Magnetic Nano Cobalt Ferrite Catalyzed Synthesis of 4H-Pyrano[3,2-h]quinoline Derivatives under Microwave Irradiation

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Abstract

A microwave irradiated magnetically separable nano cobalt ferrite catalyzed green method for the synthesis of 4-phenyl-4H-pyrano[3,2-h]quinolin-2-amine and 2-amino-4-phenyl-4H-pyrano[3,2-h]quinoline-3-carbonitrile derivatives through cyclization of aromatic aldehyde, acetonitrile/malononitrile and 8-hydroxyquinoline is developed and presented in this paper. The cubic magnetic cobalt ferrite nano particles were synthesized by sol-gel citrate precursor method and characterized by FT-IR, XRD, SEM and TEM techniques and the structures of the synthesized pyranoquinoline derivatives were assigned by IR, MASS and 1H NMR techniques. The reaction is carried out in a domestic microwave oven with a heat-resistant microwave safe glass container with a lid.

Keywords

Synthesis of 4H-Pyrano[3,2-h]quinoline Derivatives, Microwave Irradiation, Nano Cobalt Ferrite Catalyst

1. Introduction

Microwave irradiation is a powerful tool and efficient method for the synthesis of biological active compounds due to selective absorption of microwave energy by polar molecules [1]. The wide applications of microwave irradiation are to enhance the rate of the reaction and usage of non-conventional energy source for product syn-

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thesis [2].

Most of the multicomponent reactions (MCRs) proceed through convergent reaction pathway, in which two or more starting materials react to form a single product in one-pot manner without any intermediate formation [3]. Multicomponent reactions play an important role in organic chemistry due to their excellent yields, ideal atom efficiency, convergence, exploratory power leading to the straightforward synthesis of some heterocyclic compounds [4] and also they have wide applications in combinatorial synthesis [5]-[7]. Pyranoquinolines are the important moieties in natural products [8]-[10] and these compounds have shown antimalarialial [11], HIV inhibitors [12], pharmaceuticals [13], antischistosomal agents [14], antimicrobial [15] [16] and antitumor activity [17].

According to literature survey, several methods have been reported for the synthesis of pyranoquinoline derivatives such as Lanthanide chloride [18], Potassium fluoride-alumina [19], Triethylamine [20], Imino Diels-Alder reactions catalyzed by Antimony (III) sulfate [21], Molten tetra-n-butylphosphonium bromide under solvent-free conditions [22], Piperidine [23], Iodine [24], Phosphorous oxy chloride [25], Ultrasound assisted green synthesis [26], Sodium acetate [27], Ethanol:pyridine (1:1) [13], Egg shell [28], Trifluoroborane-silica [29], 1,4-diazabicyclo[2,2,2]octane [30] and Indium chloride [31]. Even though these methods have their own merits but some limitations are observed like longer reaction times [33], usage of toxic reagents [23] and difficulty of separation of catalyst [20]. The main disadvantage of these procedures involves that the catalysts are destroyed during the course of the reaction and cannot be recovered [20] [23]-[25] [27]. Our progressing research on development and application of magnetic nano ferrite catalysts for organic transformations involve green procedures, short reaction time, low temperature reaction conditions, higher yields, easy separation of catalyst and economically desirable processes. Previously, synthesis, characterization and catalytic application of nano copper and cobalt ferrite catalysts was reported by us for the one-pot synthesis of 2,4,5,-trisubstituted imidazoles [36], nano copper ferrate catalyzed one-pot synthesis of tri and tetra substituted imidazoles under ultrasonication [37], microwave assisted nickel cobalt ferrite catalyzed one-pot synthesis of β-acetamido ketones [38] and nano copper ferrate catalyzed improved procedure for one-pot synthesis of poly substituted pyridine derivatives [39].

Here we are reporting an efficient improved procedure for one-pot multi-component synthesis of 4H-pyrano [3,2-h]quinoline derivatives through aromatic aldehyde, malononitrile/acetonitrile and 8-hydroxyquinoline in presence of magnetically separable nano cobalt ferrite catalyst under microwave irradiation (Scheme 1).

2. Experimental

2.1. Chemicals and Apparatus

Chemicals used in this procedure are of AR grade without further purification. The calcined as-synthesized nano cobalt ferrite was characterized by XRD, SEM, FT-IR, BET and TEM. The XRD spectra were recorded on PANalytical-Xpertpro diffractometer and the average crystallite size was determined from the corresponding XRD data. The microstructural morphology was studied with a Scanning Electron Microscope (SEM) model JEOL-
JSM 6610 LV. FTIR spectra were recorded on BRUKER ALPHA FT-IR with Opus 6.1 version. Specific surface area (SBET) of sample was determined by BET surface area analyzer (Nova 2000 series, Quanta chrome Instruments, UK). KORYO microwave oven (model-KMS1911) with a power output-700W and microwave frequency-2450 MHz was used. The synthesized pyranoquinoline derivatives were characterized by IR, MASS and $^1$H NMR. IR spectra recorded on a (Perkin Elmer Spectra-880) spectrophotometer by using KBr pellets in the region 400 - 4500 cm$^{-1}$ and $^1$H NMR spectra was characterized by 400 MHz-(Bruker Avance) in CDCl$_3$/DMSO-d$_6$ solvent and Mass spectra was recorded at 70 eV (MASPEC low resolution mass spectrometer).

