

Environmentally benign synthesis of 14-Phenyl-8*H*-Dibenzo[*a,i*]xanthene-8,13(14*H*)-Diones using CuI nanoparticles as an efficient catalyst

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Received 10 April 2016; received in revised form 28 July 2016; accepted 18 August 2016

ABSTRACT

In this study, CuI nanoparticles as an efficient catalyst was used for the synthesis of 14-phenyl-8*H*-dibenzo[*a,i*]xanthene-8,13(14*H*)-diones using aldehydes, 2-naphthol and 2-hydroxynaphthalene-1,4-dione in aqueous media. In this study, it was found that water was the most effective solvent compared to others. Among several catalysts that were tested for this multi-component synthesis, CuI nanoparticles were the best catalyst with 4 mol% loading. The reusability of CuI nanoparticles was experienced for 6 times with a slightly decreased activity. The use of no hazardous organic solvent, atom economy, short reaction times, little catalyst loading, reusability of the catalyst and high yields of products are some of the important features of this protocol.

Keywords: Dibenzoanthene; CuI nanoparticles; Environmentally benign; Three-component reactions.

1. Introduction

Xanthenes and benzoxanthenes are an elite class of biologically active heterocyclic compounds. Some of the newly-synthesized compounds of xanthenes showed a significant activity compared to the standard drug [1]. Xanthene derivatives have also been investigated for Screening of anti-proliferative activity [2]. These compounds have a wide range of use in dyes [3] in laser technology [4], as probes of interfacial PH [5]. Consequently, looking for efficient and simple methods for the synthesis of Xanthenes is attractive. A number of methods have been reported for the preparation of xanthene derivatives, including the reaction of aromatic aldehydes with 2-naphthol [6], synthesis of 14-substituted-14*H*-dibenzo[*a,i*]xanthenes using Amberlyst-15 [7], synthesis of 14-aryl-14*H*-dibenzo[*a,i*]xanthene-8,13-diones by Silica chloride [8], synthesis of new dibenzo[*a,i*]xanthene-diones in the presence of *p*-TSA [9] synthesis of xanthenes using ethan-1,2-diyl bis (hydrogen sulfate) and DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) [10] and synthesis of xanthenes in the presence of trifluoroacetic acid as the catalyst in 1,1,3,3-*N,N,N',N'*-tetramethylguanidinium trifluoroacetate (TMGT) ionic liquid [11].

Despite the availability of these methods, there remains enough scope for an efficient and reusable catalyst with high catalytic activity for the preparation of xanthenes. Undoubtedly, the synthesis of xanthenes by multicomponent reactions (MCR) has been given much attention owing to excellent synthetic efficiency, inherent atom economy, procedural simplicity, and environmental friendliness. Therefore, the possibility of accomplishing multicomponent reactions under mild conditions with a suitable catalyst could improve their effectiveness from cost-effectiveness and ecological points of view. One-pot MCRs usually shorten reaction periods, giving higher overall chemical yields than multiple-step syntheses, and can therefore reduce utilization of energy and manpower [12-16]. MCRs are environmentally friendly and play a prominent role in green chemistry [17]. The use of water as a green solvent for organic reactions has emerged in recent years because it is safe, nontoxic, environmentally friendly, readily available, and cheap, compared with organic solvents [18]. The possibility of performing multicomponent reactions in water as a green solvent with a heterogeneous catalyst plays a prominent role in green chemistry. In recent years, nanocatalysts have emerged as an alternative approach for the improvement of many significant organic reactions. They reduce reaction times and they can be easily

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recovered from the reaction mixture by simple filtration [19]. However, when the size of active site is reduced to nanoscale dimensions, the surface free energy is increased greatly. These surface atoms behave as the centers where the chemical reactions could be catalytically activated [20-23]. Recently, copper (I) iodide nanoparticles have been used as a suitable catalyst in many reactions including synthesis of pyrazolones [24], pyrazolo[1,2-*b*]phthalazines [25], and functionalized tricarboxamides [26]. 1,4-dihydropyridines [27] coupling of heterocyclic amines and phenols with chlorobenzenes [28], selective synthesis of phenols, anilines, and thiophenols from aryl halides [29].

