



AN APPROACH TO RAPID ONE-POT MULTI-COMPONENT SYNTHESIS OF 1,4-DIHYDROPYRANO [2,3-C] PYRAZOLE CATALYZED BY CORE SHELL NiO-Co₃O₄@CuO NANOPATES UNDER SOLVENT-FREE CONDITIONS.

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ABSTRACT:

The present study describes a facile one-pot multicomponent protocol for the synthesis of series of pyranopyrazoles from ethyl acetoacetate, phenyl hydrazine, malononitrile and aryl aldehydes using core shell NiO-Co₃O₄@CuO as nanocatalyst. The structure identification of the catalyst by spectral techniques including FT-IR, UV-DRS, XRD and SEM analysis. The pyranopyrazoles derivatives were synthesized under solvent-free conditions using NiO-Co₃O₄@CuO as heterogenous catalyst. Interesting advantages this protocol is reaction proceeded smoothly with cost effective and environmentally friendly catalyst, high purity and yields (up to 96%) of product along with the retention of catalytic activity up to four cycles.

KEY WORD: Core shell NiO-Co₃O₄@CuO, 1,4-dihydropyrano[2,3-c] pyrazole, solvent free

INTRODUCTION:

In recent years, one of the fundamental research objectives in organic synthesis is use of heterogeneous nanostructures. Various research groups around the world are intrigued the advance science fields, nanoscience and nanotechnology. These fields have provided one of the most important applications, production and fabrication of nano catalysts^{i-iv}. This material is highly advantageous in organic synthesis. The development of nanocatalytic systems have served attracted sustainable, efficient, and selective chemical transformations because of their ability to raise rates of chemical reactions, promote yields and reusability after easy recoverability process^{v-viii}.

Due to changeable oxidation states transition metal oxides measured as potential materials for catalysis. Catalytic properties of nanoscale transition metal oxides are more advanced than its bulk equivalents because of their small size and high surface area^{ix-xi}.

Among the oxides of transition metals, because of potential p type semiconductors and the narrow band gap (1.2eV) Copper Oxide is a material which has many applications in nano

scale such as in gas sensor ^{xii}, field emission ^{xiii-xiv}, antibacterial and antioxidant ^{xv-xvi} and reaction catalyst ^{xvii-xix}. Environment-friendly and quite economical copper-based nanoparticles have been broadly discovered as highly selective catalysts in C–C and C-heteroatom bond forming reactions ^{xx}.

The core shell formation with CuO leading to superiority in their properties like dimensional, optical, electronic and surface area which made desirable for many applications ^{xxi-xxii}. NiO and Co₃O₄ are the promising materials in formation of core shell nanostructure ^{xxiii-xxvi}.

one-pot multicomponent reactions are significant approaches over traditional reaction. These reactions follow ideologies of green chemistry. Hence design stepwise cost saving operation, no need of intermediate isolation, easy separation of product, and minimized time ^{xxvii}. During the last few years, synthetic organic chemists are used the one-pot multicomponent reactions for synthesis of functionalized and fused heterocyclic structural scaffolds ^{xxviii-xxix}. Between the different heterocyclic molecules, oxygen- and nitrogen containing fused ring heterocycles 1,4-dihydropyrano[2,3-c] pyrazole display important role as pharmacologically and biologically active compound and an interesting moiety in medicinal chemistry ^{xxx-iii}

Based on the above description, we sought to find an effective one-pot multi-component synthesis of 1,4-dihydropyrano [2,3-c] pyrazole under solvent-free conditions catalyzed by core shell nanostructure. For this we synthesized noble, recyclable and cost-effective nanoscale heterogeneous solid catalysts, core shell NiO-Co₃O₄@CuO nanoplates. The present investigation not only describes a facile approach for synthesis of 1,4-dihydropyrano[2,3-c] pyrazole but also demonstrate the utilization of NiO-Co₃O₄@CuO nanoplates as an effective catalyst. The synthesized catalyst would be beneficial for the further development of green method in organic synthesis.

EXPERIMENT:

The chemicals used are copper nitrate (Cu (NO₃)₂.3H₂O), nickel nitrate (Ni (NO₃)₂.6H₂O), cobalt nitrate (Co (NO₃)₂.6H₂O), Sodium hydroxide (NaOH), Double distilled water (DDW) was use as a solvent in all the experiments, phenyl hydrazine, ethyl acetoacetate, Malononitrile and aldehydes were used without further purification.

