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Chinese Chemical Letters 23 (2012) 1225–1229
CHINESE CHEMICAL LETTERS
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Zinc oxide nanoparticles: A highly efficient and readily recyclable catalyst for the synthesis of xanthenes

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Received 2 July 2012
Available online 24 October 2012

Abstract

A novel and efficient route for the synthesis of 1,8-dioxooctahydroxanthenes and 14-aryl-14*H*-dibenzo[a,j]xanthenes is described through one-pot multi-component reaction of dimedone and 2-naphthol with various aryl aldehydes using ZnO nanoparticles under solvent-free conditions. This method provides a novel and improved pathway for the synthesis of xanthenes in the terms of excellent yields, short reaction times, reusability and low catalyst loading.

Keywords: ZnO nanoparticles; Xanthene; Solvent-free; Multi-component reaction; Heterogeneous catalysts

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During the last decade, nanocrystalline metal oxides have received significant attention as efficient catalysts in many organic reactions due to their high surface-to-volume ratio and coordination parts which provide a larger number of active sites per unit area in comparison with their heterogeneous counter sites [1,2]. Nanocrystalline zinc oxide is one of the extensively used surface materials for many chemical transformations, such as gas sensors [3], photoactivity and flame-retardancy [4], solar cells [5], semiconductor [6] and antibacterial materials [7]. In last decade zinc oxide nanoparticles were used as an active catalyst in many reactions including the Mannich reaction [8], the Knoevenagel condensation [9] and synthesis of coumarins [10], β-phosphono malonates [11], benzimidazole [12], β-acetamido ketones/esters [13], 4-amino-5-pyrimidinecarbonitriles [14], polyhydroquinoline [15] and the synthesis of 2,3-disubstituted quinalolin-4(1*H*)-ones [16].

In recent years, great attention has been paid to the synthesis of xanthene derivatives because of their highly absolute biological and physiological activities [17,18]. These compounds have found wide use in dyes [19], laser technologies [20] and as pH-sensitive fluorescent materials [21].

There are several methods reported in the literature for the synthesis of 1,8-dioxooctahydroxanthenes involving the condensation of two equivalent of dimedone (5,5-dimethyl-1,3-cyclohexane dione) with various aldehydes [22], which catalysis by different catalysts such as alum [23], *p*-dodecylbenzenesulfonic acid [24], Fe^{3+}-montmorilonite [25], $NaHSO_4$–SiO_2 or silica chloride [26] and amberlyst-15 [27]. The classical method for the synthesis of 14-aryl-14*H*-dibenzo[a,j]xanthenes is the condensation of 2-naphthol and aldehydes in the presence of various catalysts including AcOH–H_2SO_4 [28], *p*-TSA [29], sulfamic acid–ionic liquid [30], iodine [31], heteropolyacid [32],

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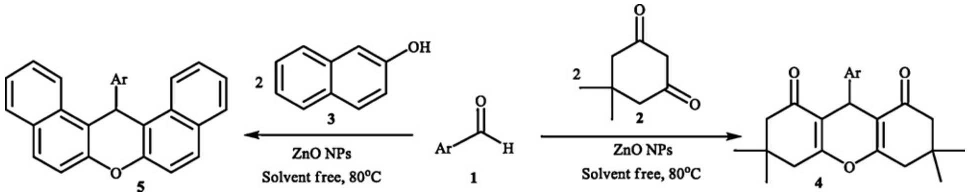
http://dx.doi.org/10.1016/j.cclet.2012.09.016



Scheme 1. ZnO nanoparticles catalyzed one-pot synthesis of xanthene derivatives.

amberlyst-15 [33], cyanuric chloride [34], LiBr [35], Yb(OTf)$_3$ [36], Sc[N(SO$_2$C$_8$F$_{17}$)$_2$]$_3$ [37], NaHSO$_4$ [38], P$_2$O$_5$, InCl$_3$ [39], tetra-*n*-butylammonium bromide [40] and nano TiO$_2$ [41].

Consequently, synthesis of 1,8-dioxooctahydroxanthene and 14-aryl-14*H*-dibenzo[a,j]xanthene derivatives with the aim to develop new drug molecules has been an active area of the research. Herein we wish to report a novel and effective method to the synthesis of xanthenes *via* multi-component coupling of dimedone and 2-naphthol with various aryl aldehydes in the presence of ZnO nanoparticles (Scheme 1).

1. Experimental

Zinc oxide nanoparticles were prepared according to the procedure reported by Shen *et al.* [42]. In a typical procedure, zinc acetate (9.10 g, 0.05 mol) and oxalic acid (5.4 g, 0.06 mol) were combined by grinding in an agate mortar for 1 h at room temperature. Afterwards, the formed $ZnC_2O_4 \cdot 2H_2O$ nanoparticles were calcinated at 450 °C for 30 min to produce ZnO nanoparticles under thermal decomposition conditions.

