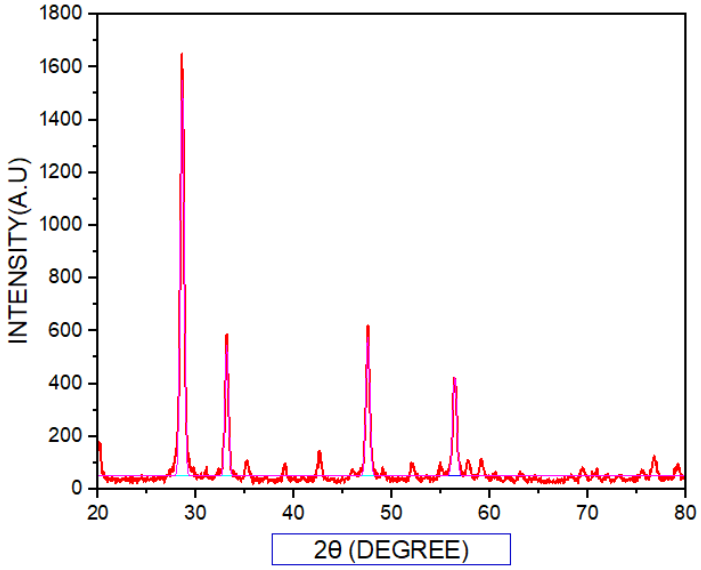


Fig.1 :XRD pattern of Nano Gd_2O_3



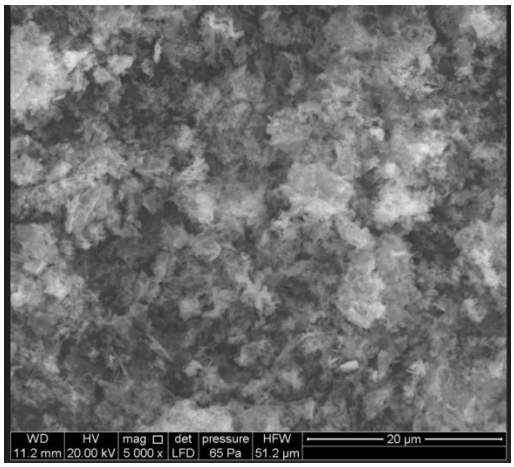


Fig.2:SEM Analysis of Nano Gd_2O_3.

