Three-component reactions of kojic acid: Efficient synthesis of Dihydropyrano[3,2-b]chromenediones and aminopyranopyrans catalyzed with Nano-Bi2O3-ZnO and Nano-ZnO

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ABSTRACT

Synthesis of pyrano-chromenes and pyrano-pyranes was developed by three-component reactions of kojic acid and aromatic aldehydes with dimethone and malononitrile, catalyzed with nano-Bi2O3-ZnO and nano-ZnO, respectively. Reactions proceeded smoothly and the corresponding heterocyclic products were obtained in good to high yields. Nano ZnO and nano Bi2O3-ZnO were prepared by sol-gel method and characterized by X-ray diffraction (XRD), energy-dispersive X-ray analysis (EDX), Fourier transform infrared (FT-IR), scanning electron microscopy (SEM), and transmission electron microscopy (TEM) techniques. Supporting Bi3+ on ZnO nanoparticles as Bi2O3 is the main novelty of this work. The simple reaction procedure, easy separation of products, low catalyst loading, reusability of the catalyst are some advantageous of this protocol.

KEYWORDS:
Kojic acid
Heterogeneous catalysis
Multicomponent reaction
Solvent-free
Nano-ZnO

1. Introduction

Multi-component reactions (MCRs) have been attracted a lot of attention in organic and pharmaceutical chemistry because of the construction of biologically active compounds. Although, these reactions are complicated than stepwise reaction, they are fast, efficient and environmentally favorable methods.

Chromenes and pyrano-pyranes are important classes of fused oxygenated heterocycles with a wide range of biological and therapeutic properties, such as antibacterial, anti-cancer, anti-anaphylactic, and anticonvulsant activities. Also, they are extensively found in natural products, such as biscopyran, Elatenyne, Calyxin I, Calyxin J, and Epicalyxin J. Therefore, the development of efficient and convenient methods for the synthesis of chromene and pyranopyran derivatives using a recyclable and environmentally benign catalyst is very necessary. Three-component reaction of kojic acid, aldehyde and 1,3-dicarbonyl compounds or malononitrile is one of the most important methodology for the synthesis of these heterocyclic systems. A various catalysts and conditions were
reported for this reaction, including InCl$_3$, CAN, Al$_2$O$_3$, Bi(OTf)$_3$, CeCl$_3$·7H$_2$O/SiO$_2$, FeCl$_3$-SiO$_2$, Fe$_3$O$_4$@SiO$_2$, ultrasonic irradiation, imidazole, piperidine, Et$_3$N, and NH$_4$VO$_3$. Kojic acid and its derivatives have wide range of applications in cosmetic, medicine, food, agriculture and chemical industries.

In the other hand, metal oxides play a crucial role in many areas of chemistry, physics and materials science. Recently, heterogeneous catalysis using metal oxides has been attracted great attention due to their potential applications in organic synthesis. Among them, bismuth and zinc oxides are as effective catalysts because of their low toxicity, ease of handling, low cost and relative insensitivity to air and moisture.

In continuing our works on the heterocyclic chemistry, we report herein a one pot three-component synthesis of chromenes and pyranopyrans from kojic acid catalyzed by nano-Bi$_2$O$_3$-ZnO and nano-ZnO, respectively.