Herein we report the use of CuI nanoparticles as an efficient catalyst for the preparation of 14-phenyl-8*H*-dibenzo[*a,i*]xanthene-8,13(14*H*)-diones by the three-component reaction of aldehydes, 2-naphthol and 2-hydroxynaphthalene-1,4-dione in aqueous media (Scheme 1).

2. Experimental

The products were isolated and characterized by physical and spectral data. ¹HNMR and ¹³CNMR spectra were recorded on Bruker Avance-400 MHz spectrometers in the presence of tetramethylsilane as the internal standard. The IR spectra were recorded on FT-IR Magna 550 apparatus using KBr plates. Melting points were determined on Electro thermal 9200 and are not corrected. The elemental analyses (C, H, N) were obtained from a Carlo ERBA Model EA 1108 analyzer. Powder X-ray diffraction (XRD) was carried out on a Philips diffractometer of X'pert Company with monochromatized Cu K α radiation ($\lambda = 1.5406 \text{ \AA}$). Microscopic morphology of products was visualized by SEM (LEO 1455VP). The mass spectra were recorded on a Joel D-30 instrument at an ionization potential of 70 eV.

2.1. Preparation of CuI nanoparticles

A solution of 0.415 g KI (25×10^{-4} mol) in 25 ml distillate water was added drop-wise to Cu(NO₃)₂·3 H₂O solution (0.55 g, 25×10^{-4} mol in 25 ml distillate

water) under ultrasound power in the presence of 0.2 g of CTAB as the surfactant. The gray as-synthesized precipitate was separated by centrifugation and washed with distillate water and ethanol to remove impurities and then it was dried overnight under vacuum.

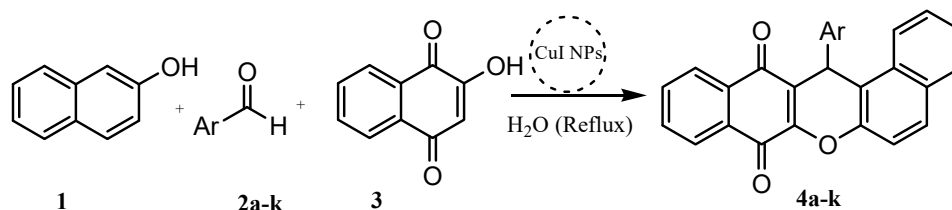
2.2. General procedure for the synthesis of 14-phenyl-8*H*-dibenzo[*a,i*]xanthene-8,13(14*H*)-diones (4a-i)

A mixture of benzaldehydes (0.11 g, 1 mmol), 2-naphthol (0.140 g, 1 mmol), 2-hydroxynaphthalene-1,4-dione (0.17 g, 1 mmol), CuI nanoparticles (4 mol%) was refluxed in water (5 mL). Progress of the reaction was continuously monitored by TLC. At the end of the reaction, the precipitate formed was collected by filtration and solved with hot dichloromethane for the separation of the catalyst. The solvent was evaporated under room temperature. The powder was washed with ethanol to afford the pure product. The structures of the products were fully established on the basis of their ¹HNMR, ¹³CNMR and FT-IR spectra (See Supporting Information).

3. Results and Discussion

The XRD pattern of the CuI nanoparticles is shown in Fig 1. The crystallite size diameter (*D*) of the CuI nanoparticles was calculated by Debye-Scherrer equation ($D = K\lambda / \beta \cos\theta$), where β FWHM (full-width at half-maximum or half-width) is in radian, which 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 λ is the X-ray wavelength (1.5406 Å for Cu K α). Crystallite size of CuI was found to be 45-52 nm. The SEM image shows particles with diameters in the range of nanometers (Fig. 2).

The choice of a suitable reaction medium is of vital importance for successful synthesis. Initially, we explored and optimized different reaction parameters for the synthesis of 14-phenyl-8*H*-dibenzo[*a,i*]xanthene-8,13(14*H*)-diones by the three-component reaction of 4-chlorobenzaldehyde, 2-naphthol and 2-hydroxynaphthalene-1,4-dione as a model reaction.



