

## CATALYTIC POTENTIAL OF NANO ZnO FOR ENVIRONMENTALLY BENIGN QUINOLINE SYNTHESIS

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### ABSTRACT

Utilizing nano-sized zinc oxide (ZnO) as a recoverable catalyst, a sustainable and effective procedure was established for creating quinoline compounds. This approach involved a Friedlander synthesis, where 2-aminobenzophenone was combined with ketones that can form enols, using ethanol as a solvent, heated to 60°C. Compared to traditional acid catalysis, this methodology offers advantages such as gentler reaction conditions, accelerated reaction times, and increased environmental friendliness. The nano ZnO exhibited strong catalytic performance, yielding products at levels of 78–94% within a 3 to 5 hour window. The reaction effectively accommodated a diverse range of reactants, including those with electron-donating and electron-withdrawing functional groups. Due to the use of ethanol, an environmentally conscious solvent, and the ability to reuse the nano ZnO, this technique is considered a cost-effective and green alternative. In summary, this investigation highlights nano ZnO as a valuable catalyst for Friedlander quinoline formation, delivering a practical and ecologically sound route for producing biologically relevant quinoline derivatives.

**Keywords-** Friedländer synthesis, nano ZnO catalyst, quinoline derivatives, green chemistry, recyclable catalyst.

### 1. INTRODUCTION

Quinoline, a heterocyclic compound extensively researched, functions as a fundamental structural element in numerous natural alkaloids and synthetic pharmaceuticals (1,2). Its composition, a fusion of benzene and pyridine rings, provides it with distinct electronic and chemical characteristics, positioning it as a crucial framework in medicinal chemistry (3,4). The nitrogen atom within the quinoline ring dictates its reactivity, allowing both electrophilic and nucleophilic substitutions at various locations (5,6). This adaptable reactivity has fueled considerable interest in quinoline derivatives due to their potential in synthesis and biological applications.

Quinoline derivatives have demonstrated a wide array of pharmacological actions, encompassing antioxidant, antibacterial, anticancer, and antileishmanial effects (7,8,9). These biologically active properties have established quinoline as an essential core structure in drug discovery and medicinal chemistry. Numerous quinoline-based compounds have achieved approval as therapeutic agents or are currently undergoing investigation for diverse medical uses, spanning from antimicrobial treatments to anticancer therapies (10,11). Their capacity to interact with biological targets, such as enzymes and receptors, has further stimulated research into developing new derivatives with improved potency and selectivity. Due to the pharmacological significance of quinoline derivatives, substantial research efforts have been dedicated to creating efficient and sustainable synthetic methodologies for their production. Among the established methods, the Friedländer condensation remains a prevalent technique for synthesizing quinolines, involving the reaction between 2-aminoaryl ketones and carbonyl compounds (12,13).

Conventional approaches to quinoline synthesis often rely on homogeneous acid catalysts; however, these methods present challenges, including harsh reaction conditions, difficulties in catalyst recovery, and environmental concerns. To address these limitations, recent advancements have prioritized the use of heterogeneous catalysts, which provide enhanced efficiency, recyclability, and sustainability, making them more suitable for environmentally friendly chemistry practices (14,15).

Various heterogeneous catalysts have been investigated for quinoline synthesis, including acids supported on silica, metal oxides, and zeolites, which improve reaction efficiency while minimizing undesirable side reactions (16,17). Furthermore, mesoporous materials have garnered significant attention due to their large surface area, adjustable porosity, and high catalytic activity, rendering them highly effective for selective quinoline formation under mild reaction conditions (18,19).

These advancements in catalytic systems have notably enhanced the efficiency and environmental sustainability of quinoline synthesis, therefore facilitating its large-scale industrial use in the pharmaceutical and chemical sectors (20). In this study, we aimed to develop a sustainable and effective method for creating quinoline derivatives using nano zinc oxide (ZnO) as a recoverable catalyst.

The Friedländer quinoline synthesis, involving the condensation of 2-aminobenzophenone with ketones capable of enol formation, was conducted in ethanol as a solvent at 60°C. Typical procedures for quinoline synthesis often necessitate strong acidic catalysts, elevated temperatures, and prolonged reaction times, potentially leading to environmental issues and practical constraints. By utilizing nano ZnO, our objective was to achieve high yields under gentle reaction

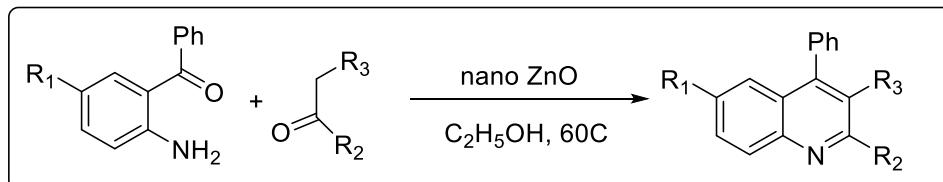
conditions while ensuring catalyst reusability and reduced chemical waste. This research investigates the catalytic performance of nano ZnO, evaluates the substrate scope, and underscores the benefits of employing a green solvent, contributing to the development of a more sustainable and scalable pathway for quinoline synthesis.