Preparation of CuO Nanoplates -

The CuO nanoplates were synthesized by coprecipitation method using copper nitrate (Cu (NO₃)₂.3H₂O), (1M) used as a precursor and triton as a surfactant was dissolved in 100ml double distilled water. The sodium hydroxide (0.1M) was slowly added drop wise under continuous stirring. The blue colored precipitate of copper nitrate was obtained. The mixture was stirred for 3 hours at 80⁰C. The precipitate obtained was filtered and washed with double distilled water. The washed precipitate was dried at 100⁰C for 12 hours. The dried precipitate was calcined at 450⁰C for 5 hours.

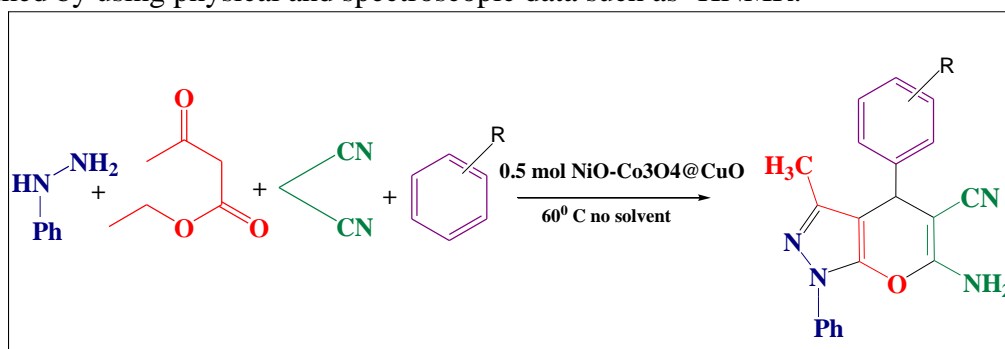
Preparation of NiO-Co₃O₄@CuO core shell nanoplates

The NiO- Co₃O₄@CuO core shell nano plate was obtained by impregnation method. The method involves loading aqueous solution of stoichiometric amount of nickel nitrate (Ni (NO₃)₂.6H₂O), cobalt nitrate (Co (NO₃)₂.6H₂O) on prepared CuO Nano plates. The mixture obtained was refluxed at 110⁰C for 12 hours then filtered and washed with double distilled water. The product obtained was dried at 100⁰C in the oven and calcined at 750⁰C for 4 hours in the air. The synthesized catalyst was characterized by UV DRS, FT-IR, XRD, SEM techniques

General procedure for preparation of 6-amino-3-methyl-1,4-diphenyl-1,4-dihydropyrano[2,3-c] pyrazole-5-carbonitrile

A mixture of aldehyde (1.5mmol), malononitrile (2mmol), Phenyl hydrazine (2mmol), ethyl acetoacetate (2mmol) and catalyst (0.5mmol) stirred at 100⁰C for appropriate time. The progress and completion of reaction was monitored by TLC. After completion of reaction, the

mixture was cooled to room temperature. The mixture was poured in cold water. The solid separated was filtered by suction to afford crude product. The obtained solid was crystallized from ethanol to get the desired compound in pure form. The structure of all products was confirmed by using physical and spectroscopic data such as $^1\text{H NMR}$.



Scheme 1: Synthesis of 1,4-dihydropyrano [2,3-c] pyrazole

RESULT AND DISCUSSION:

UV-DRS absorption spectrum of the synthesized $\text{NiO-Co}_3\text{O}_4@\text{CuO}$ core shell Nanoplates recorded in the range 200–1000 nm are shown in **Fig. 1** Spectra reveal blue shifted band at 245, 320 and 380-600 nm confirm the formation of composites.