2.2. Catalyst Preparation and Characterization

The nano cobalt ferrite has been synthesized by citrate precursor sol-gel method and characterized by FT-IR, SEM, TEM, XRD and particle size analysis as reported earlier by us [37].

2.3. General Procedure for the Synthesis of 4H-Pyrano[3,2-h]quinoline Derivatives

About 0.5 g of the catalyst was taken and activated at 500°C for 2 hours and cooled to room temperature before the experiment. Equimolar quantities of aromatic aldehyde (10 mmol), acetonitrile/malononitrile (10 mmol) and 8-hydroxyquinoline (10 mmol) were mixed together in a microwave dish and dissolved in 5 mL of ethanol and the catalyst added homogenised. The reaction mixture was irradiated in microwave oven in 2 minute intervals at Defrost mode (40% power output) as higher power levels of the microwave oven resulted in evaporation of the solvent and reactants even before the products are formed. The progress and completion of the reaction was monitored by TLC using mobile phase (n-Hexane:ethyl acetate 3:1), the formed product mixture was cooled to room temperature and ethyl alcohol added until the product was dissolved. The products were isolated by removing the catalyst magnetically from the reaction mixture and the formed products were characterized and compared by IR, $^1$H NMR and MASS spectral techniques (Table 1).

3. Results and Discussion

3.1. Catalytic Study

The procedure involves multi-component one pot cyclization reaction between aromatic aldehyde, acetonitrile/malononitrile and 8-hydroxyquinoline is described as a model reaction shown in Scheme 1. The feasibility of formation of pyranoquinoline derivatives and the reaction conditions are tabulated in Table 2.

3.1.1. Effect of Catalyst Loading on Synthesis of 4H-Pyrano[3,2-h]quinoline Derivatives

Investigation of the amount of catalyst loading was tested in this reaction procedure and the results are shown in Table 2. From this study, 500 mg of nano CoFe$_2$O$_4$ catalyst was sufficient to synthesize 92% isolated yields of pyranoquinoline derivatives (Entry 4, Table 2). From these experimental studies low concentration of catalyst is not enough to synthesize higher yields of pyranoquinoline derivatives (Entry 2, Table 2), while high concentration of nano CoFe$_2$O$_4$ catalyst loading did not produce considerable changes in the percentage of product yields (Entry 5, 6, Table 2). Hence, 500 mg of nano CoFe$_2$O$_4$ catalyst is sufficient to synthesize 4H-pyrano[3,2-h] quinoline derivatives.

3.1.2. Comparative Study of Nano Cobalt Ferrite Catalyst with Other Catalysts for the Synthesis of 4H-Pyrano[3,2-h]quinoline Derivatives

Reaction times for the formation of pyranoquinoline derivatives with various catalysts are presented in Table 3. It is observed that with other catalysts and particularly under reflux conditions the reactions times are very much higher. Under microwave conditions, synthesis of 4H-pyrano[3,2-h]quinoline derivatives catalyzed by InCl$_3$ [32] has been reported with shorter reaction times, the present method offers a comparatively very low cost and easily producible nano cobalt ferrite for effective results.

