

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

Maryam Zirak^{a*}, Mostafa Azinfar^a and Mosleh Khalili^a

^aDepartment of Chemistry, Payame Noor University, Iran

CHRONICLE

Article history:

Received January 2, 2017

Received in revised form

March 1, 2017

Accepted April 21, 2017

Available online

April 22, 2017

Keywords:

Kojic acid

Heterogeneous catalysis

Multicomponent reaction

Solvent-free

Nano-ZnO

ABSTRACT

Synthesis of pyrano-chromenes and pyrano-pyrans 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.

© 2017 Growing Science Ltd. All rights reserved.

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.¹ Although, these reactions are complicated than stepwise reaction, they are fast, efficient and environmentally favorable methods.

Chromenes and pyrano-pyrans are important classes of fused oxygenated heterocycles² with a wide range of biological and therapeutic properties, such as antibacterial,³ anti-cancer,⁴ anti-anaphylactic,⁵ and anticonvulsant activities.⁶ Also, they are extensively found in natural products, such as biscopyran,⁷ Elatinyne,⁸ Calyxin I, Calyxin J, and Epicalyxin J.⁹ 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

* Corresponding author.

E-mail address: m.zirak@pnu.ac.ir (M. Zirak)

© 2017 Growing Science Ltd. All rights reserved.

doi: 10.5267/j.ccl.2017.4.001

reported for this reaction, including InCl_3 ,¹⁰ CAN ,¹¹ Al_2O_3 ,¹² $\text{Bi}(\text{OTf})_3$,¹³ $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}/\text{SiO}_2$,¹⁴ $\text{FeCl}_3\text{-SiO}_2$,¹⁵ $\text{Fe}_3\text{O}_4@\text{SiO}_2$,¹⁶ ultrasonic irradiation,¹⁷ imidazole,¹⁸ piperidine,¹⁹ Et_3N ,²⁰ and NH_4VO_3 .²¹ Kojic acid and its derivatives have wide range of applications in cosmetic,²² medicine,²³ food,²⁴ agriculture²⁵ and chemical industries.²⁶

In the other hand, metal oxides play a crucial role in many areas of chemistry, physics and materials science.²⁷ Recently, heterogeneous catalysis using metal oxides has been attracted great attention due to their potential applications in organic synthesis.²⁸⁻²⁹ 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.³⁰

In continuing our works on the heterocyclic chemistry,³¹⁻³³ we report herein a one pot three-component synthesis of chromenes and pyranopyarns from kojic acid catalyzed by nano- $\text{Bi}_2\text{O}_3\text{-ZnO}$ 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.,³⁴ by heating a solution of $\text{Zn}(\text{NO}_3)_2$ and PEG in EtOH until forming a viscous gel, followed by drying and calcination in air at 500 °C. Then, $\text{Bi}_2\text{O}_3\text{-ZnO}$ 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- $\text{Bi}_2\text{O}_3\text{-ZnO}$ 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.³⁴ 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- $\text{Bi}_2\text{O}_3\text{-ZnO}$, accounted to the existence of $\beta\text{-Bi}_2\text{O}_3$ ³⁵ in the composition of nanoparticles (Fig. 1.).