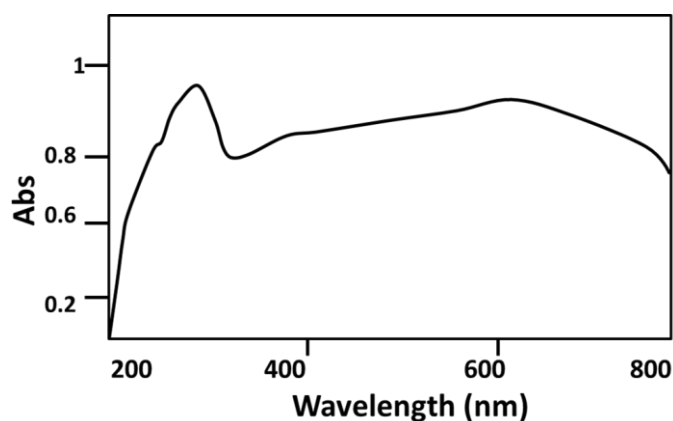


Figure 1. UV-DRS spectrum of $\text{NiO-Co}_3\text{O}_4@\text{CuO}$ core shell Nanoplates.

FT-IR spectrum of synthesized $\text{NiO-Co}_3\text{O}_4@\text{CuO}$ was taken in the region of 400-4000 cm^{-1} and is given in **Fig.2** FT-IR spectrum confirming the formation of $\text{NiO-Co}_3\text{O}_4@\text{CuO}$ nanoplates as it shows strong band at around 450.30cm^{-1} is ascribed to the representative stretching vibrations of Cu-O bond. The peak at 539.97cm^{-1} was attributed to the stretching vibration of Ni-O bond and the band at 630.27cm^{-1} was assigned to the stretching vibrations of Co-O bond.

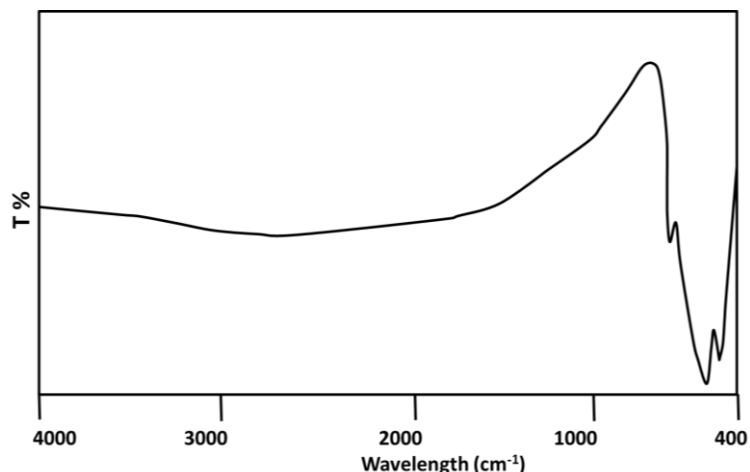


Figure 2. FT-IR spectrum of NiO–Co₃O₄@CuO core shell Nanoplates.

In XRD analysis **Fig.3** the diffraction peaks of NiO–Co₃O₄@CuO core shell nanoplates. The formation of CuO was confirmed by the XRD pattern show peaks at 33.06, 36.28, 54.06, 59.8, 67.98 and 79.76 of CuO (JCPDS card No.89–5899). Peaks at 37.88,62.96,73.32,76.76 of NiO (JCPDS No. 44-1159). Peaks at 31.90, 32.24, 49.02 and 57.98 of Co₃O₄ (JCPDS card No: 78-1970). No extra peak is observed which confirms the purity of product.

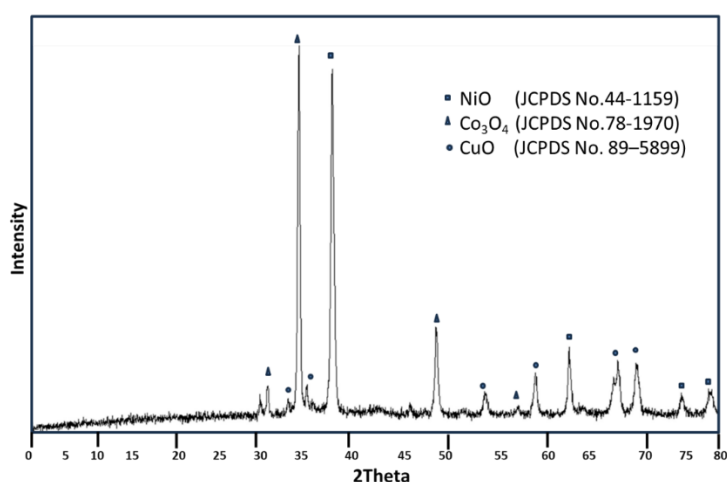


Figure 3. XRD pattern of NiO–Co₃O₄@CuO core shell nanoplates

The surface morphology of NiO–Co₃O₄@CuO core shell were analyzed by SEM analysis as shown in **Fig.4** SEM photomicrographs shows the catalyst have agglomerated plate-like

