Synthesis of functionalized piperidines by one-pot multicomponent reaction using nano-crystalline solid acid catalysts

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A simple and convenient one-pot multicomponent reaction for the synthesis of functionalized piperidines was developed. The procedure involves mixing of 1,3-dicarbonyl compounds, amines and aromatic aldehydes in ethanol at room temperature using nano-sulfated zirconia, nano-structured ZnO, nano-γ-alumina and nano-ZSM-5 zeolites, as the catalyst. The optical properties of the nano-structured organic molecules were studied. The advantages of the methods are short reaction times, mild conditions, and easy work-up. The catalysts can be recovered for the subsequent reactions and reused without any appreciable loss of efficiency.

Keywords: piperidines, nano-sulfated zirconia, nano-structured ZnO, nano-γ-alumina, nano-ZSM-5 zeolites.

INTRODUCTION

Piperidine and its analogues are widely distributed in many natural products, biologically active molecules and organic fine chemicals. [1] Some of them also act as pharmaceutical agents. [2] Compounds containing piperidine structural motif exhibit anti-hypertensive [3], anti-bacterial [4], anti-convulsant, anti-inflammatory [5] and antimalarial activities [6].

Thus, the synthesis of highly substituted piperidines has gained considerable attention [7], and a number of procedures have been developed using several approaches such as imino-Diels-Alder reactions [8], aza-Prins-cyclizations [9], intramolecular Michael reactions [10] and intramolecular Mannich reaction [11]. An alternative strategy for the synthesis of functionalized piperidines is using multicomponent reactions (MCRs).

Nowadays, one-pot multicomponent reactions have received special attention over their multistep variants for reasons of economy, energy efficiency, and general environmental friendliness. [12] The functionalized piperidines have been reported using MCRs strategy by employing catalysts, such as a combination of molecular iodine [13], L-proline [6], bromodimethylsulphonium bromide (BDMS) [14], tetrabutylammonium tribromide (TBATB) [15], InCl3 [16], ZrOCl2.8H2O [17], Bi(NO3)3.5H2O [18], CAN [19], ZrCl4 [20] and NiCl2.6H2O [21]. Therefore, there is a need for a highly efficient, versatile, and eco-friendly synthetic protocol to obtain these valuable compounds in good yields.

In the recent years, the use of nano-structured ZnO [22], nano-sulfated zirconia [23], nano-γ-alumina [24], and nano-ZSM-5 zeolite [25] catalysts has received considerable interest in organic synthesis. This extensive application of heterogeneous catalysts in synthetic organic chemistry can make the synthetic process more efficient from both environmental and economic point of view [26] and the used catalyst can be easily recycled.

As a part of our continuing efforts towards the development of useful synthetic methodologies [27], herein we report an efficient process for synthesis of functionalized piperidines by the reaction of 1,3-dicarbonyl compounds, amines and aromatic aldehydes using nano-structured ZnO, nano-sulfated zirconia, nano-γ-alumina and nano-ZSM-5 zeolites as the catalyst.

EXPERIMENTAL

Materials

All reagents were purchased from Merck and Aldrich and were used without further purification. Melting points reported were determined by an open capillary method using a Galen Kamp melting point apparatus and are uncorrected.

Instruments

Products were characterized by spectroscopy data (IR, FTIR, 1H NMR and 13C NMR spectra), elemental analysis (CHN) and melting points. A JASCO FT/IR-680 PLUS spectrometer was used to record IR spectra using KBr pellets. NMR spectra were recorded on a Bruker 400 Ultrashield NMR

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Catalyst preparation

Synthesis of nano-crystalline sulfated zirconia

Nano-crystalline sulfated zirconia was prepared by one step sol–gel technique [28]. A typical synthesis involves the addition of concentrated sulfuric acid (1.02 ml) to zirconium n-propoxide precursor (30 wt%) followed by hydrolysis with water. After 3 h aging at room temperature, the resulting gel was dried at 110°C for 12 h followed by calcination at 600°C for 2 h.

Synthesis of nano-structured ZnO

Nano-structured ZnO was prepared by one step sol–gel technique [29]. In a typical procedure, mixtures of ethanol, diethanolamine (DEA) and zinc acetate dihydrate, were prepared. The concentration of zinc acetate dihydrate in the solvent was 0.2 M. The molar ratio of zinc acetate dihydrate and diethanolamine was 1.0. pH of the mixture was adjusted to about 9. When the zinc acetate crystals were completely dissolved, sodium hydroxide (NaOH) pellets were added to the solution to increase pH of the mixture to about 11. The resultant solution was then transferred to a Teflon-lined stainless steel autoclave which was sealed and maintained at 130 °C for 24 h.