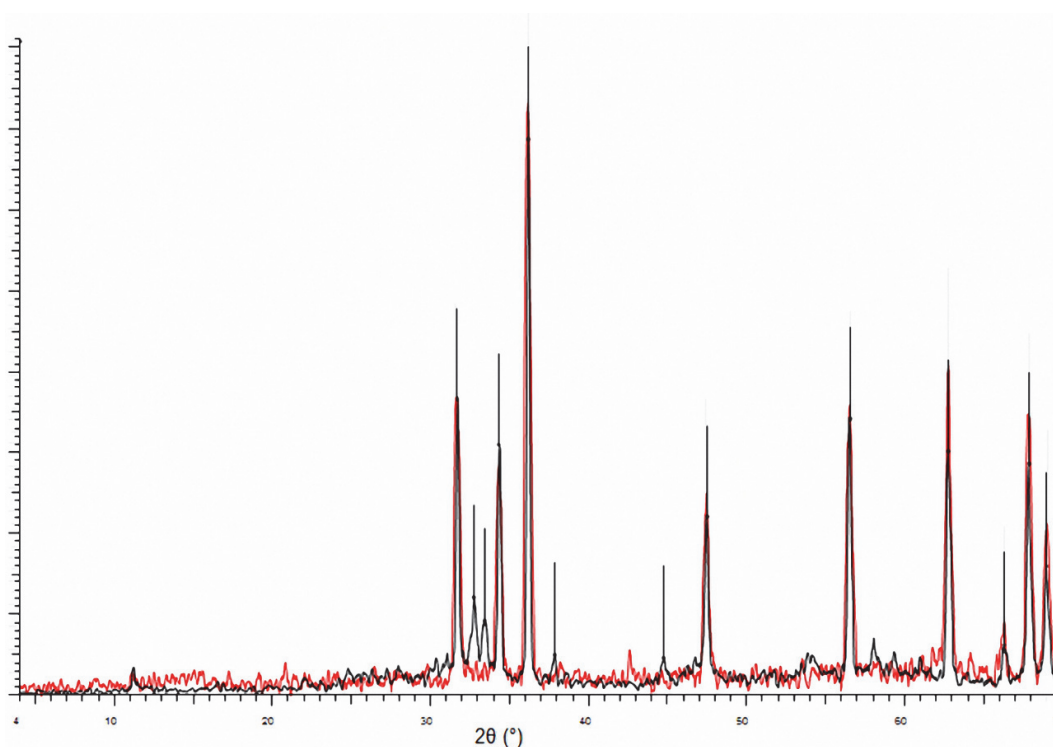


Fig. 1. XRD patterns of nano- ZnO (red) and nano- $\text{Bi}_2\text{O}_3\text{-ZnO}$ (black)

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_2O_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.).

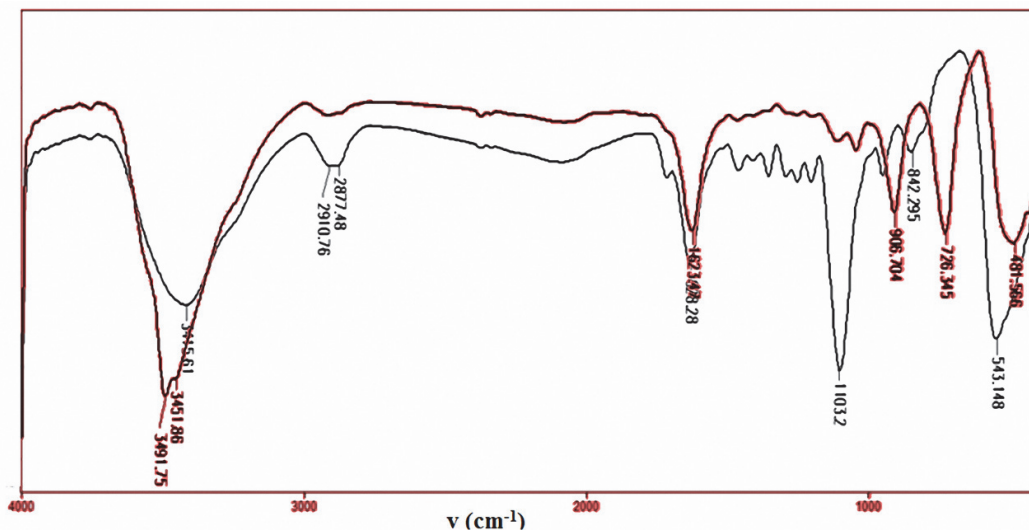


Fig. 2. FT-IR spectra of ZnO (black) and Bi_2O_3 -ZnO (red) nanoparticles

Particle morphology and textural properties of nano-ZnO and nano- Bi_2O_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_2O_3 -ZnO showed the similar shape with nano-ZnO with Puffy and wrinkled surface (Fig. 3b.). TEM images of Bi_2O_3 -ZnO revealed that the existence of ZnO nanoparticles with very tiny particles of Bi_2O_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_2O_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_2O_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_2O_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_2Cl_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_2Cl_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_2O_3 -ZnO at 100 $^\circ\text{C}$ 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 $^\circ\text{C}$), 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-Bi₂O₃-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-Bi₂O₃-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 Bi³⁺, reaction was also applied in the presence of BiCl₃ (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 CH₂Cl₂ 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-Bi₂O₃-ZnO can be reused as a catalyst (Entry 5).

