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# Greener Synthesis Of In-Situ Recrystalized Bis-Indole-2-Carboxylic Acid By Using Co-Doped-Zn Nanocatalyst

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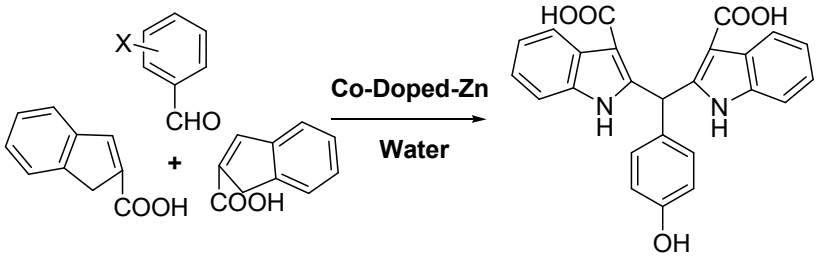
**Abstract:** An excellent yield of in-situ recrystallized bis indole 2-carboxylic acid methane like domain was obtained by catalyzing the reactions of 2-carboxylic acid indole with Co-doped-Zn nanoparticles. This recent method is easy to set up, has moderate reaction conditions, and is more eco-friendly when compared to conventional methods. All the product formation is confirmed by TLC, melting point, and has been characterized by H1 NMR and C13 NMR spectroscopic studies.

**Index Terms** - Bis-indole 2-carboxylic acid methane, Co-doped-Zn nanocatalyst, Eco-friendly doped nanocatalyst.

## Introduction

Designing organic reactions in aqueous media is one of the attractive areas in green chemistry. It offers numerous benefits such as controlling exothermic reactions, salting in and salting out, and variation of pH, as well as remarkably avoiding tedious and costly procedures that include high volumes of organic solvents [1-3]. Derivatives of indoles are important substances in medicine [4]. The indole ring system is the most pervasive heterocyclic moiety in many biological systems, commonly found in nature, showing pharmacological and biological activities. [5-6] More in several synthetic methods for the preparation of bis (indole)alkane derivatives have been documented as bis (indolyl) alkane unit is present in various natural products [7] possessing vital biological properties.[8] Being a core structure of various biologically active compounds, bis (indolyl) methane recognized as potent anti-cancer agents.

Therefore the development of efficient methods to construct such compounds has become an active area of studies. [9-10] Rani. M. and Co-worker[11] reported a convenient one-step reaction for synthesizing bis(indole)methane using ultrasonication conditions as it has emerged as a new lead in green organic synthesis and examined the nematicidal activity. [12] Organic Chemists are showing much interest in various synthetic procedures involving transition metals as catalysts. [13] The remarkable point to be mentioned is that heterocycles having complicated structures with many labile functional groups can be synthesized by the sequential catalytic process. Metals such as Zn, Fe, Cu, Co, Mn, and Ni attracted the synthetic community as they are very less expensive, nontoxic, bio-degradable, and environmentally benign. [14]




Scheme 1: General synthesis of bis (indole 2-carboxylic acid) derivative.

**EXPERIMENTAL:**

$^{1}$H NMR spectra were recorded on a 500 MHz Nuclear Magnetic Resonance (NMR) and $^{13}$C NMR spectra were recorded on a 500 MHz NMR Bruker spectrometer, respectively using $CDCl_3$ as solvent at ambient temperature. Chemical shifts are given in parts per million (ppm). All aldehyde and indole 2-carboxylic acids were used from SD-fine chemicals without purifications. Progress of the reaction was monitored on Thin Layer Chromatography (TLC) and observed under an ultraviolet chamber. The melting point were determined.

**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 nanocatalyst 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 the Cd-doped-Zn nanocatalyst is 33.08 nm. XRD and IR were used to characterize the nanocatalyst.

**Characterization of catalyst**:

The Co-doped-Zn nanoparticles were prepared by the sol-gel method[21] and 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 nanocatalyst (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.