Synthesis of nano-γ-Al₂O₃ catalyst

Nano-γ-Al₂O₃ was prepared by the sol–gel method according to a described procedure [24]. In a typical experiment, aluminum nitrate (15.614 g) was added to 400 ml of deionized water. Similarly a solution of sodium carbonate was prepared by dissolving (7.95 g) in 400 ml of deionized water. 200 ml of the deionized water was taken in a 2 l capacity round-bottom flask and was stirred well using a magnetic stirrer. Then sodium carbonate and aluminum nitrate solutions were added drop wise to 200 ml of deionized water (from separate burettes).

The temperature was maintained at 70 °C during the experiment. pH after precipitation was found to be in the range of 7.5–8.5. The mixture was stirred for 4 h. The digested precipitates were filtered and re-dispersed again in 2 l of hot deionized water, filtered and finally washed with ethanol, followed by acetone to avoid contamination by Na ions; and air dried at room temperature. The dried precipitates were calcinated in a furnace at 550 °C for 5 h to produce nano-sized γ-Al₂O₃ powders.

Synthesis of nano-ZSM-5

For synthesis of nano-ZSM-5, tetrapropyl ammonium hydroxide and tetraethyl orthosilicate were the sources of aluminum and silicon, respectively. Nano-ZSM-5 zeolite was synthesized according to a procedure described earlier [30]. The components were mixed under constant stirring. After adding all ingredients the solution was left to hydrolyze at room temperature for 48 h. The gel thus obtained was heated at 80 °C to evaporate water and ethanol formed during the reaction. The obtained solution was charged to a Teflon-lined stainless steel autoclave under pressure and static conditions at 170 °C for 48 h. The solid phase obtained was filtered, washed with distilled water several times, dried at 120 °C and then calcinated at 550 °C for 12 hours.

Characterization

X-ray diffraction patterns were recorded on a diffractometer (Philips X'pert) using CuKα radiation (λ=1.5405 Å). The angle range was between 0 and 80° (figure 1). Crystallite size of the crystalline phase was determined from the peak of maximum intensity (2θ=30.18) by using the Scherrer formula, [31] with a shape factor (K) of 0.9, as shown below:

Crystallite size = Kλ/W.cosθ, where W=W₅₅₅-W₈₀, and W₅₅₅ is the broadened profile width of the sample and W₈₀ is the standard profile width of the reference silicon sample. FT-IR spectra of the catalysts were recorded on a FT-IR spectrophotometer in the range of 400–4000 cm⁻¹ with a resolution of 4 cm⁻¹ by mixing the sample with KBr (figure 2).

Specific surface area, pore volume and pore size distribution of sulfated zirconia samples calcinated at 600°C were determined from N₂ adsorption–desorption isotherms at 77K (ASAP 2010 Micromeritics). Surface area was calculated by using BET equation; pore volume and pore size distribution were calculated by the BJH method. [32]

The samples were degassed under vacuum at 120 °C for 4 h prior to the adsorption measurement to evacuate the physisorbed moisture. The detailed imaging information about the morphology and surface texture of the catalyst was provided by SEM (Philips XL30 ESEM TMP), part of the spectral data has been published in our previous work [27]. The bulk sulfur (wt.%) retained in the sulfated zirconia samples before and after calcination at 600 °C was analyzed by a C H N S/O elemental analyzer.

GENERAL EXPERIMENTAL PROCEDURE

To the reaction mixture of amine (2 mmol) and methyl acetoacetate (1 mmol) in ethanol (5 mL) catalyst was added and the mixture was stirred at room temperature. After 30 min, aromatic aldehyde...
(2 mmol) was added to the reaction mixture and stirring was continued for completion. The reaction was monitored by TLC. After the reaction was completed, EtOAc (2×20 mL) was added to the reaction mixture and the catalyst was separated by filtration. The organic solvent was removed under reduced pressure. The obtained products were further purified by chromatography on silica gel (ethyl acetate/n-hexane 30:70) as an eluent.

Compounds were characterized by spectral data.

