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IN-SITU RECRYSTALLIZE SYNTHESIS OF BENZIMIDAZOLE DERIVATIVES BY USING Co-DOPED-Zn AS HETEROGENEOUS CATALYST

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Abstract: Benzimidazole and its derivatives has been feasibly synthesized in a prominent way using Co-doped-Zn nano catalyst with easily available o-phenyl diamine in an eco-friendly manner. This leading approach is captivating due to its easy set up and quick response to excellent yield. Melting point determination and TLC have been performed for all the products. In this study all product have been characterized by 1H NMR and 13C NMR.

Index Terms **- Benzimidazole, Co-doped-Zn, o-phenyl di-amine, eco-friendly, In-situ recrystallized.**

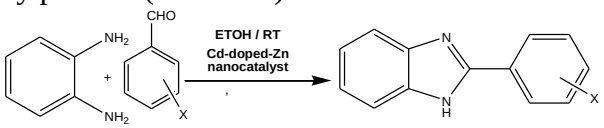
1. Introduction Nitrogen-containing heterocyclic compounds and their analogues are used in many fundamental and higher life processes because they provide the heterocyclic framework for amino acids like tryptophan, alkaloids, hormones, plant growth factors and Neurotransmitters.[1] Benzimidazoles can easily interact with the biopolymers of the living systems, which are responsible for their numerous biological activities and functions. In particular, benzimidazole derivatives exhibit antimicrobial [4-6], antiviral [6, 7], anticancer [9-11], anti-inflammatory [12-13], and antioxidant [14] activities, whereas various derivatives have been developed as therapeutic agents, such as proton pump inhibitors, level modulators[15], and antidiuretics. [16-17]

Presently chemists are drawn to the synthesis of heterocyclic on both a small and big scale in laboratories because of the reactions' robustness, dependability, and affordability to the process.[2] Numerous chemists have described attempts to prepare benzimidazole utilizing catalysis, including sodium acetate, autoclave reactions in acetic acid and nitrobenzene, SBPPSA, ethanol in the presence of ultrasonic, and many more.[19]

In recent decay, innovative and economical synthetic processes have been used to generate these reactions by replacing the traditional catalyst with Nanocatalyst. Switching to a metal-catalyzed reaction has been found to be environmentally friendly and reduce waste creation which result to report used of Nanocatalyst like CoO_x@NC-800, SBA-15 Nanocomposite (Ni/TCH@SBA-15), Ni/TCH@SBA-15, CuO, BiOCl/FeOCl/SiO_2, AlOOH–SO_3 (BNPs'SA), MnO_2, H_2O_2/TiO_2 P_{25}, (Cu@$_b$CD-PEGmesoGO), Co@Fe_2O_4 and SiO_2/Co@Fe_2O_4, Co@Fe_2O_4 and SiO_2/Co@Fe_2O_4,, (ZnO NPs), Fe_3O_4@SiO_2/collagen, nano-Fe_2O_3, nano-ZnS, CuNPs@vesicles, $CoFe_2O_4$@SiO_2@PAF-IL, copper metallovesicles, $Mo_{72}Fe_{30}$, TiO_2–Fe_2O_3, nano-Ni(II)/Y zeolite, Al_2O_3/CuI/PANI and gC_3N_4-imine/TiO_2 in the synthesis of benzimidazole.21 Organic chemists are particularly interested in eco-friendly metals including zinc, iron, copper, cobalt, manganese, and nickel because they are affordable and biodegradable.[3]

But these processes demand severe reaction conditions, costly, poisonous, and air-sensitive chemicals, or multi-step synthesis of pre-functionalized precursors, all of which have the potential to release extremely dangerous substances into the environment. Therefore, it is much desired to create synthetic processes that are safe for the environment for the production of benzimidazole. The most promising method for establishing environmentally friendly and sustainable reaction conditions is the in-situ recrystallization synthetic technique. The primary source of waste in organic syntheses, solvents and energy, are reduced by the in-situ recrystallized technique.

Zinc chemically has the tendency to wake bond formation with higher degree of co-valency, and forming stable complexes with mare N- and S-donors. Apart from wide applications of documented organo zinc compounds, Very recently ZnO nano particles have been utilized as a Catalyst in the synthesis of Benzimidazole compounds. In our recent report of catalytic modification of ZnO Nanoparticles we prove that catalytic activity of ZnO nanoparticle enhanced[20] to continuation of that research we used this modified Cd-Doped-Zn nanoparticles in present work to synthesize the benzimidazole which prove the excellent yields and environ friendly and eco-friendly process (scheme 1).