2. Results and Discussion

ZnO nanoparticles were prepared using a polyethylene glycol (PEG) sol-gel method as reported by Amini et al., by heating a solution of Zn(NO$_3$)$_2$ and PEG in EtOH until forming a viscous gel, followed by drying and calcination in air at 500 °C. Then, Bi$_2$O$_3$-ZnO nanoparticles were prepared by adding nano-ZnO to a solution of BiCl$_3$ in MeOH for 24 h, and drying in air at room temperature. Obtained nano-ZnO and nano-Bi$_2$O$_3$-ZnO were characterized using FT-IR, SEM, XRD, EDX and TEM analysis. XRD pattern of the nano-ZnO shows peaks at the positions of 31.63°, 34.31°, 36.11°, 47.48°, 56.55°, 62.80°, 66.33°, 67.90° and 69.04°, which are in good agreement with reported data. In addition to peaks related to nano-ZnO, peaks at the positions of 32.78°, 33.47°, 37.86°, 44.77° was appeared in the XRD pattern of the nano-Bi$_2$O$_3$-ZnO, accounted to the existence of β-Bi$_2$O$_3$ in the composition of nanoparticles (Fig. 1.).
FT-IR spectrum of nano-ZnO shows peaks at 842 and 543 cm\(^{-1}\) that are related to the stretching and bending vibrations of O-Zn-O bonds. The peaks of the bending and stretching vibrations of O-H were appeared at 1620 and 3415 cm\(^{-1}\), respectively. Peaks at 2877 and 2910 and 1103 cm\(^{-1}\) are attributed to vibrations of CH\(_2\) and C-O bond of PEG precursor. In the FT-IR spectrum of nano-Bi\(_2\)O\(_3\)-ZnO, peaks at 3451 and 1623 cm\(^{-1}\) are attributed to the vibrations of O-H. Peaks around 906 and 726 and 481 cm\(^{-1}\) corresponds to the stretching vibrations of Zn-O and Bi-O and bending vibrations of O-Bi-O, respectively (Fig. 2.).

![FT-IR spectra of ZnO (black) and Bi\(_2\)O\(_3\)-ZnO (red) nanoparticles](image)

Fig. 2. FT-IR spectra of ZnO (black) and Bi\(_2\)O\(_3\)-ZnO (red) nanoparticles

Particle morphology and textural properties of nano-ZnO and nano-Bi\(_2\)O\(_3\)-ZnO catalysts were studied by SEM and TEM images, in which the nanoparticles of ZnO were appeared as regular geometric shapes such as cubic and rod like materials (Fig. 3a.). SEM images of Bi\(_2\)O\(_3\)-ZnO showed the similar shape with nano-ZnO with Puffy and wrinkled surface (Fig. 3b.). TEM images of Bi\(_2\)O\(_3\)-ZnO revealed that the existence of ZnO nanoparticles with very tiny particles of Bi\(_2\)O\(_3\) on its surface (Fig. 3c,d.). Energy dispersive X-ray analysis was used for the elemental analysis of nanoparticles. EDX data of nano ZnO showed the weight percentage of 89.85% and 10.15% of Zn and O, respectively. EDX analysis of BiCl\(_3\)-ZnO composite did not exhibit the Cl in the structure, where the Zn, Bi and O weight percentage were determined as 69.39%, 19.28% and 11.33%, respectively, indicating the formation of nanoparticles of Bi\(_2\)O\(_3\) by hydrolysis of BiCl\(_3\) with water molecules on the surface of nano-ZnO in MeOH.

The catalytic activity of the prepared nano-Bi\(_2\)O\(_3\)-ZnO was investigated by reacting of dimethone and benzaldehyde with 1.1 equiv. of kojic acid in the presence of catalytic amount of nano-Bi\(_2\)O\(_3\)-ZnO in EtOH under reflux conditions for 6 h, leading to corresponding chromene 3a in 40% yield (Table 1, Entry 1). Increasing the reaction time did not improve the yield. In order to obtain the best reaction conditions, the reaction was carried out in different solvents under reflux conditions, such as water, MeCN, CH\(_2\)Cl\(_2\) and solvent-free conditions (Entries 2-5). In water Knoevenagel product 4 was obtained as major product along with the desired product in very low yield. However, reaction in MeCN did not occur. In CH\(_2\)Cl\(_2\), 23% of desired product 3a was obtained. Heating a mixture of kojic acid, dimethone and benzaldehyde in the presence of catalytic amount of nano-Bi\(_2\)O\(_3\)-ZnO at 100 °C under solvent-free conditions for 2 h, furnished the chromene 3a in 80% yield (Entry 5). By decreasing the reaction temperature (Entries 5-8), not only the reaction time was increased, but also the yield was decreased, as there is no product detected at room temperature after 8 h. When reaction was conducted at elevated temperature (110 °C), the product 3a was obtained in 66% along with formation of a mixture of non-isolable colored complex byproducts (Entry 9). In order to determine the optimum amount of catalyst,
similar reaction was performed in the presence 0.01, 0.02, 0.03 and 0.05 g of nano-Bi$_2$O$_3$-ZnO catalyst, from which the 0.03 g of catalyst was selected for the best result (Entries 5, 11-13). In the absence of nano-Bi$_2$O$_3$-ZnO catalyst, reaction did not afford the desired product (Entry 10). When reaction was conducted using nano-ZnO, chromene 3a was obtained only in 20% isolated yield, with a complex mixture of byproducts, as monitored by TLC (Entry 14). To investigate the effect of Bi$^{3+}$, reaction was also applied in the presence of BiCl$_3$ (5 mol%), resulted in formation of octahydroxanthene 5 as major product, along with formation of desired product in low yield (Entry 15). Recoverability of the catalyst was studied by separation of catalyst by simple filtration, followed by washing with CH$_2$Cl$_2$ three times, and then drying at 50 °C under vacuum. The remaining catalyst reloaded with fresh reagents under the reaction conditions for four further runs, in which no considerable decrease in the yield was observed, demonstrating that nano-Bi$_2$O$_3$-ZnO can be reused as a catalyst (Entry 5).