Scheme 1. Three-component reaction of aldehydes, β -naphthol and 2-hydroxynaphthalene-1,4-dione catalyzed by CuI NPs.

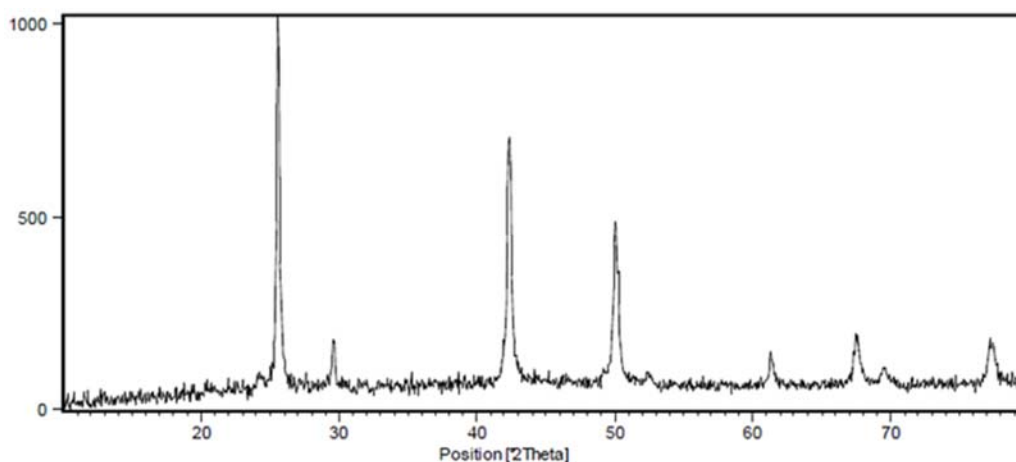


Fig. 1. The XRD pattern of copper iodide nanoparticles.

During our optimization studies, various solvents were examined and it was found that the solvent plays a significant role in terms of the reaction rate and isolated yield. As shown in Table 1, it was found that water was the most effective solvent compared to the others. We tested several catalysts for this multi-component synthesis. The results show that CuI nanoparticles is the best catalyst among those examined which are reported in Table 1. As expected, the increased surface area due to the small particle size increased reactivity of the catalyst. This factor is responsible for the accessibility of the substrate molecules on the catalyst surface. When 2, 4, and 6 mol% of CuI nanoparticles were used, the yields were 85, 89, and 89%, respectively. Therefore, performing the reaction with a higher catalyst loading (6 mol%) had no significant effect on yield. After completion of the reaction, the mixture was centrifuged and the CuI NPs catalyst was filtered. Then, nanoparticles were washed three to four times with dichloromethane and methanol and dried at 70°C for 4 h. The reusability of CuI nanoparticles was studied under similar reaction conditions 6 times with a slightly decreased activity. The reusability of the nano CuI catalyst was examined and it was found that product yields decreased to a small extent on each reuse (run 1, 89%; run 2, 89%; run 3, 88%; run 4, 87%; run 5, 85%, run 6, 84%).

Using the optimized reaction conditions (Table 1, entry 13), the scope of the reaction was tested by extending the reaction to different aldehydes. It was found that all the aldehydes were converted to the corresponding products in good to excellent yields (Table 2).

In general, the reactions are clean and high-yielding. Several substituents, such as Cl, F, OH, NO₂, OCH₃ and CH₃, are compatible under the reaction conditions. The influence of electron-withdrawing and electron-donating substituents on the aromatic ring of aldehydes

upon the reaction yields was investigated. Aromatic aldehydes having electron withdrawing groups reacted at a faster rate compared with aromatic aldehydes substituted with electron releasing groups. Under the same conditions, this reaction almost could not be observed when the aliphatic aldehyde was used as a starting material.