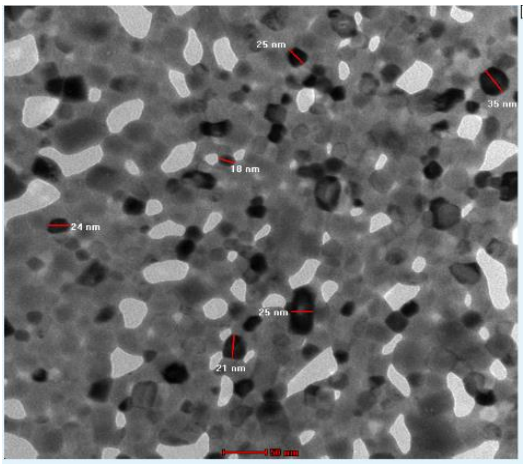


Fig.3:TEM Analysis of Nano Gd_2O_3

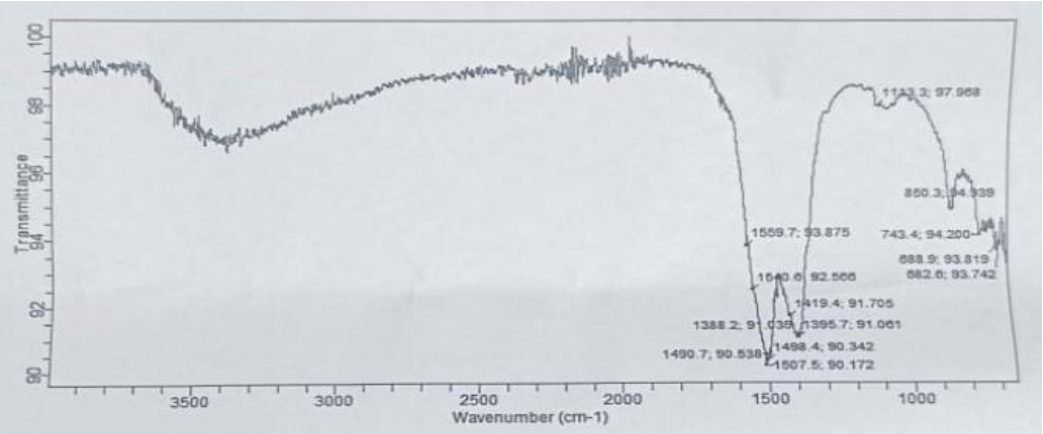


Fig.4: IR Analysis of Nano Gd_2O_3.

III. RESULT AND DISCUSSION:-

1.The study of synthesis of 2-phenyl-1H-benzimidazoles

The cyclocondensation between o-phenylenediamine (0.108 gm, 1 mmol) and benzaldehyde (0.101 ml, 1 mmol) was chosen as the model reaction for nano Gd_2O_3 (0.08 mmol) in order to determine the proper reaction conditions.

1a: Selection of Solvent

For the model reaction, a range of solvents, including polar and non-polar ones, were screened in order to choose the best one (Table 1, Entries 1 to 5). Nano Gd_2O_3 produced a discernible product yield in non-polar solvents, however the reaction time was lengthy (Table 1, Entries 1). Water did not react with any of the polar solvents (Table 1- Entry 5). When the reaction was conducted in the polar solvent CHCl3, yields increased significantly (82% and 96%, Table 1, Entry 2) at a short reaction time. Therefore, the best solvent for the model process involving nano Gd_2O_3 was determined to be $CHCl_3$

Table 1- Investigation of solvent effects for the synthesis of 2-phenyl-1H-benzimidazole (1a)*

Entry	Solvent	Nano Gd_2O_3	
		Time (min.)	Yield[c`] (%)
1	CH_2Cl_2	60	70
2	$CHCl_3$	20	96
3	CH_3CN	40	82
4	C_2H_5OH	20	85
5	H_2O	No reaction	No reaction

*Reaction conditions: o-phenylenediamine (1 mmol), benzaldehyde (1 mmol), solvent (4 ml) and catalyst (Nano Gd_2O_3) at r.t.
[cc`] Isolated Yield

1b: Selection of Catalytic loading amount

Similarly, catalytic activity of Nano Gd_2O_3 was studied with respect to its loading amount in reaction mixture (Table **2**).

Table **2**: Investigation of catalytic effect of Nano Gd_2O_3 on synthesis of 2-phenyl-1H-benzimidazoles (1a) *

Entry	Amount of Catalyst, (mmol)	Nano Gd_2O_3	
		Time (min.)	Yield[c'] (%)
1	0.01	40	70
2	0.02	35	72
3	0.04	30	75
4	0.06	20	78
5	0.08	20	96
6	0.1	20	96
7	0.2	20	96

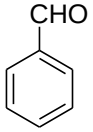
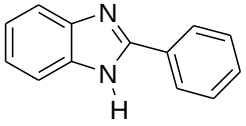
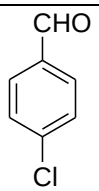
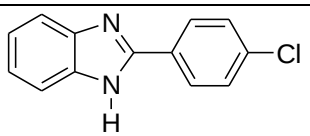
*Reaction conditions: o-phenylenediamine (1 mmol), benzaldehyde (1 mmol), solvent (4 ml) and catalyst (Nano Gd_2O_3) at r.t.
[cc'] Isolated Yield

