IRANIAN JOURNAL OF CATALYSIS

$CuO-CeO_2$ nanocomposite: A green recyclable catalyst for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones/thiones

Jalal Albadi[a]*, Azam Mansournezhad[b]

[a] *College of Science, Behbahan Khatam Alanbia University of Technologhy, Behbahan, Iran*
[b] *Department of Chemistry, Gachsaran Branch, Islamic Azad University, Gachsaran, Iran*

Received 28 March 2013; received in revised form 19 May 2013; accepted 15 June 2013

ABSTRACT

$CuO-CeO_2$ nanocomposite is reported as a green and highly efficient recyclable catalyst for the multicomponent synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones/thiones under solvent-free conditions. The catalyst was synthesized by co-precipitation method and characterized by XRD, BET specific surface area, FESEM and EDS analysis.

***Keywords**: CuO-CeO_2 nanocomposite, Biginelli reaction, Solvent-free conditions, 3,4-dihydropyrimidin-2(1H)-ones/thiones.*

1. Introduction

Dihydropyrimidone derivatives are important class of heterocyclic compounds that received significant attention from many pharmaceutical and organic chemists because of the broad spectrum of their biological and pharmaceutical properties such as antibacterial, anti-inflammatory, and antivirial properties [1]. The initial synthesis of dihydropyrimidones was reported by Biginelli involving a one pot condensation of an aldehyde, *β*-ketoester and urea under acidic conditions [2]. However, this reaction suffers from the harsh conditions, long reaction times and low yields of the products. In order to improve the efficiency of this reaction, several modified procedures have been reported [3-19]. In recent years, nanocrystalline oxides have proved to be useful to chemists in the laboratory and industry due to the good activation of adsorbed compounds and reaction rate enhancement, selectivity, easier work-up, recyclability of the supports and the eco-friendly reaction conditions [20-24]. Also the practical applications of nanocomposite metal oxides as catalysts in organic synthesis have been increased due to their high catalytic activity because of high surface area [25-26]. The catalytic application of $CuO-CeO_2$ nanostructure for oxidation of CO in H_2-rich streams is well known [27]. Recently, we have reported the preparation $CuO-CeO_2$ nanocomposite and its catalytic activity for the synthesis of aryl-14*H*-dibenzo[a-j]xanthenes [28]. In continuation of these studies and our research program to develop the efficient and green catalysts in organic synthesis [29-34], herein, we wish to report the applicability of $CuO-CeO_2$ nanocomposite as a green, recyclable and efficient catalyst for the synthesis of the dihydropyrimidone derivatives (DHPMs) under solvent-free conditions (Scheme 1).

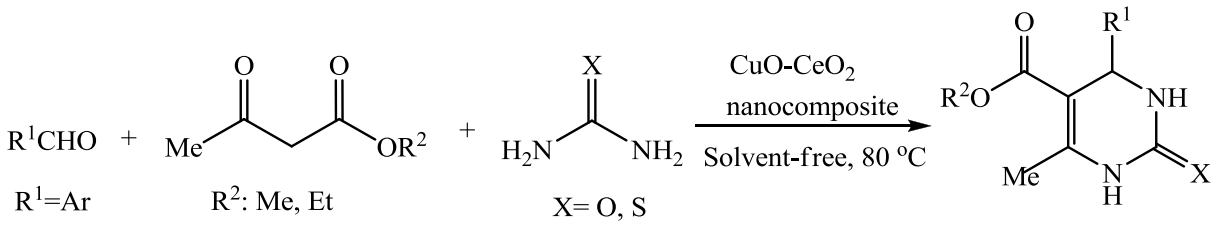
* Corresponding author: E-mail: chemalbadi@gmail.com, albadi@bkatu.ac.ir; Tel/Fax: +986712229969

2. Experimental

All products were identified by comparison of their spectral and physical data with authentic samples. Chemicals were purchased from Fluka and Merck and chemical companies. Yields refer to isolated pure products.