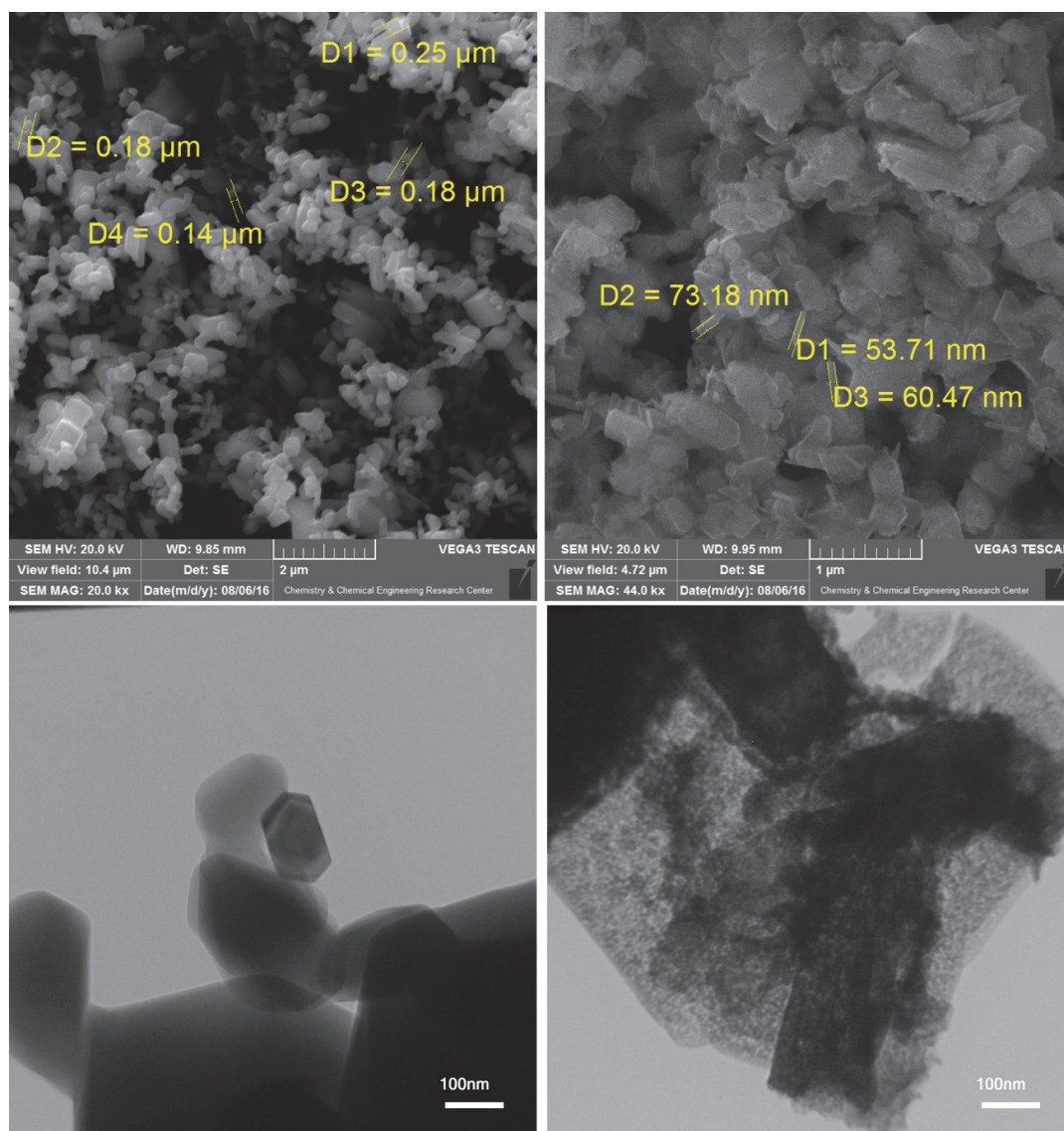
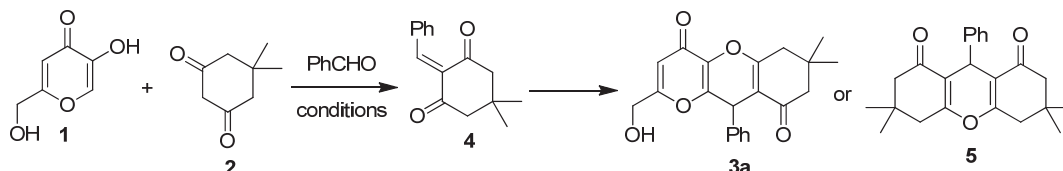


Fig. 3. SEM images of (a) ZnO and (b) Bi₂O₃-ZnO nanoparticles and TEM images of (c) ZnO and (d) Bi₂O₃-ZnO nanoparticles

With optimum conditions in hand, nano-Bi₂O₃-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-Bi₂O₃-ZnO (0.03 g, 2.8 mol% of Bi) at 100 °C for 2 h, to afford chromenes

