ANOTHER SUCCESSFUL APPLICATION OF NEWLY PREPARED NANO CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H AS HIGHLY EFFICIENT MAGNETICALLY RECYCLABLE CATALYST FOR FAST SYNTHESIS OF 14-ARYL-14*H*-DIBENZO[*a,j*]XANTHENES

Farzaneh Tajfirooz[1], Abolghasem Davoodnia[1,*], Mehdi Pordel[1], Mahmoud Ebrahimi[1], and Amir Khojastehnezhad[2]

[1] *Department of Chemistry, Mashhad Branch, Islamic Azad University, Mashhad, Iran*
[2] *Young Researchers and Elite Club, Mashhad Branch, Islamic Azad University, Mashhad, Iran*

Abstract: The newly prepared nano CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H was shown to be a highly efficient solid acid catalyst for the cyclocondensation reaction of *β*-naphthol and aryl aldehydes under solvent-free conditions, giving rise to 14-aryl-14*H*-dibenzo[*a,j*]xanthenes. The methodology presented here has the merits of environmentally friendly, easy work-up, high yields, short reaction times, and the absence of any volatile and hazardous organic solvents. Moreover, the catalyst could be easily recovered from the reaction mixture by magnetic decantation and reused several times without substantial reduction in catalytic activity.

Keywords: 14-Aryl-14*H*-dibenzo[*a,j*]xanthenes, CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H, Magnetic nanoparticles, Solvent-free conditions

Introduction
The use of traditional homogeneous acidic catalysts such as HCl, HF, H$_3$PO$_4$, H$_2$SO$_4$, or CH$_3$COOH has some major limitations including toxicity, volatility, difficulty of catalyst separation from the reaction medium, and therefore incompatibility with environment. The replacement of environmentally hazardous catalysts with cheap, recyclable, nontoxic, and easy to handle and environmentally friendly heterogeneous acidic catalysts is an attractive area in green chemistry[i-vi]. Among the heterogeneous acidic catalysts, nanoparticles having acidic functional groups have been widely investigated because of their larger surface area enhancing the catalytic activity[vii-x]. However, the recycling of nanoparticles by centrifugation or filtration causes the loss of very small particles. Magnetic separation is an attractive alternative to filtration or

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*Corresponding author. Tel.: +98-51-38435000; Fax: +98-51-38429520; E-mail: adavoodnia@mshdiau.ac.ir; adavoodnia@yahoo.com

centrifugation as it prevents loss of catalyst and enhances reusability, making the catalyst to have beneficial cost and to be promissory for industrial applications. Therefore, the use of magnetic nanoparticles (MNPs) with high thermal and mechanical stability as catalyst has attracted increasing attention in recent years. Hence, a number of functionalized MNPs have been prepared and employed in a range of organic transformations which showed excellent catalytic activities[xi-xvi]. Furthermore, MNPs have been also applied in magnetic resonance imaging (MRI)[xvii], magneto-thermal therapy[xviii], biomolecular sensors[xix], and drug and gene delivery[xx,xxi]. Xanthenes and dibenzoxanthenes are important classes of organic compounds with a large number of naturally occurring, as well as synthetic derivatives, and occupy a prominent position in medicinal chemistry. They are cited as active oxygen heterocycles possessing antibacterial[xxii], antiviral[xxiii], anti-inflammatory[xxiv], antioxidant[xxv], antiproliferative[xxvi], and anticancer[xxvii] properties. A number of these compounds are utilized as trypanothione reductase inhibitors and chloroquine potentiating agents[xxviii]. Furthermore, they are well known as fluorescent and laser dyes[xxix-xxxi]. There are several methods reported for the synthesis of xanthenes and dibenzoxanthenes, including cyclization of polycyclic aryltriflate esters[xxxii], intramolecular phenyl carbonyl coupling reactions of benzaldehydes and acetophenones[xxxiii], and cyclocondensation between 2-tetralone and 2-hydroxyaromatic aldehydes[xxxiv]. Furthermore, 14-aryl-14*H*-dibenzo[*a,j*]xanthenes are generally synthesized by cyclocondensation of *β*-naphtol with aldehydes in the presence of several promoters such as *p*-TSA[xxxv], MeSO$_3$H[xxxvi], silica sulfuric acid[xxxvii], Yb(OTf)$_3$[xxxviii], Sc[N(SO$_2$C$_8$F$_{17}$)$_2$]$_3$[xxxix], alumina supported polyphosphoric acid[xl], ionic liquids[xli,xlii], Antimony (III) acetate[xliii], 1,4-diazaniumbicyclo[2.2.2]octane diacetate[xliv], and sulfonated starch nanoparticles[xlv]. Although each of these individual methods has its own merits, many suffer from certain drawbacks including the use of relatively expensive catalysts, unsatisfactory yields, lengthy reaction times, or the use of toxic organic solvents. Thus, the development of an alternate clean procedure using efficient catalysts is highly demanding for the synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes, which surpasses those limitations.

