ZnO Nanoparticles: An Efficient Catalyst for Synthesis of (*E*)-4-(2-(4-Chlorophenyl) hydrazono)-3,3-Dimethyl-2,6-diphenylpiperidines

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Abstract

ZnO Nanoparticles is an efficient and reusable catalyst for the preparation of (E)-4-(2-(4-chlorophenyl) hydrazono)-3,3-dimethyl-2,6-diphenylpiperidines in excellent yields. The ZnO nanoparticles have good catalytic activity and reusability for up to five cycles. The synthesized (E)-4-(2-(4-chlorophenyl) hydrazono)-3,3-dimethyl-2,6-diphenylpiperidines have been characterized by IR and NMR spectral studies.

Keywords: Synthesis, ZnO catalyst, (*E*)-4-(2-(4-chlorophenyl) hydrazono)-3,3-dimethyl-2,6-diphenylpiperidines

Introduction

Recently, catalysis by metal nanoparticles have been attracted considerable attention due to their many significant properties of large and reactive surface areas, selectivity, ability to perform the reaction under milder conditions and finally ease of isolation after reactions. In recent years, the nanostructured metal oxides (NPs) have attracted considerable attention used as catalyst because of their both Lewis base and Lewis acid nature and redox properties on the surface [1]. Metal oxide reaction under milder conditions and finally the ease of isolation after reactions. In recent years, nanoparticles, including zinc, have gained significant importance as they have been demonstrated to be applicable to photovoltaic solar cells,[2] UV lasers,[3] ultraviolet (UV) photodiodes[4] and nano-generators[5]. However, in recent times; Zinc oxide nanoparticles (ZnO NPs) have also been employed as powerful catalyst for organic transformations because it can be prepared easily from inexpensive starting materials. They are also nontoxic, less corrosive and recyclable[6].

The piperidine derivatives are found to possess pharmacological activity and form an essential part of the molecular structures of some important drugs[7,8]. In recent decade piperidine derivatives have a great deal of interest in exploiting more than one proximal functional groups for designing novel structures capable of performing a variety of functions like antiviral,[9] antitumour,[10] central nervous system,[11] local anesthetic,[12] anticancer,[13] and antimicrobial activity[14]. The piperidine compounds are biologically important and also act as neurokinin receptor antagonists,[15] analgesic[16] and anti-hypertensive[17] agents.

In this present investigation, we have synthesized (*E*)-4-(2-(4-chlorophenyl)hydrazono)-3,3-dimethyl-2,6-diphenylpiperidines by the reaction of 3,3-Dimethyl-2,6-diarylpiperidin-4-ones,

4-chloro phenylhydrazine with ZnO NPs is a catalysis for the synthesis of a new application of ZnO nanoparticles as efficient catalyst in organic synthesis is described.

Experimental

All chemicals and anhydrous solvents were performed from Merck and Aldrich. The reaction process and the purity of the products were performing by thin layer chromatography. Melting points of all the synthesized piperidine compounds were measured on Open glass capillaries melting point apparatus and are uncorrected. IR spectra of all the piperidine compounds have been recorded on a Shimadzu FT-IR spectrometer and the ^{1}H & ^{13}C NMR spectral studies were carried out using Bruker 300 MHz.

3,3-Dimethyl-2,6-Diarylpiperidin-4-ones (1-4)

The compounds were synthesized as per literature procedures previously described

Synthesis of (E)-4-(2-(4-chlorophenyl)hydrazono)-3,3-dimethyl-2,6-diphenylpiperidine

A mixture of equal molar quantity of 3,3-Dimethyl-2,6-diarylpiperidin-4-ones (0.001 mol), 4-Chloro phenylhydrazine (0.001 mol) and ZnO NPs (30 mg) were taken in an open mortar and pestle the reaction mixture was thoroughly grounded at room temperature for 20–40 min. The reaction progress was monitored by TLC. After completion of the reaction mixture was washed with methanol (10 ml) for two times. The solid product was dissolved in dichloromethane; the catalyst was insoluble in ethyl acetate (5 ml) and separated by a simple filtration. The precipitate was recrystallized using ethanol to obtain the glittering solids. This same synthetic method was used for the synthesis of their derivatives. The formation of product was confirmed by the melting point determination and spectroscopic (IR, ^{1}H and ^{13}C NMR) studies. Synthetic routes of compounds are given in scheme 1.