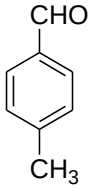
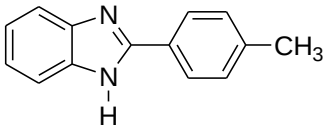
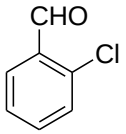
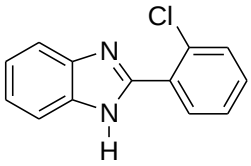
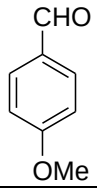
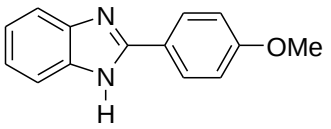
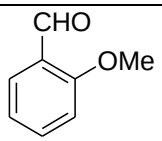
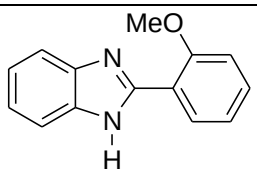
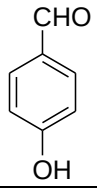
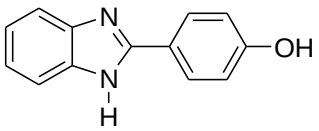
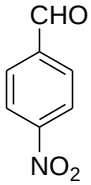
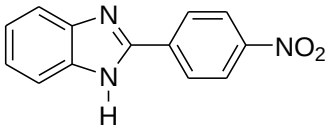
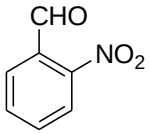
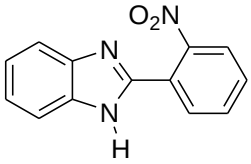
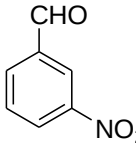
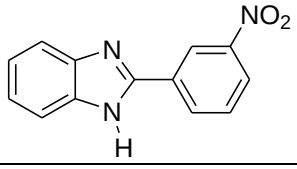
The effect of catalyst loading was studied by increasing its amount from 0.01mmol to 0.2 mmol. There was marginal increase in yield of product when amount of catalyst varied from 0.01 to 0.06 mmol (Table **2**, Entries 1 to 4). An excellent yield (96%) was observed in short reaction time when 0.08 mmol of Nano Gd_2O_3 catalyst was used. (Table **-2**, Entries 5, 6, 7).

1c Study of Scope of reaction

The effectiveness and general applicability of Nano Gd_2O_3 as a catalyst was further established by preparing different 2-phenyl benzimidazoles in presence of Nano Gd_2O_3 and the results were compared (Table 3).To assess efficacy and generality of Nano Gd_2O_3, o-phenylenediamine was reacted with various aromatic aldehydes under the optimized reaction conditions to furnish the corresponding products (Table 3). In this, the effect of electron-releasing and electron-withdrawing substituents on the reactivity of aromatic ring of aldehydes was studied.

Table-3: Synthesis of 2-phenyl benzimidazoles using Nano Gd_2O_3 catalysis*.

Entry	Aldehyde R a	Product 1(a-j)	Gd_2O_3(Nano)		M.P.(^{0}C)	M.P.(^{0}C)
			Time (min.)	Yield[c'] (%)	(Lit. Value)	(Actual)
1.			20	96	(292)[22]	290-291
2.			25	90	(292-294)[22]	291-293

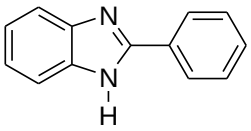
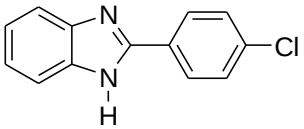
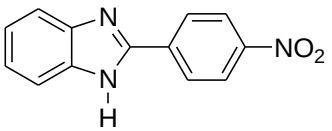
3.			20	88	(270)[22]	267-268
4.			20	85	(234)[19]	232-235
5.			20	86	(226)[19]	223-225
6.			25	80	(153)[21]	151-153
7.			20	85	(254-256)[23]	255-256
8.			15	96	(316)[22]	313-316
9.			15	96	(261-263)[20]	255-258
10.			15	93	(204-205)[20]	202-204

*Reaction conditions; Aromatic aldehyde (1 mmol), o-phenylenediamine (1.0 m mol), 0.08mmol of Nano Gd_2O_3 in $CHCl_3$ (4 mmol) at r.t.