The chemical purity of the samples as well as their stoichiometry was tested by EDAX studies. The EDAX spectra given in Fig. 1a shows the presence of Zn and O as the only elementary components.

As shown in Fig. 1b the crystalline nature of the synthesized ZnO nanoparticles sample was further verified by X-ray diffraction pattern (XRD). The crystallite size diameter (D) of the ZnO nanoparticles has been calculated by Debye–Scherrer equation ($D = K\lambda/\beta \cos \theta$). Crystallite size of ZnO has been found to be 24 nm.

In order to study the morphology and particle size of ZnO nanoparticles, SEM image of ZnO nanoparticles was presented in Fig. 1c. These results show that hexagonal ZnO NPs were gained with particle size between 20 and 30 nm.

A mixture of 5,5-dimethyl-1,3-cyclohexanedione (0.28 g, 2 mmol), various aldehydes (1 mmol) and ZnO NPs (0.01 g, 0.1 mmol, 10 mol%) was heated at 80 °C for 15–35 min. After completion of the reaction as indicated by TLC, the reaction mixture was cooled to room temperature and solid obtained was dissolved in dichloromethane, the catalyst was insoluble in CH_2Cl_2 and separated by a simple filtration. The solvent was evaporated and the residue was recrystallized from ethanol to afford the pure 1,8-dioxooctahydroxanthenes.

A mixture of 2-naphthol (0.28 g, 2 mmol), aldehyde (1 mmol) and ZnO NPs (0.01 g, 0.1 mmol, 10 mol%) in a round bottom flask was heated in the oil bath at 80 °C for 20–40 min. Upon completion, the work-up and purification of the products were performed as mentioned in previous procedure.

3,4,6,7-Tetrahydro-9-(4-isopropylphenyl)-3,3,6,6-tetramethyl-2*H*-xanthene-1,8-(5*H*,9*H*)-dione (4e). Yellow solid; mp: 203–206 °C; ^{1}H NMR (CDCl$_3$): δ 1.00 (s, 6H, 2 × CH$_3$), 1.10 (s, 6H, 2 × CH$_3$), 1.18 (d, 6H, 2 × CH$_3$), 2.16–2.26 (m, 4H, 2 × CH$_2$), 2.46 (s, 4H, 2 × CH$_2$), 2.78–2.81 (m, 1H, CH), 4.73 (s, 1H, CH), 7.04–7.06 (d, 2H, J = 8.1 Hz, Ar–H), 7.17–7.19 (d, 2H, J = 8.1 Hz, Ar–H). ^{13}C NMR (CDCl$_3$): δ 23.9, 27.4, 29.2, 31.3, 32.2, 33.6, 40.8, 50.8, 115.8,

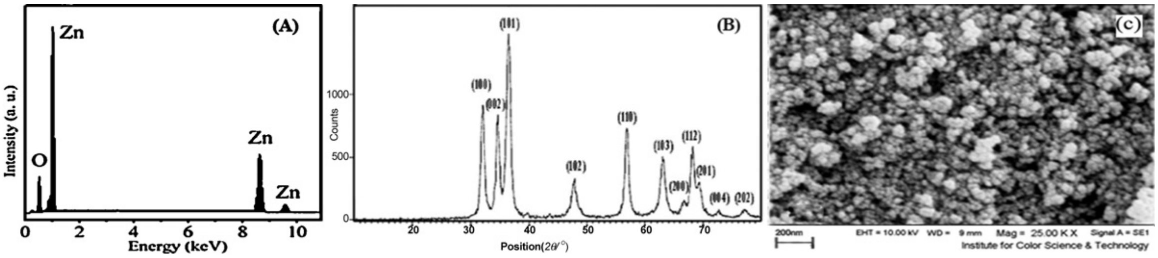


Fig. 1. (a) EDX image of ZnO NPs; (b) XRD pattern of ZnO NPs; and (c) SEM image of ZnO nanoparticles.

126.1, 128.1, 141.3, 146.5, 162.1, 196.4. FT-IR (KBr, cm^{-1}): 3071, 2961, 1665 (C═O), 1624 (C═C, Ar), 1359, 1198 (C–O). Anal. calcd. for $C_{26}H_{32}O_3$: C 79.56, H 8.22. Found C 79.39, H 8.36. MS (EI) (*m/z*): 392 (M^+).