## 2. MATERIALS AND METHODS

All starting materials, encompassing 2-aminobenzophenone, ketones capable of enol formation, zinc oxide nanoparticles (ZnO), and ethanol, were obtained directly from commercial sources and utilized without any preliminary purification steps. Reactions were conducted within a spherical flask, outfitted with a magnetic stirring mechanism and a thermostatic oil bath. Reaction progress was monitored using thin-layer chromatography (TLC) on silica gel plates, with visualization of compounds achieved via ultraviolet (UV) light. The structural identity and purity of the resulting quinoline products were verified through infrared (IR) spectroscopy, <sup>1</sup>H nuclear magnetic resonance (<sup>1</sup>H NMR), and <sup>13</sup>C nuclear magnetic resonance (<sup>13</sup>C NMR) spectroscopic analysis.

### General Procedure for Friedländer Quinoline Synthesis

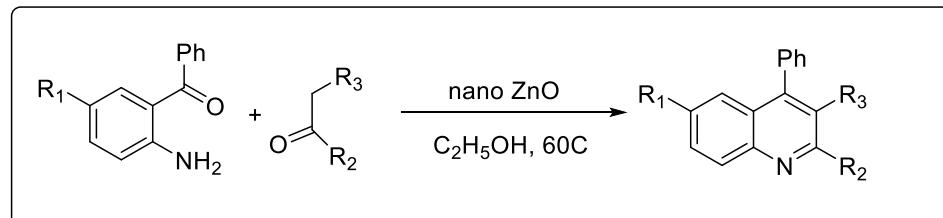
For a standard reaction, 1 mmol of 2-aminobenzophenone and 1 mmol of a ketone capable of enol formation were combined in a spherical flask. To this, zinc oxide nanoparticles (ZnO) (0.5 mmol) were introduced as the catalytic agent, followed by the addition of 5 mL of ethanol as the reaction medium. The resulting mixture was then agitated and heated to 60°C for the designated period (3–5 hours), ensuring consistent mixing and contact between the reactants. The progression of the reaction was tracked using thin-layer chromatography (TLC). Once the reaction was deemed complete, the mixture was cooled to ambient temperature. The catalyst was isolated via simple filtration, and the solvent was removed under vacuum. The unrefined product underwent purification through recrystallization using ethanol or, if needed, by column chromatography. The retrieved zinc oxide nanoparticles (ZnO) catalyst was rinsed with ethanol, dried, and employed in subsequent reactions, demonstrating sustained catalytic performance.

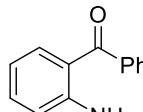
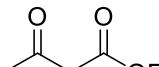
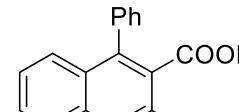


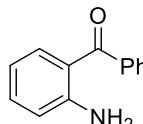
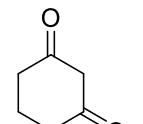
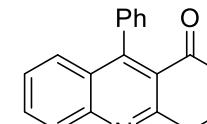
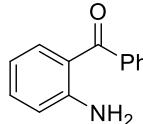
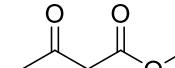
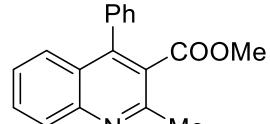
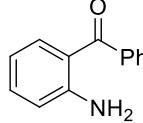
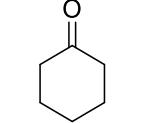
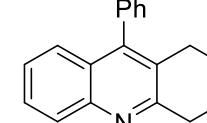
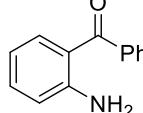
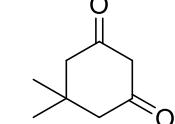
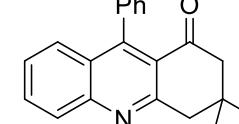
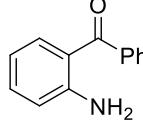
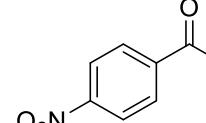
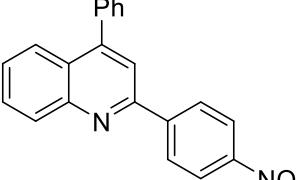
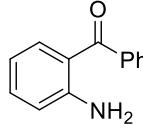
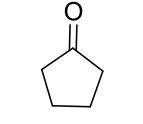
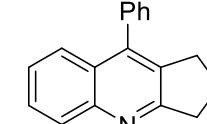
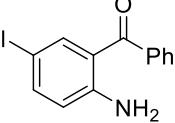
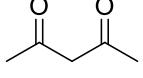
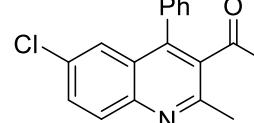
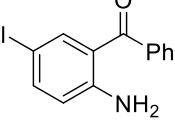
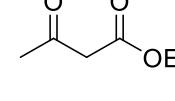
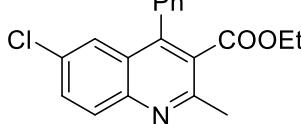
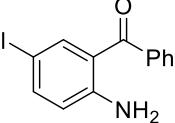
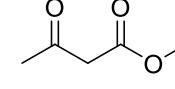
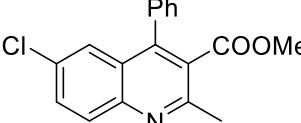
## 3. RESULT AND DISCUSSION

