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SILICA SUPPORTED ZINC OXIDE NANOPARTICLES: AN EFFICIENT AND REUSABLE HETEROGENEOUS CATALYST FOR BIGINELLI REACTION

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Abstract

Silica-supported zinc oxide (ZnO) nanoparticles were synthesized via a co-precipitation method and evaluated as an efficient heterogeneous catalyst for the Biginelli reaction. The synthesis involved depositing ZnO nanoparticles on silica, followed by calcination at 650°C for 2 h. The resulting materials were characterized using XRD, FTIR, and FESEM analyses, confirming the crystalline nature and uniform distribution of ZnO on the silica surface. The catalytic performance of silica-supported ZnO nanoparticles was tested in the one-pot synthesis of 3,4-dihydropyrimidinones (DHPMs) from various aldehydes, ethyl acetoacetate, and urea/thiourea under solvent-free conditions. The catalyst demonstrated excellent activity, affording high product yields and facile separation. Reusability studies indicated that the catalyst could be recycled up to five consecutive runs with minimal loss in activity. This work demonstrates the first successful application of silica-supported ZnO nanoparticles as a robust and recyclable heterogeneous catalyst for the Biginelli reaction.

Keywords: *Zinc oxide, Heterogeneous catalysis, Nanoparticles, Biginelli reaction, Reusability, Silica support..*

INTRODUCTION

Catalysis is the cornerstone of modern chemical synthesis, driving transformations that are critical for industrial, environmental, and pharmaceutical processes [1]. Among catalytic systems, heterogeneous catalysts are preferred for their ease of separation, reusability and environmental compatibility compared to homogeneous systems (Haruta et al., 2011; Astruc, 2018)[2]. The development of highly efficient, sustainable, and recyclable heterogeneous nanocatalysts remains an area of intense research interest [3]. Nanomaterials, particularly metal and metal oxide nanoparticles, have demonstrated exceptional catalytic activities due to their large surface-to-volume ratio and unique quantum effects (Xia et al., 2009; Daniel & Astruc, 2004). Among these, zinc oxide (ZnO) nanoparticles have emerged as promising catalysts because of their wide band gap (~3.3 eV), high thermal stability, and amphoteric nature, which allow them to act as both Lewis acids and bases (Saeed et al., 2015; Mahapatra et al., 2021). ZnO has been extensively used for various organic transformations such as esterification, aldol condensation, acylation, and coupling reactions (Pawar et al., 2019). However, aggregation of ZnO nanoparticles often reduces their catalytic efficiency by decreasing accessible active surface sites. Therefore, immobilising ZnO nanoparticles on suitable supports enhances their surface area, dispersion, and stability (Li et al., 2020; Tang et al., 2023).

Silica (SiO_2) is one of the most commonly employed supports due to its high surface area, chemical inertness, non-toxicity [4], and mild acidity. Functionalization of silica with metal oxides provides a synergistic effect that enhances catalytic activity while allowing easy recovery and recyclability (Gupta et al., 2007; Bhuyan et al., 2018). Silica-supported catalysts such as SiO_2–$CuCl_2$, SiO_2–$ZnCl_2$, SiO_2–H_2SO_4, and $HClO_4$–SiO_2 have demonstrated remarkable efficiency in various organic transformations (Kour et al., 2014; Chanu et al., 2018). In particular, ZnO supported on silica offers a dual advantage of acidic and basic sites, making it excellent bifunctional catalysts [5].

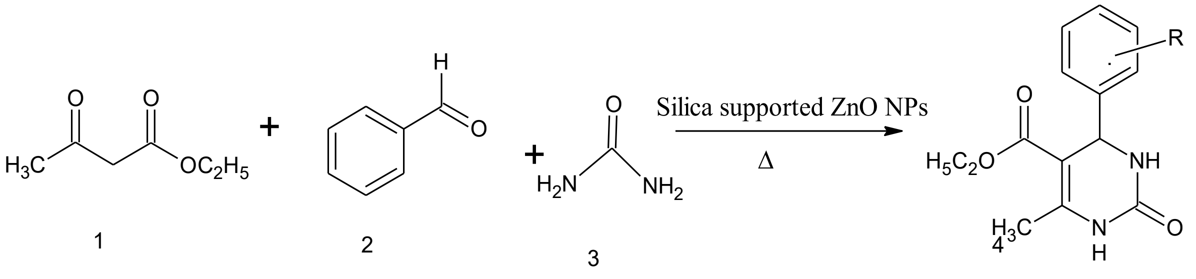
The Biginelli reaction, a three-component condensation of β-ketoester, aldehyde, and urea (or thiourea), was first reported by Pietro Biginelli in 1891 [6]. It yields 3,4-dihydropyrimidin-2(1H)-ones (DHPMs), which are valuable heterocycles with diverse biological activities, including antihypertensive, antitumor, antiviral, and antibacterial properties (Kappe, 2000; Wan & Liu, 2010; Singh et al., 2021). Traditional methods often use strong acids (HCl, H_2SO_4, or acetic acid) under harsh conditions, which generate waste and pose environmental hazards. Consequently, the search for green, solvent-free, and reusable catalytic systems for this reaction has gained importance (Polshettiwar & Varma, 2010; Martins et al., 2019).

