A novel three component synthesis of 2-amino-4H-chromenes derivatives using nano ZnO catalyst

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Abstract In this work, we attempted to synthesize organic soluble ZnO nano particles in the organic phase using zinc nitrate as a precursor. Also, ZnO nano particles have been characterized by XRD, SEM and TEM and then we report a simple and efficient method for the synthesis of 2-amino-4H-chromenes derivatives by aldehyde, malononitrile and dimedone by using ZnO nanoparticles under reflux in ethanol (Scheme 1) the products are been characterized by CHN, GC/MS, IR and 1H NMR spectroscopy.

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1. Introduction

2-Amino-4H-chromenes and their derivatives are of considerable interest as they possess a wide range of biological properties (Green et al., 1995), such as spasmylytic, diuretic, anticoagulant, anticancer and antianaphylactic activity (Foye, 1991; Witte et al., 1986). In addition, they can be used as cognitive enhancers for the treatment of neurodegenerative diseases, including Alzheimer’s disease, amyotrophic lateral sclerosis, Huntington’s disease, Parkinson’s disease, AIDS associated dementia and Down’s syndrome as well as for the treatment of schizophrenia and myoclonus (Konkoy et al., 2001). The increasing attention during recent decades for environmental protection has led modern academic and industrial groups to develop chemical processes with maximum yield and minimum cost whilst using nontoxic reagents, solvents and catalysts. One of the tools used to combine economic aspects with the environmental ones is the multicomponent reaction (MCR) strategy; this process consists of two or more synthetic steps which are carried out without the isolation of any intermediate, thus reducing time and saving money, energy and raw materials (Hall, 1994). We performed the synthesis of 2-amino-4H-chromenes through a multicomponent reaction employing Nano ZnO as a nontoxic catalyst in ethanol as a greener solvent (Scheme 1).

2. Experimental

All products are known compounds and were characterized by M.p., IR, 1H NMR and GC/MS. Melting points were measured by using the capillary tube method with an electro thermal 9200 apparatus. 1H NMR spectra were recorded on a Bruker AQS AVANCE-400 MHz spectrometer using TMS as an internal standard (CDCl3 solution). IR spectra were re-
corded from KBr disk on the FT-IR Bruker Tensor 27. GC/MS spectra were recorded on an Agilent Technologies 6890 network GC system and an Agilent 5973 network mass selective detector. Thin layer chromatography (TLC) on commercial aluminum-backed plates of silica gel, 60 F254 was used to monitor the progress of reactions. All products were characterized by spectra and physical data (see Table 1).

2.1. Preparation of ZnO nanoparticle

Aqueous solutions of zinc nitrate and urea were added into a flask under vigorous stirring (300 rpm/min). The molar ratio of Zn2+ to urea was about 1:4. In order to inhibit the growth of ZnO crystallite during the course of precipitation, a certain amount of surfactant (SDS), was added into the reaction system. Then the reaction system was heated to 95 °C and maintained at that temperature. After stirring for 2 h, a semitransparent zinc hydroxide colloid was obtained (see Fig. 1 and Scheme 2).

The precipitates were then filtered, washed with distilled water and alcohol for three or four times, dried in air at 80 °C, and finally calcined at 350 °C for 2 h to achieve samples with 80 nm particle size (Sadeghi et al., 2012).

2.2. Preparation of 2-amino-4H-chromenes: general procedure

A mixture of the aldehyde (1 mmol), malononitrile (1 mmol), dimeredone (1 mmol) and Nano ZnO catalyst (0.003 g), in ethanol (5 mL) was refluxed for 10 min. The progress of the reaction was followed by TLC. After the completion of the reaction, the mixture was filtered to remove the catalyst and the crude product was recrystallized from ethanol to obtain the pure compound (Scheme 3).

2.4. Selected spectral data

2.4.1. Compound 4c

M.p: 202–204 °C.