3.1.3. Plausible Mechanism for the Synthesis of 4H-Pyrano[3,2-h]quinoline Derivatives Catalyzed by Nano CoFe$_2$O$_4$

Initially acetonitrile/malononitrile undergo deprotonation in the presence of Lewis base (O$^{2-}$) of nano CoFe$_2$O$_4$...
<table>
<thead>
<tr>
<th>S.No</th>
<th>Reactants</th>
<th>Pyranoquinoline derivatives</th>
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<td>1</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
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<td></td>
<td>OCl</td>
<td>4-(4-chlorophenyl)-4H-pyrano[3,2-h]quinoline-2-amine (4a)</td>
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<td></td>
<td>H</td>
<td>White solid, yield: 93%, IR (KBr, (\nu_{\text{max}}) cm(^{-1})): 3424 (NH(_2) str), 3049 (-CH str), 1592 (-C=N str), 1111 (-C-O-C- str); (^1)H NMR (CDCl(_3)-400 MHz, (\delta) ppm); 8.7 - 8.8 (d, Ar-H), 8.0 - 8.1 (d, Ar-H), 8.2 (d, Ar-H), 7.4 - 7.5 (m, Ar-H), 7.3 (d, Ar-H), 7.2 - 7.3 (s, NH(_2)), 7.1 - 7.2 (d, Ar-H), 5.2 - 5.3 (d, CH-pyran ring), 4.2 - 4.3 (d, ethylene proton); ESMS: 309 [M + 1].</td>
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<tr>
<td>2</td>
<td>Br</td>
<td><img src="image3.png" alt="Image" /></td>
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<td>H</td>
<td>4-(4-Bromophenyl)-4H-pyrano[3,2-h]quinoline-2-amine (4b)</td>
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<td></td>
<td></td>
<td>White solid, yield: 88%, IR (KBr, (\nu_{\text{max}}) cm(^{-1})): 3627 (NH(_2) str), 3091 (-CH str), 1584 (-C=N str), 1223 (-C-O-C- str); (^1)H NMR (CDCl(_3)-400 MHz, (\delta) ppm); 8.9 (d, Ar-H), 8.0 (d, Ar-H), 8.1 (d, Ar-H), 7.3 (m, Ar-H), 7.3 - 7.4 (d, Ar-H), 7.1 (s, NH(_2)), 7.2 - 7.3 (d, Ar-H), 7.3 (d, Ar-H), 7.2 (d, Ar-H), 7.1 (d, Ar-H) 5.0 (d, CH-pyran ring), 4.1 - 4.2 (d, ethylene proton); ESMS: 353 [M + 1].</td>
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<td>3</td>
<td>CHO</td>
<td><img src="image4.png" alt="Image" /></td>
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<td>Cl</td>
<td>4-(3,4-dichlorophenyl)-4H-pyrano[3,2-h]quinoline-2-amine (4c)</td>
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<td></td>
<td>Cl</td>
<td>White solid, yield: 86%, IR (KBr, (\nu_{\text{max}}) cm(^{-1})): 3421 (NH(_2) str), 3089 (-CH str), 1588 (-C=N str), 1280 (-C-O-C- str); (^1)H NMR (CDCl(_3)-400 MHz, (\delta) ppm); 7.9 - 8.0 (d, Ar-H), 8.1 - 8.2 (d, Ar-H), 7.4 (d, Ar-H), 7.5 - 7.6 (m, Ar-H), 7.6 - 7.7 (d, Ar-H), 7.3 (s, NH(_2)), 5.2 - 5.3 (d, CH-pyran ring), 4.1 - 4.3 (d, ethylene proton); ESMS: 344 [M + 1].</td>
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<tr>
<td>4</td>
<td>CHO</td>
<td><img src="image5.png" alt="Image" /></td>
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<td>OCH(_3)</td>
<td>2-amino-4-(4-methoxyphenyl)-4H-pyrano[3,2-h]quinoline-3-carbonitrile (4d)</td>
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<td></td>
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<td>White solid, yield: 92%, IR (KBr, (\nu_{\text{max}}) cm(^{-1})): 3421 (NH(_2) str), 3027 (-CH str), 2221 (-CN), 1604 (-C=N str), 1236 (-C-O-C- str); (^1)H NMR (CDCl(_3)-400 MHz, (\delta) ppm); 7.9 (d, Ar-H), 7.6 - 7.7 (d, Ar-H), 7.8 (d, Ar-H), 7.5 (m, Ar-H), 7.6 (d, Ar-H), 7.3 (s, NH(_2)), 7.0 (d, Ar-H), 6.8 - 6.9 (d, Ar-H), 4.7 - 4.8 (s, CH-pyran ring), 3.9 (s, 3H, OCH(_3) ); ESMS: 330 [M + 1].</td>
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<tr>
<td>5</td>
<td>CHO</td>
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<td>4-(4-methylphenyl)-4H-pyrano[3,2-h]quinoline-2-amine (4e)</td>
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<td>White solid, yield: 86%, IR (KBr, (\nu_{\text{max}}) cm(^{-1})): 3421 (NH(_2) str), 3027 (-CH str), 2221 (-CN), 1604 (-C=N str), 1236 (-C-O-C- str); (^1)H NMR (CDCl(_3)-400 MHz, (\delta) ppm); 8.1 - 8.2 (d, Ar-H), 7.4 (d, Ar-H), 7.6 - 7.7 (d, Ar-H), 7.8 (d, Ar-H), 7.5 (m, Ar-H), 7.6 (d, Ar-H), 7.3 (s, NH(_2)), 7.0 (d, Ar-H), 6.8 - 6.9 (d, Ar-H), 4.7 - 4.8 (s, CH-pyran ring), 3.9 (s, 3H, OCH(_3) ); ESMS: 330 [M + 1].</td>
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2-amino-4-(p-tolyl)-4H-pyrano[3,2-h]quinoline-3-carbonitrile (4e)
White solid, yield; 90%, IR (KBr, $\tilde{\nu}_{\text{max}}$ cm$^{-1}$); 3495 (NH$_2$ str), 3035 (-CH str), 2223 (-CN), 1587 (-C=N str), 1149 (-C-O-C- str); $^1$H NMR (CDCl$_3$, 400 MHz, $\delta$ ppm); 7.7 (d, Ar-H), 7.3 - 7.4 (m, Ar-H), 7.2 - 7.3 (d, Ar-H), 7.0 (d, Ar-H), 6.8 - 6.9 (d, Ar-H), 7.6 (s, NH$_2$), 6.6 - 6.7 (d, Ar-H), 6.5 (d, Ar-H), 5.2 - 5.3 (s, CH-pyran ring), 2.5 (s, 3H, CH$_3$); ESMS: 314 [M + 1].