14-(4-Cyanophenyl)-14H-dibenzo[a,j]xanthene (5n). White crystal; m.p. = 218–219 °C; ^{1}H NMR ($CDCl_3$): δ 6.61 (s, 1H, CH) 7.43–7.45 (d, 2H, J = 8 Hz, Ar–H), 7.51–7.53 (d, 2H, J = 7.8 Hz, Ar–H), 7.59–7.61(t, 2H, Ar), 7.68–7.70 (d, 2H, J = 8 Hz, Ar–H), 7.84–7.87 (m, 4H, Ar), 8.00–8.02 (d, 2H, J = 7.8 Hz, Ar–H), 8.28–8.30 (d, 2H, Ar). ^{13}C NMR ($CDCl_3$): δ 36.9, 95.1, 115.9,116.2, 117.1, 120.2, 122.5, 124.8, 126.1, 128.1, 129.7, 132.6, 134.1, 135.9, 148.3, 159.1. FT-IR (KBr, cm^{-1}): 3041, 2218 (C≡N), 1622 (C═C, Ar), 1583, 1242 (C–O), 809. Anal. calcd. for $C_{28}H_{17}NO$: C 87.71, H 4.47, N 3.65. Found C 87.58, H 4.59. N 3.78. MS (EI) (*m/z*): 383 (M^+).

2. Results and discussion

In order to determine the optimized reaction conditions, we selected reaction of 4-bromo-benzaldehyde and dimedone as model study in this research. The reaction conditions were optimized on the basis of the catalysts, solvents and different temperatures for the synthesis 1,8-dioxooctahydroxanthenes (Table 1).

Afterwards, to test the efficiency of the catalytic activity, we choose to focus our initial studies using various nanocatalysts such as MgO, NiO, Mn_3O_4 and ZnO under solvent-free conditions (Table 1). As a result of these experiments we found that ZnO NPs (Table 1, entry 5) is the most effective catalyst for these condensation reactions. During optimization of reaction conditions the model reaction was performed in different solvents and also under solvent-free conditions. In according to Table 1 no product was obtained in the absence of the catalyst and in the presence of the catalyst at room temperature (Table 1, entries 1 and 2), indicating the catalyst and high temperature are necessary for these reactions. We found that the best results were obtained when the reaction was carried out at 80 °C under solvent-free conditions. Also the resulting of Table 1 shows the optimum amount of the catalyst was 0.01 g (0.1 mmol, 10 mol%) of ZnO NPs which increasing of this amount did not show any significant change in yield and time of reaction.

In the continuations of this research, we encouraged testing reaction of 2-naphthol and aldehydes. Thus, we used the optimized reaction conditions in the presence of ZnO NPs to produce 14-aryl-14*H*-dibenzo[a,j]xanthene derivatives. A series of experiments were carried out and as a result of these we prepared a number of 14-aryl-14*H*-dibenzo[a,j]xanthenes in high yields and short reaction times.

In the present work, we successfully synthesized ZnO nanoparticles and used it in synthesis of 1,8-dioxooctahydroxanthene and 14-aryl-14*H*-dibenzo[a,j]xanthene derivatives (Scheme 1). Application of this catalytic system effectively gives desired products in excellent yields (Table 2). As seen from Table 2, aromatic aldehydes with electron-withdrawing groups such as NO_2 and Cl reacted faster than those with electron-releasing groups such as isopropyl and methoxy as expected; also sterically hindered aromatic aldehydes required longer reaction times.

A plausible mechanism for the synthesis of 14-aryl-14*H*-dibenzo[a,j]xanthenes using ZnO NPs has been shown in Scheme 2. We suppose that zinc oxide nanoparticles behave as the Lewis acid and coordinate with carbonyl and hydroxyl groups to promote cyclization reaction, so interaction of nanocatalyst with reactants leading to speed up the rate of reaction. Finally the product was obtained and the ZnO NPs being released for further reactions. Moreover the

Table 1
Optimization of model reaction by catalyst amount of ZnO NPs, solvent and temperature.[a]

Entry	Catalyst (mol%)	Solvent	T (°C)	Time (min)	Yield (%)[b]
1	None	Solvent-free	80	300	None
2	MgO NPs (20%)	Solvent-free	rt	100	30
3	NiO NPs (20%)	Solvent-free	80	60	45
4	Mn_3O_4 NPs (20%)	Solvent-free	80	40	60
5	ZnO NPs (20%)	Solvent-free	80	17	92
6	ZnO NPs (15%)	Solvent-free	80	17	92
7	ZnO NPs (10%)	Solvent-free	80	17	92
8	ZnO NPs (5%)	Solvent-free	80	20	85
8	ZnO NPs (10%)	CH_2Cl_2	Reflux	150	45
9	ZnO NPs (10%)	CH_3CN	Reflux	120	60
10	ZnO NPs (10%)	EtOH	Reflux	180	50