IR(KBr) \( \nu_{\text{max}} = 3370 (\text{NH}_2), 3316 (\text{NH}_2), 3252 (\text{sp}^2 \text{CH}), 2925 (\text{sp}^3 \text{CH}), 2190 (\text{C}"\text{N}), 1680 (\text{C}'\text{O}), 1653 (\text{C}'\text{C Alifatic}), 1606 (\text{C}'\text{C aromatic}), 1249 (\text{C}−\text{O}), 1208 (\text{C}−\text{O}), 1029 (\text{C}−\text{N}).

1H NMR (DMSO, 500 MHz): \( \delta_H = 0.94 (s, 3H, \text{CH}_3), 1.04 (s, 3H, \text{CH}_3), 2.08 (d, 1H, J = 16.3 Hz, \text{CH}_2), 2.23 (d, 1H, J = 16.0 Hz, \text{CH}_2), 2.49 (s, 2H, \text{CH}_2), 3.71 (s, 3H, OCH_3), 4.11 (s, 1H, CH), 6.93 (s, 2H, NH_2), 6.83 (d, 2H, J = 14.4 Hz, Ar-H), 7.04 (d, 2H, J = 11.5 Hz, ArH).

GC/Ms: 324(M+).

2.4.2. Compound 4d

M.p: 205–207 °C.

IR(KBr) \( \nu_{\text{max}} = 3395 (\text{NH}_2), 3345 (\text{NH}_2), 3260 (\text{sp}^2 \text{CH}), 2960 (\text{sp}^3 \text{CH}), 2185 (\text{C}"\text{N}), 1683 (\text{C}'\text{O}), 1651 (\text{C}'\text{C Alifatic}), 1605 (\text{C}'\text{C aromatic}), 1249 (\text{C}−\text{O}), 1208 (\text{C}−\text{O}), 1012 (\text{C}−\text{N}).

1H NMR (DMSO, 300 MHz): \( \delta_H = 0.95 (s, 3H, \text{CH}_3), 1.03 (s, 3H, \text{CH}_3), 2.05 (d, 1H, CH_2, H-6', J = 16.0 Hz), 2.24 (d,1H,CH_2, H-6, J = 16.0), 2.40 (s,2H, CH_2, H-8), 3.73 (s, 3H, OCH_3), 4.46 (s, 1H, H-4), 6.83 (s, 2H, NH_2), 6.86 (m, 1H, Ar-H), 6.95 (dd, J = 8.1, 7.4 Hz, 2H, Ar-H), 7.26 (t, 1H, J = 7.2 Hz, Ar-H).

Anal. Calcd. for C_{19}H_{20}N_{2}O_{3}: C, 70.37; H, 6.17; N, 8.64. Found: C, 70.1; H, 6.6; N, 8.5.

2.4.3. Compound 4g

M.p: 217–219 °C.

IR(KBr) \( \nu_{\text{max}} = 3420 (\text{NH}_2), 3365 (\text{NH}_2), 3255 (\text{sp}^2 \text{CH}), 2955 (\text{sp}^3 \text{CH}), 2185 (\text{C}−\text{N}), 1676 (\text{C}−\text{O}), 1650 (\text{C}−\text{C Alifatic}).

Table 1: Synthesis of 2-amino-4H-chromenes derivatives using Nano ZnO catalyst.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>Product</th>
<th>Yield (%)</th>
<th>M.P. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C_{6}H_{5}</td>
<td>4a</td>
<td>90</td>
<td>236–238</td>
</tr>
<tr>
<td>2</td>
<td>4-NMe_{2}C_{6}H_{4}</td>
<td>4b</td>
<td>80</td>
<td>214–218</td>
</tr>
<tr>
<td>3</td>
<td>4-OCH_{3}C_{6}H_{4}</td>
<td>4c</td>
<td>78</td>
<td>202–204</td>
</tr>
<tr>
<td>4</td>
<td>2-O_{Me}C_{6}H_{4}</td>
<td>4d</td>
<td>75</td>
<td>205–207</td>
</tr>
<tr>
<td>5</td>
<td>3,4-(OMe)<em>{2}C</em>{6}H_{3}</td>
<td>4e</td>
<td>80</td>
<td>132–141</td>
</tr>
<tr>
<td>6</td>
<td>2-NO_{2}C_{6}H_{4}</td>
<td>4f</td>
<td>85</td>
<td>234–238</td>
</tr>
<tr>
<td>7</td>
<td>3-NO_{2}C_{6}H_{4}</td>
<td>4g</td>
<td>92</td>
<td>217–219</td>
</tr>
<tr>
<td>8</td>
<td>2,4-(Cl)<em>{2}C</em>{6}H_{3}</td>
<td>4h</td>
<td>80</td>
<td>123–126</td>
</tr>
<tr>
<td>9</td>
<td>4-ClC_{6}H_{4}</td>
<td>4i</td>
<td>80</td>
<td>214–218</td>
</tr>
<tr>
<td>10</td>
<td>4-BrC_{6}H_{4}</td>
<td>4j</td>
<td>95</td>
<td>213–215</td>
</tr>
</tbody>
</table>

