ChemTech

International Journal of ChemTech Research
CODEN (USA): IJCRGG, ISSN: 0974-4290, ISSN(Online):2455-9555
Vol.9, No.07 pp 366-377, 2016

Chromium doped nano In_2O_3 – An efficient catalyst for synthesis of benzoxazoles and 3, 4-dihydropyrimidin-2(1H)-ones

Vishvanath Patil*, Jyotsna Thakur, Nagesh Sutar

Orgnic Chemistry Research Laboratory, Department of Chemistry, C.K.Thakur A.C.S College, New Panvel, Raigad,Maharashtra, India

Abstract : Gel-combustion method was used to prepare nano In_2O_3 and nano In_2O_3 doped with Chromium. The prepared nano materials were characterized by powder XRD, Transmission electron microscopy (TEM) and standard BET technique. The effect of doping of Chromium upon catalytic activity of nano In_2O_3 was evaluated by using it in synthesis of important pharmacophores such as benzoxazoles and 3, 4-dihydropyrimidin-2(1H)-ones. Even if both nano materials were found to be useful in carrying out conversions, nano In_2O_3 doped with Chromium was found to be more effective as a catalyst in terms of reaction time and yields. The heterogeneous nature of nano materials in reaction medium made its recycling possible making overall process cost effective.

Keywords : Gel-combustion method, doped, chromium, catalytic activity, pharmacophores, effective, heterogeneous nature, recycling, cost effective.

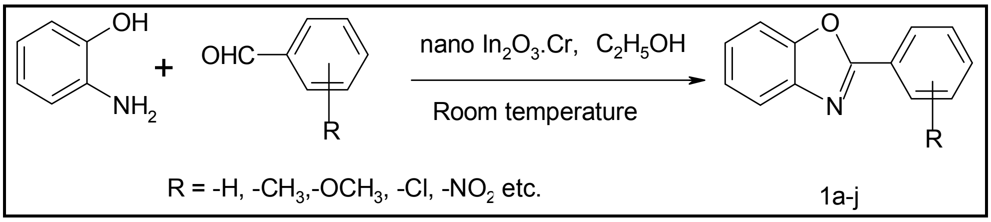
1. Introduction

In recent years, Nanoscience has emerged as an upcoming field for research and has been playing an important role in overall development process[1,2]. Nano materials are found to be useful in various fields of applications including catalysis[3,4,5]. Nanocrystalline metal oxides are found to be efficient as catalyst in various organic syntheses due to their high surface area to volume ratio and large number of coordination sites. Moreover, by using nano crystalline metal oxides it is possible to frame environment friendly, high yield giving organic synthesis[6,7,8]. The literature survey shows that biologically active organic compounds such as benzoxazoles have been synthesized using nano-sized metal oxides[9]. The literature survey shows that chromium is possessing catalytic properties [10] which encouraged to dope Chromium in nano In_2O_3.

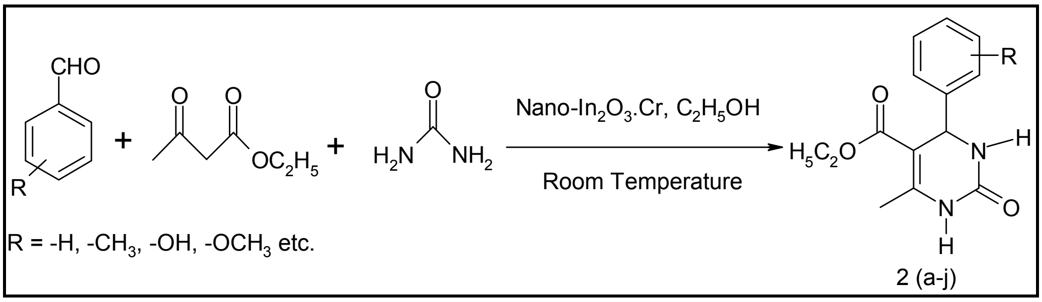
Benzoxazoles constitutes an important class of natural as well as synthetic heterocyclic compounds. Some benzoxazole derivatives exhibit biological properties such as antitumour, antiviral and antimicrobial properties[11]. Due to this, benzoxazoles are considered as important pharmacophores. Several methods have been reported in the literature for the synthesisof benoxazoles. These includes coupling of 2-aminophenols with carboxylic acids in presence of strong acids as catalyst[12] or microwaves as a source of energy.[13] The second method involves oxidative cyclization of phenolic Schiff'bases obtained from the condensation of 2-amino phenols and aldehydes in presence of various oxidants such as DDQ[14] ,$Mn(OAc)_3$[15] , $PhI(Oac)_2$[16] ,$Th^+.ClO_4^-$[17] , $BaMnO_4$[18] , NiO_2.[19] Some synthetic protocols involve use of different Lewis acids such as $FeCl_3$, $CeCl_3$ as catalysts.[20] The nucleophilic addition & metal-free *ortho*-C–H functionalization are few more pathways to synthesize these important pharmacophores[21]. Even if these protocols are effective in carrying out desired conversions, some of these protocols suffer from one or other disadvantages such as vigorous reaction condition conditions, prolonged reaction time, low yields, use of expensive toxic chemicals etc. Therefore, a search for mild and still more effective protocols for synthesis of benzoxazoles is continued.