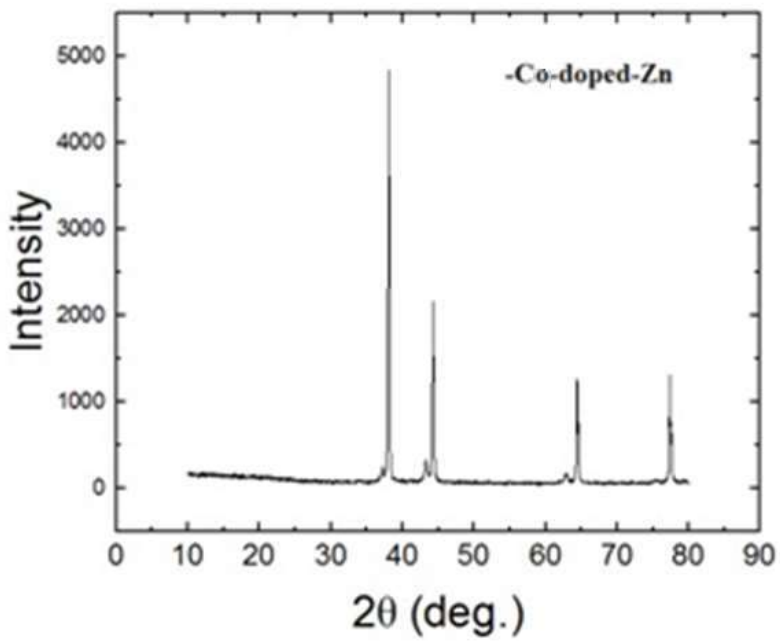



Fig. 1: XRD pattern of Cd-doped-Zn Nano Catalyst

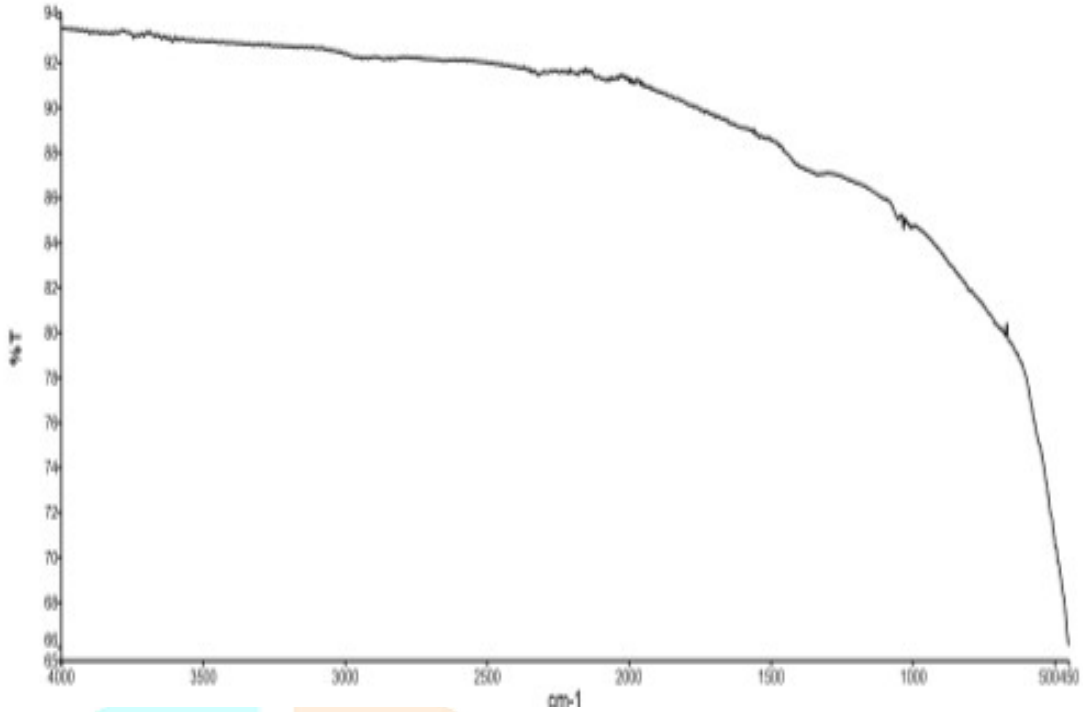



Fig. 2-IR of Co-Doped-Zn Nanocatalyst

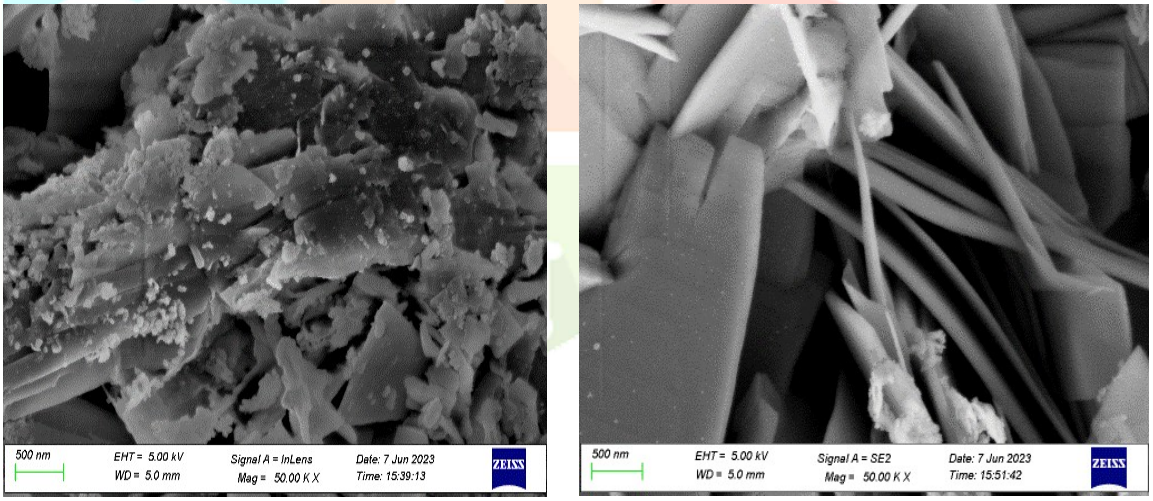



Fig. 3-FE-SEM of Co-Doped-Zn Nanocatalyst

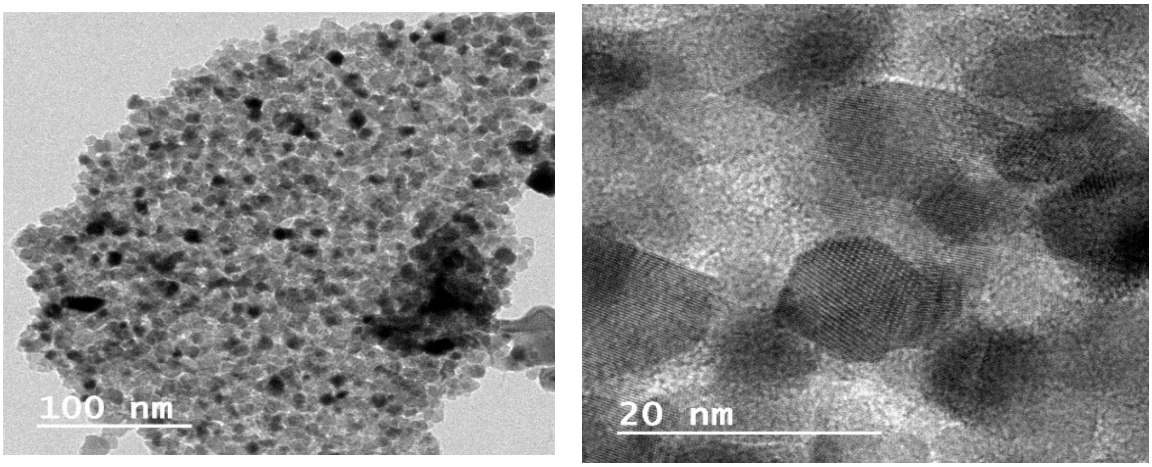



Fig. 4-TEM of Co-Doped-Zn Nanocatalyst

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

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