Various green methods using microwave-assisted synthesis and various solid acid catalysts are also reported for the synthesis of dihydropyrimidones and other pharmaceutical intermediates [7,8,9] Recent literature highlights the use of solid acid catalysts such as zeolites, clays, and metal oxide nanocomposites for Biginelli reactions. However, challenges such as catalyst deactivation, poor recyclability, or metal leaching persist (Bhuyan et al., 2018; Mondal et al., 2012). In this context, the present study introduces silica-supported ZnO nanoparticles as a green, reusable, and efficient heterogeneous catalyst for the Biginelli reaction [10]. The catalyst combines the advantages of both ZnO and silica, demonstrating excellent catalytic activity, solvent-free reaction conditions, and recyclability [11]. This work contributes to the growing field of sustainable nanocatalysis, providing insights into the design of environmentally benign systems for multicomponent reactions [12].

EXPERIMENTAL

Silica-supported ZnO nanoparticles were synthesized via a co-precipitation method. Silica gel (60–120 mesh, 25 g) was added with stirring to 100 mL of 1 M zinc nitrate hexahydrate solution. 1 M NaOH solution was then added dropwise to maintain the pH at 10.8 under continuous stirring, resulting in the formation of a white precipitate. The precipitate was filtered, washed with deionized water several times, and dried in an oven at 80°C. The obtained powder was calcined at 650°C for 2 hours to yield the final catalyst. For the catalytic test, a mixture of benzaldehyde (30 mmol), ethyl acetoacetate (30 mmol), and urea (30 mmol) was heated in an oil bath with 1 g of the catalyst under solvent-free conditions. The reaction was monitored by TLC using n-hexane: ethyl acetate (3:2). Upon completion, the solid product was separated using acetone, filtered, and purified by recrystallization from alcohol.

2.1 Reaction Scheme:



Where R=H, 4ˉOH, 4ˉˉNO_2, 4ˉCl etc

Figure 1: Reaction scheme for Biginelli reaction.

2.2 Optimization of reaction parameters:

Reaction was optimized using ZnO powder, Silica and Silica Supported ZnO nanoparticles at 120 C° heating and at different reaction times. Silica-supported ZnO nanoparticles gave better results compared to ZnO powder and only Silica reaction.

Catalyst	Weight	Time and temp.C°	Yield %
ZnO powder	0.250 g	2 hr. 120	59
Silica (60-120 mesh)	0.500 g	3.5 hr. 140	38
Silica supported ZnO Nanoparticles	1 g	40 min. 120	92

Table 1: Optimization of reaction parameters for the Biginelli reaction

2.3 Reusability of catalyst:

Silica suppoted nanoparticles were reused for 5 times for the same reaction without losing much activity.Results are as shown in table 2.

Cycle	Time /Temperature C°	Yield %
1	40 min. 120	92
2	40 min. 120	89
3	40 min. 120	87
4	40 min. 120	87
5	40 min. 120	85

Table 2: Reusability study of the catalyst.

Aldehyde	Urea/Thiourea	Time and temperature C°	Yield %	M.P. (lit)
Benzaldehyde	Thiourea	40 min. 120	89	202-204 (207-208)
4-hydroxybenzaldebhyde	Urea	40 min. 120	85	226-228 (227-229)
4-nitrobenzaldehyde	Urea	40 min. 120	87	204-205 (206-209)
4-chlorobenzaldehyde	Urea	45 min. 120	84	219-221 (221-223)

Table 3: Silica-supported ZnO catalyzed Biginelli reaction.

CHARACTERIZATION

The synthesized silica-supported ZnO nanoparticles were comprehensively characterized using multiple analytical techniques to confirm structural, morphological, and chemical properties.

