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Original article

Nickel oxide nanoparticles catalyzed synthesis of poly-substituted quinolines *via* Friedlander hetero-annulation reaction

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ABSTRACT

Reusable acidic nickel oxide nanoparticles have been synthesized, characterized and applied as a catalyst to convert 2-aminoaryl ketones and β-ketoesters/ketones into the corresponding quinolines in good yields with high selectivity. This could serve as a simple and convenient procedure for the Friedlander annulations.

1. Introduction

Quinolines are an important class of heterocycles due to their wide range of pharmacological properties such as antimalarial, anti-inflammatory, anti-asthmatic, antibacterial, antihypertensive, tyro-kinase PDGF-RTK inhibitory activities. The derivatives of quinolines are also used as synthetic building blocks in the synthesis of heterocycles [1–6]. The classical methods to synthesize quinolines require harsh reaction conditions and the yields are unsatisfactory in most cases [7]. The Friedlander annulation, which involves the condensation of an aromatic 2-amino aldehyde/ketone with ketone/aldehyde containing active methylene group followed by cyclization, is the simplest and most straightforward synthetic method for the synthesis of quinoline derivatives, especially for the highly substituted 3-functionalized quinolines [8]. Hydrochloric acid, sulfuric acid, *p*-toluenesulfonic acid and PPA have been employed as catalysts for this conversion [9–12]. Some of the methods reported for the synthesis of quinolines also involve the use of catalysts such as $SnCl_2$, $BiCl_3$, I_2 [12,13], montmorillonite KSF clay [14], ionic liquids [15], $Bi(OTf)_3$ [16], $Y(OTf)_3$ [17], silver dodecatungstophosphate [18], silica sulfuric acid, sulfamic acid, neodymium nitrate [19,20], dodecylphosphonic acid (DPA) [21], proline [22], silica supported phosphomolybdic acid [23], and sodium ethoxide [24]. However, most of these methods suffered from certain drawbacks such as harsh reaction conditions, use of expensive catalysts, and long reaction time, *etc.* Thus, a simple and environmentally benign procedure with an inexpensive and readily available reagent is desirable, which prompted us to test the feasibility of NiO nanoparticles (NiO NPs) as a catalyst for the synthesis of quinolines without any co-catalysts or additives. Hence in continuation of our earlier effort on quinolines [25–33] syntheses, herein we report an efficient, cost effective and environmentally benign procedure for the synthesis of multi-substituted quinolines (Scheme 1).

2. Experimental

2.1. General

Chemicals were purchased from Sigma Aldrich, Fluka and used as received. IR spectra were recorded using an AVATAR 330 equipped with a DTGS detector. NMR spectra were recorded on a Bruker AMX-400 instrument in $CDCl_3$ using TMS as an internal reference. Mass spectra were recorded either on an ABI QSTAR XL ESI-TOF Mass spectrometer (Sciex Model) or an LC–MS using Agilent 1200 series LC and Micromass zQ spectrometer. Melting points were determined in open capillaries and were uncorrected. Powder X-ray diffraction analysis was carried out using a Bruker D8 Advance diffractometer and lanthanum hexaboride (LaB_6) was used to calibrate the instrument before analysis.

2.2. Synthesis of the catalyst

To a solution of 2.3 g of $Ni(NO_3)_2{\cdot}6H_2O$ in 10 mL distilled water, 10 mL of 15% NaOH was added drop wise with constant stirring.

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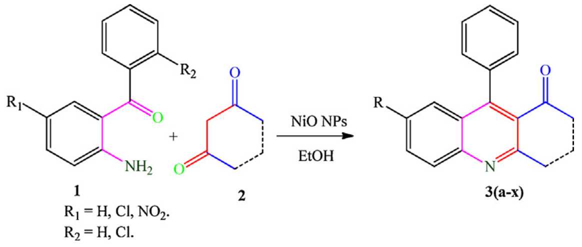

Scheme 1. Synthesis of poly-substituted quinolones.

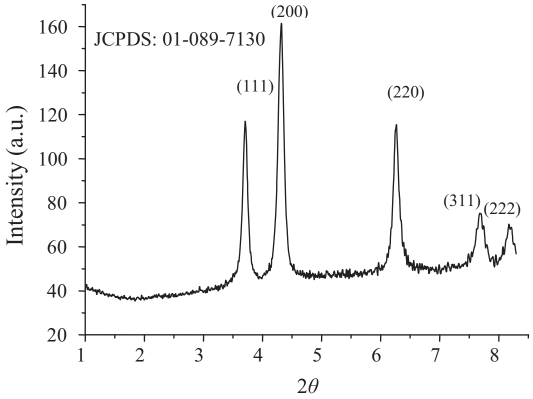

Fig. 1. XRD pattern of synthesized NiO nanoparticles.