Spectral data

(E)-4-(2-(4-chlorophenyl)hydrazono)-3,3-dimethyl-2,6-diphenylpiperidine

Yellow glittering solid; Yield 80%., M.P: 191°C, IR (KBr, cm^{-1}): 3462, 3068, 2935, 1547; ^{1}H-NMR ($CDCl_3$) 7.21-8.18 (m, Ar-**H**), 7.28 (1H, N-**H**), 2.16 (1H, N-**H**), 3.01(1H, H5ax,), 3.13 (1H, H5eq), 3.88 (1H, H_2), 3.54 (1H, H_6), 1.62 (3H, C**H**$_3$); 13C NMR (100 MHz, CDCl3, δ, ppm):160.09 (C=N), 120.17-146.32 (Ar-C), 66.72 C(2), 56.41 C(6), 44.34 C(3), 34.15C(5), 26.06 (CH_3). MF: $C_{25}H_{26}ClN_3$; elemental analysis: Calcd (%): C, 69.82, H, 5.87; N, 9.81; found (%):C, 69.11; H, 5.16; N, 8.79.

(E)-2,6-bis(4-chlorophenyl)-4-(2-(4-chlorophenyl)hydrazono)-3,3-dimethylpiperidine

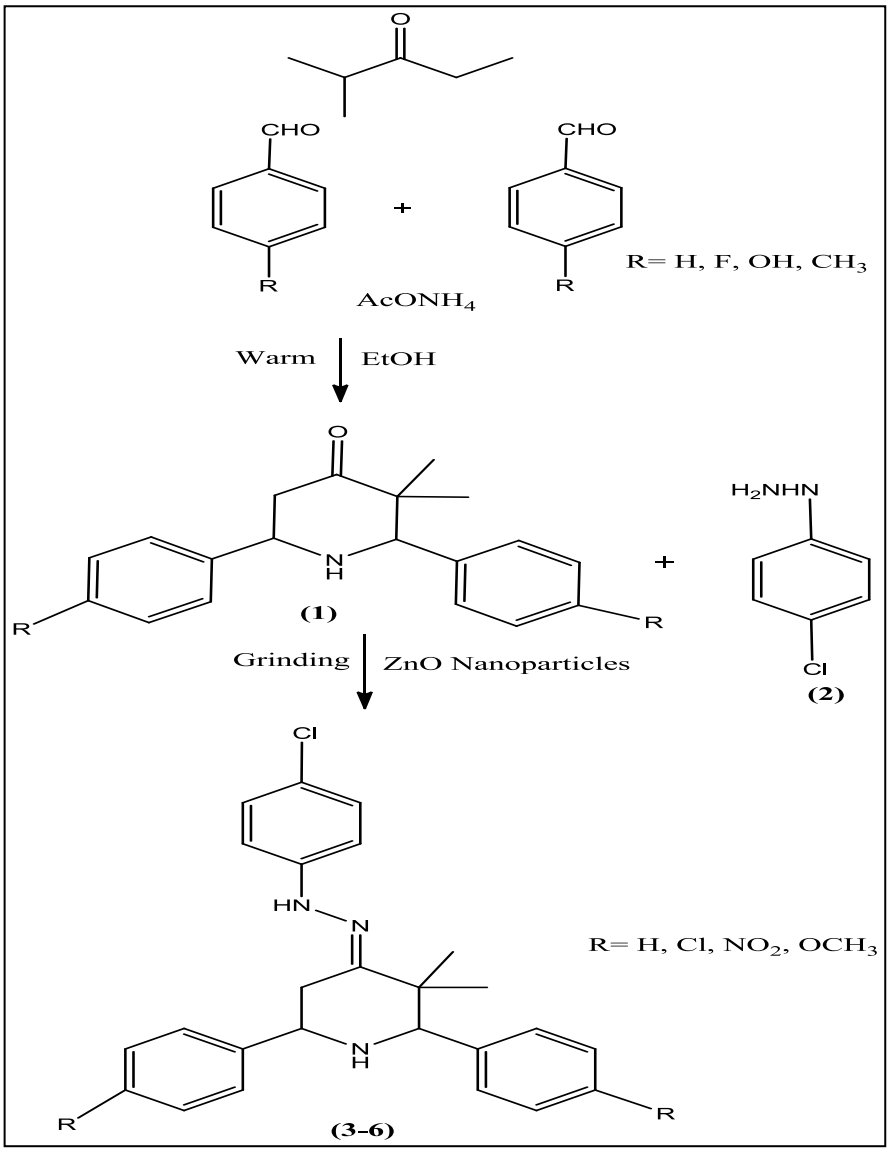
Yellow solid; Yield 85%., M.P: 204°C, IR (KBr, cm^{-1}): 3472, 3064, 2920, 1574; ^{1}H-NMR ($CDCl_3$) 7.14-7.78 (m, Ar-**H**), 7.26 (1H, N-**H**), 2.18 (1H, N-**H**), 3.36 (1H, H_2), 2.18 (1H, H5ax,), 2.54 (1H, H5eq), 4.00 (1H, H_6), 1.61 (3H, C**H**$_3$); ^{13}C NMR (100 MHz, CDCl3, δ, ppm): 156.38 (C=N), 118.11-148.12 (Ar-C), 66.92 C(2), 57.97 C(6), 42.58 C(3), 38.23 C(5), 14.43 (CH_3). MF: $C_{25}H_{24}Cl_3N_3$; elemental analysis: Calcd (%): C, 68.92; H, 5.82; N, 9.09;; found (%):C, 67.98; H, 5.79; N, 9.02.