**Spectral data for compound (1a) m.p. 180-182 °C, FTIR (KBr, cm⁻¹) \( \nu_{max} \): 3447, 2918, 1663, 1593, 1517, 1452, 1318, 1077; ¹H NMR spectrum (DMSO-d₆, 400 MHz), \( \delta \) ppm: 10.26 (1H, s, NH), 7.39-7.25 (5H, m, ArH), 7.12 (2H, d, ArH), 7.07 (2H, t, ArH), 7.05 (2H, d, ArH), 7.01 (2H, d, ArH), 6.62 (1H, t, ArH), 6.43 (2H, d, ArH), 6.38 (2H, d, ArH), 6.32 (1H, s, H-2), 5.05 (1H, d, H), 3.88 (3H, s, OMe), 2.80 (1H, dd, H), 2.71 (1H, dd, H); ¹³C NMR spectrum (100MHz, CDCl₃), \( \delta \) ppm: 168.5, 156.1, 147.3, 144.2, 142.7, 137.7, 129.1, 128.3, 128.4, 128.0, 127.2, 126.6, 126.3, 125.9, 125.5, 116.1, 113.3, 98.2, 58.1, 55.4, 51.6, 33.6; MS: m/z (M⁺+1): 530.14; Anal. Calcd for C₁₃H₁₉BrN₂O₂: C, 60.21; H, 4.24; N, 4.53. Found: C, 60.05; H, 4.13; N, 4.91.

**Spectral data for compound (1d) m.p. 236-238 °C, FTIR (KBr, cm⁻¹) \( \nu_{max} \): 3356, 2950, 1660, 1593, 1514, 1463, 1347, 1182, 1070; ¹H NMR spectrum (DMSO-d₆, 400 MHz), \( \delta \) ppm: 10.23 (1H, s, NH), 8.12 (2H, d, ArH), 8.10 (2H, d, ArH), 7.46 (2H, d, ArH), 7.25 (2H, d, ArH), 7.15-7.11 (3H, m, ArH), 7.07 (1H, ArH), 7.05 (1H, ArH), 6.66 (1H, t, ArH), 6.44 (1H, s, H-2), 6.40-6.35 (4H, m, ArH), 5.23-5.21 (1H, m, H), 3.93 (3H, s, OMe), 2.83 (2H, d, CH₂); ¹³C NMR spectrum (100MHz, CDCl₃), \( \delta \) ppm: 168.1, 155.5, 151.6, 149.2, 147.4, 146.8, 145.6, 137.1, 129.7, 129.2, 127.3, 127.1, 126.8, 125.9, 123.9, 123.3, 118.3, 113.4, 96.4, 57.3, 55.2, 51.4, 34.2; MS: m/z (M⁺+1): 551.19; Anal. Calcd for C₁₃H₁₉BrN₂O₂: C, 67.63; H, 4.76; N, 10.18. Found: C, 67.50; H, 4.63; N, 10.29.

**Spectral data for compound (1f) m.p. 184-186 °C, FTIR (KBr, cm⁻¹) \( \nu_{max} \): 3259, 3206, 2947, 1654, 1593, 1517, 1452, 1318, 1077; ¹H NMR spectrum (DMSO-d₆, 400 MHz), \( \delta \) ppm: 10.27 (1H, s, NH), 7.72 (2H, d, ArH), 7.12 (2H, d, ArH), 7.09 (1H, t, ArH), 7.08 (2H, d, ArH), 7.07 (2H, d, ArH), 6.83 (4H, d, ArH), 6.62 (1H, t, ArH), 6.54 (2H, d, ArH), 6.40-6.36 (3H, m, ArH), 5.09 (1H, d, H), 3.94 (3H, s, OMe), 3.81 (3H, s, OMe), 3.80 (3H, s, OMe), 2.87 (1H, dd, H), 2.77 (1H, dd, H); ¹³C NMR spectrum (100MHz, CDCl₃), \( \delta \) ppm: 168.6, 158.6, 158.0, 156.3, 147.2, 138.5, 136.1, 134.8, 129.0, 127.8, 127.6, 125.8, 125.6, 115.9, 114.1, 113.5, 113.1, 98.0, 57.7, 55.2, 54.5, 50.8, 34.1; MS: m/z (M⁺+1): 522.24; Anal. Calcd for C₁₃H₂₃N₄O₃: C, 76.13; H, 6.20; N, 5.38. Found: C, 76.03; H, 6.09; N, 5.45.