Similarly, It is observed that 3, 4-dihydropyrimidin-2(1H)-ones constitutes a class of organic compounds which posses therapeutic and pharmacological properties such as anti-tumor, anti-inflammatory, anti-viral and anti-malarial activities.[22] These compounds also serve as calcium channel blockers and neuropeptides Y (NPY) antagonists.[23] Apart from original reaction condition various new reaction conditions have been introduced for the classical Biginelli reaction which includes use of solvent free conditions, microwave and ultrasound irradiation etc.[24-29] Some of these synthesis are performed in presence of Lewis acid catalysts such as $BF_3.Oet_2$, $InBr_3$, $LaCl_3.H_2O$, $Yb(Otf)_3$, $CuCl_2$ etc.[30-34] These protocols suffer from one or other drawbacks such as requirement of sophisticated apparatus, sensitive and costly reagents which are difficult to handle, long reaction time, low yields etc. So search for still more convenient synthetic pathways for the classical as well as Biginelli like reactions is continued.

The present study deals with preparation of nano In_2O_3 doped with Cr using Gel-combustion method which possess several advantages such as simplicity and cost effectiveness [35]. The synthesized nano material is used effectively in synthesis of biologically active organic compounds such as benzoxazoles (Scheme 1) and 3, 4-dihydropyrimidin-2(1H)-ones (Scheme 2). Further, the obtained data is also compared with data when same Schemes were performed with nano In_2O_3 as catalyst.



Scheme 1



Scheme 2

2. Experimental

2.1 Materials and Methods

All necessary chemicals were AR grade and used without further purification. The reactions were monitored by thin-layer chromatography (TLC) using 0.25 mm E-Merck Silica Gel 60F254 percoated plates and were observed with U.V. light. ^{1}HNMR spectra of synthesized compounds were recorded on 400 MHz Varian FT-NMR spectrometer. The values of all the chemical shifts were expressed in terms of δ with reference to Tetramethylsilane (TMS, δ=0) as an internal standard and expressed as ppm. All IR spectra were recorded on Perkin Elmer FT-IR spectrometer as KBr pellets. Melting points were determined by open capillary method and used without correction.

2.2 Typical procedure for synthesis of Benzoxazoles using nano In_2O_3 and nano In_2O_3 doped with Cr as catalyst.

A reaction mixture prepared by mixing 2-aminophenol (1.0 mmol), aromatic aldehyde (1.0 mmol) dissolved in ethyl alcohol (3.0 ml) with nano catalyst (0.08 mmol) was stirred magnetically at room temperature. After completion of reaction as indicated by TLC, the catalyst was removed through filtration and product was extracted in Ethyl acetate. The solvent was evaporated and obtained product was further purified by using column chromatography using Silica gel (Size- 60 to 120 mesh) and system of Pet ether and Ethyl acetate (10:4). The identity of products was established by comparison of melting point and spectral data with those reported in the literature. The separated catalyst was washed with Ethyl acetate and reused for two more batches.

2.2a Spectral data of selected Benzoxazole derivatives

Entry (1a) 2-Phenylbenzoxazole (White solid crystals)

^{1}HNMR (400MHz, $CDCl_3$) δ= 8.30-8.25 (m, 2H, Ar-H), 7.83 (t, J=7.7Hz, 1H, Ar-H), 7.61-7.49 (m, 4H, Ar-H), 7.37-7.32 (m, 2H, Ar-H). IR (KBr): 1050, 1248, 1452, 1614, 2976 cm^{-1}

2.3 Typical procedure for synthesis of 3, 4-dihydropyrimidin-2(1H)-ones

A reaction mixture was prepared by dissolving aromatic aldehyde (1.0 mmol), ethyl acetoacetate (1.0 mmol) and urea (1.0 mmol) in C_2H_5OH (3.5 ml) followed by addition of nano catalyst (0.1mmol). The reaction mixture was stirred magnetically at room temperature and progress of reaction mixture was studied by using TLC. After the completion of reaction as indicated by TLC, the reaction mixture was filtered and catalyst was separated and washed thoroughly with ethyl acetate and reused for the next round of same set of reaction. The catalyst was found to be active to form corresponding product with considerable yield for at least three rounds. The remaining content of reaction mixture was dried over anhydrous Na_2SO_4 and further concentrated under reduced pressure to get crude product. The purification of product was done using hot ethyl alcohol.

2.3a Spectral data for selected 5-unsubstituted 3, 4-dihydropyrimidinones.

Entry 2a - 5-Ethoxycarbonyl-4-phenyl-6-methyl-3, 4-dihydropyrimidin-2(1H)-one

IR (KBr): 1092, 1225, 1650, 1705, 1728, 3120, 3242 cm^{-1}

^{1}H NMR (400MHz, DMSO-d_6): δ= 1.12 (t, 3H, J=7.2Hz), 2.28 (s,3H), 3.97 (q, 2H, J=7.2Hz), 5.12(d, 1H, J=3.2Hz), 7.22-7.32 (m, 5Hz, Ar-H), 7.75 (s,1H, NH), 9.20(s,1H,NH)

3. Results and Discussion

3.1 Characterization of nano In_2O_3 and nano In_2O_3 doped with Cr

We prepared nano In_2O_3 and nano In_2O_3 doped with Cr using Gel-combustion method. The prepared nano materials were successfully used to synthesize various benzoxazoles and 3, 4-dihydropyrimidin-2(1H)-ones. Further, catalytic activity of both materials was evaluated by comparing respective data for synthesis. X-ray diffraction (XRD) pattern of nano In_2O_3 is shown in Fig.1

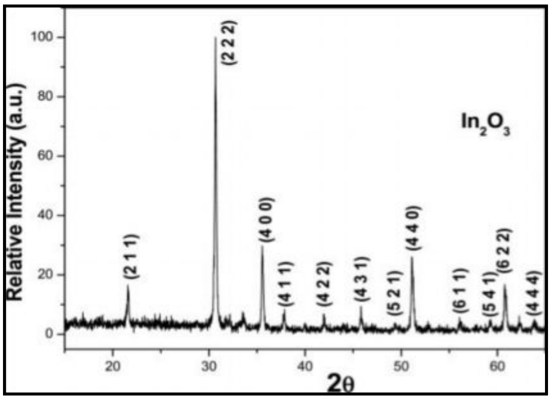


Fig.1 XRD pattern of nano In_2O_3

The powder XRD pattern of nano In_2O_3 proved single-phasic nature of the material. All diffraction peaks were in agreement with JCPDS card no. 06-0416. The crystallite size, as calculated by using Scherrer's equation was found to be 48 nm. The specific surface area was found to be 47.55 m^2 /g. TEM image of nano In_2O_3 (Fig.2) showed presence of chains of irregular shaped nano particles.