In order to show the merit of the present work in comparison with some reported protocols, we compared the results of the synthesis of dibenzo[a,i]xanthenes in Table 3. However, some of the reported methods tolerate disadvantages including long reaction times, harsh reaction conditions and use of toxic and non-reusable catalysts. Therefore, to avoid these limitations, the exploration of an efficient, easily available catalyst with high catalytic activity and short reaction times and use of water as a green solvent for the preparation of dibenzo[a,i]xanthenes was still favored.

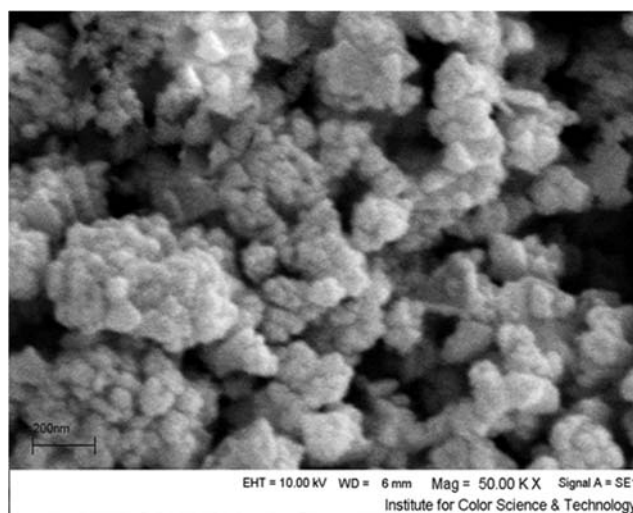


Fig. 2. SEM images of CuI nanoparticles.

Table 1. Optimization of reaction conditions using different catalysts.^a

Entry	Solvent (reflux)	Catalyst (mol%)	Time (min)	Yield (%) ^b
1	neat	None	500	-----
2	CH ₂ Cl ₂	CuO (5)	350	11
3	H ₂ O:EtOH(5:5)	ZrO ₂ (5)	200	42
4	CH ₃ CN	InCl ₃ (3)	210	35
5	H ₂ O:EtOH(5:5)	CuBr (7)	200	40
6	H ₂ O	CuI (5)	180	52
7	H ₂ O:EtOH(5:5)	CuCl (9)	250	35
8	CH ₃ CN	CuO (5)	250	32
9	CH ₃ CN	CuI NPs (3)	150	65
10	DMF	CuI NPs (3)	150	61
11	EtOH	CuI NPs (3)	150	78
12	H ₂ O	CuI NPs (2)	145	85
13	H₂O	CuI NPs (4)	120	89
14	H ₂ O	CuI NPs (6)	118	89

^a4-chlorobenzaldehyde, 2-naphthol and 2-hydroxynaphthalene-1,4-dione as a model reaction.

^bIsolated yields.

Table 2. Synthesis of 14-phenyl-8*H*-dibenzo[*a,i*]xanthene-8,13(14*H*)-diones using CuI NPs under reflux conditions in water.

Entry	Aldehyde	Product	Time (min)	Yield (%) ^a	m.p.(°C)		Ref.
					Found	Reported	
1	<i>C</i> ₆ <i>H</i> ₅ - <i>CHO</i>	4a	127	84	294-296	294-297	[9]
2	4-Cl- <i>C</i> ₆ <i>H</i> ₄ - <i>CHO</i>	4b	120	89	281- 283	281-284	[9]
3	4-F- <i>C</i> ₆ <i>H</i> ₄ - <i>CHO</i>	4c	125	87	297- 299	>300	[31]
4	4-NO ₂ - <i>C</i> ₆ <i>H</i> ₄ - <i>CHO</i>	4d	125	86	325-327	>320	[30]
5	3-NO ₂ - <i>C</i> ₆ <i>H</i> ₄ - <i>CHO</i>	4e	125	85	300-302	304-305	[8]
6	4-Me- <i>C</i> ₆ <i>H</i> ₄ - <i>CHO</i>	4f	130	79	257-259	256-258	[30]
7	2,4-diCl- <i>C</i> ₆ <i>H</i> ₃ - <i>CHO</i>	4g	124	85	298- 302	301-302	[8]
8	4-Br- <i>C</i> ₆ <i>H</i> ₄ - <i>CHO</i>	4h	124	85	292-294	294-298	[9]
9	4-OMe- <i>C</i> ₆ <i>H</i> ₄ - <i>CHO</i>	4i	135	77	278-280	279-280	[8]
10	<i>n</i> -hexanal	4j	300	trace	-	-	-

^aIsolated yields.