(E)-4-(2-(4-chlorophenyl)hydrazono)-3,3-dimethyl-2,6-bis(4-nitrophenyl)piperidine

Yellow glittering solid; Yield : 85%., M.P: 172°C, IR (KBr, cm^{-1}): 3387, 3048, 2918, 1558; ^{1}H-NMR ($CDCl_3$) 7.38-8.11 (m, Ar-**H**), 7.10 (1H, N-**H**), 2.37 (1H, N-**H**), 3.19 (1H, H_2), 2.37 (1H, $H5_{ax}$), 2.56 (1H, $H5_{eq}$), 4.76 (1H, H_6), 1.86 (3H, C**H**$_3$), ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 154.63 (C=N), 118.89-148.41 (Ar-C), 65.05 C(2), 55.59 C(6), 44.98 C(3), 42.83 C(5), 14.93 (CH_3). MF: $C_{25}H_{24}ClN_5O_4$, elemental analysis: Calcd (%):C,81.57; H, 7.86; N, 10.57; found (%):C, 80.98; H, 6.69; N, 9.53.

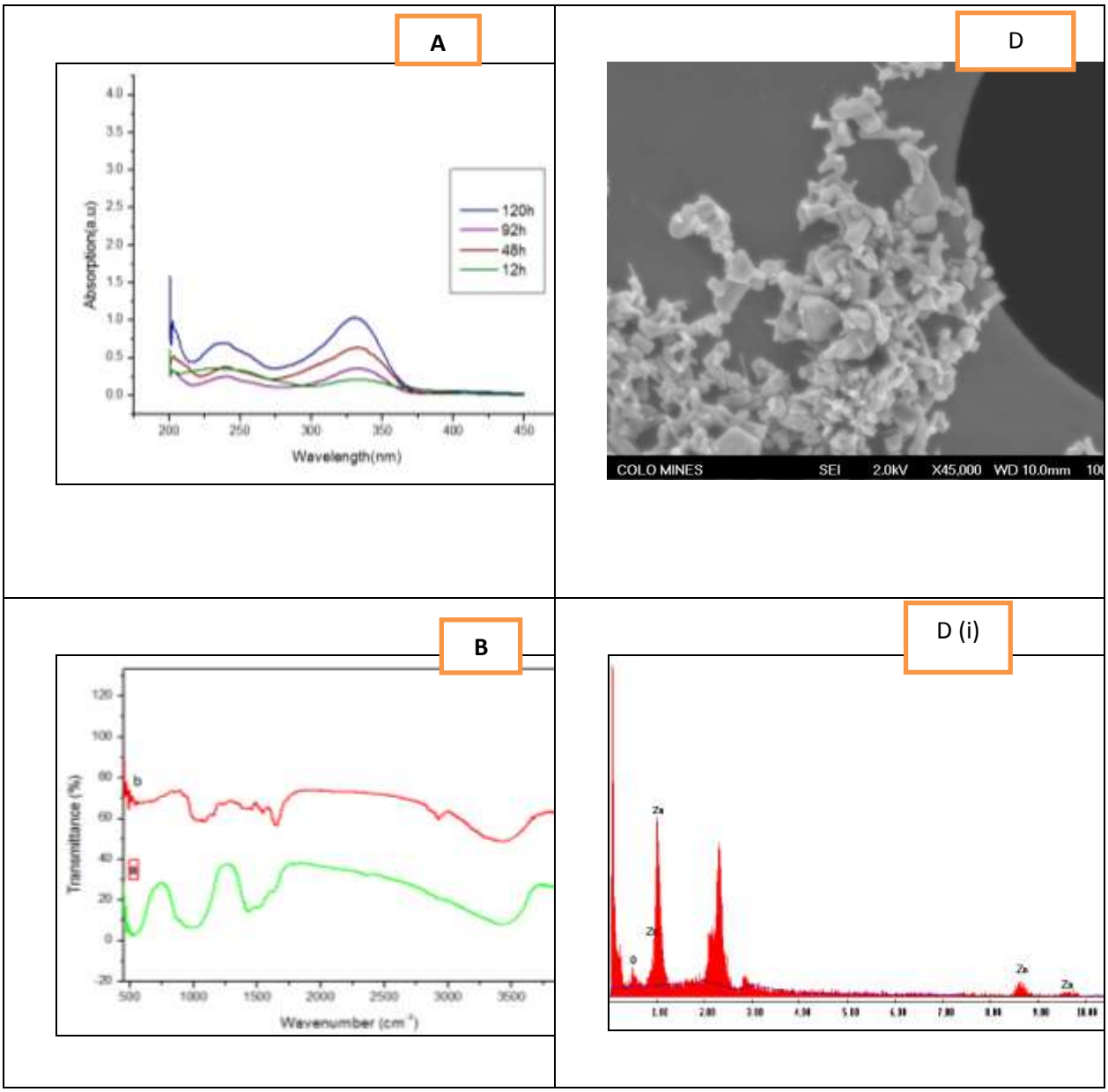
(E)-4-(2-(4-chlorophenyl)hydrazono)-2,6-bis(4-methoxyphenyl)-3,3-dimethylpiperidine

Yellow glittering solid; Yield 80%., M.P: 214°C, IR (KBr, cm^{-1}): 3462, 3067, 2917, 1596; ^{1}H-NMR ($CDCl_3$) 7.16-7.59 (m, Ar-H), 6.65 (1H, N-H), 2.18 (1H, N-H), 3.62 (1H, H_2), 2.39 (1H, H5ax,), 3.48 (3H, OCH_3), 2.67 (1H, H5eq), 1.63 (3H, CH_3), 3.64 (1H, H6); ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 154.95 (C=N), 54.29 C(6), 67.12 C(2), 122.56-155.90 (Ar-C), 50.40 C(5), 53.09 C(3), 20.15 (CH_3), 64.52 (OCH3). Anal. calcd for $C_{27}H_{30}CClN_3O_2$; elemental analysis: Calcd (%):C, 72.38; H, 7.00; N, 8.89; O, 6.88. Found (%): C, 71.12; H, 6.89; N, 8.65.



Results and Discussion

At first, ZnO NPs have been prepared by 20 ml of murraya koenigii seed extract, 80 ml of zinc nitrate $Zn(NO_3)_2$ and few drops of 2.0 M sodium hydroxide solution was added with continuous and vigorous shaking for 3–5 h, after completion of the reaction the black coloured solution is formed and then incubated for overnight at room temperature. The white coloured precipitate was settled down at the bottom of the conical flask. The formation of the synthesized zinc oxide nanoparticles (nano-sized ZnO) was indicated by UV-Vis study (λ_{max} = 330 nm) (Figure 1a) which was further confirmed by Infrared spectral study (zinc and oxygen bond at 525.35 cm^{-1}) (Figure 1a).