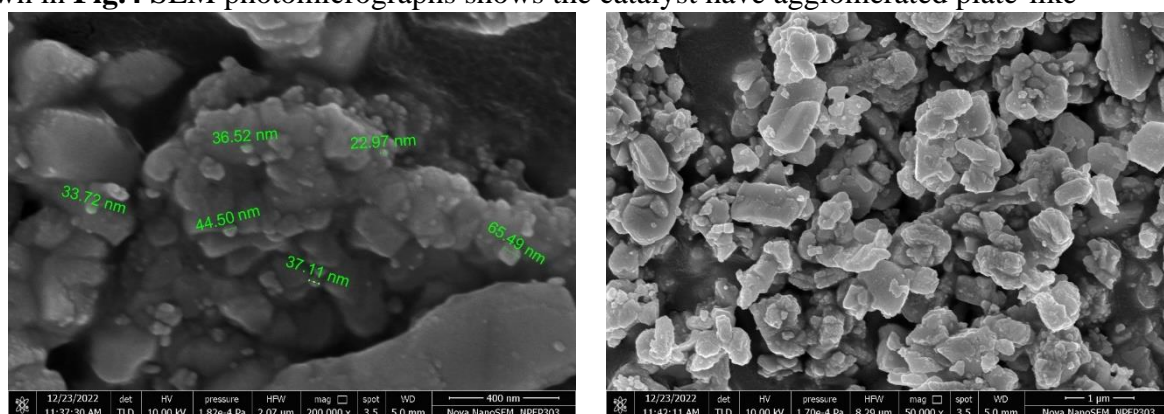


Figure 4. SEM image of NiO–Co₃O₄@CuO core shell nanoplates

morphology and the average particle sizes may be varied from 22 to 65 nm.

The catalytic performance of NiO-Co₃O₄@CuO nanocomposite catalyst was measured by One-pot multi-component condensation reaction of 4-fluoro benzaldehyde, malononitrile, Phenyl hydrazine and ethyl acetoacetate. In order to get maximum conversion and yield of the product, we examined reaction parameters such as the reaction temperature, reaction time, amount of catalyst and effect of solvent.

To check the effectiveness of NiO-Co₃O₄@CuO we tried synthesized CuO, NiO and Co₃O₄ independently for condensation reaction of aldehyde. CuO gave good yield but required more time as compared to modified NiO-Co₃O₄@CuO catalyst summarized in Table 1. To optimize amount of catalyst required for condition we tried various mole equivalent of the catalyst. It was found that when the reaction was carried out with 0.5 mol equivalent the yield was found 95% (Table 2.). The active sites of catalyst are blocked due to the adsorption of product over surface area of catalyst, hence further increased in amount of catalyst was decreased the % yield. At 60°C temperature maximum yield was found Table 3.

Table 1. Effect of catalytic performance on the synthesis of 1,4-dihydropyrano [2,3-c] pyrazole

Entry	Catalyst	Time (min)	Yield (%)
1	Without catalyst	160	Reaction incomplete
2	CuO	30	76
3	NiO	25	73
4	Co ₃ O ₄	40	61
5	NiO- Co ₃ O ₄ @CuO	10	97

Table 2. Effect of mole percentage of NiO-Co₃O₄ @CuO.

Entry	Amount of catalyst(mol)	Time(min)	Yield (%)
1	0.1	35	65
2	0.3	30	76
3	0.4	15	82
4	0.5	10	95
5	0.8	10	82

Table 3. Effect of temperature on the synthesis of 1,4-dihydropyrano [2,3-c] pyrazole

Entry	Temperature(°C)	Time(min)	Yield (%)
1	40	15	50
2	50	15	69
3	60	10	95
4	80	20	43
5	100	30	41

After optimizing the reaction conditions, we have investigated the applicability of this synthetic methodology for 1,4-dihydropyrano [2,3-c] pyrazole derivatives with series of reaction of ethyl acetoacetate(2mmol), phenyl hydrazine (2mmol), malononitrile (2mmol) and a wide range of structurally diverse aldehyde (1.5mmol) were treated in presence of NiO-Co₃O₄@CuO at 60⁰C. Almost in all cases desired product was obtained in good to excellent yield Table 4.

