Synthesis and characterization of ZnO nanoparticles: Application to one-pot synthesis of benzo[b][1,5]diazepines

Mohammad Ali Ghasemzadeh and Javad Safaei-Ghomi

Cogent Chemistry (2015), 1: 1095060
Synthesis and characterization of ZnO nanoparticles: Application to one-pot synthesis of benzo[b][1,5]diazepines

Mohammad Ali Ghasemzadeh* and Javad Safaei-Ghomi

Abstract: The pharmaceutical and biologically active heterocyclic compounds including benzo[b][1,5]diazepines were efficiently synthesized via three-(in situ five-) component reactions of aromatic diamines, Meldrum’s acid, and isocyanide derivatives in the presence of zinc oxide nanoparticles at room temperature. ZnO nanoparticles, as an effective, mild, and reusable catalyst, significantly improved the reaction times and also the products were obtained in excellent yields. The prepared zinc oxide nanoparticles were fully characterized by EDX, XRD, BET, SEM, IR, and TEM analyses.

Keywords: ZnO; nanoparticles; multi-component reaction; benzo[b][1,5]diazepine; heterocyclic

1. Introduction

Multi-component reactions (MCRs) have become a significantly important device for the fast preparation of various compound libraries. MCRs suggest several benefits over traditional methods for the synthesis of a broad variety of compounds with pharmaceutical and biological properties (Evano, Blanchardan, & Toumi, 2008; Weber, 2002). Benzodiazepines belong to a significant group of nitrogen-containing compounds which have numerous medicinal and biological activities. In recent years, the synthesis of seven-membered heterocyclic rings has received great attention because of their applications in pharmaceutical and medicinal chemistry as analgesic, sedative, anticonvulsant, hypnotic, anti-inflammatory, and antidepressive agents (Fryer, 1991; Landquist, 1984).

Among various benzodiazepine structures, several representative drugs possessing high medicinal activity such as olanzapine 1 and clozapine 2 (schizophrenia treatment) (Leyva-Pérez, Cabrero-Antonino, 1984).
& Corma, 2010), clobazam (3, anxiolytic agents) (Kruse, 1982), and 3-carbamoyl-1,5-benzodiazepine (selective CCK-B antagonists as potential anxiolytic drugs) (Tranquillini et al., 1997) exhibit 1,5-benzodiazepin template (Figure 1).

The synthesis of 1,5-benzodiazepines has interested great attention and there are many reported methods for the synthesis of 1,5-benzodiazepine scaffolds. Ways for the synthesis of these compounds mainly are the reactions of 1,2-phenylenediamines with various ketones (Reddy & Sreekanth, 2003), chalcones (Sarda, Jadhav, Kolhe, Landge, & Pawar, 2009), alkynes (Qian, Liu, Cui, & Xu, 2012), 4,6-di-o-benzyl-2,3-dideoxy-aldehydo-D-erythro-trans-hex-2-enose (Yadav, Reddy, Satheesh, Srinivasulu, & Kunwar, 2005), and 3-acetyl-4-hydroxy-6-methyl-2H-pyran-2-one (Kaoua et al., 2011).

On the other hand, in accordance with interest in benzodiazepines synthesis, herein we report an efficient method for the preparation of a class of 1,5-benzodiazepin-2-one scaffolds including tetrahydro-2,4-dioxo-1H-benzo[b][1,5]diazepine-3-yl-2-methylpropanamide derivatives.

Recently, Shaabani, Rezayan, Keshipour, Sarvary, and Ng (2009) have reported a novel and efficient method for the synthesis of some tetrahydro-2,4-dioxo-1H-benzo[b][1,5]diazepine-3-yl-2-methylpropanamide derivatives. This method has valuable advantages such as mild reaction conditions, good yields, and no undesirable byproducts. The duration of the reported method as well as yields is not sufficiently good. So, in spite of the aforementioned advantages of this method, we decided to promote some aspects of this research including the reactivity of substrates. Therefore, we carried out the three-component reactions of 1,2-phenylenediamines, isocyanides, and Meldrum’s acid using metal oxide nanoparticles as efficient catalysts.

Transition metal nanoparticles have interested great attention during the twenty-first century because of their significant properties such as high chemical activity and large surface-to-volume ratio in comparison with their bulk counter parts.