**EDAX**

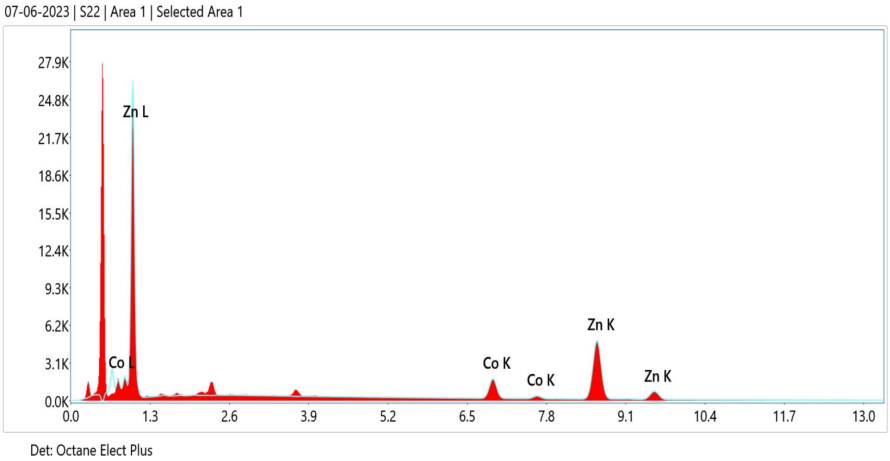



Fig. 5-Elemental Analysis of prepared catalyst

| 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 indicates the doping of the cobalt in the cluster of zinc, and also it shows the percentage of ceria content in material that matches with the charged amount of the ceria nitrate (11.7%). The mapping image of the prepared catalyst shows the uniform distribution of cobalt Nanoparticles in the cluster of the zinc nanoparticles.