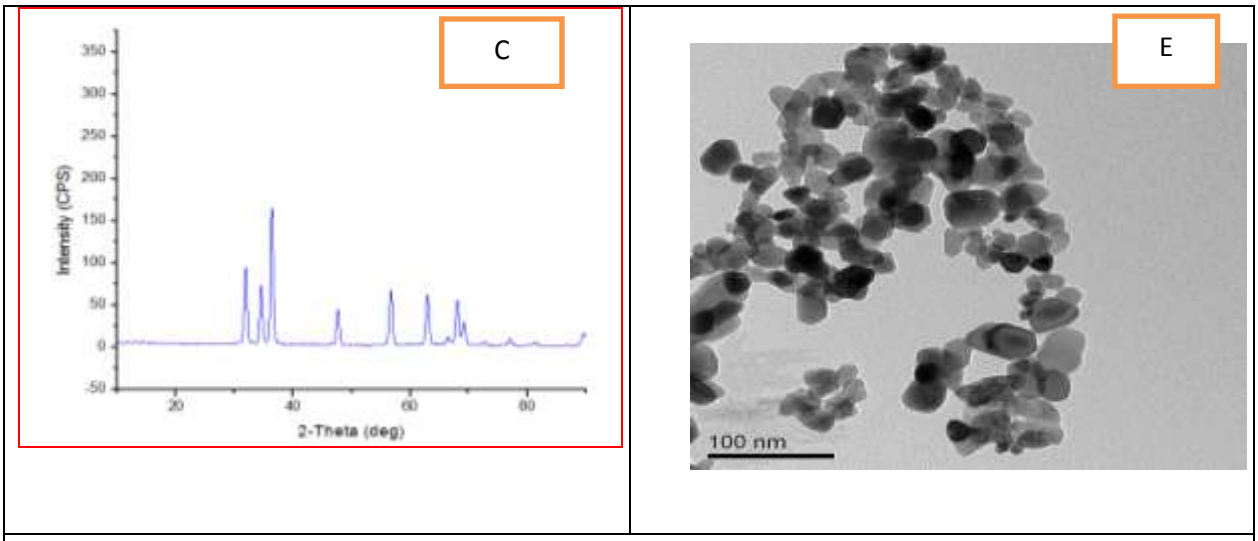


Fig. 1: (**A**) UV–visible absorption spectra of zinc oxide nanoparticles with different incubation time, **(B)** FT-IR spectra of (i) murraya koenigii seed extract and (ii) zinc oxide nanoparticles (ZnNPs), (C) XRD patterns of zinc oxide nanoparticles synthesized after 120 h of incubation, **(D)** (i) FESEM micrographic image of synthesized ZnO NPs (ii) EDX of the zinc oxide nanoparticles showing chemical composition, **(E)** TEM images of synthesized zinc oxide nanoparticles using extract of murraya koenigii seed extract.

The powder XRD diffraction pattern obtained at 69.07°, 67.9°, 56.6°, 47.5°, 36.2°, 34.4° and 31.80° are observed corresponding to (2 0 1), (1 1 2), (1 1 0), (1 0 2), (1 0 1), (0 0 2) and (1 0 0) planes. This planes suggesting the face-centered cubic (fcc) crystalline nature of the Zinc Oxide nanoparticle. The SEM images have been measured and topographical analysis was performed based upon the surface study. The SEM image shows triangle, radial, spherical, rod, rectangle, and hexagonal shapes. The size of the zinc oxide is about 100 nm as obtained by the bio-synthesis process. The TEM image of ZnO NPs shows different sizes such as radial, triangle, rod, hexagonal, and rectangle with size of 100 nm. On the basis of the characterization of the prepared nano catalyst have been utilised for the preparation of new organic molecules.