Among the various metal oxide nanoparticles, zinc oxide nanoparticles have been widely used in many chemical transformations. Recently, zinc oxide nanoparticles have been applied in solar cells (Matsubara et al., 2003), catalysts (Huang, Fang, & Wang, 2005), antibacterial materials (Sánchez, Peral, & Doménech, 1996), gas sensors (Zhang et al., 2005), luminescent materials (Zhang, Yu, & Zhang, 2002), and in influencing the growth rate of *Cicer arietinum* (Pandey, Sanjay, & Yadav, 2010). In addition, ZnO nanoparticles (ZnO NPs) were used as an efficient heterogeneous catalyst in several organic reactions such as: the Mannich reaction (MaGee, Dabiri, & Salehi, 2011), the Knoevenagel condensation reaction (Hosseini-Sarvari, Sharghi, & Etemad, 2008), and the synthesis of tetrahydrobenzo[b]pyrans (Bhattacharyya, Pradhan, Paul, & Das, 2012), β-phosphono malonates (Hosseini-Sarvari & Etemad, 2008), benzimidazole (Alinezhad, Salehian, & Biparva, 2012), β-acetamido ketones/esters (Mirjafary, Saeidian, Sadeghi, & Moghaddam, 2008), naphtho[1,2-e]oxazinone (Dharma Rao, Kaushik, & Halve, 2012), polyhydroquinoline (Kassaee, Masrouri, & Movahedi, 2010), and dihydropyrano[2,3-c]chromenes (Paul, Bhattacharyya, & Das, 2011).

Figure 1. Some biologically important benzodiazepines.
In agreement with the above-mentioned importance of ZnO NPs and significant importance of benzodiazepine derivatives and also in continuation of our interest in sustainable approaches for the preparation of organic compounds using nanocatalysts (Ghasemzadeh, Safaei-Ghani, & Molaei, 2012; Ghasemzadeh, Safaei-Ghani, & Zahedi, 2013; Mirhosseini-Eshkevari & Ghasemzadeh, 2014; Safaei-Ghani & Ghasemzadeh, 2012, 2013a, 2013b; Safaei-Ghani, Ghasemzadeh, & Mehrabi, 2013), herein we wish to report a convergent one-pot synthesis of tetrahydro-2,4-dioxo-1H-benzo[b][1,5]diazepine-3-yl-2methylpropanamides via MCRs of 1,2-phenylenediamines, isocyanides, and Meldrum’s acid in the presence of zinc oxide nanoparticles (Scheme 1).

2. Results and discussion

In the preliminary experiments, nanocrystalline zinc oxide was prepared and characterized by EDX, XRD, BET, SEM, IR, and TEM analyses.

The chemical composition of the prepared sample as well as its stoichiometry was determined by EDX studies. The EDX spectrum of ZnO NPs shows the presence of zinc and oxygen as the only elementary components (Figure 2(A)).

The crystalline nature of the synthesized ZnO NPs sample was further verified by XRD. The XRD pattern of the ZnO NPs is shown in Figure 2(B). All reflection peaks in Figure 2(B) can be easily indexed to pure spherical phase of ZnO with P63mc group (JCDPS No. 36-1451). The crystallite size diameter ($D$) of the ZnO NPs has been calculated by Debye–Scherrer equation ($D = K\lambda/\beta \cos \theta$), where $\beta$ FWHM (full-width at half-maximum or half-width) is in radian and $\theta$ is the position of the maximum of diffraction peak, $K$ is the so-called shape factor, which usually takes a value of about 0.9, and $\lambda$ is the X-ray wavelength (1.5406 Å for Cu–Kα). Crystallite size of ZnO has been found to be 25 nm.

In addition, the specific surface area was measured by nitrogen physisorption (the BET method); the specific surface area was approximately 88 m$^2$ g$^{-1}$. Also, the theoretical particle size was calculated from the surface area and zinc oxide density (6.11 g cm$^{-3}$) from the equation was 10.6 nm.

$$D_{BET} = \left(\frac{6,000}{\rho \times S}\right)$$

Figure 2. EDX (A) and XRD (B) of ZnO NPs.

Scheme 1. One-pot preparation of tetrahydro-2,4-dioxo-1H-benzo[b][1,5]diazepine-3-yl-2methylpropanamides catalyzed by ZnO NPs.

$$R_1 = \text{H, CH}_3$$

$$R_2 = \text{cyclohexyl, tert butyl, n-pentyl, 4-methoxyphenyl, benzyl}$$

$\text{NH}_2$ $\text{NH}_2$

$\text{O}$ $\text{O}$

$\text{NC}$ $\text{R}_2$

$\text{N}$

$\text{O}$ $\text{O}$

$\text{HN}$ $\text{R}_2$

$\text{R}_1$

$\text{CH}_2\text{Cl}_2$, r.t.

$\text{ZnO NPs}$

$\text{ZnO NPs}$
In the FT-IR spectrum of ZnO NPs (Figure 3), the band from 500 to 600 cm\(^{-1}\) is assigned to the stretching vibrations of (Zn–O) bond. The broad band with low intensity at 3,422 cm\(^{-1}\) is related to the vibration mode of (OH) group, indicating the presence of little amount of water adsorbed on the zinc oxide nanoparticles’ surfaces (Ambrožič, Škapin, Žigon, & Orel, 2010; Sasidharan et al., 2011).