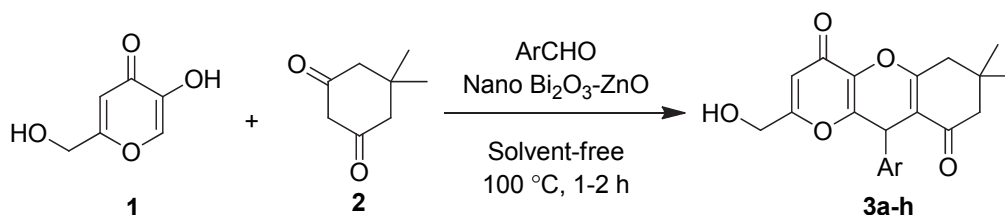
3a-h in 75-84% yields. The results are summarized in Table 2. As shown in Table 2, not only electron-withdrawing substituted benzaldehydes, such as Cl and NO₂ substituted benzaldehydes afforded corresponding desired products in high yields, but also electron donating substituted benzaldehydes, 4-Me and 4-MeO substituted benzaldehydes worked well under the reaction conditions.

Table 1. Optimization of the reaction conditions^a



Entry	Catalyst	Catalyst loading (g) [Bi mol%] ^b	Solvent	Temp. (°C)	Time (h)	Yield (%)
1	Nano-Bi ₂ O ₃ -ZnO	0.03 [2.8]	EtOH	Reflux	6	40
2	Nano-Bi ₂ O ₃ -ZnO	0.03 [2.8]	Water	Reflux	6	<10% ^d
3	Nano-Bi ₂ O ₃ -ZnO	0.03 [2.8]	CH ₂ Cl ₂	Reflux	6	23
4	Nano-Bi ₂ O ₃ -ZnO	0.03 [2.8]	MeCN	Reflux	6	NR ^e
5	Nano-Bi ₂ O ₃ -ZnO	0.03 [2.8]	SF ^c	100	2	80, 78, 78, 72 ^f
6	Nano-Bi ₂ O ₃ -ZnO	0.03 [2.8]	SF	rt	8	NR
7	Nano-Bi ₂ O ₃ -ZnO	0.03 [2.8]	SF	60	8	27
8	Nano-Bi ₂ O ₃ -ZnO	0.03 [2.8]	SF	80	5	64
9	Nano-Bi ₂ O ₃ -ZnO	0.03 [2.8]	SF	110	2	66
10	-	-	SF	100	6	NR
11	Nano-Bi ₂ O ₃ -ZnO	0.01 [0.9]	SF	100	2	58
12	Nano-Bi ₂ O ₃ -ZnO	0.02 [1.8]	SF	100	2	70
13	Nano-Bi ₂ O ₃ -ZnO	0.05 [4.7]	SF	100	2	81
14	Nano-ZnO	0.03 [0.0]	SF	100	2	20
15	BiCl ₃	0.02 [6.3]	SF	100	2	35 ^g

^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.



Scheme 1. Nano Bi₂O₃-ZnO-catalyzed synthesis of pyrano-chromenes

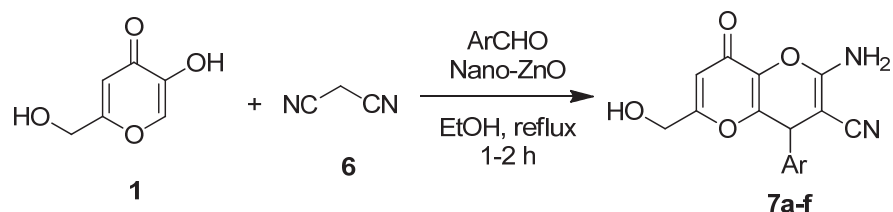
Table 2. Nano-Bi₂O₃-ZnO catalyzed synthesis of dihydropyrano[3,2-*b*]chromenediones^a

Entry	Ar	Product	Yield (%)	Mp (°C)	
				Measured	Reported
1	C ₆ H ₅	3a	80	186-188	184-185 [14]
2	4-ClC ₆ H ₄	3b	82	194-196	205-206 [14]
3	2-ClC ₆ H ₄	3c	79	218-220	216-217 [14]
4	3-NO ₂ C ₆ H ₄	3d	84	214-216	212-213 [14]
5	4-NO ₂ C ₆ H ₄	3e	81	233-235	229-230 [14]
6	2,4-Cl ₂ C ₆ H ₃	3f	78	168-170	166-167 [14]
7	4-OMeC ₆ H ₄	3g	75	177-179	178-179 [14]
8	4-MeC ₆ H ₄	3h	77	216-217	214-215 [14]

^aReactions were carried out under solvent-free conditions at 100 °C for 1-2 h.