![SEM images of (a) ZnO and (b) Bi$_2$O$_3$-ZnO nanoparticles and TEM images of (c) ZnO and (d) Bi$_2$O$_3$-ZnO nanoparticles](image)

**Fig. 3.** SEM images of (a) ZnO and (b) Bi$_2$O$_3$-ZnO nanoparticles and TEM images of (c) ZnO and (d) Bi$_2$O$_3$-ZnO nanoparticles

With optimum conditions in hand, nano-Bi$_2$O$_3$-ZnO catalyzed three component synthesis of chromene derivatives were investigated using various substituted benzaldehydes (Scheme 1). Reactions were carried out by heating a mixture of a substituted benzaldehyde, dimethone and 1.1 equiv. of kojic acid in the presence of nano-Bi$_2$O$_3$-ZnO (0.03 g, 2.8 mol% of Bi) at 100 °C for 2 h, to afford chromenes
3a-h in 75-84% yields. The results are summarized in Table 2. As shown in Table 2, not only electron-withdrawing substituted benzaldehydes, such as Cl and NO₂ substituted benzaldehydes afforded corresponding desired products in high yields, but also electron donating substituted benzaldehydes, 4-Me and 4-MeO substituted benzaldehydes worked well under the reaction conditions.

Table 1. Optimization of the reaction conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Catalyst loading (g) [Bi mol%]</th>
<th>Solvent</th>
<th>Temp. (°C)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nano-Bi₂O₃-ZnO</td>
<td>0.03 [2.8]</td>
<td>EtOH</td>
<td>Reflux</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>Nano-Bi₂O₃-ZnO</td>
<td>0.03 [2.8]</td>
<td>Water</td>
<td>Reflux</td>
<td>6</td>
<td>&lt;10% d</td>
</tr>
<tr>
<td>3</td>
<td>Nano-Bi₂O₃-ZnO</td>
<td>0.03 [2.8]</td>
<td>CH₂Cl₂</td>
<td>Reflux</td>
<td>6</td>
<td>23</td>
</tr>
<tr>
<td>4</td>
<td>Nano-Bi₂O₃-ZnO</td>
<td>0.03 [2.8]</td>
<td>MeCN</td>
<td>Reflux</td>
<td>6</td>
<td>NR e</td>
</tr>
<tr>
<td>5</td>
<td>Nano-Bi₂O₃-ZnO</td>
<td>0.03 [2.8]</td>
<td>SF f</td>
<td>100</td>
<td>2</td>
<td>80, 78, 78, 72 f</td>
</tr>
<tr>
<td>6</td>
<td>Nano-Bi₂O₃-ZnO</td>
<td>0.03 [2.8]</td>
<td>SF</td>
<td>rt</td>
<td>8</td>
<td>NR</td>
</tr>
<tr>
<td>7</td>
<td>Nano-Bi₂O₃-ZnO</td>
<td>0.03 [2.8]</td>
<td>SF</td>
<td>60</td>
<td>8</td>
<td>27</td>
</tr>
<tr>
<td>8</td>
<td>Nano-Bi₂O₃-ZnO</td>
<td>0.03 [2.8]</td>
<td>SF</td>
<td>80</td>
<td>5</td>
<td>64</td>
</tr>
<tr>
<td>9</td>
<td>Nano-Bi₂O₃-ZnO</td>
<td>0.03 [2.8]</td>
<td>SF</td>
<td>110</td>
<td>2</td>
<td>66</td>
</tr>
<tr>
<td>10</td>
<td>-</td>
<td>-</td>
<td>SF</td>
<td>100</td>
<td>6</td>
<td>NR</td>
</tr>
<tr>
<td>11</td>
<td>Nano-Bi₂O₃-ZnO</td>
<td>0.01 [0.9]</td>
<td>SF</td>
<td>100</td>
<td>2</td>
<td>58</td>
</tr>
<tr>
<td>12</td>
<td>Nano-Bi₂O₃-ZnO</td>
<td>0.02 [1.8]</td>
<td>SF</td>
<td>100</td>
<td>2</td>
<td>70</td>
</tr>
<tr>
<td>13</td>
<td>Nano-Bi₂O₃-ZnO</td>
<td>0.05 [4.7]</td>
<td>SF</td>
<td>100</td>
<td>2</td>
<td>81</td>
</tr>
<tr>
<td>14</td>
<td>Nano-ZnO</td>
<td>0.03 [0.0]</td>
<td>SF</td>
<td>100</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>15</td>
<td>BiCl₃</td>
<td>0.02 [6.3]</td>
<td>SF</td>
<td>100</td>
<td>2</td>
<td>35 g</td>
</tr>
</tbody>
</table>