SEM of ZnO NPs Figure 4(A) shows that zinc oxide nanoparticles were obtained from anhydrous ZnCl\(_2\) and NaOH with dimensions ranging from 25 to 30 nm under ultrasound power.

The size and morphology of zinc oxide nanoparticles were analyzed by TEM (Figure 4(B)). The result shows that the smallest sizes of nanoparticles are obtained with a crystalline size about 30 nm, confirming the results calculated from Scherrer’s formula based on the XRD pattern.

In the continuation of this research, in order to determine the optimized reaction conditions, the reaction of o-phenylenediamine, Meldrum’s acid, and cyclohexyl isocyanide was selected as a model reaction and the reaction conditions were optimized on the base of solvent and catalyst and different temperatures for the preparation of benzodiazepines by Scheme 2.

Initially, we found that the reaction results are significantly depending on the nature of the solvent. Various types of solvents were used and as a result of these experiments, we discovered that
the solvent has a great role in promoting the reaction. The model study was carried out several times using different solvents in the presence of zinc oxide nanoparticles.

As shown in Table 1, the reaction efficiently proceeded in dichloromethane in comparison with other solvents such as ethanol, DMF, toluene, water, and acetonitrile.

To evaluate the best catalyst, the research continued using various catalytic systems for the synthesis of tetrahydro-2,4-dioxo-1H-benzo[b][1,5]diazepine-3-yl-2-methylpropanamides by three-component coupling in dichloromethane at room temperature (15 mol% of each catalyst was used separately).

The results are shown in Table 2. Clearly, ZnO NPs are superior to any of the other catalysts tested with respect to reaction time (3.5 h) and yield (93%) of the obtained product (Entry 10).

The increased catalytic activity of ZnO NPs compared to the other catalysts and also over the commercially available bulk ZnO is related to the high surface area-to-volume ratio of nanoparticles which provides an enormous driving force for diffusion.

Next, we examined the effect of amounts of zinc oxide nanoparticles on the synthesis of 1,5-benzodiazepin-2-one 4a. The reaction was performed in the presence of various quantities of ZnO NPs. The best result was obtained using 10 mol% of nanocatalyst in dichloromethane at room temperature (Table 3, Entry 4).

The use of 10 mol% of this catalyst was enough to progress the reaction and an increase in the amount of the catalyst did not change the yield and the reaction time of the model study.

It was demonstrated that multi-component synthesis of tetrahydro-2,4-dioxo-1H-benzo[b][1,5]diazepine-3-yl-2-methylpropanamide derivatives could be performed using a diversity of structurally different isocyanides and diamines in the presence of zinc oxide nanoparticles (Scheme 1 and Table 4).

The summarized results of Table 4 show that both mono and disubstituted aromaticdiamines reacted with isocyanides to afford the corresponding 1,5-benzodiazepin-2-ones in excellent yields under optimized conditions (91–96%, Entries 1–10, Table 4). Although the reactions containing 4-methyl-substituted o-phenylenediamines were smoothly performed, in addition, both aliphatic and aromatic isocyanides produced corresponding benzodiazepine derivatives in excellent yields as shown in Table 4. In this case, we observed that the best results were obtained when we used tert-butyl isocyanide as substrate in the cyclization reaction (95 and 96%, Entries 2 and 7, Table 4).

| Entry | Solvent | Time (h) | Yield (%)b |
|-------|---------|----------|------------|
| 1     | EtOH    | 8        | 30         |
| 2     | DMF     | 6        | 42         |
| 3     | PhCH₃   | 6        | 50         |
| 4     | H₂O     | 10       | Trace      |
| 5     | CH₃CN   | 8        | 45         |
| 6     | CH₂Cl₂  | 3.5      | 93         |

*aReaction conditions: o-phenylenediamine (1 mmol), Meldrum’s acid (1 mmol), cyclohexyl isocyanide (1 mmol), and ZnO NPs (10 mol%) in 5-mL CH₂Cl₂.

*bIsolated yields.
Table 2. Effect of various catalysts in the model reaction

| Entry | Catalyst | Time (h) | Yield (%)<sup>b</sup> |
|-------|----------|----------|------------------------|
| 1     | None     | 8        | 58                     |
| 2     | CuO      | 6        | 52                     |
| 3     | MnO      | 7        | 45                     |
| 4     | p-TSA    | 8        | 34                     |
| 5     | Ni       | 6        | 45                     |
| 6     | NaOH     | 6        | –                      |
| 7     | Triethylamine | 6   | 28                     |
| 8     | Piperidine | 6     | 33                     |
| 9     | ZnO      | 5        | 62                     |
| 10    | ZnO NPs  | 3.5      | 93                     |

<sup>a</sup>Reaction conditions: o-phenylenediamine (1 mmol), Meldrum’s acid (1 mmol), and cyclohexyl isocyanide (1 mmol), 15 mol % of each catalyst separately in 5-mL CH<sub>2</sub>Cl<sub>2</sub>.