2.1. Preparation of the catalyst

$CuO-CeO_2$ nanocomposite was prepared by co-precipitation method using aqueous solution of cerium and copper nitrate and drop-wise KOH as precipitant agent under vigorous mixing at 80 ºC to precipitate the Cu and Ce cations at pH of 10 [27]. Then acquired sample was filtered, washed and calcined to obtain final catalyst for using synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones/thiones. X-ray diffraction (XRD), BET specific surface area, emission scanning electron microscopy (ESEM) and energy dispersive spectroscopy (EDS) analysis were used to characterize the catalyst.



Scheme 1. Synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones/thiones catalyzed by CuO-CeO_2 nanocomposite.

2.2. General procedure for the synthesis of 3,4-dihydropyrimidin-2(1H)-ones/thiones

A mixture of aldehyde (1 mmol), *β*-ketoester (1 mmol), urea or thiourea (1 mmol) and CuO-CeO_2 nanocoposite (0.05 g), was heated in an oil bath (80 ºC) for the appropriate times (Table 1). After completion of the reaction as followed by TLC, 10 mL of acetone was added to the mixture and filtered. The catalyst washed with hot acetone, dried and stored for another consecutive reaction run. Evaporation of the solvent from the filtrate and recrystallization of the solid residue from hot ethanol afforded the pure products in high yields.

3. Results and Discussion

The CuO-CeO_2 nanocomposite catalyst was prepared by a coprecipitation method and characterized by X-ray diffraction (XRD), BET specific surface area, emission scanning electron microscopy (ESEM) and energy dispersive spectroscopy (EDS) analysis. According to the ESEM images, the average size of the nanoparticles was estimated to be 7-30 nm (Figure 1). It seems that 7 nm particles calculated based on the BET surface area, are agglomerated to approximately 33 nm sized clusters and made bigger nanostructure CuO-CeO_2 catalyst.

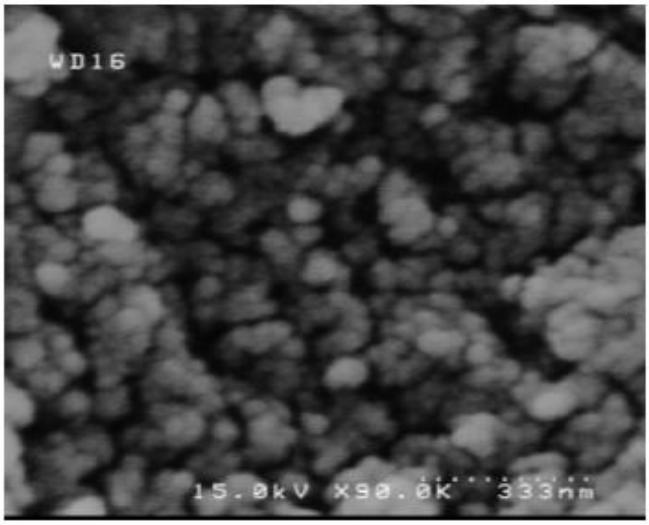


Figure 1. ESEM image of the CuO–CeO_2 nanocomposite.

Sharp peaks were observed in the XRD patterns, which were consistent with only CeO_2 crystallite. There was no peak related to the CuO phase, probably due to the fine dispersion of CuO nanoparticles on the surface of ceria (Figure 2). The average crystallite size of ceria was also determined from X-ray line broading using the Debye–Scherrer formula (obtained size: 7.5 nm). The calculated average crystal size of the ceria in the catalyst based on dominant peak at 2θ of 28.5o using Debye–Scherrer equation was 7.5 nm.

EDS analysis showed the presence of about 5.8 wt.% CuO in the CuO–CeO_2 catalyst (Figure 3).

Initially, for the optimization of reaction conditions, the condensation of benzaldehyde, ethyl acetoacetate and urea was chosen as a model and its behavior was studied under a variety of conditions. The best result was achieved by carrying out the reaction of each substrate (with 1mmol) in the presence of 0.05 g of CuO-CeO_2 nanocomposite oxide at 80 °C under solvent-free conditions (Table 1, entry 1). In order to study the generality of the method, different kinds of aromatic aldehydes were reacted with ethyl acetoacetate or methyl acetoacetate and urea or thiourea under optimized conditions (Table 1). Aromatic aldehydes containing both electron-donating and electron-withdrawing groups were reacted under the same reaction conditions to produce the corresponding products in good to high yields.