Table 4. Synthesis of different of 1,4-dihydropyrano [2,3-c] pyrazole derivatives catalyzed by NiO-Co₃O₄ @CuO.

Entry	R group	Time (min)	Yield (%)	MP (°C) (Observed)
a	H	15	88	172-174
b	4-F	10	95	175-177
c	4-Cl	15	92	178-180
d	4-OH	05	94	213-214
e	4-Me	20	89	175-177
f	3-NO ₂	10	93	187-189
g	4-OMe	15	91	172-173

To explore the catalyst reusability, the separated core shell NiO-Co₃O₄@CuO from the model reaction washed with alcohol and dried in the oven at 110⁰C for 3h. This activated catalyst reused further and showed insignificant loss of the catalytic activity till 4th reaction cycle which indicate cost effectivity of synthesized catalyst.

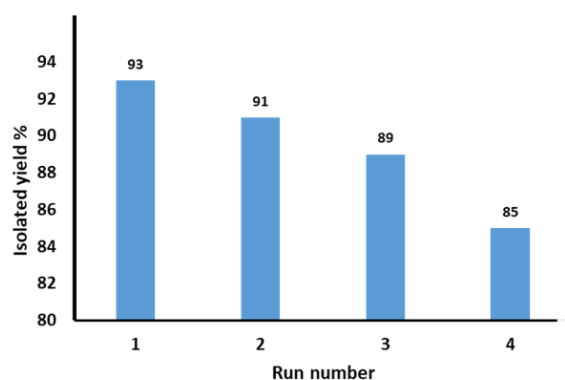


Figure 5. Reusability of catalyst in synthesis of 1,4-dihydropyrano [2,3-c] pyrazole

CONCLUSION:

In conclusion, a feasible method was proposed to prepare a Core shell NiO-Co₃O₄@CuO nanoplates. Then, characterization of synthesized catalysts was carried out by several techniques such as UV-DRS, FT-IR, XRD, SEM. we have demonstrated that Core shell NiO-Co₃O₄@CuO nanoplates is novel, recoverable and cost-effective nanoscale heterogeneous solid catalysts for one-pot multi-component solvent free synthesis of 1,4-dihydropyrano [2,3-c] pyrazole derivatives. The present study recommends numerous advantages for instance: excellent yields, short reaction times, ease of separation of catalyst and environmentally benign reaction conditions.

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SPECTRAL DATA OF PREPARED COMPOUNDS:

b)6-amino-3-methyl-4-(4-florophenyl)-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile

¹HNMR (400MHz CDCl₃): δ (ppm) 1.80 (s, 3H), 4.66 (s, 1H), 4.68(s, NH₂), 7.02-7.06 (m, 2H), 7.21-7.24 (m, 2H), 7.32 (t, 1H), 7.45-7.48 (t, 2H), 7.63-7.65 (t, 2H)

d)6-amino-3-methyl-4-(4-hydroxyphenyl)-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile

¹HNMR (400MHz CDCl₃): δ (ppm) 1.79 (s, 3H, CH₃), 4.56 (s, 1H), 4.62(s, 2H, NH₂), 6.72 (d, 2H), 7.04 (d, 2H), 7.29-7.33(m, 1H), 7.49 (d, 2H), 7.78 (d, 2H).

e)6-amino-3-methyl-4-(4-methylphenyl)-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile

¹HNMR (400MHz CDCl₃): δ (ppm) 1.76(s, 3H) 2.25 (s, 3H), 4.57(s, 1H), 4.70 (s, 2H, NH₂), 7.04 (d, 2H), 7.10 (d, 2H), 7.26-7.29(m, 1H), 7.41 (d, 2H), 7.75 (d, 2H).

f)6-amino-3-methyl-4-(3-nitrophenyl)-1-phenyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile

¹HNMR (400MHz CDCl₃): δ (ppm) 1.83 (s, 3H), 4.80(s, 1H), 4.96(s, NH₂), 7.31 (t, 1H), 7.54 (t, 2H), 7.72 (t, 1H), 7.89 (m, 3H), 8.12-8.15 (m, 2H).

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