<sup>b</sup>Isolated yields.

Table 3. Effect of quantity of ZnO NPs on the model reaction

| Entry | Amount (mol %) | Time (h) | Yield (%)<sup>b</sup> |
|-------|----------------|----------|------------------------|
| 1     | 3              | 7        | 64                     |
| 2     | 5              | 5.5      | 72                     |
| 3     | 7              | 5        | 85                     |
| 4     | 10             | 3.5      | 93                     |
| 5     | 12             | 3.5      | 93                     |

<sup>a</sup>Reaction conditions: o-phenylenediamine (1 mmol), Meldrum’s acid (1 mmol), and cyclohexyl isocyanide (1 mmol) in 5-mL CH<sub>2</sub>Cl<sub>2</sub>.

<sup>b</sup>Isolated yields.

Scheme 3. Proposed reaction pathway for the synthesis of 1,5-benzodiazepin-2-ones by ZnO NPs.
A plausible mechanism on the basis of our experimental results together with some literature (Shaabani et al., 2009) for the synthesis of tetrahydro-2,4-dioxo-1H-benzo[b][1,5]diazepine-3-yl-2-methylpropanamide by ZnO NPs is shown in Scheme 3. Initially, we suppose that ZnO NPs coordinate with carbonyl groups of Meldrum’s acid and accelerate the nucleophilic attack of

| Entry | R₁ | R₂ | Products (4a-4j) | Time (h) | Yield (%)¹ |
|-------|----|----|-----------------|---------|------------|
| 1     | H  | Cyclohexyl | 3.5            | 93      |
| 2     | H  | Tert-butyl | 3              | 95      |
| 3     | H  | Benzyl     | 3.5            | 91      |
| 4     | H  | n-Pentyl   | 3.5            | 92      |
| 5     | H  | 4-Methoxyphenyl | 4       | 91      |
| 6     | CH₃| Cyclohexyl | 3              | 95      |
| 7     | CH₃| Tert-butyl | 3              | 96      |
| 8     | CH₃| Benzyl     | 3.5            | 94      |
| 9     | CH₃| n-Pentyl   | 3.5            | 95      |
| 10    | CH₃| 4-Methoxyphenyl | 3.5   | 93      |

¹Reaction conditions: aromatic diamines (1 mmol), Meldrum’s acid (1 mmol), isocyanides (1 mmol), and ZnO NPs (10 mol %) in 5-mL CH₂Cl₂.

²Isolated yields.
1,2-phenylenediamine. In other words, interaction between ZnO NPs as a Lewis acid with substrates and other intermediates promoted the rate of reaction.

3. Experimental

3.1. General

Chemicals were of commercial reagent grade and obtained from Merck or Fluka and used without further purification. Zinc oxide nanoparticles were prepared according to the procedure reported by Shen et al. (2006). All products were characterized by comparison of their FT-IR and NMR spectra and physical data with those reported in the literature. All yields refer to the isolated products. Progress of reactions was followed by TLC on silica gel Polygram SILG/UV 254 plates. IR spectra were run on a Shimadzu FT-IR-8300 spectrophotometer. NMR spectra were recorded on a Bruker-Avance DRX instrument (400 MHz) with DMSO-d₆ as solvent using tetramethylsilane (TMS) as an internal standard, the chemical shift values are in δ. The elemental analyses (C, H, N) were obtained from a Carlo ERBA model EA 1108 analyzer. The mass spectra were recorded on a Joel D-30 instrument at an ionization potential of 70 eV. The N₂ adsorption/desorption analysis (BET) was performed at −196°C using an automated gas adsorption analyzer (Tristar 3000, Micromeritics). Microscopic morphology of products was visualized by SEM (LEO 1455VP). Powder X-ray diffraction (XRD) was carried out on a Philips diffractometer of X’pert Company with monochromatized Cu–Kα radiation (λ = 1.5406 Å). The compositional analysis was done by energy dispersive analysis of X-ray (EDX, Kevex, Delta Class I). TEM was performed with a Jeol JEM-2100UHR, operated at 200 kV.

3.2. Preparation of ZnO NPs

To a solution of anhydrous ZnCl₂ in deionized water, NaOH was added to maintain a pH of 12. Then, the mixture was ultrasonically irradiated for 30 min. The white as-synthesized precipitate was separated by centrifugation and washed with deionized water to remove impurities for several times and then dried at 120°C for 24 h. Finally, the formed nanoparticles were calcined at 600°C for 12 h to obtain a fine white powder.