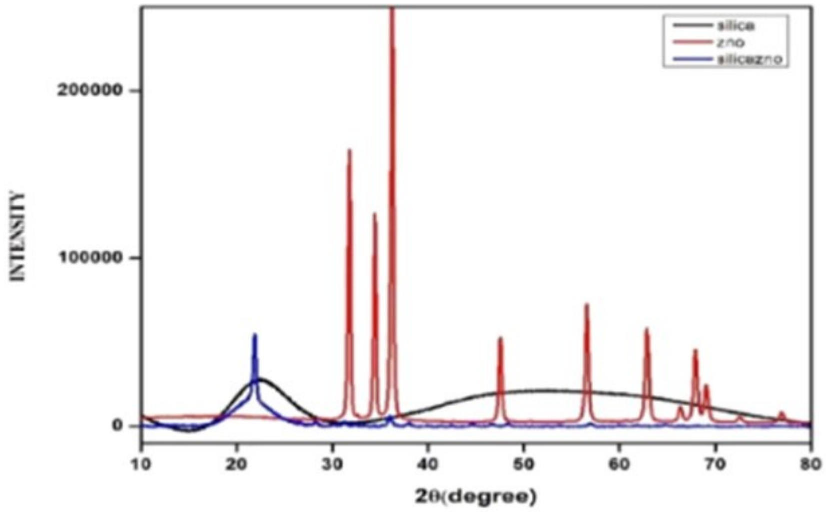


Figure 2- XRD pattern of silica, ZnO NPs, and silica-coated ZnO NPs

X-ray diffraction (XRD) analysis was performed to confirm the crystalline phase of the material. The characteristic diffraction peaks observed at 2θ = 31.70°, 34.42°, 36.26°, 47.62°, 56.73°, 62.65°, 67.98°, 72.54°, and 76.90° correspond well with the standard JCPDS card No. 36-1451 for hexagonal wurtzite ZnO (Zhang et al., 2019). The absence of additional peaks indicates the purity of the product. The broadening of the peaks suggests nanoscale crystallite size, estimated to be around 25–35 nm using the Scherrer equation.

Fourier Transform Infrared (FTIR) spectroscopy confirmed the successful formation of ZnO nanoparticles on the silica surface. The broad band at 1055 cm^{-1} corresponds to asymmetric Si–O–Si stretching, while the band near 493 cm^{-1} is characteristic of Zn–O stretching vibrations (Choudhury et al., 2017). The absence of peaks for nitrates or hydroxyl groups confirms effective calcination and removal of residual precursors.

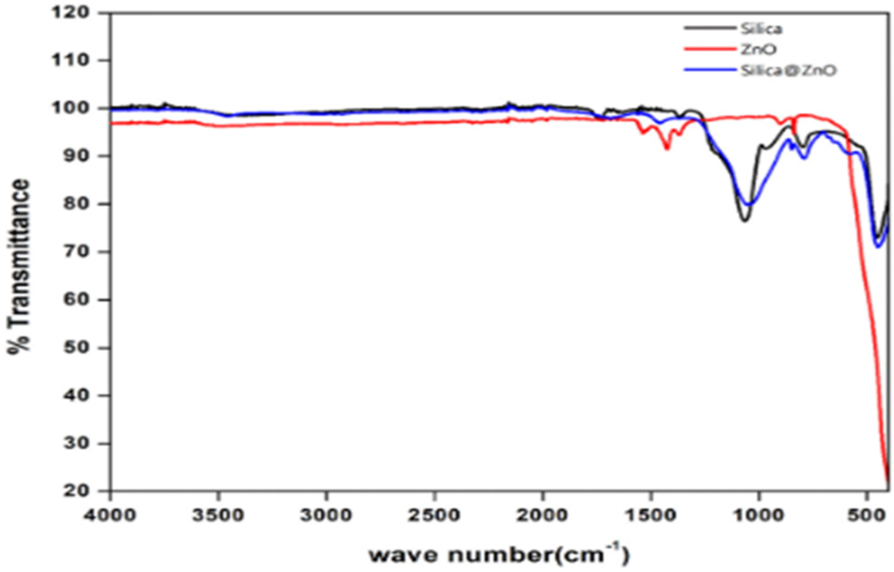


Figure 3 .-FTIR of silica, ZnO, Silica coated by ZnO NPs

Field Emission Scanning Electron Microscopy (FESEM) images revealed uniform distribution of ZnO nanoparticles across the silica surface, forming a well-dispersed and porous morphology. This morphology facilitates efficient mass transfer and provides numerous accessible catalytic sites (Kumar et al., 2021). Energy-