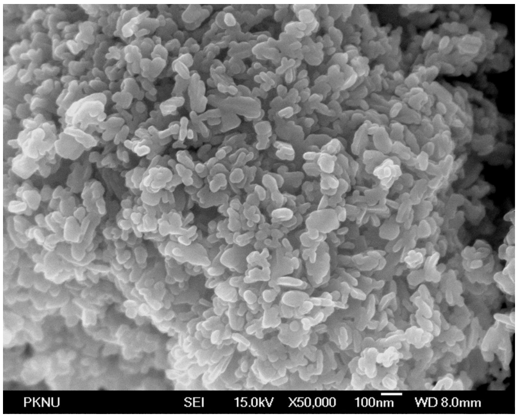

Fig. 2. SEM micrograph of synthesized NiO nanoparticles.

After 15 min the obtained products were collected by centrifugation, washed thoroughly with distilled water and dried at 100 °C. Then the dried sample was heated at 400 °C for 3 h.

$$2\text{NaOH(s)} \rightarrow 2\text{Na}^{+}\text{(aq)} + 2\text{OH}^{-}\text{(aq)}$$

$$\text{Ni(NO}_3)_2{\cdot}6\text{H}_2\text{O(s)} \rightarrow \text{Ni}^{2+}\text{(aq)} + 2\text{NO}^{3-}\text{(aq)} + 6\text{H}_2\text{O(aq)}$$

$$\text{Ni}^{2+}\text{(aq)} + 2\text{OH}^{-}\text{(aq)} + x\text{H}_2\text{O(aq)} \rightarrow \text{Ni(OH)}_2{\cdot}x\text{H}_2\text{O(s)}\downarrow$$

$$\text{Ni(OH)}_2{\cdot}x\text{H}_2\text{O(s)} \rightarrow \text{Ni(OH)}_2\text{(s)} + x\text{H}_2\text{O(g)}\uparrow$$

$$\text{Ni(OH)}_2\text{(s)} \rightarrow \text{NiO(s)} + \text{H}_2\text{O(g)}\uparrow$$

2.3. Test to determine the phase formation of NiO NPs

The synthesized NiO NPs were characterized using an XRD Bruker D8 Advance Diffractometer (Bruker AXS, Germany) with Cu Kα radiation (λ = 1.54 Å). The XRD pattern of NiO NPs powder samples was recorded over a 2θ range of 10–90°, which revealed that the synthesized NiO NPs were crystalline (Fig. 1). The XRD pattern showed four distinct diffraction peaks at 37.05, 43.19, 62.67, 75.12 and 79.02, which could be assigned to (1 1 1), (2 0 0), (2 2 0), (3 1 1) and (2 2 2) of cubic NiO NPs, respectively, and were in agreement with the database of Joint Committee on Powder Diffraction Standards (JCPDS No. 01-089-7130).

2.4. Test to determine the morphology of NiO NPs

To determine the morphologies, the image of NiO NPs was taken using a scanning electron microscope (SEM) (Carl Zeiss Oxford Instrument) at various magnifications. The SEM micrographs (Fig. 2.) at lower magnification clearly revealed that the formation of well dispersed rod shaped nickel oxide nanostructures. SEM demonstrates that all the particles were in the size range of less than 100 nm.

2.5. General procedure for the synthesis of quinoline derivatives

To a mixture of 2-aminoaryl ketone (1 mmol) and α-methylene carbonyl compound (1 mmol) in ethanol (5 mL) was added NiO NPs (10 mol%) and the mixture was refluxed. The progress of the reaction was monitored by TLC analysis. After the completion of the reaction, the reaction mixture was dissolved in ethanol to recover the catalyst by filtration and solvent was removed under reduced pressure. The obtained products were recrystallized using chloroform, characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. The melting points and spectral data for the known compound are found to be identical to the values reported in the literature and for newly reported compounds the data are given below.

3. Results and discussion

By considering the advantageous surface characteristics of NiO NPs, we decided to investigate the behavior of different 2-aminoaryl ketones with various simple ketones, cyclic ketones and β-keto esters in the presence of NiO NPs as a catalyst. The compound **3a** has been taken as a representative example and it was synthesized by treating 2-aminobenzophenone with ethyl acetoacetate in the presence NiO NPs as a catalyst in various solvents. Ethanol served as a better solvent than other solvents such as toluene, acetonitrile, dichloromethane and THF. After finding the suitable solvent the concentration of the catalyst was varied and optimized as 10 mol%. The yields of the products were found to be lower at lower amount than the optimized amount of

Table 1
Optimization the reaction conditions under various solvents and various concentrations of the NiONPs catalyst for the representative compound **3a**.[a]

Entry	Solvent	Catalyst (mol%)	Time (min)	Conversion (%)
1	Acetonitrile	10	240	58
2	Toluene	10	300	Trace
3	THF	10	300	65
4	Dichloromethane	10	240	68
5	Ethanol	10	150	97
6	Ethanol	20	150	97
7	Ethanol	10[b]	300	92

[a] Reaction conditions: 2-aminobenzophenone (1 mmol), ethylacetoacetate (1 mmol), NiO NPs (10 mol%).
[b] Commercially available NiO.