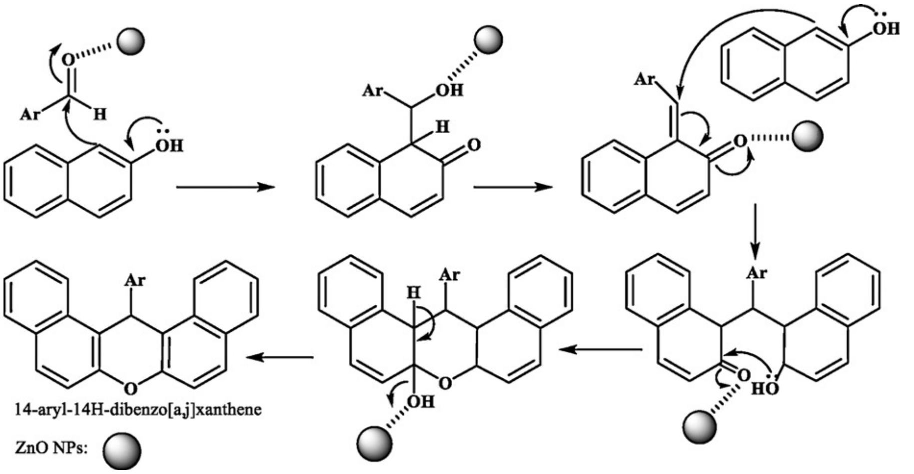
[a] Reaction conditions: dimedone (2 mmol) and 4-bromo-benzaldehyde (1 mmol).

[b] Isolated yields.

Table 2
Synthesis of 1,8-dioxooctahydroxanthenes (**4**) and 14-aryl-14*H*-dibenzo[a,j]xanthenes (**5**) catalyzed by ZnO NPs.

Entry	Aldehyde	Products **4(a–o)**	M.p. (°C) Ref.	Products **5(a–o)**	M.p. (°C) Ref.
		Time (min)/yield (%)[a]		Time (min)/yield (%)[a]	
1	C_6H_5	22/91	201–203 [23]	28/87	181–183 [39]
2	4-$CH_3C_6H_4$	32/87	214–215 [23]	31/83	227–229 [39]
3	4-HOC_6H_4	23/88	248–250 [23]	28/84	135–136 [41]
4	4-$MeOC_6H_4$	30/86	241–243 [23]	37/80	203–204 [39]
5	4-$(CH_3)_2CHC_6H_4$	35/82	203–205[b]	40/78	152–154 [39]
6	4-ClC_6H_4	15/96	227–229 [23]	20/94	287–289 [39]
7	4-BrC_6H_4	17/92	240–241 [23]	23/92	296–297 [39]
8	4-$NO_2C_6H_4$	15/97	225–226 [23]	20/95	310–312 [39]
9	3-$NO_2C_6H_4$	19/91	166–168 [23]	28/90	211–212 [29]
10	3-ClC_6H_4	24/91	183–184 [23]	25/86	211–212 [41]
11	4-FC_6H_4	17/93	225–226 [23]	24/92	239–240 [39]
12	2-$NO_2C_6H_4$	34/84	246–248 [22]	35/86	213–215 [41]
13	4-$CHOC_6H_4$	20/93	211–213[b]	25/92	252–254[b]
14	4-NCC_6H_4	19/95	216–217[b]	28/94	218–219[b]
15	4-$MeSC_6H_4$	32/86	256–257[b]	37/86	264–266[b]

[a] Isolated yield.
[b] New products.



Scheme 2. The proposed mechanism for the synthesis of 14-aryl-14*H*-dibenzo[a,j]xanthenes catalyzed by ZnO NPs.

influence of catalytic behavior of ZnO NPs for the synthesis of 1,8-dioxooctahydroxanthenes is the same as above-mentioned mechanism for the preparation of 14-aryl-14*H*-dibenzo[a,j]xanthenes.

3. Conclusion

In conclusion, we have demonstrated an efficient, one-pot method for the synthesis of 1,8-dioxooctahydroxanthene and 14-aryl-14*H*-dibenzo[a,j]xanthene derivatives using zinc oxide nanoparticles as a mild, green and eco-environmentally catalyst under solvent-free conditions. The simplicity, easy workup, as well as safety and reusability of catalyst are advantages of this procedure over the previously reported ones.

Acknowledgments

The authors are grateful to University of Kashan for supporting this work by Grant 159196/VII. Also we thank Iran National Science Foundation for supporting this work.

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