**RESULTS AND DISCUSSION**

Firstly, we compared the results of functionalized piperidines synthesis from aromatic aldehyde, aniline and methyl acetoacetate using nano-structured ZnO, nano-sulfated zirconia, nano-γ-alumina and nano-ZSM-5 zeolites as the catalyst (Table 1).

We further investigated the reaction of various aromatic aldehydes having substituents, such as Me, OMe, Cl, Br and NO₂ with aniline and methyl acetoacetate under the same reaction conditions (Table 1, entries 2-6). To find the generality and scope of this MCR, various amines were also examined. A wide variety of anilines tethered with substituents such as Me, OMe, Cl and NO₂ were treated with benzaldehyde and methyl acetoacetate under similar reaction conditions. All reactions occurred smoothly to provide the corresponding
piperidine derivative 1g-j, in moderate to good yields (Table 1, entries 7-10). Some interesting observations were made during these studies: p-methyl and p-methoxy aniline reacted faster than aniline, and reactions were completed within 5 h rather than 7 h. p-Nitroaniline and 4-chloroaniline reacted very slowly, which is undoubtedly due to the reduced nucleophilicity of these anilines compared to p-methyl and p-methoxy aniline and aniline. The results showed that nano-crystalline sulfated zirconia (SZ) promoted the reaction more effectively than nano-structured ZnO, nano-γ-alumina and nano-ZSM-5 zeolites, as far as the amount of catalyst and reaction time are concerned. (Table 1)

In a systematic study (Table 2), benzaldehyde was added to a solution of aniline, methyl acetacetate and catalyst in ethanol and the reaction mixture was stirred under reflux conditions. In an initial endeavor, a blank reaction was carried out using 2.0 equivalents of benzaldehyde, 2.0 equivalents of aniline and 1.0 equivalent of methyl acetacetate in the presence of a catalyst. The reaction mixture was stirred in ethanol; even after 8 h, 10% of the expected product was obtained in the absence of catalyst. To further improve the yield and to optimize the reaction conditions, the same reaction was carried out in presence of 10 mol % of a catalyst under similar conditions. A tremendous improvement was observed and the product yield increased up to 87% after stirring the mixture for 6h.

To minimize the formation of byproducts and to achieve good yield of the desired product, the reaction was optimized by varying the amount of catalyst (5, 10 and 15 mg). An increase in the amount of nano SZ from 5 to 15 mg increased the yield of the desired product to a great extent (80–87%, Table 2, entries 2-4). The percentage yield of the product with 5, 10 and 15 mol% of nano-ZnO as a catalyst are 72%, 74% and 70%, respectively (Table 2, entries 5-7). For nano-γ-alumina and nano-ZMS-5 as the catalyst, the increase in the catalyst amount to 15 mg, lead to a decrease in the product yield to 74% (Table 2, entry 10) and 68% (Table 2, entry 13), respectively. Therefore, it was considered that the use of 10 mol % of the catalyst was sufficient to promote the reaction, and greater amounts of the catalyst did not improve the yields.

Table 3 compares the efficiency of the present method with that of other methods in the synthesis of piperidine derivatives. As can be seen, SZ shows better efficiency than other catalysts and only ZrOCl₂·8H₂O is slightly better than the sulfated zirconia catalyst. The effect of different solvents on the reaction rate and the yields of products was also investigated and the results are summarized in Table 4. Ethanol, methanol and acetonitrile provided excellent yields and proved to be the solvents of choice, whereas THF, water and dichloromethane afforded lower yields.

Table 1: Acid-catalyzed synthesis of functionalized piperidines.