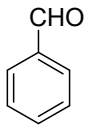
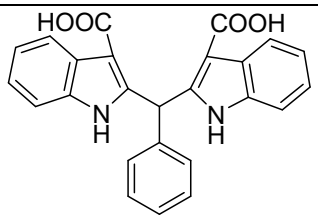
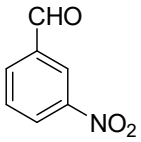
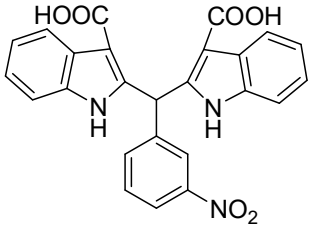
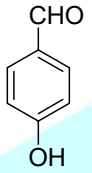
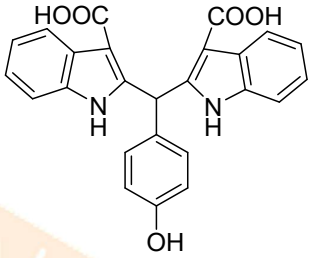
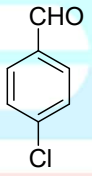
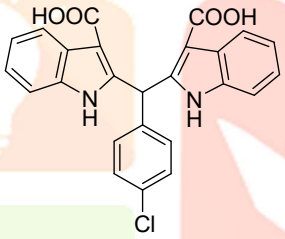
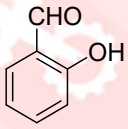
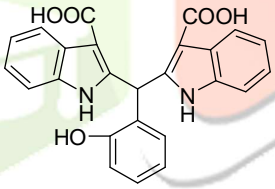
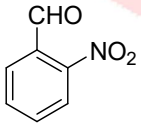
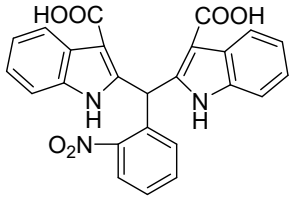
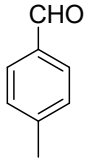
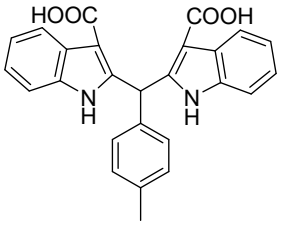
**General Procedure for the Preparation of bis-Indole-2-carboxylic acid methane derivative:**

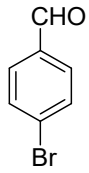
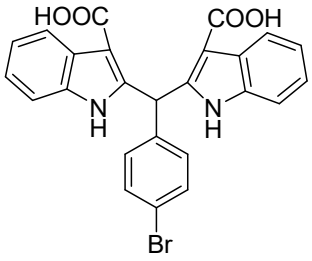
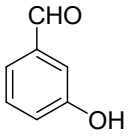
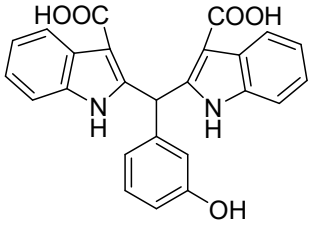
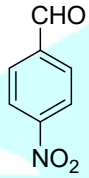
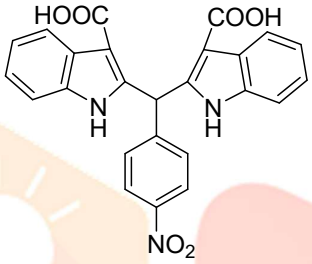
In an RB flask, stir a combination of Indole-2-carboxylic acid (2mol) and aldehyde (1mol) with distilled water (5ml) then heat up to reflux and string on a magnetic stirrer with Co-doped-Zn nanocatalyst. The progress of the reaction was examined using thin-layer chromatography, with spots exposed to a UV chamber. In-situ recrystallization of the product was performed after the reaction was completed by filtering the hot reaction mixture. The residue is a pure product and unreacted 2-carboxylic acid indole gets separated in mother liquor.