3.3. Typical procedure for the synthesis of tetrahydro-2,4-dioxo-1H-benzo[b][1,5]diazepine-3-yl-2-methyl propanamides (4a–4j)

ZnO NPs (0.007 g, 0.1 mmol, 10 mol %) were added to a mixture of 1,2-phenylenediamines (1 mmol), Meldrum’s acid (1 mmol), and isocyanide (1 mmol) in 5 mL dichloromethane. The reaction mixture was stirred for 3–4 h at room temperature. Progress of the reaction was continuously monitored by TLC. After the reaction was completed, the residue was dissolved in methanol and then centrifuged for the separation of the catalyst. The solvent was evaporated under vacuum and the solid obtained was washed several times with acetone to afford the pure benzodiazepines.

Spectral data of the new products are given below.

The selected spectral data

N-n-pentyl-2-(2,4-dioxo-2,3,4,5-tetrahydro-1H-benzo[b][1,5]diazepin-3-yl)-2-methyl propanamide (4d).

White solid; m.p. 286–288°C. ¹H NMR (400 MHz, DMSO-d₆): δ = 0.81–0.84 (t, 3H, CH₃ (pentyl)), 1.17–1.43 (m, 12H, 3 × CH₂ and 2 × CH₃), 2.96–2.97 (t, 2H, CH₂–NH), 3.39 (s, 1H, CH), 7.11–7.18 (m, 4H, ArH), 7.58 (bs, 1H, NH), 10.33 (bs, 2H, 2NH).¹³C NMR (100 MHz, DMSO-d₆): δ = 14.4, 22.3, 28.9, 29.1, 29.8, 43.4, 48.1, 52.6, 112.4, 125.3, 130.4, 167.4, 177.1. FT-IR (KBr): 3,347 (NH), 1,700 (C=O), 1,660 (C=O), 1,546 (C=C) cm⁻¹. MS (EI) (m/z): 331 (M⁺). Anal. Calcd. for: C₁₉H₂₅N₃O₃ (Mr = 331.19): C 65.23, H 7.60, N 12.58. Found: C 65.09, H 7.71, N 12.69.

N-(4-methoxyphenyl)-2-(2,4-dioxo-2,3,4,5-tetrahydro-1H-benzo[b][1,5]diazepin-3-yl)-2-methyl propanamide (4e).

Spectral data of the new products are given below.
White solid; m.p. > 300°C. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 1.48–1.53 (s, 6H, 2 × CH$_3$), 3.43 (s, 1H, CH), 3.69 (s, 3H, OCH$_3$), 6.82–6.82 (d, 2H, J = 8 Hz, ArH), 7.16–7.18 (m, 4H, ArH), 7.42–7.44 (d, 2H, J = 8 Hz, ArH), 9.53 (bs, 1H, NH), 10.47 (bs, 2H, 2NH).$^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ = 21.8, 43.1, 48.5, 56.1, 122.2, 125.5, 131.4, 133.6, 135.8, 136.2, 140.1, 167.8, 177.2. FT-IR (KBr): 3,424 (NH), 1,695, 1,654 (C=O), 1,510 (C=C), 1,253 (C–O) cm$^{-1}$. MS (EI) (m/z): 367 (M$^+$. Anal. Calcd. for: C$_{20}$H$_{21}$N$_3$O$_4$ ($M_r$ = 367.15): C 65.38, H 5.67, N 11.44. Found: C 65.51, H 5.59, N 11.35.

N-n-pentyl-2-methyl-2-(7-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1Hbenzo[b][1,5]diazepin-3-yl)propanamide (4i).

White solid; m.p. 246–248°C. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 0.92–0.95 (t, 3H, CH$_3$ (pentyl)), 1.22–1.51 (m, 12H, 3 × CH$_2$ and 2 × CH$_3$), 2.22 (s, 3H, CH$_3$), 2.93 (t, 2H, CH$_2$–NH), 3.34 (s, 1H, CH), 7.09–7.16 (m, 3H, ArH), 8.11 (bs, 1H, NH), 10.43 (bs, 2H, 2NH).$^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ = 15.6, 19.8, 21.4, 22.8, 29.2, 29.7, 43.4, 48.2, 53.1, 112.4, 125.3, 126.7, 127.5, 128.4, 133.2, 167.2, 177.1. FT-IR (KBr): 3,339 (NH), 1,698 (C=O), 1,659 (C=O), 1,566 (C=C) cm$^{-1}$. MS (EI) (m/z): 345 (M$^+$. Anal. Calcd. for: C$_{19}$H$_{27}$N$_3$O$_3$ ($M_r$ = 345.21): C 66.06, H 7.88, N 12.16. Found: C 66.18, H 7.79, N 12.04.

N-(4-methoxyphenyl)-2-methyl-2-(7-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1Hbenzo[b][1,5]diazepin-3-yl)propanamide (4j).