aReactions were performed using dimethone (1 mmol), benzaldehyde (1 mmol) and kojic acid (1.1 mmol); bThe mol% of Bi was calculated using EDX analysis data as 19.28 w% Bi content of the catalyst; cSF = Solvent-free; dKnoevenagel product 4 was obtained as major product; eNR = No reaction; fYields for runs with recovered catalyst. gOctahydroxanthene 5 was obtained as major product.

The results encouraged us to investigate the synthesis of pyrano-pyran derivatives 7 via nano-Bi₂O₃-ZnO catalyzed three-component reaction between kojic acid, substituted benzaldehydes and malononitrile. By treatment of malononitrile with kojic acid and benzaldehyde in the presence of
catalytic amount of nano-Bi$_2$O$_3$-ZnO at 100 °C for 5 h, reaction did not proceed smoothly and only 24% yield of product was obtained, along with a complex mixture of byproducts. So, the reaction was examined under different conditions, including various solvents, temperatures and using other catalysts such as BiCl$_3$ and nano-ZnO. Conducting reaction with 0.03 g of nano-ZnO in refluxing EtOH resulted in formation of corresponding pyrano-pyran 7a in 94% yield, within 2 h of reaction time. Then, the scope of the reaction was investigated by reaction of variety of aromatic aldehydes, in which the corresponding pyrano-pyrans 7a-f were obtained in 81-95% yields (Scheme 2, and Table 3).

![Scheme 2. Nano-ZnO-catalyzed synthesis of pyranopyrans](image)

Table 3. Nano-ZnO catalyzed synthesis of aminopyrano-pyrans$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ar</th>
<th>Product</th>
<th>Yield (%)</th>
<th>Mp (°C)</th>
<th>Measured</th>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C$_6$H$_5$</td>
<td>7a</td>
<td>94</td>
<td>222-224</td>
<td>220-222</td>
<td>[15]</td>
</tr>
<tr>
<td>2</td>
<td>4-BrC$_6$H$_4$</td>
<td>7b</td>
<td>90</td>
<td>231-233</td>
<td>228-230</td>
<td>[16]</td>
</tr>
<tr>
<td>3</td>
<td>3-NO$_2$C$_6$H$_4$</td>
<td>7c</td>
<td>95</td>
<td>238-240</td>
<td>236-238</td>
<td>[16]</td>
</tr>
<tr>
<td>4</td>
<td>3,4-(OCH$_2$O)C$_6$H$_3$</td>
<td>7d</td>
<td>81</td>
<td>220-222</td>
<td>New</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1-naphthyl</td>
<td>7e</td>
<td>88</td>
<td>258-260</td>
<td>New</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>thiophen-2-yl</td>
<td>7f</td>
<td>85</td>
<td>231-233</td>
<td>235-237</td>
<td>[15]</td>
</tr>
</tbody>
</table>

$^a$Reactions were carried out in refluxing EtOH for 1-2 h.