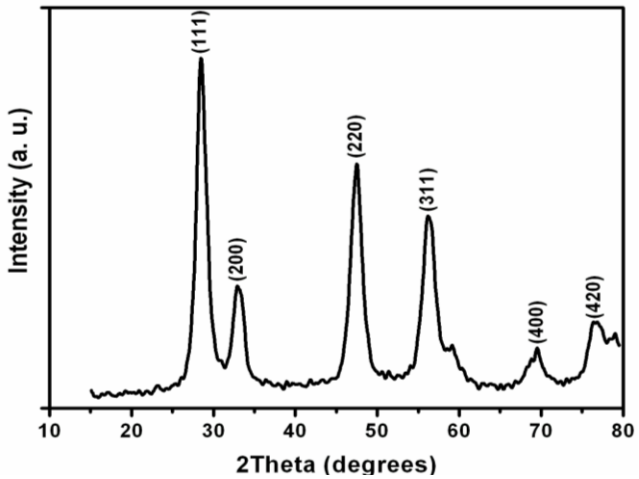


Figure 2. XRD pattern of the CuO–CeO_2 nanocomposite.

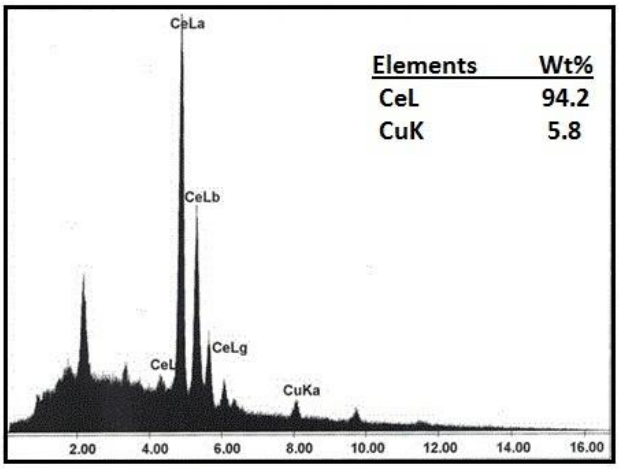


Figure 3. EDS analysis of the CuO–CeO_2 nanocomposite

Aliphatic aldehydes remain intact under the same reaction conditions. Therefore, the method can be useful for the chemoselective synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones/thiones from aromatic aldehydes in the presence of aliphatic ones. The experimental procedure with this catalyst is very simple and the catalyst can be removed easily by filtration. The solid products were easily recrystallized from hot ethanol and were obtained in good to high yields during short reaction times. Very low amount of the catalyst is needed. Moreover, our procedure is environmentally friendly as it does not use any toxic auxiliary or solvent.

Moreover the recyclability of the catalyst is also important. To investigate these properties, the reaction of benzaldehyde, ethyl acetoacetate and urea was selected again as the model (Table 2). After completion of the reaction, the recovered catalyst was washed with hot acetone and after dryness was reused in the next similar run. This procedure was repeated for 10 consecutive runs and the desired product was obtained in high yields after 1-10 runs, respectively.

In order to show the efficiency of our method, Table 3 compares the results from the synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones from benzaldehyde, ethyl acetoacetate and urea in the presence of CuO-CeO_2 nanocomposite and some of the previously reported catalysts. In comparison with previously reported methods, CuO-CeO_2 nanocomposite promoted the reaction very effectively, gave the desired product in very short times at high yields. This catalyst easy to handle and its preparation is simple and straightforward. It can be recovered simply by filtration and can be reused in the next runs without significant yield decrease of the products.

Table 1. Synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones/thiones catalyzed by CuO-CeO_2 nanocomposite.