In the present work, we describe a simple and effective method for the synthesis of (*E*)-4-(2-(4-chlorophenyl)hydrazono)-3,3-dimethyl-2,6-diphenylpiperidine derivatives catalysed by ZnO nanoparticles shown in (Scheme 1). The effect of catalyst on the reaction rate and the product yield was investigated and summarized in Table 1. As a result, application of this catalytic system effectively gives desired products in excellent yields (Table 1). This table indicates that the yield was increased to some extent when 0.5 g of ZnO nano-particles is used. No substantial improvement in the yield was observed by increasing the quantity of ZnO nano-catalyst to 1.0 g. Finally, in this investigation the optimum amount of the catalyst is found to be 0.5 g for the synthesis of piperidine derivatives (Figure.2). The aromatic aldehydes with nitro and chloro electron-withdrawing substituents reacted faster than those that reacted with electron-releasing methoxy substituent as expected. Also, aromatic aldehydes required longer reaction times due to sterical hindrance. The products were characterized by IR, ^{1}H NMR and ^{13}C NMR spectral analysis.

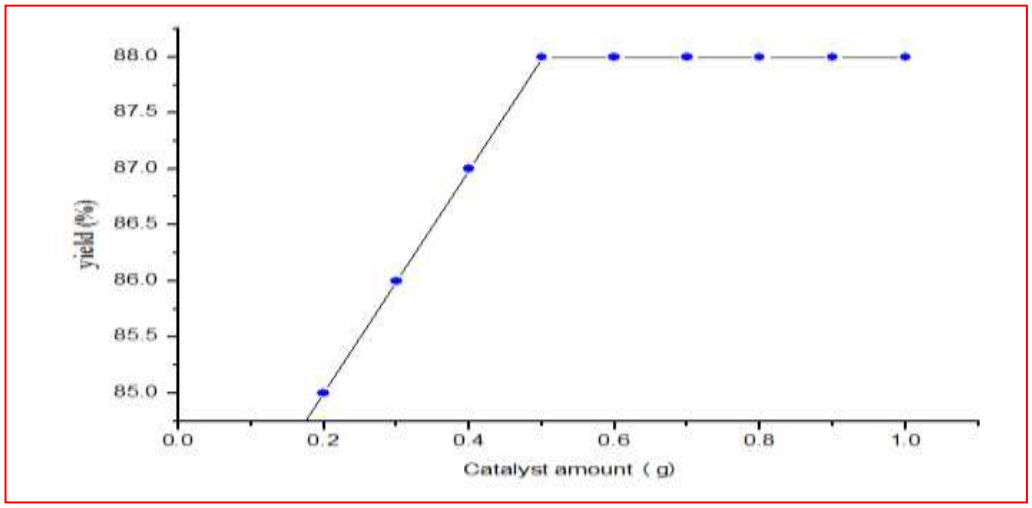
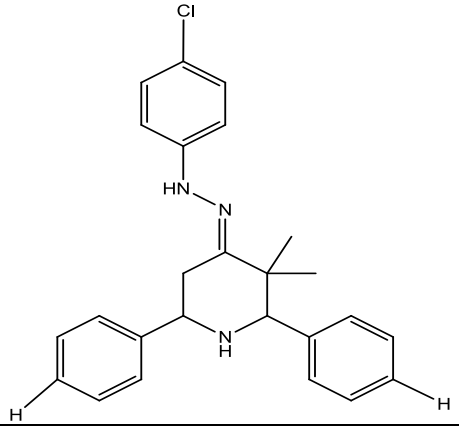
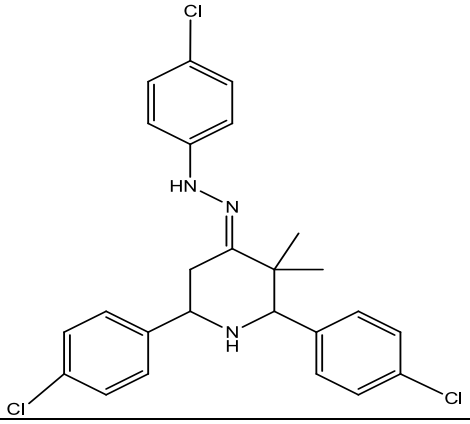
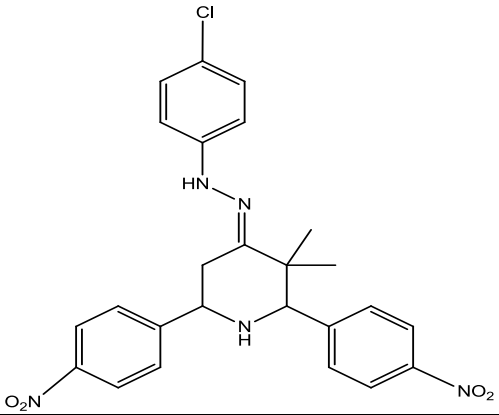
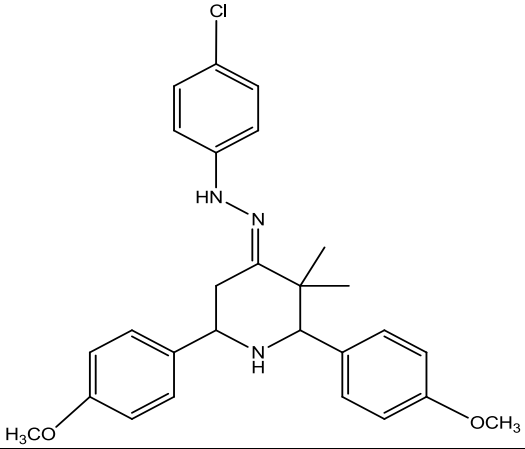