White solid; m.p. 283–285°C. $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 1.31–1.35 (s, 6H, 2 × CH$_3$), 2.22 (s, 3H, CH$_3$), 3.45 (s, 1H, CH), 3.81 (s, 3H, OCH$_3$), 6.91–6.93 (d, 2H, J = 7.9 Hz, ArH), 7.14–7.17 (m, 3H, ArH), 7.53–7.55 (d, 2H, J = 7.9 Hz, ArH), 9.66 (bs, 1H, NH), 10.44 (bs, 2H, 2NH).$^{13}$C NMR (100 MHz, DMSO-$d_6$): $\delta$ = 19.9, 42.8, 43.5, 55.1, 56.7, 122.6, 123.7, 125.6, 128.4, 130.7, 131.4, 135.2, 136.5, 138.3, 142.1, 167.6, 169.9. FT-IR (KBr): 3,448 (NH), 1,705 (C=O), 1,662 (C=O), 1,518 (C=C), 1,246 (C–O) cm$^{-1}$. MS (EI) (m/z): 381 (M$^+$. Anal. Calcd. for: C$_{21}$H$_{23}$N$_3$O$_4$ ($M_r$ = 381.17): C 66.13, H 6.08, N 11.02. Found: C 66.24, H 5.99, N 10.93.

3.4. Catalyst recovery

After completion of the process, to study the recoverability and reusability of the catalyst, the zinc oxide nanoparticles were separated by centrifugation and then were washed three to four times with acetone and methanol and then dried at 100°C for 5 h. The separated catalyst was used several times with a slightly decreased activity as shown in Figure 5.

Funding

This work is funded by the Research Affairs Office of the Islamic Azad University, Qom Branch, Qom, I.R. Iran [grant number 2014-13929].

Author details

Mohammad Ali Ghasemzadeh$^1$
E-mail: ghasemzadeh@qom-iau.ac.ir
Javad Safaei-Ghomi$^1$
E-mail: jsafaei2015@gmail.com