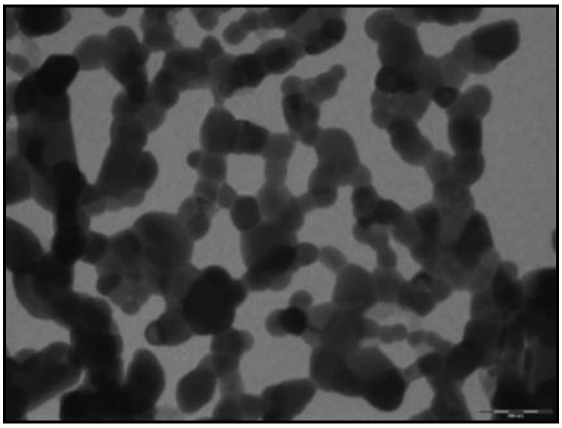


Fig.2 TEM image of nano In_2O_3

Similarly, powder XRD of nano In_2O_3 doped with Cr (Fig.3) showed single-phasic nature of the material and all diffraction peaks were in agreement with the JCPDS card no. 06-0416.

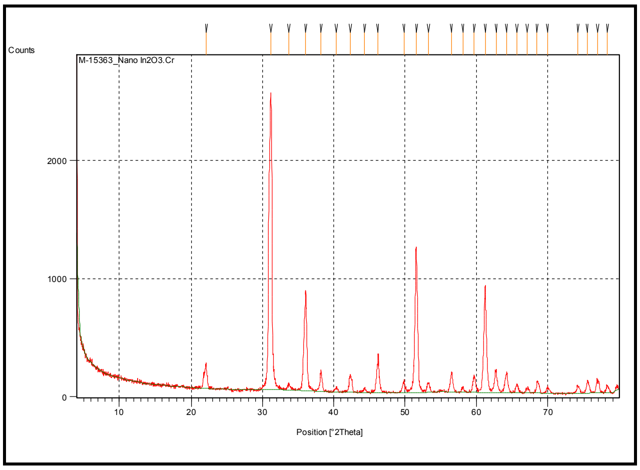


Fig.3 XRD pattern of nano In_2O_3 doped with Cr.

The crystallite size was found to be 22.4 nm as calculated by using Scherrer's equation. The specific surface area was found to be 75.6 m^2 /g. Thus, nano In_2O_3 doped with Cr was found to have large surface area as compare to that of nano In_2O_3.

3.2 Study of synthesis of benzoxazoles using nano In_2O_3 and nano In_2O_3 doped with Cr

The prepared nano materials were used to synthesize benzoxazole derivatives. Accordingly, reaction between o-aminophenol (0.109 gm, 1.0 mmol) and benzaldehyde (1.0 mmol) to form 2-phenyl benzoxazole was selected as model reaction and performed in presence of both nano In_2O_3 and nano In_2O_3 doped with Cr.

A suitable solvent was selected by performing model reaction in a series of solvents with increasing polarity as shown in Table 1.

Table1.Investigation of solvent effects for the synthesis of 2-pheny benzox- azole (1a) using nano In_2O_3 and nano In_2O_3 doped with Cr at room temperature

Entry	Solvent	Nano-In_2O_3		Nano-In_2O_3.Cr	
		Time (min.)	Yield[c] (%)	Time (min.)	Yield[c'] (%)
1	CH_2Cl_2	60	76	40	88
2	$CHCl_3$	55	77	35	90
3	CH_3CN	50	79	25	81
4	C_2H_5OH	45	86	10	93
5	H_2O	No reaction	No reaction	No reaction	No reaction

[cc']Isolated Yields

Thus, a maximum yield of product was obtained when model reactions were performed in C_2H_5OH as a polar solvent. Similarly, amount of catalyst to be added was determined by performing model reactions in presence of increasing amount of catalyst as shown in Table 2.

Table 2.Investigation of catalytic effect of nano In_2O_3 and nano In_2O_3 doped with Cr on synthesis of 2-phenyl benzoxazole (1a) in C_2H_5OH at room temperature

Entry	Amount of Catalyst (mmol)	Nano-In_2O_3		Nano-In_2O_3.Cr	
		Time (min.)	Yield[c] (%)	Time (min.)	Yield[c'] (%)
1	0.02	55	79	35	83
2	0.04	52	83	30	85
3	0.06	50	85	25	86
4	0.08	48	86	10	93
5	0.1	45	86	10	93
6	0.2	45	86	10	93

[cc']Isolated Yields

The maximum yield was obtained when 0.1 mmol of nano In_2O_3 and 0.08 mmol of nano In_2O_3.Cr were used. To study the general applicability of the Scheme 1, different aromatic aldehydes containing either electron-donating or electron withdrawing substituents were made to react with o-aminophenol. All reactions proceeded smoothly and gave corresponding benzoxazole derivatives in good to excellent yield without any side product (Table 3).