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-Bi₂O₃-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 BiCl₃ 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

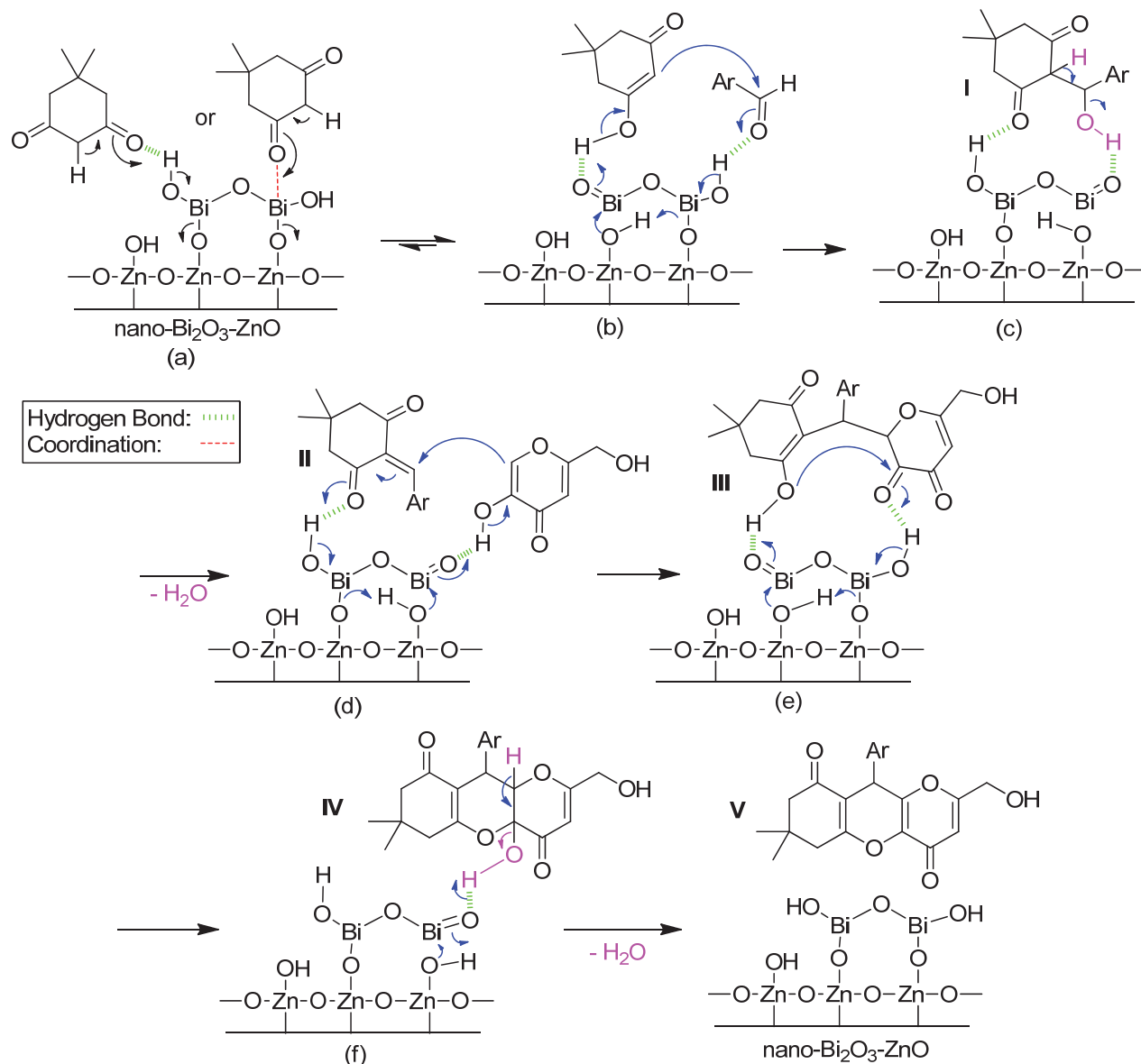
Table 3. Nano-ZnO catalyzed synthesis of aminopyrano-pyrans^a

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

^aReactions were carried out in refluxing EtOH for 1-2 h.