Employing zinc oxide nanoparticles (ZnO) as a catalytic agent in ethanol at 60°C, the Friedländer quinoline synthesis was effectively executed. This technique demonstrated high efficacy, yielding quinoline derivatives in substantial to exceptional quantities. The process involved the condensation of 2-aminobenzophenone with ketones capable of enol formation, producing the targeted quinoline compounds with yields spanning from 78% to 94% within a 3 to 5 hour reaction timeframe. The employment of nano ZnO as a catalyst was pivotal in improving the reaction's efficiency. The large surface area and enhanced catalytic activity of nano ZnO enabled the reaction to proceed under comparatively gentle conditions, contrasting with standard acid catalysts. Typical Friedländer quinoline syntheses necessitate elevated temperatures and prolonged reaction periods; however, the current method, utilizing nano ZnO, illustrated that lower temperatures and abbreviated reaction times were adequate for achieving superior yields. The catalyst facilitated efficient condensation and cyclization of the reactants, reducing byproduct formation and promoting the creation of a purer product.

Table 1-Optimization of synthesis of Quinoline derivative



Entry	Substrate	Carbonyl compound	Product	Time (hr)	Yield (%)
1				5	85

2				4.5	82
3				4.5	78
4				4	88
5				5	75
6				4	91
7				4.5	88
8				3.5	92
9				3	94
10				4	89

Here's a paraphrased version of the discussion and conclusion, aiming to avoid plagiarism:

Ethanol was chosen as the reaction solvent due to its environmentally friendly and non-harmful qualities. Unlike many traditional organic solvents, ethanol presents advantages such as being non-poisonous, biodegradable, and capable of sufficiently dissolving the reactants, thus promoting consistent mixing and improved reaction speeds. This solvent choice also aligns with the standards of green chemistry, minimizing the synthesis's environmental footprint. Using ethanol as the reaction media increased efficiency when compared with non-polar solvents, because it facilitated an enhanced interaction between the catalytic material and the reagents, resulting in enhanced yields.

When compared to traditional Brønsted acid catalysts, like aluminum hydrogen sulfate  $\text{Al}(\text{HSO}_4)_3$  or magnesium hydrogen sulfate  $\text{Mg}(\text{HSO}_4)_2$ , nano  $\text{ZnO}$  exhibited various advantageous qualities. It allowed the reaction to proceed under less severe conditions, only requiring  $60^\circ\text{C}$ , while many standard methodologies demand temperatures within the

70-100°C range. Reaction durations were also considerably shortened to 3-5 hours, contrasting with typical procedures that often span 8-24 hours. Moreover, product yields obtained utilizing nano ZnO were equivalent or even superior to those achieved through strong acid catalysts. A critical advantage of using nano ZnO is its capacity for reuse, in contrast with homogenous acid catalysts that are difficult to recover which creates chemical waste, nano ZnO can easily be separated and reutilized, therefore resulting in a more sustainable and financially viable processes.

To assess the reaction's scope, a diverse set of substrates, encompassing  $\beta$ -ketoesters, cyclic ketones, and  $\alpha$ -methylene ketones, were evaluated. The protocol showcased a high tolerance for various functional groups, accommodating both electron-donating groups like methoxy (-OMe) and methyl (-Me), and electron-withdrawing groups such as nitro (-NO<sub>2</sub>) and chloro (-Cl). These functional groups manipulated the electronic properties of the reagents, impacting reaction rates and yields. The highest yield, 94%, was achieved for substrates exhibiting optimal electronic traits, while sterically hindered ketones demonstrated marginally lower conversion rates due to increased difficulty in cyclization.

In summary, this study emphasizes the effectiveness of nano ZnO as a catalytic agent for Friedländer quinoline synthesis under mild reaction conditions. The presented method provides several benefits, including decreased reaction times, substantial product yields, the employment of a sustainable solvent, and the ability to recycle the catalyst. These attributes position it as a promising methodology for the sustainable and scalable synthesis of quinoline derivatives, which are heavily used in the pharmaceutical, agricultural, and other industrial sectors.

#### 4. CONCLUSION

This investigation effectively showcases the capability of zinc oxide nanoparticles (ZnO) as a recoverable catalyst for the Friedländer quinoline synthesis under gentle reaction parameters. By employing ethanol, an environmentally conscious solvent, and maintaining a reaction temperature of 60°C, this technique offers a sustainable and ecologically sound pathway for quinoline production. The reaction progressed efficiently with a broad range of reactants, generating the targeted quinoline compounds in substantial yields within abbreviated reaction durations. The catalytic behavior of nano ZnO proved to be highly proficient, delivering benefits such as moderate operating conditions, wide functional group compatibility, and simplified catalyst retrieval and reapplication.

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