dispersive X-ray spectroscopy (EDS) confirmed the presence of Si, Zn, and O elements, verifying the composition of the composite catalyst.
Additionally, the Brunauer–Emmett–Teller (BET) surface area analysis of the silica-supported ZnO catalyst exhibited a specific surface area of ~185 m^2/g, higher than that of bulk ZnO (~35 m^2/g). This enhanced surface area contributes directly to the improved catalytic performance observed in the Biginelli reaction (Gandhi et al., 2020). The combination of structural integrity, nanoscale particle size, and high surface area validates the suitability of silica-supported ZnO nanoparticles as a robust and recyclable catalyst.
Synthesized dihydropyrimidin-2-ones are characterized by IR, NMR and Mass Spectroscopy.
Representative Characterization of the compound is as follows:
4a. ethyl 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate: IR(KBr):3340, 3240, 1704, 1643, 740 cm^{-1}; ^{1}H NMR (DMSO-d_6),300 MHz: δ(ppm) 9.20 (,1H,s,NH), 7.75(,1H,s,NH), 7.22-7.34(,5H,m,Ar-H,J=7.6 Hz), 4.13-5.14(1H,d,CH,J=3.24 Hz),3.94-4.01(2H,q,CH_2), 2.46(3H,s,CH_3), 0.99-1.47(3H,t,CH_3, J=7.3 Hz);

RESULTS AND DISCUSSION

The catalytic performance of the silica-supported ZnO nanoparticles was systematically evaluated for the Biginelli reaction between various aldehydes, ethyl acetoacetate, and urea/thiourea under solvent-free conditions. The model reaction using benzaldehyde produced 3,4-dihydropyrimidin-2(1H)-one with an isolated yield exceeding 92% within 30 minutes at 90°C. This demonstrates the high catalytic efficiency of the developed system.

The superior activity of the silica-supported ZnO catalyst can be attributed to the synergistic effect between ZnO and the mildly acidic silica surface. ZnO provides Lewis acidic sites that activate the carbonyl group of aldehydes, while the silica support promotes adsorption and stabilization of the intermediates (Kour et al., 2014; Gupta et al., 2007). This dual activation facilitates the Biginelli condensation through an iminium–enolate coupling mechanism (Sweet & Fissekis, 1973).
The reaction mechanism involves initial formation of an imine intermediate between the aldehyde and urea, followed by nucleophilic addition of the β-ketoester enolate, leading to cyclization and dehydration. The heterogeneous catalyst surface stabilizes transition states, lowering activation energy and accelerating the reaction rate (Polshettiwar & Varma, 2010; Wan & Liu, 2010).
Optimization of reaction conditions indicated that the best results were obtained using 1 g of catalyst at 90°C under solvent-free conditions. Using higher temperatures did not significantly improve yields but caused minor decomposition, while lower catalyst loading decreased conversion. Reactions performed without the catalyst or with pure silica exhibited negligible product formation, confirming the crucial role of ZnO active sites.
The catalyst was tested with a series of substituted benzaldehydes (electron-donating and withdrawing groups) to evaluate substrate scope. All reactions proceeded smoothly, giving yields between 85–95%. Electron-withdrawing substituents enhanced reaction rates due to increased electrophilicity of the aldehyde carbonyl carbon.
Reusability tests revealed that the catalyst maintained its activity for up to five consecutive cycles with only a minor decrease in yield (from 92% to 88%), demonstrating its stability. Post-reaction XRD and FTIR analyses showed no significant structural changes, confirming catalyst integrity. Minimal Zn leaching was detected by atomic absorption spectroscopy (AAS), supporting the robustness of the silica support.
The performance of this catalyst compares favorably with other reported heterogeneous systems such as Fe_3O_4@SBA-15 (Mondal et al., 2012), SiO_2–$CuCl_2$ (Kour et al., 2014), and ZnO@Al_2O_3 (Bhuyan et al., 2018). Moreover, the solvent-free conditions and high recyclability highlight the potential of silica-supported ZnO as a green catalyst for multicomponent reactions. These findings suggest that this system could be extended to other condensation or coupling reactions, aligning with the principles of sustainable chemistry.

CONCLUSION

A novel heterogeneous catalyst comprising silica-supported ZnO nanoparticles has been successfully synthesized and applied for the Biginelli reaction. The catalyst exhibited high efficiency, solvent-free operation, easy recovery, and excellent recyclability. These findings suggest that silica-supported ZnO nanoparticles can serve as a green and sustainable alternative to conventional acid catalysts in multicomponent organic reactions.

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