Scheme 1: General synthesis of Benzimidazole and its derivatives

2. Experimental:-

Material and methods: - In the experiment, ^{1}H Nuclear Magnetic Resonance (NMR) and ^{13}C spectra were recorded on a 500 MHz using $CDC1_3$ as a solvent at ambient temperature. Chemical shifts were expressed relative to the solvent as values in parts per million (ppm). All aldehydes and o-phenyl diamine are commercially available. On silica- coated aluminium plates, thin layer chromatography (TLC) was carried out and seen through an ultraviolet chamber. Melting points were determined. All solvents were employed without purification and no measures were made to eliminate ambient moisture. Glasswares were dried in an oven at 85 °C for at least one hour prior to use.

Preparation of Co-doped-Zn Nanocatalyst:

Utilizing zinc nitrate (5.0 gm) as a source of zinc ions, cobalt nitrate (1.0 gm) as a source of Co ions, and a predicted amount of glycine and L-ascorbic acid taken in the least amount of de-ionized water, the synthesis of Cd-doped-Zn nano catalyst was completed. After removing superfluous water, it is cooked on a hot plate to achieve a homogenized gel. Gel absorbs more heat and produces brownish gasses in two to three seconds. Ultimately, the powder was calcined for four hours at 500°C in a Muffle furnace. The average particle size of the resulting crystalline powder of Cd-doped-Zn nano catalyst is 33.08 nm. XRD and IR were used to characterize the nano catalyst.

General Experimental Procedure for benzimidazole:

In an RB flask a mixture of o-phenylenediamine (1mmol), aromatic aldehyde (1 mmol) and solvent ethanol 2-3 ml was continuously stirred at room temperature with a cobalt-doped-Zinc nano catalyst (scheme 1); the progress of the reaction was monitored by thin-layer chromatography and melting point were taken. After the reaction was complete, the mixture was recrystallized in-situ with existing ethanol (8 ml) and the crystallized product formed was filtered, dried and characterized by H^{1}-NMR, C^{13}-NMR, and FT-IR.

Characterization of catalyst:

The Co-doped-Zn nanoparticle were prepared by the sol-gel method[21] shown to have a single-phase powder XRD pattern (fig. 1a), and the crystallite size was confirmed to be 33.06 nm by Scherrer's equation to the broadening diffraction peak. The Zn-O and Co-O stretching bands formed at 610–710 cm^{-1} and 1400–1500 cm^{-1}, respectively, were visible in the FTIR spectra of the Co-doped-Zn nano catalyst (Fig. 1b), which were in the 450–4000 cm-1 range. The catalyst is stable to moisture as there are no wide peaks in the 3100–3500 cm–1 range.