a Yields refer to isolated products.
ic), 1601 (C=–C aromatic), 1529 (N=–O), 1340 (N=–O), 1252 (C=O), 1208 (C=O), 1035 (C=N).

$^1$H NMR (DMSO, 500 MHz): $\delta$H = 0.95 (s, 3H, CH3), 1.04 (s, 3H, CH3), 2.11 (d, 1H, CH2, $J = 16.0$ Hz), 2.49 (s, 2H, CH2), 2.26 (d, 1H, CH2, $J = 16.0$ Hz), 4.41 (s, 1H, CH), 7.16 (s, 2H, NH2), 7.61 (t, 1H, $J = 7.8$ Hz, Ar-H), 7.66 (d, 1H, $J = 7.7$ Hz, Ar-H), 7.97 (s, 1H, Ar-H), 8.07 (d, 1H, $J = 9.9$ Hz, Ar-H).

GC/Ms: 339 (M$^+$).

2.4.4. Compound 4j

M.p: 223–224 °C.

IR(KBr)  $\nu_{\text{max}}$ = 3390 (NH2), 3350(NH2), 3250 (sp$^2$CH), 2955 (sp$^3$CH), 2190 (C=O), 1710(C=O), 1677 (C=–C Alifatic), 1648 (C=–C aromatic), 1604 (N-H), 1252 (C=O), 1209 (C=O), 1035 (C=N).

$^1$H NMR (DMSO, 300 MHz): $\delta$H = 0.93 (s, 3H, CH3), 1.02 (s, 3H, CH3), 2.08 (s, 2H, H=8), 2.1 (d, 1H, H=6, $J = 15.8$ Hz), 2.24 (d, 1H, H=6, $J = 15.8$ Hz), 4.16 (s, 1H, H=4), 7.07 (s, 2H, NH2), 7.1 (d, 2H, $J = 6.7$ Hz), 7.47 (d, 2H, $J = 6.6$ Hz).

3. Results and discussion

In this paper we report a facile one pot multicomponent reaction of aldehydes, malononitrile and dimedone allowing the
formation of 2-amino-4H-chromene catalyzes by ZnO nano particles as catalysts in ethanol as a greener solvent under reflux condition. The progress of the reaction was monitored by TLC and was completed in 10 min to furnish 2-amino-4H-chromene in a good yield. The catalyst and product were separated by a simple workup procedure. The literature survey has been done and revealed that ethanol is used as green and effective solvent for carrying out carbon–carbon, carbon-heteroatom bond forming reactions under both homogeneous and heterogeneous conditions (Ballini and Bosica, 1996, 1997; Ballini et al., 1997, 1999; Bigi et al., 1999a,b).

4. Conclusion

In this work we report a mild procedure for the synthesis of 2-amino-4H-chromenes derivatives by solid phase catalyst with improved yields. This procedure offers several advantages including mild reaction conditions, cleaner reaction, high yields of products as well as a simple experimental and work-up procedure which makes it a useful and attractive process for the synthesis of these compounds. So we can say this method is faster and easier than other published methods.

References