Entry	R^1	R^2	X	Time(min)	Yield (%) [a]	M. P. (^{O}C)	
						Found	Reported
1	C_6H_6	Et	O	10	91	203-204	204-206[33]
2	2-Cl- C_6H_4	Et	O	12	90	214-215	213-216[33]
3	4-Cl- C_6H_4	Et	O	10	94	211-213	209-211[33]
4	4-NO_2- C_6H_4	Et	O	7	89	209-210	209-211[33]
5	4-MeO- C_6H_4	Et	O	20	90	201-203	200-202[33]
6	3,4,5-MeO- C_6H_4	Et	O	45	90	179-181	178-180[19]
7	Ph	Et	S	10	90	206-208	205-206[33]
8	2-Cl-Ph	Et	S	12	89	168-170	167-169[33]
9	4-Cl-Ph	Et	S	10	92	183-185	181-183[33]
10	3-NO_2-Ph	Et	S	14	88	205-206	205-207[33]
11	4-Cl-C_6H_4	Me	O	12	92	205-207	204-206[33]
12	4-MeO-C_6H_4	Me	O	20	87	191-193	190-192[33]
13	4-Me-C_6H_4	Me	O	12	92	212-214	214-215[19]
14	3,4,5-MeO-C_6H_4	Me	O	45	91	197-198	198-199[19]
15	$CH_3CH_2CH_2$	Et	O	60	-	-	-
16	$PhCH_2CH_2$	Et	O	60	-	-	-

[a]Ioslated yield.

Table 2. Recyclability of $CuO\text{-}CeO_2$ nanocomposite.

Run	1	2	3	4	5	6	7	8	9	10
Time(min)	10	10	10	10	12	12	15	15	18	20
Yield (%)[a]	91	91	90	90	90	90	90	89	89	88

[a]Ioslated yield

Table 3. Comparison of the efficiency of $CuO\text{-}CeO_2$ nanocomposite in the synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones from benzaldehde, ethyl acetoacetate and urea with other reported methods.

Entry	Reagent	Conditions	Time(h)	Yield (%) [a]	Reference
1	$Cu(OTf)_2$	EtOH/100 °C, M.W	1	95	[4]
2	$PPA\text{-}SiO_2$	CH_3CN/reflux	1	88	[6]
3	$\alpha\text{-}Zr(CH_3)_{1.2}(O_3PC_6H_4SO_3H)_{0.8}$	Solvent-free/80 °C	18	89	[7]
4	sulfated tungstate	Solvent-free/80 °C	1	92	[8]
5	$CD\text{-}SO_3H$	Solvent-free/80 °C	2	89	[9]
6	DBSA	Water/54 °C	7	89	[16]
7	$CuO\text{-}CeO_2$ nanocomposite	Solvent-free/80 °C	10 (min)	91	This Work

4. Conclusion

In conclusion, we have developed a simple, green and efficient procedure for the multicomponent synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones/thiones catalyzed by $CuO\text{-}CeO_2$ nanocomposite under solvent-free conditions. The introduced catalyst can promote the yields and reaction times over 10 runs without appreciable loss in its activity and efficiency. Moreover, high yields of products, short reaction times, ease of work-up and clean procedure, will make this procedure a useful addition to the available methods.

Acknowledgement

We are thankful to the Behbahan Khatam Alanbia University of Technology for the partial support of this work.