<table>
<thead>
<tr>
<th>Entry/Product</th>
<th>R</th>
<th>R'</th>
<th>Time (h)/Yield (%)</th>
<th>MP°C (lit.) [Ref.]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>nano-ZnO</td>
<td>nano-γ-alumina</td>
</tr>
<tr>
<td>1 (1a)</td>
<td>Ph</td>
<td>Ph</td>
<td>6/74</td>
<td>6/76</td>
</tr>
<tr>
<td>2 (1b)</td>
<td>4-ClC₆H₄</td>
<td>Ph</td>
<td>6/80</td>
<td>6/80</td>
</tr>
<tr>
<td>3 (1c)</td>
<td>4-BrC₆H₄</td>
<td>Ph</td>
<td>6/70</td>
<td>6/75</td>
</tr>
<tr>
<td>4 (1d)</td>
<td>4-NO₂C₆H₄</td>
<td>Ph</td>
<td>7/60</td>
<td>7/64</td>
</tr>
<tr>
<td>5 (1e)</td>
<td>4-CH₃C₆H₄</td>
<td>Ph</td>
<td>6/71</td>
<td>6/73</td>
</tr>
<tr>
<td>6 (1f)</td>
<td>4-OCH₃C₆H₄</td>
<td>Ph</td>
<td>6/68</td>
<td>6/74</td>
</tr>
<tr>
<td>7 (1g)</td>
<td>Ph</td>
<td>4-ClC₆H₄</td>
<td>7/75</td>
<td>7/76</td>
</tr>
<tr>
<td>8 (1h)</td>
<td>Ph</td>
<td>4-NO₂C₆H₄</td>
<td>7/77</td>
<td>7/80</td>
</tr>
<tr>
<td>9 (1i)</td>
<td>Ph</td>
<td>4-CH₃C₆H₄</td>
<td>5/74</td>
<td>5/77</td>
</tr>
<tr>
<td>10 (1j)</td>
<td>Ph</td>
<td>4-OCH₃C₆H₄</td>
<td>5/72</td>
<td>5/74</td>
</tr>
</tbody>
</table>

The products were characterized by IR, 1H-NMR, 13C-NMR, and mass spectroscopy.

Isolated yields
Table 2: Reaction of methyl acetoacetate with aniline and benzaldehydes in ethanol catalyzed by different catalysts

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Catalyst (mol%)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>-</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>nano-SZ</td>
<td>5 (mg)</td>
<td>6</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>nano-SZ</td>
<td>10 (mg)</td>
<td>6</td>
<td>87</td>
</tr>
<tr>
<td>4</td>
<td>nano-SZ</td>
<td>15 (mg)</td>
<td>6</td>
<td>83</td>
</tr>
<tr>
<td>5</td>
<td>nano-ZnO</td>
<td>5 (mol%)</td>
<td>6</td>
<td>72</td>
</tr>
<tr>
<td>6</td>
<td>nano-ZnO</td>
<td>10 (mol%)</td>
<td>6</td>
<td>74</td>
</tr>
<tr>
<td>7</td>
<td>nano-ZnO</td>
<td>15 (mol%)</td>
<td>6</td>
<td>70</td>
</tr>
<tr>
<td>8</td>
<td>nano-γ-γ-alumina</td>
<td>5 (mg)</td>
<td>6</td>
<td>72</td>
</tr>
<tr>
<td>9</td>
<td>nano-γ-γ-alumina</td>
<td>10 (mg)</td>
<td>6</td>
<td>76</td>
</tr>
<tr>
<td>10</td>
<td>nano-γ-γ-alumina</td>
<td>15 (mg)</td>
<td>6</td>
<td>74</td>
</tr>
<tr>
<td>11</td>
<td>nano-ZMS-5</td>
<td>5 (mg)</td>
<td>6</td>
<td>66</td>
</tr>
<tr>
<td>12</td>
<td>nano-ZMS-5</td>
<td>10 (mg)</td>
<td>6</td>
<td>70</td>
</tr>
<tr>
<td>13</td>
<td>nano-ZMS-5</td>
<td>15 (mg)</td>
<td>6</td>
<td>68</td>
</tr>
</tbody>
</table>

*a* Yields after isolation of products

Table 3: Comparison of the efficiency of nano-crystalline SZ with other reported catalysts in the synthesis of functionalized piperidines

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol %)</th>
<th>Condition</th>
<th>Time</th>
<th>Yield (%)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>nano-crystalline SZ</td>
<td>EtOH/rt</td>
<td>6 h</td>
<td>87%</td>
<td>This work</td>
</tr>
<tr>
<td>2</td>
<td>10% I₂</td>
<td>MeOH /rt</td>
<td>8 h</td>
<td>81%</td>
<td>13</td>
</tr>
<tr>
<td>3</td>
<td>TBATB</td>
<td>EtOH /rt</td>
<td>24 h</td>
<td>74%</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>InCl₃</td>
<td>MeCN/reflux</td>
<td>24-48 h</td>
<td>60%</td>
<td>16</td>
</tr>
<tr>
<td>5</td>
<td>ZrOCl₂.8H₂O</td>
<td>EtOH/reflux</td>
<td>4 h</td>
<td>91%</td>
<td>17</td>
</tr>
<tr>
<td>6</td>
<td>Bi(NO₃)₃.5H₂O</td>
<td>EtOH/reflux</td>
<td>12 h</td>
<td>81%</td>
<td>18</td>
</tr>
</tbody>
</table>

Benzaldehyde, aniline and methyl acetoacetate were taken in 2:2:1 ratio in presence of catalyst.