$^1$ Department of Chemistry, Qom Branch, Islamic Azad University, Qom, I.R. Iran.
nanoparticles. Synthetic Communications, 42, 102-108. [http://dx.doi.org/10.1080/003397911.2010.522294
Ambrožič, G., Škapin, S. D., Žigon, M., & Orel, Z. C. (2010). The synthesis of zinc oxide nanoparticles from zinc acetate dihydrate and 1-tutan or isobutanol. Journal of Colloid and Interface Science, 346, 317-323.
Bhattacharyya, P., Pradhan, K., Paul, S., & Das, A. R. (2012). Nano crystalline ZnO catalyzed one pot multiprotocatalytic reaction for an easy access of fully decorated 4H-pyran scaffolds and its rearrangement to 2-pyridine nucleus in aqueous media. Tetrahedron Letters, 53, 4687-4691. [http://dx.doi.org/10.1016/j.tetlet.2012.06.086
Dharma Rao, G. B., Kaushik, M. P., & Halve, A. K. (2012). An efficient synthesis of naphtha[1,2-e]oxazineone and 14-substituted-14H-dibenzo[a,j]xanthene derivatives promoted by zinc oxide nanoparticle under thermal and solvent-free conditions. Tetrahedron Letters, 53, 2751-2754. [http://dx.doi.org/10.1016/j.tetlet.2012.03.085
Evan, G., Blanchardard, N., & Touri, M. (2008). Copper-mediated coupling reactions and their applications in natural products and designed biomolecules synthesis. Chemical Reviews, 108, 3105-3131. [http://dx.doi.org/10.1021/cr0005005
Fryer, R. L. (1991). Bicyclic diazepines. In E. C. Taylor (Ed.), Comprehensive heterocyclic chemistry (Vol. 50, Chap. II). New York, NY: Wiley.
Ghasemzadeh, A., Safaei-Ghomi, J., & Zahedi, S. (2013). Fe3O4 nanoparticles: A highly efficient and easily reusable catalyst for the one-pot synthesis of xanthenes derivatives under solvent-free conditions. Journal of the Serbian Chemical Society, 78, 769-779. [http://dx.doi.org/10.2298/JSC120624156G
Ghasemzadeh, M. A., Safaei-Ghomi, J., & Mehrabi, M. (2013). FeO nanoparticles: As an efficient, green and magnetochemically reusable catalyst for the one-pot synthesis of xanthene derivatives under solvent-free conditions. Comptes Rendus Chimie, 15, 969-974. [http://dx.doi.org/10.1016/j.crci.2012.08.010
Hosseini-Sarvari, M., & Etemad, S. (2008). Nanosized zinc oxide as a catalyst for the rapid and green synthesis of 1-phosphono malonates. Tetrahedron, 64, 5519-5523. [http://dx.doi.org/10.1016/j.tet.2008.03.095
Hosseini-Sarvari, M., Sharholl, H., & Etemad, S. (2008). Nanocrystalline ZnO for Knoevenagel condensation and reduction of the carbon, carbon double bond in conjugated alkenes. Helvetica Chimica Acta, 91, 715-724. [http://dx.doi.org/10.1002/hlca.200701017
Huang, W., J., Feng, G. C., & Wang, C.-C. (2006). A nano-meter-ZnO catalyst to enhance the ozonation of 2,4,6-trichlorophenol in water. Colloids and Surfaces A: Physicochemical and Engineering Aspects, 260, 45-51. [http://dx.doi.org/10.1016/j.colsurfa.2005.01.031
Kapou, R., Bennmame, N., Bakkho, S., Benadjis, S., Rabia, C., & Nedjar-Kolli, B. (2011). Synthesis of substituted 1,4-diazepines and 1,5-benzodiazepines using an efficient heteropolyacid-catalyzed procedure. Molecules, 16, 92-99.
Kassoe, M. Z., Masrou, H., & Movahedi, F. (2010). ZnO-nanoparticle-promoted synthesis of polyhydroquinoline derivatives via multicomponent Hantzsch reaction. Monatshefte für Chemie - Chemical Monthly, 141, 317-322. [http://dx.doi.org/10.1007/s00706-010-0252-1
Kruze, H. (1981). Clobazam: Induction of hyperlocomotion in a new nonautomated device for measuring motor activity and exploratory behavior in mice: Comparison with dizepam and critical evaluation of the results with an automated hole-board apparatus ("Planche à Troux"). Drug Development Research, 2, 145-151. [http://dx.doi.org/10.1080/003397911.2010.522294
Landquist, J. K. (1984). In A. R. Katritzky & C. W. Rees (Eds.), Comprehensive heterocyclic chemistry (Vol. 1, pp. 166-170). Oxford: Pergamon.
Levy-Pérez, A., Cabrero-Antoniano, J. R., & Corma, A. (2012). Functionalized solid catalysts for chemoselective hydrogenation-cyclisation-amination cascade reactions of relevance for the synthesis of pharmaceuticals. Tetrahedron, 66, 8203-8209. [http://dx.doi.org/10.1016/j.tet.2010.08.022
McGee, D. I., Dabiri, M., & Salehi, P. (2011). Highly efficient one-pot three-component Mannich reaction catalyzed by ZnO-nanoparticles in water. Archive for Organic Chemistry, 11, 156-164.
Matsubara, K., Fons, P., Iwata, K., Yamada, A., Sakurai, K., Tampoand, H., & Niki, S. (2008). ZnO transparent conducting films deposited by pulsed laser deposition for solar cell applications. Thin Solid Films, 431-432, 369-372. [http://dx.doi.org/10.1016/j.tsf.2006.09.030
Mirhosseini-Eshkevari, B., & Ghasemzadeh, M. A. (2014). An efficient and green one-pot synthesis of indazol[1,2-b]-phthalazinetriones via three-component reaction of aldehydes, dimedone, and phthalhydrazide using FeO@SiO2 core-shell nanoparticles. Research on Chemical Intermediates, 40, 1845-1854. [http://dx.doi.org/10.1007/s11071-014-1854-8
Mirjafary, Z., Saédien, H., Sadeghi, A., & Moghadam, F. M. (2008). ZnO nanoparticles: An efficient nanocatalyst for the synthesis of β-o-acetamido ketones/esters via a multi-component reaction. Catalysis Communications, 9, 299-308. [http://dx.doi.org/10.1016/j.catcom.2007.06.018
Pandey, A. C., Sanjay, S. S., & Yadav, R. S. (2010). Application of ZnO nanoparticles in influencing the growth rate of Cicer arietinum. Journal of Experimental Nanoscience, 5, 488-497. [http://dx.doi.org/10.1016/j.jenano.2010.09.004
Paul, S., Bhattacharyya, P. & Das, A. R. (2011). One-pot synthesis of dihydroxyran[2,3-c]chromenes via a three component coupling of aromatic aldehydes, malononitrile, and 3-hydroxycoumarin catalyzed by nanostructured ZnO in water: A green protocol. Tetrahedron Letters, 52, 4636-4641.
Qian, J., Liu, Y., Cui, J., & Xu, Z. (2012). Gold(I)-catalyzed synthesis of 1,5-benzodiazepines directly from o-phenylenediamines and aldehydes. The Journal of Organic Chemistry, 77, 4484-4490. [http://dx.doi.org/10.1021/jo300543s
Reddy, B. M., & Sreekanti, P. M. (2003). An efficient synthesis of 1,5-benzodiazepine derivatives catalyzed by a solid superacid sulfated zirconia. Tetrahedron Letters, 44, 4464-4467. [http://dx.doi.org/10.1016/S0040-4039(03)01034-7
Safaei-Ghomi, J., & Ghasemzadeh, M. A. (2012). Zinc oxide nanoparticles: A highly efficient and readily recyclable catalyst for the synthesis of xanthenes. Chinese Chemical Letters, 23, 1225-1229. [http://dx.doi.org/10.1016/j.cclet.2012.09.016
Safaei-Ghomi, J., & Ghasemzadeh, M. A. (2013a). Cu nanoparticles: A highly active and easily recyclable catalyst for the synthesis of 2-amino-3,5-dicyano-6-sulfanyl pyridines. Journal of Sulfur Chemistry, 66, 446-447. [http://dx.doi.org/10.1016/S0040-6090(03)00234-8
Safaei-Ghomi, J., & Ghasemzadeh, M. A. (2013b). SiO2 core–shell nanoparticles: A highly efficient and easily reusable catalyst for the one-pot synthesis of xanthenes derivatives. Nanoscale, 5, 5496-5504. [http://dx.doi.org/10.1039/c2nr30821a
Safaei-Ghomi, J., & Ghasemzadeh, M. A. (2014). Silver nanoparticles as an efficient and reusable catalyst for one-pot synthesis of benzofurans under aqueous conditions. Chemical Science, 5, 1003-1008. [http://dx.doi.org/10.1039/c3sc51068a
Safaei-Ghomi, J., Ghasemzadeh, M. A., & Mehrabi, M. (2013). Calcium oxide nanoparticles catalyzed one-step multicomponent synthesis of highly substituted pyridines in aqueous ethanol media. Scientia Iranica Transactions C, 20, 549-554. [http://dx.doi.org/10.1016/j.scitetj.2012.08.002