A plausible reaction mechanism involves the nano-Bi$_2$O$_3$-ZnO induced enolization of dimethone via hydrogen bond or coordination to Bi atom (a), which attached to hydrogen bond activated aldehyde (b) to give intermediate I. Water removing from I led to knoevenagel intermediate II (c), which underwent conjugate addition with kojic acid, activated with hydrogen bond with Bi=O (d), to generate intermediate III. Intermediate III was converted to final product V by intramolecular cyclization to IV (e), followed by water removal (f). As shown in Scheme 3, the Zn-O-Bi-O bonds, produced as hydrat form of Bi$_2$O$_3$ on nano-ZnO, and hydrogen bonds formed between starting components and also in-situ generated intermediates, played an important role in catalytic activity of Bi$_2$O$_3$-ZnO, for this type of transformation. As mentioned above (Table 1, entry 14), the Bi$_2$O$_3$ is essential for the reaction of dimethone, benzaldehyde and dimethone. Due to the high reactivity of malononitrile, in the presence of Bi$_2$O$_3$-ZnO the reaction is uncontrollable, leading to a complex mixture. While nano-ZnO in the absence of Bi$_2$O$_3$ exhibited acceptable catalytic activity.

The comparison of the catalytic activity of nano-Bi$_2$O$_3$-ZnO in the three-component reaction of aromatic aldehydes, kojic acid and dimethone with some of the reported catalytic systems was summarized in Table 4. However the reaction temperatures and yields of the products are comparable, but due to the low mol% of catalyst loading, nano-Bi$_2$O$_3$-ZnO is efficient and effective catalytic system. In the case of cyclocondensation of aromatic aldehydes, kojic acid and malononitrile using nano-ZnO, reaction temperature and times, along with the yields of the corresponding products are also comparable with reported ones.
Scheme 3. Plausible reaction mechanism

Table 4. Comparison of the catalytic activity of nano-Bi$_2$O$_3$-ZnO with other catalysts.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalytic system</th>
<th>Reaction conditions</th>
<th>mol% of catalyst (catalyst loading)</th>
<th>Yield (%)$^{\text{ref}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1$^a$</td>
<td>CAN</td>
<td>120°C, 30 min</td>
<td>10 mol%</td>
<td>94$^{11}$</td>
</tr>
<tr>
<td>2$^a$</td>
<td>FeCl$_3$-SiO$_2$</td>
<td>100°C, 60 min</td>
<td>5 mol% FeCl$_3$</td>
<td>91$^{15}$</td>
</tr>
<tr>
<td>3$^a$</td>
<td>Bi(OTf)$_3$</td>
<td>120°C, 20 min</td>
<td>5 mol%</td>
<td>91$^{13}$</td>
</tr>
<tr>
<td>4$^a$</td>
<td>Alum</td>
<td>100°C, 50 min</td>
<td>10 mol%</td>
<td>94$^{12}$</td>
</tr>
<tr>
<td>5$^a$</td>
<td>CeCl$_3$.7H$_2$O</td>
<td>110°C, 40 min</td>
<td>5 mol%</td>
<td>96$^{14}$</td>
</tr>
<tr>
<td>6$^a$</td>
<td>InCl$_3$</td>
<td>120°C, 80 min</td>
<td>10 mol%</td>
<td>96$^{10}$</td>
</tr>
<tr>
<td>7$^a$</td>
<td>Nano-Bi$_2$O$_3$-ZnO</td>
<td>100°C, 60 min</td>
<td>2.8 mol% of Bi$^{3+}$</td>
<td>82$^{\text{This work}}$</td>
</tr>
<tr>
<td>8$^b$</td>
<td>MCM-41-SO$_3$H</td>
<td>Water, 90°C, 50 min</td>
<td>30 mg</td>
<td>94$^{36}$</td>
</tr>
<tr>
<td>9$^b$</td>
<td>Imidazole</td>
<td>EtOH, reflux, 90°C</td>
<td>20 mol%</td>
<td>88$^{37}$</td>
</tr>
<tr>
<td>10$^b$</td>
<td>Nano-ZnO</td>
<td>EtOH, reflux, 90°C</td>
<td>30 mg</td>
<td>94$^{\text{This work}}$</td>
</tr>
</tbody>
</table>

