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CuO Nanoparticles as an Efficient and Reusable Catalyst for the One-pot Friedlander Quinoline Synthesis

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The quinoline ring system[1] is presents in a number of natural[2] and synthetic products often endowed with interesting pharmacological or physical properties.[3] Quinoline derivatives are utilized as antimalarial,[4] antitumor,[5] and antibacterial agents.[6,7] Due to their importance, the synthesis of quinolines attracted widespread attention. Despite quinoline usage in pharmaceutical and other industries, comparatively few methods for their preparation have been reported. The Friedlander annulation is one of the simplest and most straightforward methods for the synthesis of poly substituted quinolines.[10] Modified methods employing acid catalysts such as lewis acids, brønsted acids and ionic liquid have been reported for the quinoline synthesis.[11] Although these approaches are satisfactory for a one-pot synthesis of quinolines, they suffer from at least one of the following drawbacks such as long reaction times, low yields of the products requiring stoichiometric amounts of catalysts, excess amounts of diketone compounds or use of additives. Such reactions under solvent-free condition have received more attention in comparison with their homogeneous counterparts, due to economical and environmental demands.

Metal oxide nanoparticles are known to generate a very high catalytic activity toward a wide range of catalytic-based applications.[12,13] In recent years, methods have been developed for the preparation of novel nanostructures of oxides.[14] They can be generated by a number of preparation methods that typically are described as physical and chemical methods.[15] Recently, nano ctystalline Al_2O_3 and γ-Fe_2O_3 nanoparticles have been used for Freindlander reaction.[16] In another hand, CuO nanoparticles have been previously used as heterogeneous and recyclable catalyst for α-aminophosphonate synthesis and cross coupling reactions.[17] The solvent-less protocol has an added advantage in the green context. The major benefits of the CuO nano as a heterogeneous catalytic process are the fast reactions, solvent-free environment, and improved yields. The catalytical activity of CuO is well known. The CuO catalyst is prepared by PEG assisted method with a few modification.[18] The size of the prepared catalyst is found to be 25-27 nm and surface area about 214 m^2/g. The prepared Cuo nanoparticles were characterized by XRD and SEM.

Model reaction was carried out by taking the mixture of 2-aminobenzophenone, ethyl acetoacetate and 5 mol % of catalyst in solvent free condition at 60 °C. TiO_2, SiO_2, Al_2O_3, ZnO, MgO, CuO bulk and nano CuO have been used. In our screening CuO nano was the best. This would be a novel application of CuO nano catalyst for the Friedlander quinoline synthesis.

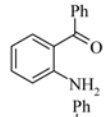
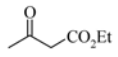
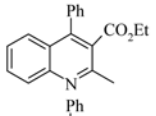
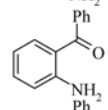
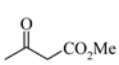
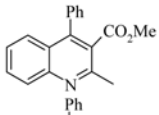
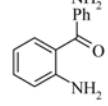
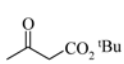
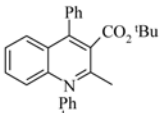
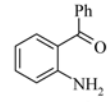
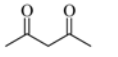
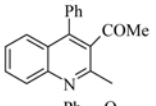
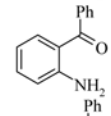
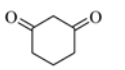
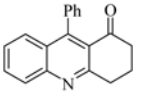
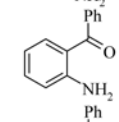
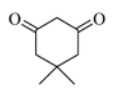
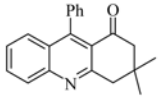
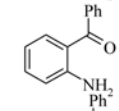
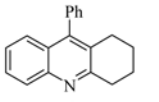
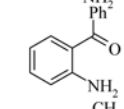
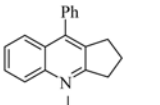
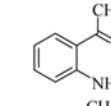
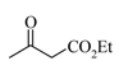
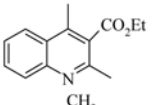
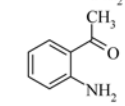
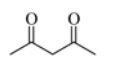
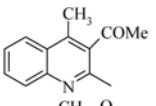
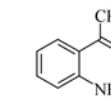
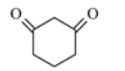
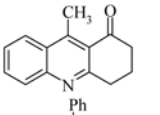
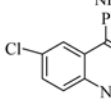
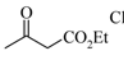
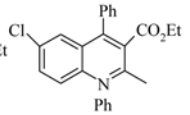
Various reaction parameters are optimized for this reaction. The reaction was carried out with and without solvents keeping the catalyst amount constant. It is observed that solvent-free condition gave the excellent yield of product than that in the presence of solvents.

Subsequently, we applied the optimized conditions to a variety of 2-aminoaryl ketones, active methylene compounds and simple cyclic ketones which furnished diversely substituted quinoline derivatives (Table 1). The solid products could be easily separate by using organic solvent and heterogeneous catalyst was separated by simple filtration. To determine the applicability of catalyst recovery, catalyst was washed with diethyl ether to remove residual product, dried, and reused over five successive cycles without any pretreatment of the catalyst.

In summary, the advantages of performing the Friedlander reaction in the presence of CuO nano as catalyst can be summarized as follows: (1) use of a safe, nonvolatile, non-corrosive catalyst; (2) high yields of recovering of catalyst at the end of the reactions by simple filtration; (3) the target products are obtained generally in excellent yields under easy and mild reaction conditions; and (4) the reactions are carried out under solvent free conditions with economic benefits.

General Procedure for One-Pot Synthesis of Quinolines: To a mixture of 2-aminoaryl ketones (2 mmol) and β-ketoester/1,3-diketone/cyclic ketone (2 mmol) was added CuO nanoparticles (5 mol %). The mixture was stirred at 60 °C until completion of the reaction, as indicated by TLC. The nanocatalyst was separated from the reaction mixture by

Table 1. Synthesis of Quinoline derivatives catalyzed by CuO nano[a]

Entry	Compound **1**	Compound **2**	Product	Time (h)	Yield (%)
a				1	98
b				1	96
c				3	94
d				1	98
e				5	90
f				5	88
g				8	85[b]
h				8	85[b]
i				1	96
j				1	94
k				3	88
l				2	94

[a]Reaction condition: 2 mmol **1**, 2 mmol **2** and 5 mol % $CuFe_2O_4$ at 60 °C. [b]5 mol % catalyst, 80 °C; 1.5 eq of 2 was used.

simple filtration. The products being soluble in CH_2Cl_2 and could be separated by filtration.

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