A plausible reaction mechanism involves the nano-Bi₂O₃-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 hydrate form of Bi₂O₃ on nano-ZnO, and hydrogen bonds formed between starting components and also in-situ generated intermediates, played an important role in catalytic activity of Bi₂O₃-ZnO, for this type of transformation. As mentioned above (Table 1, entry 14), the Bi₂O₃ is essential for the reaction of dimethone, benzaldehyde and dimethone. Due to the high reactivity of malononitrile, in the presence of Bi₂O₃-ZnO the reaction is uncontrollable, leading to a complex mixture. While nano-ZnO in the absence of Bi₂O₃ exhibited acceptable catalytic activity.

The comparison of the catalytic activity of nano-Bi₂O₃-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-Bi₂O₃-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-Bi₂O₃-ZnO with other catalysts.

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

^aThree component reaction between 4-chlorobenzaldehyde, dimethone and kojic acid under solvent free condition. ^bThree 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 is 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 Galactic Industries Corporation, spectrometer. X-ray diffraction (XRD) patterns were measured using a Bruker D8 Advance with CuK (α) radiation ($\lambda = 0.15406$ nm) in the range $4^\circ < 2\theta < 70^\circ$. 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. $^1\text{H-NMR}$ (500 MHz, DMSO- d_6): 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. $^1\text{H-NMR}$ (500 MHz, CDCl₃): δ = 7.23-7.32 (m, 4H, Ph), 6.55 (s, 1H, CH pyrone), 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. $^1\text{H-NMR}$ (500 MHz, DMSO- d_6): 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, 1 H, CH pyran), 4.21 (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.

2-Amino-4-(benzo[d][1,3]dioxol-6-yl)-4,8-dihydro-6-(hydroxymethyl)-8-oxopyrano[3,2-b]pyran-3-carbonitrile (7d): IR (KBr): ν (cm^{-1}) = 3000-3400, 3309, 3195, 3074, 2968, 2897, 2195, 1644, 1592, 1489, 1412, 1248, 1219. $^1\text{H-NMR}$ (500 MHz, DMSO- d_6): 7.20 (s, 2H, NH₂), 6.91 (d, J = 7.0 Hz, 1H, Ph), 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. $^{13}\text{C NMR}$ (125 MHz, DMSO- d_6): 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.

2-Amino-4,8-dihydro-6-(hydroxymethyl)-4-(naphthalene-1-yl)-8-oxopyrano[3,2-b]pyran-3-carbonitrile (7e): IR (KBr): ν (cm^{-1}) = 3000-3400, 3299-3193, 3061, 2961, 2188, 1644, 1592, 1444, 1412, 1267, 1216. $^1\text{H-NMR}$ (500 MHz, DMSO- d_6): 7.41-7.95 (m, 7H, CH naphthyl), 7.27 (s, 2H, NH₂), 6.34 (s, 1H, CH pyrone), 5.64 (s, b, 1H, OH), 4.98 (s, 1H, CH pyran), 4.09-4.16 (m, 2H, CH₂) ppm. $^{13}\text{C NMR}$ (125 MHz, DMSO- d_6): δ = 41.0, 57.3, 60.1, 114.6, 119.3, 124.5, 126.2, 126.5, 126.6, 127.0, 127.7, 128.5, 131.8, 133.7, 140.5, 141.3, 155.7, 159.2, 166.7, 179.1 ppm.