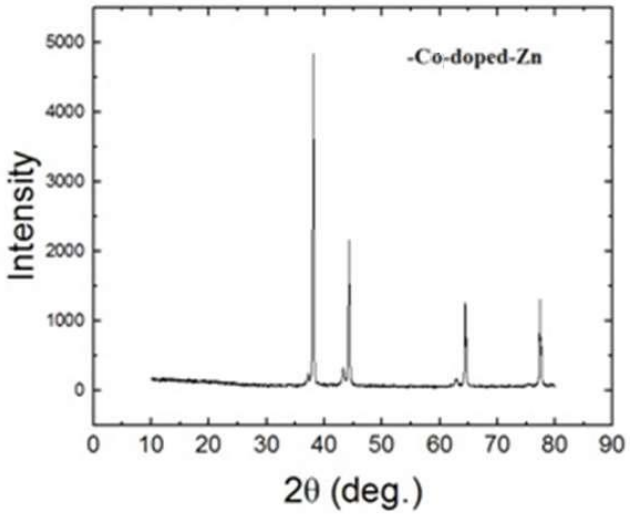


Fig. 1: XRD pattern of Cd-doped-Zn Nano Catalyst

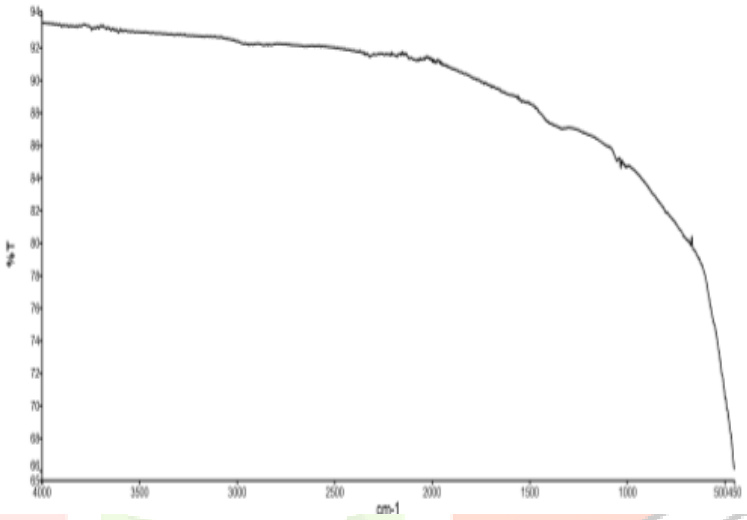


Fig. 2-IR of Co-Doped-Zn Nanocatalyst

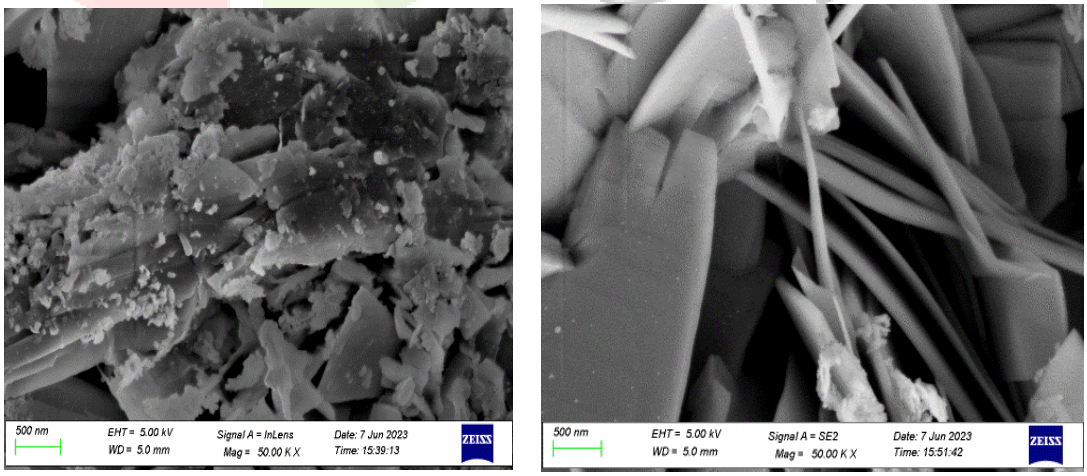


Fig. 3-FE-SEM of Co-Doped-Zn Nanocatalyst

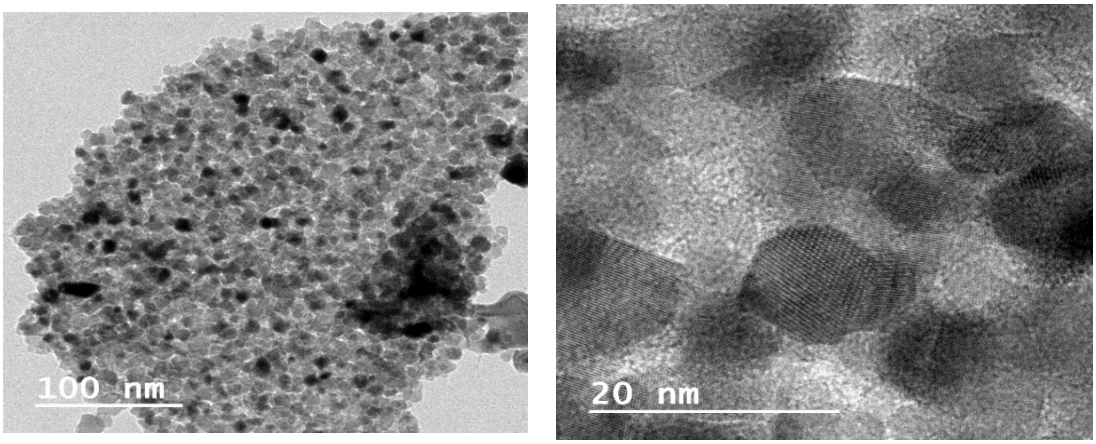


Fig. 4-TEM of Co-Doped-Zn Nanocatalyst

SEM image (fig. 3.) shows that the prepared catalyst is combination of Co and Zn particles with Nanoflex structure with size average 10-50 nm of which improve the catalytic activity of the materials

TEM image (fig. 4.) revealed that the majority of the particles are below 20 nm and porous in nature with porous size in less than 20 nm which increase the effective surface of the catalyst that help to improve the catalytic activity of the catalyst