$^a$Three component reaction between 4-chlorobenzaldehyde, dimethone and kojic acid under solvent free condition.  $^b$Three component reaction between benzaldehyde, malononitrile and kojic acid.
3. Conclusions

In summary, ZnO and Bi₂O₃-ZnO nanoparticles were synthesized and characterized using FT-IR, XRD, SEM, EDX and TEM techniques. This the first report on the preparation of Bi₂O₃ supported on ZnO nanoparticles by simple hydrolyzing BiCl₃ in the presence of ZnO nanoparticles. Three-component reaction of kojic acid, aldehyde and dimethone was catalyzed with nano-Bi₂O₃-ZnO and pyranochromenes were obtained in good to high yields. In the case of malononitrile, reaction was not progressed in the presence of nano-Bi₂O₃-ZnO, but reaction catalyzed with nano-ZnO and pyranopyranes were produced in high yields. The recoverability of the catalyst was studied, in which the catalyst was reused in four further runs without loss of efficiency.

Acknowledgements

We are grateful to the Payame Noor University for financial support.

4. Experimental

4.1. Material and Methods

All chemicals were purchased from Merck and Sigma-Aldrich and used without any further purification. Solvents were used as received from commercial suppliers. NMR spectra were recorded using a Bruker instrument at 500 MHz and 125 MHz for proton and carbon nuclei, respectively, in CDCl₃ or DMSO-d₆. FT-IR spectra were measured as a KBr disc using a Win-Bomem, version 3.04 Galatic Industries Corporation, spectrometer. X-ray diffraction (XRD) patterns were measured using a Bruker D8 Advance with CuKα radiation (λ = 0.15406 nm) in the range 4° < 2θ < 70°. Scanning electron microscope (SEM) images and EDX analysis were obtained using a VWGA3 TESCAN (20.0 KV) microscope. Transmission electron microscopy (TEM) images were recorded using a Philips CM120 microscope.

4.2. Synthesis of nano-ZnO

Zn(NO₃)₂.6H₂O (1.0 g) was dissolved in the solution of PEG (1.5 g) and ethanol (20 ml) with constant stirring at 150 °C until forming a viscous gel. After that the obtained viscous gel was dried at 350 °C for 30 min, and then the dried precursors were ground into powder and calcined in air at 500 °C for 6 h, to produce ZnO nanoparticles.

4.3. Synthesis of nano-Bi₂O₃-ZnO

Nano-ZnO (1.46 g) was added to a solution of BiCl₃ (0.63 g) in MeOH (10 ml) and stirred at room temperature for 24 h. Then, the solvent was evaporated and the obtained solid material was dried at room temperature in air, overnight.

4.4. General procedure for the synthesis of pyrano-chromenes

To a mixture of kojic acid (1.1 mmol), dimethone (1 mmol) and an aldehyde (1 mmol) was added nano-Bi₂O₃-ZnO (0.03 g) and stirred at 100 °C under solvent free condition for 1-2 h. After completion of the reaction (monitored by TLC), CH₂Cl₂ was added and catalyst was removed by filtration. Solvent was evaporated and crude products were purified by flash chromatography on silica gel using hexane-acetone (7:3) as an eluent. Obtained products were characterized by FT-IR, NMR and melting points in comparison with authentic samples.
4.5. General procedure for the synthesis of pyrano-pyrans

Nano-ZnO (0.03 g) was added to a solution of kojic acid (0.5 mmol), malononitrile (0.5 mmol) and aldehyde (0.5 mmol) in EtOH (10 mL) and refluxed for 1-2 h. After completion of the reaction (monitored by TLC), catalyst was separated by filtration, and the reaction mixture was cooled and desired product recrystallized from the solution. Obtained products were characterized by FT-IR, NMR and melting points in comparison with authentic samples.