Fig.3: Optimization of catalyst amount.

Table No.1: ZnO NPs catalyzed synthesis of piperidine derivatives

Entry	Product	Time (min)	Yield (%)
3		180	80
4		170	85

5		**175**	**85**
6		**185**	**80**

The ZnO nano-catalyst had been examined for the reusability. ZnO nano-catalyst was recovered through filtration from the reaction mixture and washed with ethyl acetate, and reused for subsequent experiments (up to five cycles) under similar reaction conditions. The ZnO nanoparticles catalyzed the reaction well without significant loss in activity (Figure. 3). This figure indicate that the catalyst have good catalytic activity.

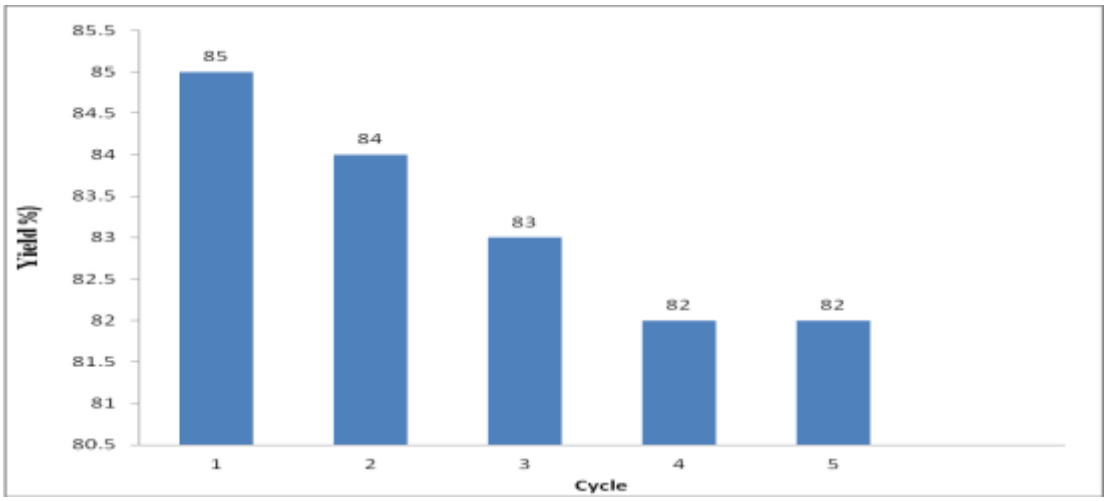


Fig. 2: Recyclability of the ZnO NPs in synthesis of piperidine derivatives

Conclusion

We have successfully synthesized some (*E*)-4-(2-(4-chlorophenyl)hydrazono)-3,3-dimethyl-2,6-diphenylpiperidine derivatives from 3,3-Dimethyl-2,6-diarylpiperidin-4-ones with4-chlorophenyl hydrazine using zinc oxide nano particle is an efficient catalyst in this investigation. This method offer several advantages such as avoidance of organic solvent, recyclable, ease of separation, and high yield. The ZnO nano catalyst is compatible with environment and can be considered as green and sustainable issues.

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