Table 3. Synthesis of benzoxazole derivatives using nano In_2O_3 and nano In_2O_3 doped with Cr separately in C_2H_5OH at room temperature

Entry	R[a]	Product[b] 1(a-j)	Nano In_2O_3		Nano In_2O_3.Cr		M.P.(°C) Observed (Literature Value)
			Time (min.)	Yield[c] (%)	Time (min.)	Yield[c'] (%)	
1	-H	1a	45	86	10	93	102 (101)[36]
2	4-CH_3	1b	50	82	20	88	113 (113-114)[36]
3	4-Cl	1c	40	84	15	93	146 (147)[36]
4	4-NO_2	1d	45	85	10	95	267 (266-268)[36]
5	4-OCH_3	1e	55	83	20	87	103 (101)[36]
6	2-NO_2	1f	50	81	15	90	102 (104-105)[40]
7	4-CF_3	1g	35	85	10	94	144 (143-145)[37]

8	2-CH_3	1h	55	80	25	85	66 (63-66)[38]
9	2-OH	1i	38	82	25	86	86-88 (87)[39]
10	2-NH_2	1j	35	79	22	88	102-103 (106-108)[41]

[a]Aldehydes(1.0mmol) were reacted with o-aminophenol (1.0mmol) in presence of nano-In_2O_3 and nano-In_2O_3.Cr in C_2H_5OH as catalyst

[b]All products were identified by comparing their spectral data and melting points with similar data from literature

[cc’]Isolated Yields

In Scheme 1, as the catalysts were found to be heterogeneous in reaction mixture they were removed by filtration and washed with ethyl acetate. The recovered catalysts were found to be effective in carrying out conversions for two more cycles (Table 4).

Table 4 Study of reusability of heterogeneous nano catalysts

Entry	**Run**	**Nano-In_2O_3**		**Nano-In_2O_3.Cr**	
		Time (min.)	**Yield[c] (%)**	**Time (min.)**	**Yield[c’] (%)**
1	1	45	86	10	93
2	2	48	81	15	90
3	3	55	75	25	88

[cc’]Isolated Yields

Under the established reaction condition, different aromatic aldehydes reacted smoothly. Aromatic aldehydes bearing electron withdrawing substituents gave maximum yield in short reaction time (Table 3, Entries 3, 4, 6, 7) as compare to those with electron donating substituents (Table 3, Entries 2, 5, 8, 9, 10). Both nano-In_2O_3 and nano-In_2O_3 doped with Cr were found to be effective catalysts in synthesis of benzoxazoles. When data of catalytic activity of both nano-In_2O_3 and nano-In_2O_3 doped with Cr was compared, it was observed that nano In_2O_3 doped with Cr could catalyze the conversions more effectively in terms of both yields and reaction time. There was considerable decrease in reaction time with enhancement in yield when nano In_2O_3 doped with Cr was used as catalyst (Table 3, Entries 1 a-j).

3.3 Study of synthesis of 3, 4-dihydropyrimidin-2(1H)-ones using nano In_2O_3 and nano In_2O_3 doped with Cr

The suitable reaction conditions were established by selecting condensation between benzaldehyde, ethylacetoacetate and urea as model reaction. The model reaction was performed in presence of both nano In_2O_3 and nano In_2O_3 doped with Cr. When model reaction was performed in polar and non-polar solvents, it was observed that maximum yield of corresponding product was obtained in short reaction time when reaction was performed in C_2H_5OH, a polar solvent (Table 5. Entry 4)

Table 5.Investigation of solvent effects for the synthesis of 5-Ethoxycarbonyl -6-methyl-4-phenyl-3, 4-dihydropyrimidin-2(1H)-one (1b) at room temperature

Entry	**Solvent**	**Nano-In_2O_3**		**Nano-In_2O_3.Cr**	
		Time (min.)	**Yield[c] (%)**	**Time (min.)**	**Yield[c’] (%)**
1	CH_2Cl_2	75	45	60	48
2	$CHCl_3$	70	43	68	49
3	CH_3CN	60	55	50	61
4	C_2H_5OH	32	91	20	96
5	H_2O	NR	NR	NR	NR

[cc’]Isolated Yields

Similarly, catalytic activity of both nano In_2O_3 and nano In_2O_3 doped with Cr was studied with respect to loading amount in reaction mixture (Table 6)

Table 6.Investigation of catalytic effect of nano In_2O_3 and nano In_2O_3.Cr on synthesis of 5-Ethoxycarbonyl-6-methyl-4-phenyl-3, 4-dihydropyrimidin-2(1H)-one (1b)

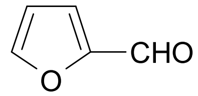
Entry	Amount of Catalyst (mmol)	Nano-In_2O_3		Nano-In_2O_3.Cr	
		Time (min.)	Yield[c] (%)	Time (min.)	Yield [c'] (%)
1	0.02	60	46	45	49
2	0.04	58	48	41	53
3	0.06	55	48	42	60
4	0.08	50	49	40	62
5	0.1	32	91	20	96
6	0.2	32	91	19	96

[cc']Isolated Yields

Thus, both nano In_2O_3 and nano In_2O_3 doped with Cr were effective in small amount that is 0.1mmol (Table 6, Entry 5). Even if the amount of catalyst was increased to 0.2 mmol hardly any improvement in terms of yield and reaction time was observed.

The effectiveness of both catalysts was further studied by performing Scheme 2 in presence of nano In_2O_3 and nano In_2O_3 doped with Cr separately and the results were compared (Table 7).