4.6. Physical and Spectral Data, for example:

2-(hydroxymethyl)-7,7-dimethyl-10-phenyl-7,8-dihydropyrano[3,2-b]chromene-4,9(6H,10H)-dione (3a): IR (KBr): ν (cm⁻¹) = 3361, 3080, 3025, 2962, 2929, 1678, 1667, 1637, 1441, 1377, 1219, 1192, 1078, 955, 852, 712. ¹H-NMR (500 MHz, DMSO-d₆): δ = 7.19-7.52 (m, 5H, Ph), 6.28 (s, 1H, CH pyrone), 5.66 (br, 1H, OH), 4.79 (s, 1H, CH pyran), 4.07-4.20 (m, 2H, CH₂ pyrone), 2.55-2.66 (m, 2H, CH₂), 2.09-2.24 (m, 2H, CH₂), 1.02 (s, 3H, CH₃), 0.94 (s, 3H, CH₃) ppm.

10-(4-chlorophenyl)-2-(hydroxymethyl)-7,7-dimethyl-7,8-dihydropyrano[3,2-b]chromene-4,9(6H,10H)-dione (3b): IR (KBr): ν (cm⁻¹) = 3325, 3095, 2960, 2927, 1673, 1641, 1597, 1443, 1376, 1217, 1190, 1078, 852. ¹H-NMR (500 MHz, CDCl₃): δ = 7.23-7.32 (m, 4H, Ph), 4.92 (s, 1H, CH pyran), 4.39-4.48 (m, 2H, CH₂ pyrone), 2.63-2.73 (m, 2H, CH₂), 2.21-2.32 (m, 2H, CH₂), 1.14 (s, 3H, CH₃), 1.08 (s, 3H, CH₃) ppm.

2-Amino-4,8-dihydro-6-(hydroxymethyl)-8-oxo-4-phenylpyrano[3,2-b]pyran-3-carbonitrile (7a): IR (KBr): ν (cm⁻¹) = 3412, 3356, 3186, 2194, 1639, 1597, 1446, 1406, 1207. ¹H- NMR (500 MHz, DMSO-d₆): 7.38-7.41 (m, 2 H, Ph), 7.31-7.34 (m, 1 H, Ph), 7.29-7.31(m, 2H, Ph), 7.23 (s, 2H, NH₂), 6.33 (s, 1 H, CH pyrone), 5.68 (t, J = 6.2 Hz, 1H, OH), 4.79 (s, 1H, CH pyran), 4.12 (dd, J = 15.8 Hz, 1H, CH₂ pyrone), 4.12 (dd, J = 15.8 Hz, J = 6.2 Hz, 1H, CH₂ pyrone), 4.12 (dd, J = 15.8 Hz, J = 6.2 Hz, 1H, CH₂ pyrone) ppm. ¹³C NMR (125 MHz, DMSO-d₆): δ = 40.3, 56.2, 59.7, 101.3, 107.7, 108.9, 114.5, 119.3, 126.7, 140.5, 141.1, 146.7, 148.1, 159.1, 169.3, 169.9 ppm.

2-Amino-4,8-dihydro-6-(hydroxymethyl)-8-oxo-4-phenylpyrano[3,2-b]pyran-3-carbonitrile (7d): IR (KBr): ν (cm⁻¹) = 3000-3400, 3299-3193, 3061, 2968, 2897, 2195, 1644, 1592, 1489, 1412, 1248, 1219. ¹H- NMR (500 MHz, DMSO-d₆): 7.20 (s, 2H, NH₂), 6.83 (s, 1H, Ph), 6.76 (d, J = 7.1 Hz, 1H, Ph), 6.32 (s, 1H, CH pyrone), 6.02 (s, 2H, CH₂), 5.68 (s, b, 1H, OH), 4.72 (s, 1H, CH pyran), 4.12-4.23 (m, 2H, CH₂) ppm. ¹³C NMR (125 MHz, DMSO-d₆): δ = 40.3, 56.2, 59.7, 101.3, 107.7, 108.9, 114.5, 119.3, 126.7, 140.5, 141.1, 146.7, 148.1, 155.9, 159.1, 169.3, 169.9 ppm.
References


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