EDAX

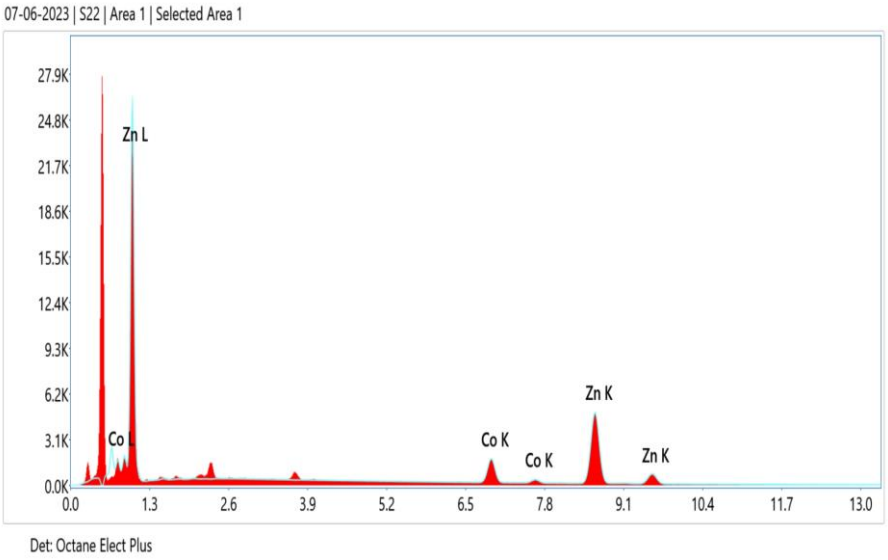


Fig. 5-Elemental Analysis of prepared catalyst

Element	Weight %	Atomic %	Net Int.	Error %	R	A	F
Co K	**11.7**	12.8	804.1	4.9	0.8895	0.9631	1.3652
Zn K	**88.3**	87.2	2673.2	2.7	0.9097	0.9700	1.0447

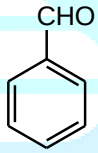
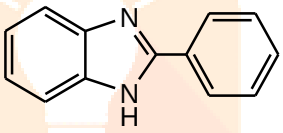
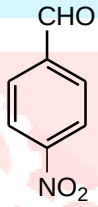
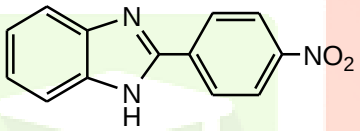
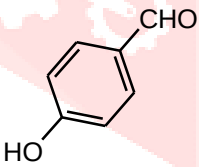
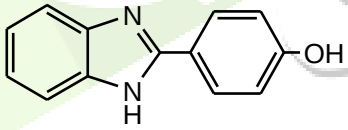
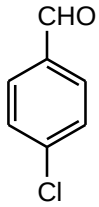
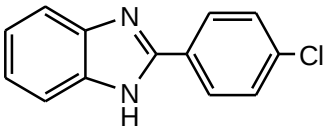
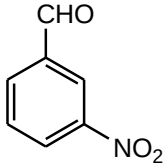
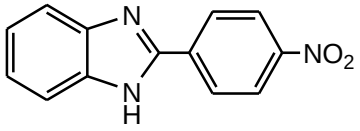
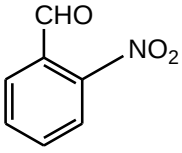
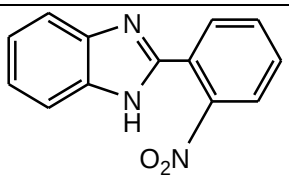
EDAX analysis indicating the doping of the cobalt in the cluster of zinc, also its shows the percentage of ceria content in material that match with the charged amount of the ceria nitrate (11.7%). Mapping image of prepared catalyst shown the uniform distribution of cobalt Nanoparticles in the cluster of the zinc nanoparticles.

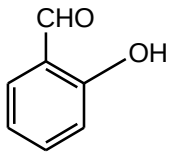
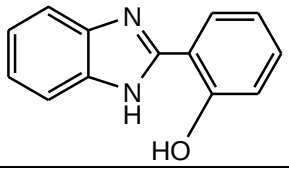
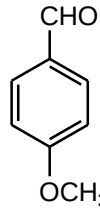
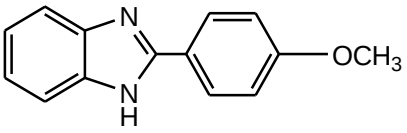
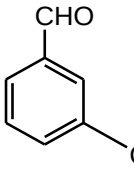
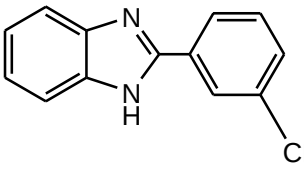
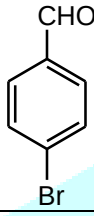
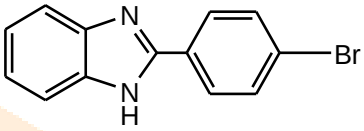
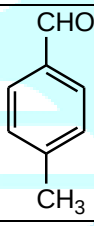
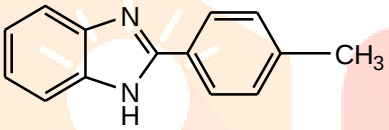
3. RESULTS AND DISCUSSION:

In order to optimize the reaction conditions, we first performed a model reaction using para-nitro benzaldehyde, 1mol equivalent of o-phenylenediamine, and 8 time volume ratio solvent in the presence of a catalyst. The reaction was carried out with solvent at room temperature with catalyst loading of 1.5 mg, yielding the best results in terms of reaction time and yield of the products 2-phenyl-1H-benzo[d]imidazole,4-(1H-benzo[d]imidazole-2-yl)phenol, 2(-4-chlorophenyl)-1H-benzo[d]imidazole, and 2(-4-nitrophenyl)-1H-benzo[d]imidazole. We performed the reaction with varying dopent cobalt percentage compositions, and a 16% w/w composition produced a great yield.

We used a variety of aromatic aldehydes and applied optimal reaction conditions to prepare a wide range of benzimidazole derivative. The results are summarized in table 1. Aromatic aldehydes (1mol) and o-phenylenediamine (1 mol) were treated with (1 mol) ethanol and stirred at room temperature to give excellent yields. Sterically hindered reactant gives considerable yield (Table 1. Entry 5 and 6).

Table 1. Synthesis of benzimidazole derivatives using Co-doped-Zn catalyst.

Entry	Aldehyde	Product	Time (min)	Yield %	M.P.(°C)
1 [b]			60	96 %	210-215°C
2[b]			75	94 %	220-223ºC
3[b]			55	92 %	322-325º C
4 [b]			50	95 %	295-296ºC
5			75	94 %	220-223ºC
6			65	87%	256-258ºC

7			70	84%	323-325ºC
8			75	90%	255-257ºC
9			65	92%	233-235ºC
10			55	86%	280-284ºC
11			65	89%	234-236ºC

Spectral characterization of selected Compounds

Entry 1, 2-phenyl-1H-benzo[d]imidazole:- Molecular formula: $C_{13}H_{10}N_2$, **Yield** 0.42 g(96%), m.p. 256-258°C, **^{1}H NMR** (500 MHz, CDCl3): 5 (s,1H, NH), 7.70-7.26 (m,4H, ArH), 7.48-7.22 (m, 5H, ArH). **^{13}CNMR** (500 MHz, $CDCl_3$): δ 129.11,129.36, 130.38, 126.64, 123.17

Entry 3, 4-(1H-benzo[d]imidazol-2-yl) phenol:- Molecular formula: $C_{13}H_{10}N_2O$, **Yield** 0.45 g(94%), m.p ,**^{1}H NMR** (500 MHz, CDCl3): 5 (s,1H, NH),5(s ,1H,OH),7.70-7.26 (m,4H, ArH), 7.38-6.79(m, 4H, ArH). **^{13}CNMR**(500 MHz,CDCl3): δ134.68, 130.60, 120.32, 118.67, 116.78, 115.77, 115.39.

Entry 4, 2-(4-chlorophenyl)-1H-benzo[d]imidazole:- Molecular formula: $C_{13}H_9N_2Cl$, **Yield** 0.50 g(92%), **m.p.** 295-296 º C , **^{1}H NMR** (500 MHz, CDCl3): 5 (s,1H, NH), 7.70-7.26 (m,4H, ArH), 8.25-7.74 (m, 4H, ArH). **^{13}CNMR**(500 MHz, CDCl3):δ 149.40, 129.47, 128, 124.29, 114.85

Entry 2, 2-(4-nitrophenyl)-1H-benzo[d]imidazole:- Molecular formula: $C_{13}H_9N_3O_2$, **Yield** 0.52 g(95%), m.p. , **^{1}H NMR** (500 MHz, CDCl3): 5 (s,1H, NH), 7.70-7.26 (m,4H, ArH), 7.42-7.33 (m, 4H, ArH). **^{13}CNMR**(500 MHz, CDCl3): δ147.19, 132.531, 33.02, 130.76, 124.66, 124.74, 125.26, 123.60, 113.81

4. Conclusion

The insight from Co-doped-Zn nanocatalyst is appealing in synthesis of desired compound such as benzimidazole and its derivative which in-situ recrystallized, since it is simpler to set up to yield more and has modest reaction conditions when compared to standard and traditional methods.

Acknowledgement

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