Sánchez, L., Peral, J., & Domènech, X. (1996). Degradation of 2,4-dichlorophenoxyacetic acid by in situ photogenerated Fenton reagent. Electrochimica Acta, 41, 1981–1985. http://dx.doi.org/10.1016/0013-4686(95)00486-6

Sarda, S. R., Jadhav, W. N., Kolhe, N. B., Landge, M. G., & Pawar, R. P. (2009). Solvent-free one pot synthesis of benzo-[b]-1,4-diazepines using reusable sulfamic acid catalyst. Journal of the Iranian Chemical Society, 6, 477–482. http://dx.doi.org/10.1007/BF03246524

Sasidharan, A., Chandran, P., Menon, D., Ramam, S., Nair, S., & Kayakutty, M. (2011). Rapid dissolution of ZnO nanocrystals in acidic cancer microenvironment leading to preferential apoptosis. Nanoscale, 3, 3657–3669. http://dx.doi.org/10.1039/c1nr10272a

Shaabani, A., Rezayan, A. H., Keshipour, S., Sovary, A., & Ng, S. (2009). A Novel one-pot three- (in situ five-)component condensation reaction: an unexpected approach for the synthesis of tetrahydro-2,4-dioxo-1H-benzo[b][1,5]diazepine-3-yl-2-methylpropanamide derivatives. Organic Letters, 11, 3342–3345. http://dx.doi.org/10.1021/ol0901196. Shen, L., Bao, N., Yanagisawa, K., Domen, K., Gupta, A., & Grimes, C. A. (2006). Direct synthesis of ZnO nanoparticles by a solution-free mechanochemical reaction. Nanotechnology, 17, 5117–5123. http://dx.doi.org/10.1088/0957-4484/17/20/013

Tranquillini, M. E., Cassara, P. G., Corsi, M., Curotto, G., Donati, D., Finizio, G., ... Van Amstelred, F. T. M. (1997). Novel 1,5-benzodiazepines as CCK-B ligands. Effect of arylcarbamoyl substituents at the c-3 position together with halogen substitution on the benzo-fused ring. Archiv der Pharmazie, 330, 353–357.

Weber, L. (2002). The application of multi-component reactions in drug discovery. Current Medicinal Chemistry, 9, 2085–2093. http://dx.doi.org/10.2174/0929867023368719

Yadav, J. S., Reddy, B. V. S., Satheesh, G., Srinivasulu, G., & Kunwar, A. C. (2005). InCl3-catalyzed stereoselective synthesis of 1,5-benzodiazepines. Archive for Organic Chemistry, ii, 221–227.

Zhang, J., Yu, W., & Zhang, L. (2002). Fabrication of semiconductor ZnO nanobelts using a halide source and their photoluminescence properties. Physics Letters A, 299, 276–281. http://dx.doi.org/10.1016/S0375-9601(02)00622-9

Zhang, Q., Xie, C., Zhang, S., Wang, A., Zhu, B., Wang, L., & Yang, Z. (2005). Identification and pattern recognition analysis of Chinese liquors by doped nano ZnO gas sensor array. Sensors and Actuators B: Chemical, 110, 370–376. http://dx.doi.org/10.1016/j.snb.2005.02.017