References

- Domling A. (2006) Recent developments in isocyanide based multicomponent reactions in applied chemistry. *Chem. Rev.*, 106 (1) 17-89.
- Pratap R., and Ram V. J. (2014) Natural and synthetic chromenes, fused chromenes, and versatility of dihydrobenzo[*h*]chromenes in organic synthesis. *Chem. Rev.*, 114 (20) 10476-10526.
- Kumar D., Reddy V. B., Sharad S., Dube U., and Kapur S. (2009) A facile one-pot green synthesis and antibacterial activity of 2-amino-4*H*-pyrans and 2-amino-5-oxo-5,6,7,8-tetrahydro-4*H*-chromenes. *Eur. J. Med. Chem.*, 44 (9) 3805-3809.
- Shestopalov A. M., Litvinov Y. M., Rodinovskaya L. A., Malyshev O. R., Semenova M. N., and Semenov V. V. (2012) Polyalkoxy substituted 4*H*-chromenes: Synthesis by domino reaction and anticancer activity. *ACS Comb. Sci.*, 14 (8) 484-490.
- Bonsignore L., Loy G., Secci D., and Calignano A. (1993) Synthesis and pharmacological activity of 2-oxo-(2*H*) 1-benzopyran-3-carboxamide derivatives. *Eur. J. Med. Chem.*, 28 (6) 517-520.
- El-Nagger A. M., Abdel-El-Salam A. M., Latif M. S. A., and Ahmed F. S. M. (1981) Synthesis of some biologically active visnagin-9-sulfonylamino acid and dipeptide derivatives. *Chemischer Informationsdienst. Pol. J. Chem.*, 55 793-797.
- Evidente A., Andolfi A., Maddau L., Franceschini A., and Marras F. (2005) Biscopyran, a Phytotoxic Hexasubstituted Pyranopyran Produced by *Biscogniauxia mediterranea*, a Fungus Pathogen of Cork Oak. *J. Nat. Prod.*, 68 (4) 568-571.
- Sheldrake H. M., Jamieson C., and Burton J. W. (2006) The Changing Faces of Halogenated Marine Natural Products: Total Synthesis of the Reported Structures of Elatenyne and an Enyne from *Laurencia majuscula*. *Angew. Chem. Int. Ed.*, 45 (43) 7199-7202.
- Cakir S. P., Stokes S., Sygula A., and Mead K. T. (2009) Evidence for π -Stacking as a Source of Stereocontrol in the Synthesis of the Core Pyranochromene Ring System common to Calyxin I, Calyxin J, and Epicalyxin J. *J. Org. Chem.*, 74 (19) 7529-7532.
- Li Y., Meng X., Cai G., Du B., and Zhao B. (2014) CAN-catalyzed synthesis of 10-arylpyrano[3,2-*b*]chromene-4,9-diones under solvent-free conditions. *Res. Chem. Intermed.*, 40 (2) 699-709.
- Subba Reddy B. V., Ramana Reddy M., Narasimhulu G. and Yadav J. S. (2010) InCl₃-catalyzed three-component reaction: a novel synthesis of dihydropyrano[3,2-*b*]chromenediones under solvent-free conditions. *Tetrahedron Lett.*, 51 (43) 5677-5679.
- Li W. L., Wu L. Q., and Yan F. L. (2011) Alum-catalyzed one-pot synthesis of dihydropyrano[3,2-*b*]chromenediones. *J. Braz. Chem. Soc.*, 22 (11) 2202-2205.
- Pourshahrestani S. Mohammadpoor-Baltork I., Moghadam M., Tangestaninejad S., Khosropour A. R., and Mirkhani V. (2015) Bismuth triflate, Bi(OTf)₃, as an efficient and reusable catalyst for synthesis of dihydropyrano[3,2-*b*]chromenediones. *J. Iran. Chem. Soc.*, 12 (4) 573-580.
- Zhang G., and Qu Y. (2013) CeCl₃·7H₂O/SiO₂ as an efficient and recyclable catalyst for the synthesis of dihydropyrano[3,2-*b*]chromenediones. *J. Chem.*, 1-4.
- Li W. L., Liang J. Y., Wang T. B. and Yang Y. Q. (2011) FeCl₃-SiO₂ as heterogeneous catalysts for the preparation of dihydropyrano[3,2-*b*]chromenediones. *Collect. Czech. Chem. Commun.*, 76 (12) 1791-1797.
- Maleki A., and Azadegan S. (2017) Preparation and characterization of silica-supported magnetic nanocatalyst and application in the synthesis of 2-amino-4*H*-chromene-3-carbonitrile derivatives. *Inorg. Nano-Met. Chem.*, 47 (6) 917-924.
- Banitaba S. H., Safari J., and Dehghan Khalili S. (2013) Ultrasound promoted one-pot synthesis of 2-amino-4,8-dihydropyrano[3,2-*b*]pyran-3-carbonitrile scaffolds in aqueous media: A