References

[1] K.S. Atwal, B.N. Swanson, S.E. Unger, D.M. Floyd, S. Moreland, A. Hedberg, B.C. O'Reilly, J. Med. Chem. 34 (1991) 806-811.
[2] P. Biginelli, Gazz. Chim. Ital. 23 (1893) 360-413.
[3] A. Bamoniri, B.F. Mirjalili, S. Nazemian, Iran. J. Catal. 2 (2012) 17-21.
[4] K.K. Pasunooti, H. Chai, C.N. Jensen, B.K. Gorityala, S. Wang, X.-W. Liu, Tetrahedron Lett. 52 (2011) 80-84.
[5] Z. Fang, Y. Lam, Tetrahedron Lett. 67 (2011) 1294-1297.
[6] M. Zeinali-Dastmalbaf, A. Davoodnia, M.M. Heravi, N. Tavakoli-Hoseini, A. Khojastehnezhad, H.A. Zamani, Bull. Korean Chem. Soc. 32 (2011) 656-658.
[7] O. Rosati, M. Curini, F. Montanari, M. Nocchetti, S. Genovese, Catal. Lett. 141 (2011) 850-853.
[8] S.D. Salim, K.G. Akamanchi, Catal. Lett. 12 (2011) 1153-1156.
[9] S. Asghari, M. Tajbakhsh, B. Jafarzadeh Kenari, S. Khaksar, Chin. Chem. Lett. 22 (2011) 127-130.
[10] L. Khazdooz, A. Zarei, A. R. Hajipour, N. Sheikhan, Iran. J. Catal. 2 (2012) 173-178.
[11] H. Sharghi, M. Jokar, Synth. Commun. 39 (2009) 958-979.
[12] F. Shirini, M.A. Zolfigol, E. Mollarazi, Synth. Commun. 36 (2006) 2307-2310.
[13] M.M. Heravi, K. Bakhtiari, F. Bamoharram, Catal. Commun. 7 (2006) 373-376.
[14] K.K. Pasunooti, H. Chai, J. Chantel Nixon, G. Bala Kishan, W. Siming, L. Xue-Wei, Tetrahedron Lett. 52 (2011) 80-84.
[15] G.B. Dharma Rao, B.N. Acharya, S.K. Verma, M.P. Kaushik, Tetrahedron Lett. 52 (2011) 809-812.
[16] M.A. Bigdeli, G. Golami, E. Sheikhhosseini, Chin. Chem. Lett. 22 (2011) 903-906.
[17] Q. Liu, N. Pan, J. Xu, W. Zhang, F. Kong, Synth. Commun. 43 (2013) 139-146.
[18] M. Mirzai, H. Valizadeh, Synth. Commun. 42 (2012) 1268-1277.
[19] N.D. Abhishek, K.P. Vaibhav, K.R. Dipak, J. Chem. Sci. 124 (2012) 921-926.

[20] H. Sharghi, M. Hosseini, Synthesis. (2002)1057-1059.
[21] S. M. Hosseini, H. Sharghi, J. Org. Chem. 69 (2004) 6953-6956.
[22] S.F. Yin, B.Q. Xu, S.J. Wang, C.F. Ng, C.T. Au, Catal. Lett. 96 (2004) 113-116
[23] M.T. Drexler, M.D. Amiridis, Catal. Lett. 79 (2002) 175-181.
[24] R.S. Varma, Green. Chem. 1 (1999) 43-55.
[25] S. Samantaray, D.K. Pradhan, G. Hota, B.G. Mishra, Chem. Eng. J. 193 (2012) 1-9.
[26] S.Li, W. Zhang, M.H. So, C.M. Che, R. Wang, R. Chen, J. Mol. Catal. A: Chem. 359 (2012) 81-87.
[27] A. Razeghi, A. Khodadadi, H. Ziaie-Azad, Y. Mortazavi, Chem. Eng. J. 164 (2010) 214-220.
[28] J. Albadi, A. Razeghi, A. Mansournezhad, H. Abbaszadeh, J. Nanoparticles 9 (2013) 83-889.
[29] J. Albadi, M. Keshavarz, M. Abedini, M. Vafaie-nezhad, Chin. Chem. Lett. 23 (2012) 797-800.
[30] J. Albadi, M. Keshavarz, F. Shirini, M. Vafaie-nezhad, Catal. Commun. 27 (2012) 17-20.
[31] J. Albadi, N. Iravani, M. Khoshakhlagh, Iran. J. Catal. 2 (2012) 85-89.
[32] J. Albadi, N. Iravani, F. Shirini, F. Dehghan, J. Chem. Res. (2012) 610-611.
[33] F. Shirini, M. A. Zolfigol, J. Albadi, Chin. Chem. Lett. 22 (2011) 318-321.
[34]. J. Albadi, A. Mansournezhad, M. Baghernezhad, N. Frozan, 57 (2013) 169-171.