2-amino-4-(4-chlorophenyl)-4H-pyrano[3,2-h]quinoline-3-carbonitrile (4f)
White solid, yield; 90%, IR (KBr, $\tilde{\nu}_{\text{max}}$ cm$^{-1}$); 3421 (NH$_2$ str), 3097 (-CH str), 2225 (-CN), 1637 (-C=N str), 1094 (-C-O-C- str); $^1$H NMR (CDCl$_3$, 400 MHz, $\delta$ ppm); 7.8 - 7.9 (d, Ar-H), 7.7 (d, Ar-H), 7.5 (d, Ar-H), 7.3 (d, Ar-H), 7.1 - 7.2 (d, Ar-H), 7.0 (s, NH$_2$), 6.5 - 6.7 (d, Ar-H), 6.4 (d, Ar-H), 5.1 - 5.2 (d, CH-pyran ring); ESMS: 334 [M + 1].

2-amino-4-(3-hydroxy-4-methoxyphenyl)-4H-pyrano[3,2-h]quinoline-3-carbonitrile (4g)
Lemon yellow solid, yield; 88%, IR (KBr, $\tilde{\nu}_{\text{max}}$ cm$^{-1}$); 3394 (NH$_2$ str), 3082 (-CH str), 2228 (-CN), 1619 (-C=N str), 1281 (-C-O-C- str); $^1$H NMR (CDCl$_3$, 400 MHz, $\delta$ ppm); 7.5 (d, Ar-H), 7.2 - 7.3 (s, NH$_2$), 6.9 (d, Ar-H), 6.6 - 6.7 (m, Ar-H), 6.5 - 6.6 (m, Ar-H), 6.4 - 6.5 (d, Ar-H), 6.3 - 6.4 (d, Ar-H), 6.0 (s, Ar-H), 5.5 - 5.7 (s, OH proton), 4.7 - 4.9 (s, CH-pyran ring), 4.0 (s, OCH$_3$); ESMS: 346 [M + 1].

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<th>Table 2. Effect of catalyst loading.</th>
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<th>Table 3. Comparative study of nano CoFe$_2$O$_4$ catalyst with other catalysts.</th>
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catalyst to form carbanion which further react with aromatic aldehyde leads condensation reaction in the presence of Lewis acid (Fe$^{3+}$) to form an intermediate arylidenemalononitrile (1-Knoevenagel product). This intermediate undergo Michael addition with 8-hydroxyquinoline, leads to cyclization followed by rearrangement reaction produce 4$H$-pyrano[3,2-h]quinoline derivatives shown in Scheme 2.

4. Recycling of the Catalyst

Catalyst reusability is of major concern in heterogeneous catalysis. Catalyst recycling was achieved by fixing the catalyst magnetically at the bottom of the microwave dish with a strong Neodymium magnet, after which the solution containing the product was taken off with a pipette, the catalyst washed thrice with ethyl acetate, dried and the fresh reactants dissolved in ethyl alcohol was introduced into the microwave dish, followed by microwave irradiation, allowing the reaction to proceed for the next run. The catalyst was consecutively reused for five times without any noticeable loss of its catalytic activity.

5. Conclusion

In this present study, we report an efficient method for the synthesis of pyranoquinoline derivatives using nano cobalt ferrite as heterogeneous catalyst. This method has several advantages like improved yield of products, microwave assisted reaction, less reaction times, easy separation of the catalyst by strong Neodymium magnet, recyclability and reusability of the catalyst.

![Scheme 2. Plausible mechanism for the synthesis of 4$H$-pyrano[3,2-h]quinoline derivatives catalyzed by nano CoFe$_2$O$_4$.](image-url)
Acknowledgements

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References


Ferrite Catalyzed Sonochemical, One-Pot Three and Four Component Synthesis of Poly Substituted Imidazoles. *Modern Research in Catalysis*, 5, 31-44. [http://dx.doi.org/10.4236/mrc.2016.51004](http://dx.doi.org/10.4236/mrc.2016.51004)