Table 7 Synthesis of 3, 4-dihydropyrimidin-2(1H)-ones using nano In_2O_3 and nano In_2O_3 doped with Cr separately in C_2H_5OH at room temperature

Entry	R[a]	Product[b] 2(a-j)	Nano In_2O_3		Nano In_2O_3.Cr		M.P.(°C) Observed (Literature)
			Time (min.)	Yield[c] (%)	Time (min.)	Yield[c'] (%)	
1	-H	2a	32	91	20	96	205 (206-208)[42a]
2	4-CH_3	2b	35	92	25	95	168-169 (169-171)[44]
3	4-OCH_3	2c	28	89	20	93	203 (202-204)[42d]
4	4-Cl	2d	25	88	15	92	216 (213-215)[42d]
5	2-Cl	2e	30	87	20	90	221-223 (222-224)[43]
6	4-NO_2	2f	32	85	18	89	210-211 (211-213)[42b]
7	3-NO_2	2g	30	88	20	91	228-230 (229-231)[42d]
8	2-NO_2	2h	28	90	20	91	220-222 (221)[42c]
9	4-OH	2i	30	84	22	88	231 (230-232)[42d]
10		2j	28	86	20	89	205-207 (206-208)[42e]

[a]Aldehydes(1.0mmol) were reacted with ethylacetoacetate (1.0mmol) & urea(1.0mmol)in presence of Nano-In_2O_3 and Nano-In_2O_3.Cr in C_2H_5OH as catalyst

[b]All products were identified by comparing their spectral data and melting points with data from literature

[cc']Isolated Yields

Study of recyclability of nano In_2O_3 and nano In_2O_3 doped with Cr

Both catalysts were found to be heterogeneous in reaction mixtures during synthesis. Moreover, it was easy to recover catalysts from reaction mixtures which encouraged checking their reusability. It was observed that catalysts could afford corresponding products for at least three times without much loss in catalytic activity as shown in Table 8.

Table 8 Study of reusability of heterogeneous nano catalysts

Entry	Run	Nano-In_2O_3		Nano-In_2O_3.Cr	
		Time (min.)	Yield^c (%)	Time (min.)	Yield$^{c'}$ (%)
1	1	32	91	20	96
2	2	40	87	25	91
3	3	48	84	35	89

$^{cc'}$Isolated Yields

During synthesis of 3, 4-dihydropyrimidinones also, nano In_2O_3 doped with Cr was found to be more effective in carrying out conversions in terms of reaction time and yields (Table 7, Entries 2a-j) as compare to that of nano- In_2O_3. The nature of substituents was found to have hardly any effect upon reactivity of aromatic aldehydes under the present reaction condition (Table 7, Entries 2a-j).

4. Conclusion

In conclusion, we could successfully prepare nano-In_2O_3 and nano-In_2O_3 doped with Cr using Gel-combustion method. Both nano materials were found to be quite effective as catalyst in synthesize of benzoxazoles and 3, 4-dihydropyrimidin-2(1H)-ones. It was observed that nano-In_2O_3 doped with Cr was found to be more efficient one. The presence of Cr which itself is good catalyst must be responsible for the high efficiency of the material as catalyst. The high catalytic activity of nano In_2O_3 doped with Cr could be further attributed to small crystallite size (22.4 nm), large specific surface area (75.6 m^2 /g). Moreover, it was required in minimum amount (0.08 mmol) as compare to nano-In_2O_3 (0.1 mmol) in synthesis of benzoxazoles. During recycling also, its catalytic activity was found to be more sustainable as compare to that of nano-In_2O_3. The advantages of the present protocol include the ease of preparation of nano catalysts, reusability and heterogeneous nature of nano catalysts, mild reaction conditions, easy work up and overall convenient nature of the process.

Acknowledgement

The authors are thankful to the Principal, C. K. Thakur A.C.S. College, New Panvel, Maharashtra, India for kind support to this work.

References

1. (a) Vishvanath DP, Jyotsna ST, Shramesha M, Medha G, Aarti J. Synthesis and Characterization of Nanocrystalline In_2O_3 and Its Efficacy as a Catalyst for the One Pot Synthesis of Amidoalkyl Naphthols. Synthesis and Reactivity in Inorganic, metal-organic and non metal chemistry, 2013, 43; 471-478.
   (b) Hariprasad S, Susheela Bai G, Santhoshkumar J, Madhu CH, Sravani D. Greensynthesis of Copper Nanoparticles by Arevalanata Leaves Extract and their Anti Microbial Activites. International Journal of ChemTech Research , 2016, 9: 98-105
   (c) Singh S ,Vanaja J, Raghunathan VS and Balasubramanian K. Process Optimization for the Synthesis of Nanocrystalline and Anhydrous Lanthanide Fluoride. International Journal of ChemTech Research, 2014-2015, 7: 1537-1543.
2. (a) Rodger P., Nanoscience and Technology, a collection of reweaves from Nature journals,World Scientific, Singapore, 2009.
   (b) Saha S, Ramesh R. Nanotechnology for Controlled Drug Delivery System. International Journal of PharmTech Research, 2014-2015, 7: 616-628.

(c) Amalthi P, Vijaya JJ, Kennedy LJ, Bououdina M. A Comparative study on the synthesis of Co-doped manganese ferrite [Mn(1-x) CoxFe2O4 (x = 0.0, 0.1, 0.2, 0.3, 0.4, 0.5)] nanoparticles via microwave assisted and conventional combustion method. International Journal of ChemTech Research, 2014-2015, 7: 1237-1246.