- complementary 'green chemistry' tool to organic synthesis. *Ultrasonics Sonochem.*, 20 (1) 401-407.
- 18 Nasim Khan M. D., Pal S., Karamthulla S. and Choudhury L. H. (2014) Imidazole as organocatalyst for multicomponent reactions: diversity oriented synthesis of functionalized hetero- and carbocycles using *in situ*-generated benzyldenemalononitrile derivatives. *RSC Adv.*, 4, 3732-3741.
- 19 Piao M. Z., and Imafuku K. (1997) Convenient synthesis of amino-substituted pyranopyranones. *Tetrahedron Lett.*, 38 (30) 5301-5302.
- 20 Shestopalov A. A., Rodinovskaya L. A., Shestopalov A. M. and Litvinov V. P. (2004) One-step synthesis of substituted 4,8-dihydropyrano[3,2-*b*]pyran-4-ones. *Russ. Chem. Bull. Int. Ed.*, 53 (3) 724-725.
- 21 Shitole B., Shitole N., Shingare M., and Kakde G. (2016) An efficient one pot three-component synthesis of dihydropyrano[3,2-*c*]chromenes using ammonium metavanadate as catalyst. *Curr. Chem. Lett.*, 5 (4) 137-144.
- 22 Lin C. H., Wu H. L. and Huang Y. L. (2007) Combining high-performance liquid chromatography with on-line microdialysis sampling for the simultaneous determination of ascorbyl glucoside, kojic acid, and niacinamide in bleaching cosmetics. *Anal. Chim. Acta.*, 581 (1) 102-107.
- 23 Brtko J., Rondah L., Fickova M., Hudecova D., Eyb V., and Uher M. (2004) Kojic acid and its derivatives: history and present state of art. *Cent. Eur. J. Pub. Health.*, 12, S16-S18.
- 24 Son S. M., Moon K. D. and Lee C. Y. (2001) Inhibitory effects of various antibrowning agents on apple slices. *Food Chem.*, 73 (1) 23-30
- 25 Chen J. S., Wei C., Rolle R. S., Steven Otwell W., Balaban M. O. and Marshall M. R. (1991) Inhibitory effect of kojic acid on some plant and crustacean polyphenol oxidases. *J. Agric. Food Chem.*, 39 (8) 1396-1401.
- 26 Buchta K. (1982) Organic acids of minor importance in biotechnology biomass, microorganisms for special application, microbial products, energy from renewable resources. *Bioehringer, Ingelheim Federal Republic of Germany*, 447.
- 27 Cao J., Zhu Y., Shi L., Zhu L., Bao K., Liu S., and Qian Y. (2010) Double-Shelled Mn₂O₃ Hollow Spheres and Their Application in Water Treatment. *Eur. J. Inorg. Chem.*, 2010 (8) 1172-1176
- 28 Shinde S. S., Bhosale C. H., and Rajpure K. Y. (2011) Photocatalytic activity of sea water using TiO₂ catalyst under solar light. *J. Photochem. Photobiol. B: Biol.*, 103 (2) 111-117.
- 29 Maleki A., Aghaei M., Hafizi-Atabak H. R., and Ferdowsi M. (2017) Ultrasonic treatment of CoFe₂O₄@B₂O₃-SiO₂ as a new hybrid magnetic composite nanostructure and catalytic application in the synthesis of dihydroquinazolinones. *Ultrason. Sonochem.*, 37, 260-266.
- 30 Bao J., Zimmler M. A., and Capasso F. (2006) Broadband ZnO Single-Nanowire Light-Emitting Diode. *Nano Lett.*, 6 (8) 1719-1722.
- 31 Eftekhari-sis B., and Zirak M. (2015) Chemistry of α -Oxoesters: A Powerful Tool for the Synthesis of Heterocycles. *Chem. Rev.*, 115 (1) 151-264.
- 32 Eftekhari-sis B., Zirak M., and Akbari A. (2013) Aryl glyoxals in synthesis of heterocyclic compounds. *Chem. Rev.*, 113 (5) 2958-3043
- 33 Zirak M., and Eftekhari-sis B. (2015) Kojic acid in organic synthesis. *Turk. J. Chem.*, 39, 439-496.
- 34 Amini M., and Ashrafi M. (2016) Photocatalytic degradation of some organic dyes under solar light irradiation using TiO₂ and ZnO nanoparticles. *Nano. Chem. Res.*, 1 (1) 79-86.
- 35 Cerva H., and Russwurm W. (1988) Microstructure and crystal structure of bismuth oxide phases in zinc oxide varistor ceramics. *J. Am. Ceram. Soc.*, 71 (7) 522-530.
- 36 Sarrafi Y., Mehrasbi E., and Mashalchi S. Z. (2015) MCM-41-SO₃H: an efficient, reusable, heterogeneous catalyst for the one-pot, three-component synthesis of pyrano[3,2-*b*]pyrans. *Res.*

Chem. Intermed., published online; doi: 10.1007/s11164-015-2275-z.

37 Khan M. N., Pal S., Karamthulla S., and Choudhury L. H. (2014) Imidazole as organocatalyst for multicomponent reactions: diversity oriented synthesis of functionalized hetero-and carbocycles using in situ-generated benzyldenemalononitrile derivatives. *RSC Adv.*, 4 (8) 3732-3741.



© 2016 by the authors; licensee Growing Science, Canada. This is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC-BY) license (<http://creativecommons.org/licenses/by/4.0/>).