[cc] Isolated Yield.

Nano Gd_2O_3 were found to be effective in synthesis of Benzimidazoles (Table 3). The electron donating substituents in aromatic aldehydes were found to increase the reaction time to some extent (Table 3, Entries 3, 5, 6). Otherwise, all aromatic aldehydes bearing either electron donating or withdrawing substituents were found to be reacting smoothly under the established reaction condition in terms of yield and reaction time (Table 3).

SPECTRAL DATA OF THE PRODUCTS OF SCHEME 1(TABLE-4)

Entry	Products	Spectral Data
1		2-Phenylbenzimidazole M.P. 290-291^{o}C I.R.(KBr) cm^{-1}:1500 & 1600 (Ar- C=C), 3300 (-NH),1358 Pyrrazole ring H^{1}NMR(500MHz,$CDCl_3$): δ=5.0 (s,1H,NH), 7.70-7.26(m ,4H,Ar-H),7.48-7.22(m, 5H, Ar-H) C^{13}NMR (500MHz,$CDCl_3$): δ= 129.11, 129.36, 130.38, 126.64, 123.17
2		2-(4-chlorophenyl)benzimidazole M.P. 291-293^{o}C I.R.(KBr) cm^{-1}:1500-1600 (Ar- C=C), 3000 (-NH), 1348 Pyrrazole ring H^{1}NMR(500MHz, $CDCl_3$): δ=5 (s,1H, NH),7.70-7.26(m,4H,Ar-H), 8.25-7.74(m,4H,Ar-H). C^{13}NMR(500MHz, $CDCl_3$): δ= 149.40, 129.47, 128, 124.29, 114.85.
3		2-(4-nitrophenyl)benzimidazole M.P. 313-316^{o}C I.R.(KBr) cm^{-1}:1500 (Ar- C=C), 3100 (-NH), 1410 Pyrazole ring H^{1}NMR(500MHz, $CDCl_3$):δ=5 (s,1H,NH), 7.70-7.26 (m,4H,Ar-H), 7.42-7.33(m,4H,Ar-H), C^{13}NMR(500MHz, $CDCl_3$): δ= 147.19, 132.53, 133.02, 126.76, 124.66, 124.74, 125.26, 123.60, 113.81.

IV. Proposed Mechanism (Fig. 5):-

The proposed mechanism which is consistent with literature[xxii] is shown in the fig.5. It involves activation of aromatic aldehyde by Nano Gd_2O_3. Ortho-phenylenediamines attacks the carbon of carbonyl group of activated aldehyde and forms intermediate (I) which undergo elimination of water molecule to form Imine intermediate (II). The formed intermediate is activated by Gd_2O_3 of Nano catalyst to form new intermediate (III) which undergo air oxidation to form product (IV).