3. Seyed MV, Shima GR and Saeed B. Application of nano SnO_2 as a green and recyclable catalyst for the synthesis of 2-aryl or alkylbenzoxazole derivatives under ambient temperature. J. Chem. Sci. 2014, 126(3):579–585
4. (a) Pnea V and Bond GC., Catalysis by Metals and Alloys (Amsterdam: Elsever) 1995, Vol.95.
   (b) Ganeshan S ,Dhanalakshmi R ,Vijayalakshmi R. Synthesis and Characterization of LiCoO2 by Sol gel method. International Journal of ChemTech Research, 2014-2015, 7: 1085-1089.
5. Bond GC. Heterogenous catalysis: Principles and Applications (Oxford: Oxford Science Publications, Clarendon press) 1987.
6. Vutukuri PR, Akkilagunta V, Kokkirala S, Kokulapati RR. Nano Indium Oxide as aRecyclable Catalyst for C−S Cross-Coupling of Thiols with Aryl Halides under Ligand Free conditions. Org.Lett. 2009, 11:1697-1700.
7. (a) Sadjadi S, Rasouli S. An efficient synthesis of imidazo[1,2-a]azine using nanocrystallinealumina powder. Int. J. Nano. Dim., 2011, 1:177-186.
   (b) Abishek S , Elathiraiyan S , Deepa E , Helen Annal Therese. Green synthesis of silver nanoparticles using Alternanthera dentata and its anti-bacterial activities. International Journal of ChemTech Research, 2014-2015, 7: 780-785.
8. Laxmikantam M, Mahendar K, Bhargava S. One-pot, three-component synthesis ofhighly substituted pyridines and 1,4-dihydropyridines by using nanocrystalline magnesium oxide. J. Chem. Sci. 2010, 122:63-69.
9. (a) Saha P, Ali MA, Punniyamurthy T. Ligand-Free Copper(II) Oxide Nanoparticles Catalyzed Synthesis of Substituted Benzoxazoles. Organic Syntheses, 2012, 398–405
   (b) Banerjee S, Payra S, Saha A, Sereda G. ZnO nanoparticles: a Green efficient catalyst for the room temperature synthesis of biologically active 2-aryl-1,3- benzothiazole and 1,3-benzoxazole derivatives. Tetrahedron Letters,2014, 5515–5520.
   (c) Teimouri A, Chermahini AN, Salavati H, Ghorbanian L. An efficient and one-pot synthesis of benzimidazoles, benzoxazoles, benzothiazoles and quinoxalines catalyzed via nano-solid acid. Journal of Molecular Catalysis A: Chemical , 2013, 373:38-45
10. (a) Ali I, Hassan A, Shabaan S, El-Nasser K. Synthesis and characterization of composite catalysts Cr/ZSM-5 and their effects toward photocatalytic degradation of p-nitrophenol. Arabian Journal of Chemistry, 2013, http://dx.doi.org/10.1016/j. arabjc.2013.07.042.
   (b) Ryashentseva MA, Afanas'yeva YuA, Abramovich VB, Minachev KhM. Synthesis of thiophen from butane-butylene fractions and hydrogen sulphide on oxide catalysts containing chromium. Petroleum Chemistry U.S.S.R. 1975, 15(2):118-124.
   (c) Zhang Z, Zhao Z(Kent). Production of 5-hydroxymethylfurfural from glucose catalyzed by hydroxyapatite supported chromium chloride. Bioresource Technology, February, 2011, 102(4):3970–3972.
   (d) Michorczyk P, Ogonowski J, Zeńczak K. Activity of chromium oxide deposited on different silica supports in the dehydrogenation of propane with CO_2 – A comparative study. Journal of Molecular Catalysis A: Chemical, 2011, 349(1-2):1-12.
11. (a) Heravi MM, Sadjadi S, Oskooie HA, Shoar RH and Bamoharram FF.One-Pot Synthesis of 2-Arylbenzoxazoles Promoted by Heteropolyacids. Journal of the Chinese Chemical Society, 2008, 55:890-895
   (b) Sato Y, Yamada M, Yoshida S, Soneda T, Ishikawa M, Nizato T, Suzuki K, Konno F. Benzoxazole Derivatives as Novel 5-HT_3 Receptor Partial Agonists in the Gut. J. Med.Chem. 1998, 41:3015-3021.
   (c) Sato S, Kajiura T, Noguchi M, Takehana K, Kobayashi T, Tsuji T. AJI9561, a new cytotoxic benzoxazole derivative produced by *Streptomyces* sp. J. Antibiot. 2001,54:102-104.
12. (a) Terashima M, Ishii M, Kanaoka Y. A Facile Synthesis of 2-Substituted Benzoxazoles. Synthesis, 1982, 6:484-485.
   (b) Patil VD, Patil KP. Synthesis of Benzimidazole and Benzoxazole Derivatives Catalyzedby Nickel Acetate as Organometallic Catalyst. International Journal of ChemTech Research, 2015, 8: 457-465.

13. (a) Bourgrin K, Loupy A, Soufiaoui M. Trois nouvelles voies de synthèse des dérivés 1,3-azoliques sous micro-ondes. Tetrahedron, 1998, 54:8055-8064.

    (b) Pottorf RS, Chadha NK, Katkevics M, Ozola V, Suna E, Ghane H, Regberg T,Player MR. Parallel synthesis of benzoxazoles via microwave-assisted dielectric heating. Tetrahedron Lett., 2003, 44:175-178.
14. (a) Chang J, Zhao K, Pan S. Synthesis of 2-arylbenzoxazoles via DDQ promoted oxidative cyclization of phenolic Schiff bases—a solution-phase strategy for library synthesis.Tetrahedron Lett. 2002, 43:951-954.