**Results and Discussion:**

As part of our investigation, we used water as the reaction to create green chemistry through the use of solvent-free environments to carry out organic reactions. In the initial step, we used a catalyst and (1 mmol) of 3-nitro benzaldehyde and (2 mmol) of indole-2-carboxylic acid as model reaction conditions. The model reaction was examined to determine the impact of several reaction parameters, such as the catalyst-doped composition, temperature, and time of loading. We generate a wide range of bis (indole-2 carboxylic acid) derivatives by using a variety of aromatic aldehydes and applying ideal reaction conditions. The outcome is summarized in Table 1. A high yield was achieved by stirring and heating aromatic aldehyde (1 mmol) and indol-2-carboxylic acid (2 mmol) in water while the catalyst was present.

Table 1: The above reaction scheme with varying substituents of aldehyde gives the following observation:

| Entry | Aldehyde | Product | Time | Yield | MP °C |
|---|---|---|---|---|---|
| 1 |  |  | 2hr | 96% | 210-213 |
| 2 |  |  | 2hr | 96% | 230-235 |
| 3 |  |  | 2hr | 84% | 190-195 |
| 4 |  |  | 2hr | 92% | 190-193 |
| 5 |  |  | 2hr | 92% | 185-187 |
| 6 |  |  | 2hr | 93% | 205-210 |
| 7 |  |  | 2hr | 90% | 180-184 |

| | | | | | |
|---|---|---|---|---|---|
| 8 |  |  | 2hr | 92% | 190-192 |
| 9 |  |  | 2hr | 97% | 235-237 |
| 10 |  |  | 2hr | 97% | 235-237 |

**Compound Characterization:**

**Entry 1:- 3,3(benzylidene) bis-indol-2-carboxylic acid:** Molecular Formula :($C_{25}H_{20}O_4N_2$) (Table -1 entry. 1), Yield -1.67g, (96%), M.P-(210-213), 1H NMR (500MHZ, Cdcl3) δ 1.2-1.3 (S,3H, ArH), δ6.84-6.98 (S,3H, Ar-H), δ 7.17-7.19 (S,2H, ArH), δ7.22-7.28 (S,4H-ArH), δ 7.33-7.42 (S,4H, ArH).

**Entry 2:- 3,3 (3-nitrobenzylidene) bis-indol-2-carboxylic acid :** Molecular Formula : ($C_{25}H_{19}O_6N_3$) (Table- 1 entry 2.), Yield1.85g, (96%), M.P(230235), 1HNMR(500MHZ, Cdcl3) δ1.251.29 (d,3H,CH), 7.16(M,1H,ArH), 7.18-7.25(d,3H,ArH), 7.35-7.41(S,4H,ArH), 7.44-7.73(S,4H,ArH), 8.7(NH), 10.12(OH). 13CNMR(Cdcl3): δ189.761, 166.384, 137.30, 134.67, 130.38. 126.11, 127.45, 128.62,124.55, 122.89, 121.08, 112.00, 110.8.

**Entry 3:- 3,3 (4-hydrobenzylidene)bis indole-2-carboxylic acid**: Molecular Formula :($C_{25}H_{20}O_5N_3$) (Table -1 entry 3.), Yield -1.51 g, (84% ), M.P-(190-195), 1H NMR (500MHZ, Cdcl3):δ 1.2(3H, CH), 7.17-7.35(S,5H, ArH), 7.37-7.44 (S,4H, Ar), 7.46-7.73(S,4H, ArH), 8.95(NH). 13C NMR ($CdCl_3$): δ 166.40, 137.23, 127.45, 126.14, 122.89, 121.09, 111.99, 110.28.

**Entry 4:- 3,3(4-chloro benzylidene) bis indole -2-carboxylic acid**: Molecular Formula :($C_{25}H_{19}O_4N_2CI$) (Table -1 entry. 4), Yield – 1.73 g ,(92%) ,M.P-(190-193) , 1H NMR (500MHZ, Cdcl3) δ1.2(3H,CH), 7.18-7.39(S,5H,ArH), 7.44-7.73(S,4H,ArH), 8.0(NH). 13C-NMR(Cdcl3): δ 166.40, 137.23, 127.45, 126.14, 122.89, 121.09, 111.99, 110.28.

**Conclusion**

Modern methodology to synthesize bis-indole-2-carboxylic acid methane and its derivative is more facile using a Co-doped-Zn nanocatalyst. This is appealing since it is eco-friendly, in-situ purified, quick to set up, and produces results rapidly.

**Acknowledgement**

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