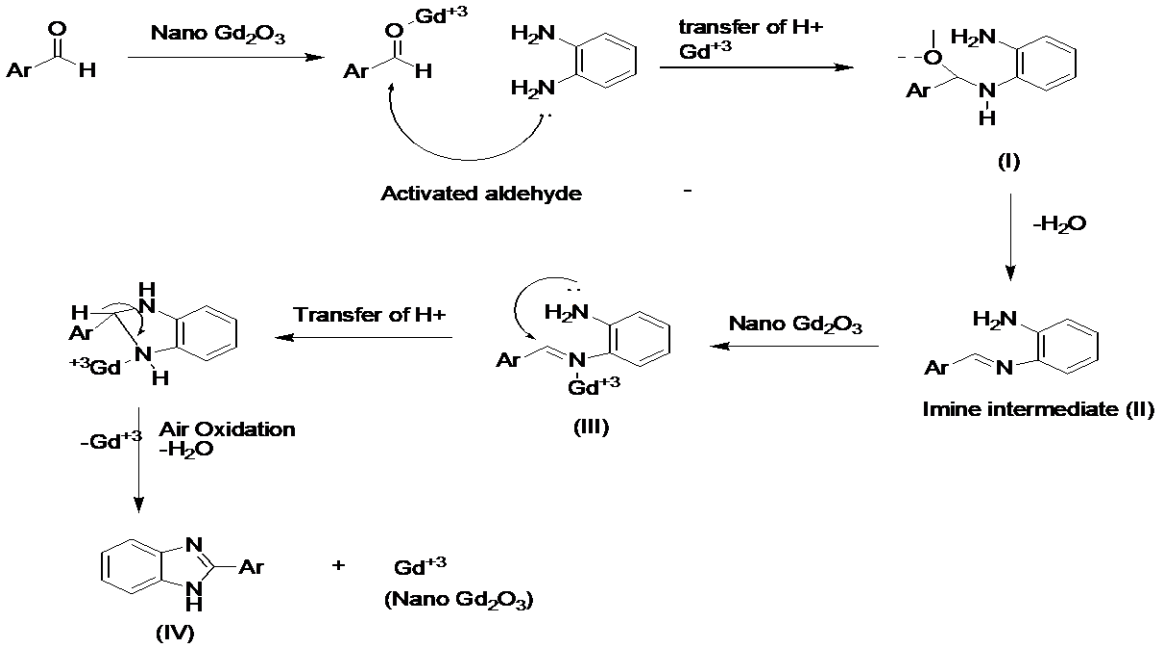


Fig. 5

1d:Study of reusability of Nano Gd_2O_3.

Nano Gd_2O_3 was found to be heterogeneous in reaction mixture during synthesis of 2-phenyl benzimidazoles. The easy recovery of catalyst encouraged to check its reusability in Scheme

1. It was observed that Nano Gd_2O_3 could afford corresponding products for at least three times without much loss in its catalytic activity as shown in Table 5.

Table 5 : Study of reusability of Nano Gd_2O_3 in synthesis of 2-phenyl-1H-benzimidazole (1a)*

Run No.	1	2	3
Time (min.)	20	25	30
Yield[c] (%)	96	93	90

*Reaction conditions; Aromatic aldehyde (1 mmol), o-phenylenediamine (1.0 mol), 0.08mmol of Nano Gd_2O_3 in $CHCl_3$ (4 mmol) at r.t. [c]Isolated Yield

V. CONCLUSION:

It was discovered that nano Gd_2O_3 was a reusable and heterogeneous catalyst for the production of 2-phenyl benzimidazole. Under the specified circumstances, it is more efficient.

VI. ACKNOWLEDGMENT

The authors would like to sincerely thank the Department of Chemistry at C.K. Thakur A.C.S. College in New Panvel, University of Mumbai, for their support and provision of the tools required to complete this work.

VII. REFERENCES:

I Patil, V. D., Patil, J., Rege, P., & Dere, G. (2010). *Mild and Efficient Synthesis of Benzimidazole Using Lead Peroxide Under Solvent-Free Conditions. Synthetic Communications, 41(1), 58–62 (2011).*

II Hazelton,J.C.; Iddon, B.; Suschitzky, H.; Woolley,L.H., Tetrahedron,1995,51,10771- 10794.

III Meisel, P.; Heidrich, H.J.; Jaensch, H.J.; Kretzschmar, E.; Henker, S.; Laban, G., DD patent 243284,1987; Chem. Abstr. 1987, 107, 217629.

IV Preston, P.N.,Chem.Rev.,1974, 74, 279-314.