Table 4: Effect of solvent on the reaction times and yields.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H₂O</td>
<td>8</td>
<td>40%</td>
</tr>
<tr>
<td>2</td>
<td>EtOH</td>
<td>8</td>
<td>87%</td>
</tr>
<tr>
<td>3</td>
<td>MeOH</td>
<td>8</td>
<td>65%</td>
</tr>
<tr>
<td>4</td>
<td>CH₃CN</td>
<td>8</td>
<td>70%</td>
</tr>
<tr>
<td>5</td>
<td>CH₂Cl₂</td>
<td>8</td>
<td>65%</td>
</tr>
<tr>
<td>6</td>
<td>THF</td>
<td>8</td>
<td>60%</td>
</tr>
</tbody>
</table>

*a* Reaction was performed with benzaldehyde (2 mmol), aniline (2 mmol) and methyl acetoacetate (1 mmol) in the presence of a catalyst in various solvents.

*b* Reaction time monitored by TLC.

*c* Isolated yield.

The FT-IR spectra of alumina samples calcined at 550 °C (Figure 1) showed an intense band centered around 3500 cm⁻¹ and a broad band at 1650 cm⁻¹, these are assigned to stretching and bending modes of adsorbed water. The Al–O–Al bending stretching vibrations observed at around 1150 cm⁻¹ are due to symmetric and asymmetric bending modes, respectively. The OH torsional mode observed at 800 cm⁻¹ overlaps with Al–O stretching vibrations. The weak band at 2091 cm⁻¹ is assigned to a combination band. The bands observed at 617 and 481 cm⁻¹ may be attributed to stretching and bending modes of Al₂O₃ [33].

The morphology of the as prepared nano-size γ-Al₂O₃ and nano-sized ZnO powders analyzed by SEM is shown in Figs. 3-4. The SEM image clearly demonstrates the formation of spherical ZnO nanoparticles. The γ-Al₂O₃ powders indicated strong agglomeration of particles with various spherical sizes.

![Fig. 1. XRD pattern of nano-γ-alumina catalyst](image-url)
One of the most important advantages of heterogeneous catalysis over homogeneous one is the possibility of reusing the catalyst by simple filtration, without loss of activity. The recovery and reusability of the catalyst in product formation was investigated. After completion of the reaction, the catalyst was separated by filtration, washed 3 times with 5 ml acetone, then several times with redistilled water and dried at 110 °C. The recovered catalyst was used in the next run. The results of three consecutive runs showed that the catalyst can be reused several times without significant loss of its activity (see figure 5).

CONCLUSIONS
In conclusion, an efficient one-pot synthesis of functionalized piperidines was developed by reactions of aromatic aldehydes, acetoacetic esters, and amines in the presence of nano-sulfated zirconia, nano-structured ZnO, nano-γ-alumina and nano-ZSM-5 zeolites. The nano-sulfated zirconia demonstrated higher activity. Compared to previously reported methods, the mild reaction conditions, high yields, easy work-up, clean reaction profiles and lower catalyst loading render this approach an interesting alternative to the existing methods.

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Синтез на функционализирани пиеридини чрез единедноетапна многокомпонентна реакция с използване на нано-кристални киселинни катализатори

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(Резюме)

Разработена е една проста и удобна едноетапна многокомпонентна реакция за синтез на функционализирани пиеридини е. Процедурата включва смесване на 1,3-дикарбонилни съединения, амини и ароматни алдехиди в етанол при стайна температура, използващи нано-сульфатиран цирконив наноструктуриран ZnO, нано-г-двуалуминия тристоксин и нано-ZSM-5 зеолити, като катализатор. Проучени са оптичните свойства на наноструктурираните органични молекули. Предимствата на метода са кратки срокове за реакция, меки условия, както и лесно извършване. Катализаторите могат да бъдат ренерирани за следващите реакции и да се използват отново, без значителна загуба на ефективност.