    (b) Manish KG, Sonal, Neeraj KS, Priyanka, Jha KK. Pharmacological Profile and Pharmaceutical Importance of Substituted Benzoxazoles: A Comprehensive Review. International Journal of ChemTech Research, 2012, 4: 640-650.
15. Varma RS, Kumar D. Manganese triacetate oxidation of phenolic schiffs bases: Synthesis of 2-arylbenzoxazoles. J. Heterocycl. Chem. 1998, 35:1539-1540.
16. Varma RS, Saini RK, Prakash O. Hypervalent iodine oxidation of phenolic schiff'sbases: Synthesis of 2-arylbenzoxazoles. Tetrahedron Lett.1997, 38:2621-2622.
17. Park KH, Jun K, Shin SR, Oh SW. 2-Arylbenzoxazoles from phenolic schiff's bases by thianthrene cation radical. Tetrahedron Lett.1996, 37: 8869-8870.
18. Srivastava RG, Venkataramani PS. Barium Manganate Oxidation in OrganicSynthesis: Part III: Oxidation of Schiff'S Bases to Benzimidazoles Benzoxazoles and Benzthiazoles. Synth.Commun. 1988, 18:1537-1544.
19. Nakagawa K,Onoue H, Sugita J. Oxidation with nickel peroxide. iv. the preparation of benzoxazoles from schiff's bases. Chem. Pharm. Bull.1964, 12:1135-38
20. (a) Cao Ke, Yong Qiang TU & Zhang FuMin. Synthesis of substituted benzoxazoles by the iron(III)-catalyzed aerobic oxidation process. SCIENCE CHINA, 2010, 53(1):130–134.

    (b) Zhu X, Wei Y. An efficient synthesis of 2-substituted benzoxazoles using cerium(III) chloride/sodium iodide as catalyst. Heterocyclic Communications, 10/2012, 18(4).DOI: 10.1515/hc-2012-0054
21. (a) Nicolai A Aksenov, Alexander V Aksenov, Oleg N Nadein, Dmitrii A Aksenov,Alexander N Smirnov and Michael Rubin. One-pot synthesis of benzoxazoles *via* the metal-free *ortho*-C–H functionalization of phenols with nitroalkanes. RSC Adv., 2015, 5:71620-71626.

    (b) Alexander V Aksenov, Alexander N. Smirnov, Nicolai A Aksenov, Asiyat S Bijieva, Inna V Aksenova and Michael Rubin. Benzimidazoles and benzoxazoles*via* the nucleophilic addition of anilines to nitroalkanes. Org. Biomol. Chem., 2015,13: 4289-4295
22. (a) Focher F, Ubiali D, Pregnolato M, Zhi C, Gambino J, Wright GE and Spadari S. Novel Nonsubstrate Inhibitors of Human Thymidine Phosphorylase, a Potential Target for Tumor-Dependent Angiogenesis. J. Med. Chem., 2000, 43: 2601-2607.

    (b) Kappe CO.4-Aryldihydropyrimidines via the Biginelli Condensation: Aza- Analogsof Nifedipine-Type Calcium Channel Modulators. Molecules, 1998,3:1-9.

    (c) Ravnyak GC, Kimball SD, Beyer B, Cucinatta G, Dimarco JD, Gougouta J, Hedberg A, Malley M, McCarthy JP, Zhang RA, Morreland S.CalciumEntry Blockers and Activators: Conformational and Structural Determinants of Dihydropyrimidine Calcium Channel Modulators. J. Med.Chem, 1995,38:119-129.
23. Pendergast W, Dickerson SH, Johnson JV, Dev IK, Ferone R, Duch DS and Smith GK. Benzoquinazoline inhibitors of thymidylate synthase: Enzyme inhibitory activity and cytotoxity of some sulfonamidobenzoylglutamate and related derivatives. J.Med. Chem., 1993, 36:3464-3471.
24. (a) Stadler A, Kappe CO. Microwave-mediated Biginelli reactions revisited. On the nature of rate and yield enhancements, *J. Chem. Soc. Perkin. Trans.,*2000,2: 136-1368.

    (b) Patil PA , Bhole RP, Chikhale RV, Bhusari KP. Synthesis of 3,4-Dihydropyrimidine-2(1H)-one Derivatives using Microwave for their Biological screening. International Journal of ChemTech Research, 2009, 1: 373-384.
25. Al-Mousawi SM, El-Apasery MA and Elnagdi MH. Enaminones in Heterocyclic Synthesis: A Novel Route to Tetrahydropyrimidines, Dihydropyridines, Triacylbenzenes and Naphthofurans under Microwave Irradiation. Molecules, 2010,15:58-67.
26. (a) Desai B, Dallinger D and Kappe CO. Microwave-assisted solution phasesynthesis of dihydropyrimidine C5 amides and esters. Tetrahedron, 2006, 62:4651-4644.

(b) Patel A , PashaTY ,Modi A. Synthesis and Biological Evaluation of 4-Aryl substituted -2- (5-carboxylicacid-1, 6-dihydro)-2-thiophenylethylene-6-oxopyrimidine as Protein Tyrosine Phosphatase (PTP-1B) Inhibitors. International Journal of PharmTech Research, 2015, 8: 136-143.