V Nannapaneni, D. T.; Gupta, A. V.; Reddy, M.I.; Sarva, RCh., J. Young Pharm.,2010, 2(3), 273-279

VI Dekhane,D. V.; Pawar,S. S.;Gupta,S. V.; Shingare,M. S.;Thore,S. N.,Chinese Chemical Letters, 2010, Volume 21,Issue 5, 519-523

VII Murugulla A. C.; Zaied-A-Mosaa;,Donthabakthuni S.; Malayalamal,S., InternationalJournal of Organic Chemistry, 2013, 3, 243-250.

VIII Gorepatil, P. B.; Mane,Y. D. and Ingle,V. S.,Journal of Chemistry, 2013, Volume 2013, Article ID 108318,7 pages, http://dx.doi.org/10.1155/2013/108318.viiiNile, S.H.; Kumar,B.; Park,SeW.,Arabian Journal of Chemistry, 2015, Volume 8, Issue 5, 685–691

IX Bai,G-Yi;Lan,X-Wang; Chen,G-Feng; Liu,X-Fang; Li,T-Yu; Shi,LJuan,UltrasonicsSonochemistry, 2014, Volume 21, Issue 2, 520–526

X Tarpada,U. P.; Thummar, B. B.; Raval,D. K., Journal of Saudi Chemical Society,2016, 20, 530–535.

XI Bhavsar, A.; Makone, S.; Shirodkar, S., International Journal of Advanced Research in Science, Engineering and Technology, 2016, Vol. 3, Issue 8, 2485-2487.

XII Liu,W-Hua; Gao,S-Tao; Zhang,P-Hui; Zhou, X. and Wang,C., Asian Journal of Chemistry, 2014,Vol. 26, No. 7, 1980-1982.

XIII Zolfigol,M.A.; Khakyzadeh,V.; Moosavi-Zare, A. R.; Zare,A.; Arghavani-Hadi,P.; Mohammadi, Z.andBeyzavi, M.H.,S. Afr. J. Chem., 2012, 65, 280–285.

XIV Rajabi,F.; De,S.; Luque,R.,Catalysis Letters,2015, DOI 10.1007/s10562-015-1546-z.

XV Ghafuri,H.;Esmaili,E.; Talebi,M., ComptesRendusChimie, 2016,Volume 19, Issue 8, Pages 942–950

XVI Taher,M. A.; Karami, C.; Arabi,M. S.; Ahmadian,H.; Karami,Y.,Int. Nano Lett., 2016, 6, 85–90.

XVII Inamdar,S. M.; More,V. K.; Mandal,S. K.,Tetrahedron Letters, 2013, 54, 579–583

XVIII Bandyopadhyay,P.; Sathe,M.;Prasad,G.K.;Sharma,P.;Kaushik,M. P.,Journal of Molecular Catalysis A: Chemical,2011,Volume 341, Issues 1–2, 77–82 Sharghi, H.; Asemani, O. and Khalifeh, R.,SyntheticCommun., 2008, 38, 1128-1136

XIX Gadekar, L. S.; Arbad, B. R. and Lande, M. K.,Chin. Chem.Lett.,2010; 21,1053-1056

XX Perumal, S.; Mariappan, S.; Selvaraj, S.,Arkivoc, 2004, 8, 46-51

XXI Alloum, A. B.; Bougrin, K. and Soufiaoui, M.,TetrahedronLett., 2003, 44,

5935-5937.

XXII Khan, T.A.; Tasneem, P.; Choudhury, L.H.A.,Synth.Commun., 2009; 39, 2339-2346.

XXIII Zolfigol, M.A.; Khakyzadeh, V.; Moosavi-Zare, A.R.; Zare, A.; Arghavani-Hadi, P.; Mohammadi, Z. and Beyzavi, M.H., S. Afr. J. Chem., 2012, 65, 280–285

Received on May 11, 2025.