Table 3. Comparison the results of the synthesis of dibenzo[*a,i*]xanthenes using different catalysts.

Entry	Catalyst	Amount of catalyst	Conditions	Time (min)	Yield (%) ^a	Ref.
1	<i>p</i> -TSA	0.1 g	H ₂ O (reflux)	600	88	[9]
2	Poly(4-vinylpyridinium) hydrogen sulfate	2 mol%	Neat/100 °C	60	90	[30]
3	silica chloride	200 mg	Neat/110 °C	60	88	[8]
4	[bmim]HSO ₄	20 mol%	Neat/60 °C	45	90	[31]
5	CuI nanoparticles	4 mol%	H ₂ O (reflux)	120	89	This work

^aIsolated yields.

A plausible mechanism for the preparation of 14-phenyl-8*H*-dibenzo[*a,i*]xanthene-8,13(14*H*)-diones by CuI NPs is shown in Scheme 2. β-Naphthol undergoes condensation with aldehyde in the presence of CuI NPs to afford α, β-unsaturated carbonyl compound. Michael addition reaction between α, β-unsaturated carbonyl compound **I** and 2-hydroxynaphthalene-1,4-dione would give the desired of 14-phenyl-8*H*-dibenzo[*a,i*]xanthene-8,13(14*H*)-dione.

4. Conclusion

In conclusion, we have developed a flexible and highly efficient protocol for the synthesis 14-phenyl-8*H*-dibenzo[*a,i*]xanthene-8,13(14*H*)-diones using CuI nanoparticles in aqueous media. These polycyclic compounds will provide promising candidates for chemical biology and drug discovery. The advantages offered by this method include easy workup, the employment of a cost-effective catalyst, short reaction

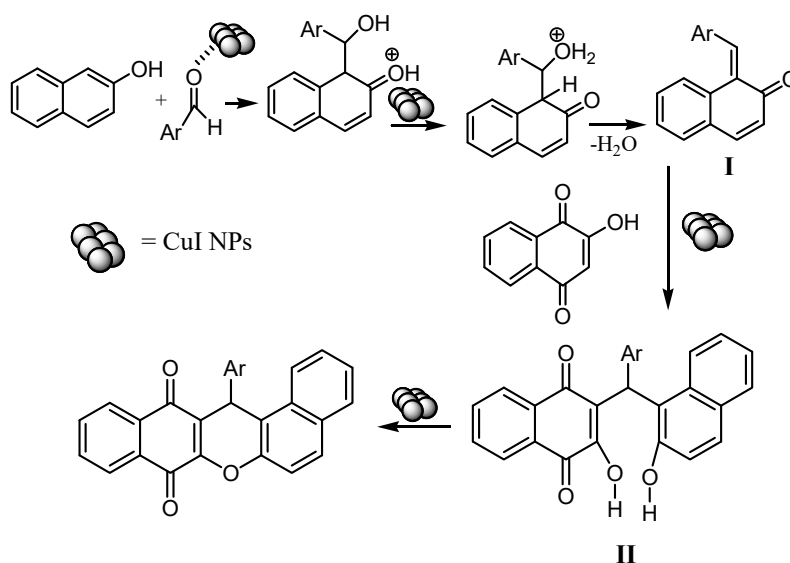
times, excellent yields and the use of no hazardous organic solvent, which is considered to be relatively environmentally benign.

Acknowledgements

The authors acknowledge a reviewer who provided helpful insights. The authors are grateful to Islamic Azad University, Qom Branch for supporting this work. Also authors are grateful to Dr. Hossein Shahbazi-Alavi for his help.

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**Scheme 2.** A plausible mechanism for the preparation of 14-phenyl-8*H*-dibenzo[*a,i*]xanthene-8,13(14*H*)-dione.

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