27. Yadav JS, Reddy BVS, Reddy KB, Raj KS and Prasad AR.Ultrasound- accelerated synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones with ceric ammonium nitrate. J. Chem. Soc.Perkin. Tran., 2001, I:1939-1941.
28. Azizian J, Mohammadi AA, Karimi AR and Mohammadizadeh MR. $KAl(SO_4)_2\cdot 12H_2O$ supported on silica gel as a novel heterogeneous system catalyzed biginelli reaction: One-pot synthesis of di-hydropyrimidinones under solvent-free conditions. App. Cat. A: Gen., 2006 , 300:85-88.
29. Hong M, Cai CJ. Three-component one-pot synthesis of pyrimidinone derivatives in fluorous media: Ytterbium bis(perfluorooctanesulfonyl)imide complex catalyzed Biginelli-type reaction. Heterocy. Chem., 2009, 46:1430-1432.
30. Fu N-Y, Yuan Y-F, Cao Z, Wang S-W, Wang J-T and Peppe C. Indium(III) bromide-catalyzed preparation of dihydropyrimidinones: improved protocol conditions for the Biginelli reaction. Tetrahedron, 2002,58:4801-4807.
31. Hu EH, Sidler DR and Dolling U-H.Unprecedented Catalytic Three Component One-PotCondensation Reaction: An Efficient Synthesis of 5-Alkoxycarbonyl- 4-aryl-3,4- dihydropyrimidin-2(1H)-ones. J. Org. Chem., 1998, 63:3454-3457.
32. Lu J, Bai Y, Wang Z, Yang B and Ma H.One-pot synthesis of 3,4- dihydropyrimidin-2(1H)-ones using lanthanum chloride as a catalyst. Tetrahedron Lett., 2000, 41:9075-9078.
33. Ma Y, Qian C, Wang L and Yang M.'Lanthanide Triflate Catalyzed Biginelli Reaction. One-Pot Synthesis of Dihydropyrimidinones under Solvent-Free Conditions; J. Org. Chem., 2000, 65:3864-3868.
34. Mirza-Aghayan M, Moradi A, Bolourtchian M and Boukheroub R. Cheap and Efficient Protocol for the Synthesis of Tetrahydroquinazolinone, Dihydropyrimidinone, and Pyrimidinone Derivatives. Syn. Commun., 2009, 40:8-20.
35. (a) Patil KC, Aruna ST, Ekambaram SA. Combustion synthesis, Curr. Open.Solid state Mater. Sci., 1997, 2:158-165.

    (b) Tyagi AK, Chavan SV, Purohit RD. Visit to the fascinating world of nano-ceramic powders via solution-combustion. *Ind. J. Pure Appl. Phys.*, 2006, 44:113-118.

    (c) Bedekar V, Chavan SV, Tyagi AK. Highly sinter-active nanocrystalline RE_2O_3 (RE = Gd, Eu, Dy) by a combustion process, and role of oxidant-to-fuel ratio in preparing their different crystallographic modifications. *J. Mater. Res.,* 2007, 22:587-594.
36. Varma RS, Saini RK, Prakash O. Hypervalent iodine oxidation of phenolic schiff's bases: Synthesis of 2-arylbenzoxazoles. Tetrahedron Lett., 1997, 38:2621-2622.
37. Lewis JC, Wiedemann SH, Bergman RG, Ellman JA. Arylation of Heterocycles via Rhodium-Catalyzed C−H Bond Functionalization. *Org. Lett.*, 2004, 6(1):35-38.
38. Ravikumar K, Satyanarayana PVV, Srinivasa Reddy B. *Direct and practical synthesis of 2-Arylbenzoxazoles promoted by Silica supported sodium hydrogen sulphate.* Der Pharma Chemica. 2012, 4(2):761-766.
39. Suryavanshi AW, Mane NA, Gundgole SS, Mathapati SR, Mathkari SS andSomwanshi JL. Alumina catalyzed synthesis of benzoxazole derivatives – a Green approach. *Heteroletters*, 2014,4(2):199-202.
40. 40. Bourgrin K, Loupy A, Soufiaoui M. Trois nouvelles voies de synthèse des dérivés 1,3-azoliques sous micro-ondes, *Tetrahedron,* 1998, 54:8055-8064.
41. Button KM, Gossage RA. Oxazoline chemistry part III. Synthesis and characterisation of [2-(2′-anilinyl)-2-oxazolines] and some related compounds. *J. Heterocycl. Chem.*2003, 40:513-517.
42. (a) Su W, Li J, Zheng Z and Shen Y.One-pot synthesis of dihydropyrimidiones catalyzed by strontium(II) triflate under solvent-free conditions. *Tetrahedron Lett.*, 2005, 46:6037-6040.

    (b) Sun Q, Wang Y, Ge Z, Cheng T and Li R. A highly efficient solvent-free synthesis of dihydropyrimidinones catalyzed by zinc chloride. Synthesis, 2004 ,7:1047-1051.

    (c) Heravi MM, Bakhtiari K and Bamoharram FF. 12-Molybdophosphoricacid: A recyclable catalyst for the synthesis of Biginelli-type 3,4-dihydropyrimidine-2(1H)-ones. *Catal.Commun.*, 2006, 7, 373-376.

    (d) Fu N, Yuan Y, Cao Z, Wang S, Wang J and Peppe C. Indium(III)bromide–catalyzed preparation of dihydropyrimidinones: Improved protocol conditions for the Biginelli reaction. *Tetrahedron*, 2002, 58, 4801-4807.

(e) Zheng RW, Wang X X, Xu H and Du JX. Brønsted acidic ionic liquid:An efficient and reusable catalyst for the synthesis of 3,4-dihydropyrimidin-2(1H)-ones,*Synth.Commun.,* 2006, 36, 1503-1513.

43. Fu NY, Yuan YF, Cao Z, Wang SW, Wang JT and Peppe C. Indium(III)bromide–catalyzed preparation of dihydropyrimidinones: Improved protocol conditions for the Biginelli reaction. *Tetrahedron*, 2002, 58:4801–4807.
44. Rashmi SV, Sandhya NC, Raghava B, Kumara MN, Mantelingu K and RangappaKS. Trifluoroethanol as a metal-free homogeneous and recyclable medium for the efficient one-pot synthesis of dihydropyrimidinones. *Synthetic Communications*, 2012, 42:424-433.
45. Reddy CV, Mahesh M, Raju PVK, Babu TR and Reddy VVN. Zirconium(IV) chloride catalyzed one-pot synthesis of 3,4-dihydropyrimidin-2(1H)- ones. *Tetrahedron Lett.*, 2002, 43:2657-2659.

*****