Considering the unique properties of MNPs, very recently, we have synthesized and characterized novel CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H MNPs by immobilizing of phosphorus pentoxide (P$_2$O$_5$)$_2$ on CuFe$_2$O$_4$@SiO$_2$ nanoparticles[xlvi] (Scheme 1). This new reusable catalyst performed well and showed a high level of catalytic activity in the synthesis of 1,8-dioxo-octahydroxanthenes. Prompted by these facts and as part of our research on the development of environmentally friendly methods for the synthesis of organic compounds using reusable catalysts[xlvii-xlxiii], and in heterocycles[xlxiv-xlxviii] we report here another application of CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H MNPs as catalyst in the synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes **3a-j** *via* the reaction of *β*-naphthol **1** and aryl aldehydes **2a-j** under neat conditions (Scheme 2).

CuFe$_2$O$_4$@SiO$_2$ CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H
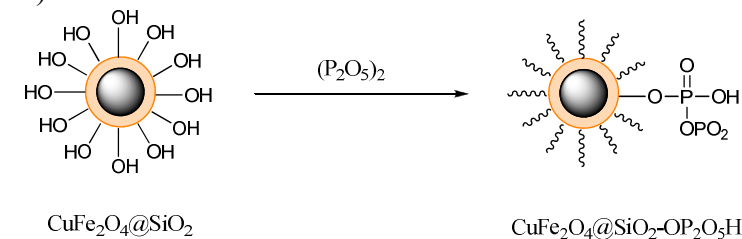
Scheme 1. Preparation of CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H MNPs
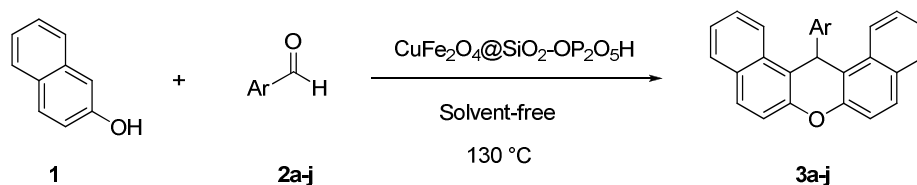
Scheme 2. CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H MNPs catalyzed synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes

Experimental

All chemicals were purchased from Merck and Aldrich and used without purification. Melting points were measured on a Stuart SMP3 melting point apparatus. The ^{1}H NMR spectra were measured on a Bruker 300 and 500 spectrometers using tetramethyl silane (TMS) as internal standard. IR spectra were recorded on a Tensor 27 Bruker spectrophotometer in KBr disks.

Preparation of CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H MNPs

A mixture of CuFe$_2$O$_4$@SiO$_2$ MNPs (0.5 g) and (P$_2$O$_5$)$_2$ (0.5 g) was ground vigorously in a mortar for 30 min. The resulting new MNPs were repeatedly washed with ethanol (10 ml), ethyl acetate (15 ml), and small portion of water (5 ml) and then dried under vacuum at 60 °C for 1 h[xlvi].

General procedure for the synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes 3a-j catalyzed by CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H MNPs

A mixture of *β*-naphthol **1** (2 mmol), an aromatic aldehyde **2a-j** (1 mmol), and CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H (0.04 g) was heated in the oil bath at 130 °C for 1-20 min. During the procedure, the reaction was monitored by TLC. Upon completion, the reaction mixture was cooled to room temperature and hot acetone was added. The catalyst was readily recycled by simple magnetic decantation, washed with ethyl acetate, dried under vacuum at 60 °C for 1 h, and then used in the next run. The solvent was evaporated in *vacuo* and the residue crude product was recrystallized from ethanol to give compounds **3a-j** in high yields.

Results and discussion

In order to evaluate the catalytic activity of CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H MNPs in the synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes, at first, the synthesis of compound **3c** was selected as a test reaction to determine suitable reaction conditions. The reaction was carried out by heating a mixture of *β*-naphthol **1** (2 mmol) and 4-chlorobenzaldehyde **2c** (1 mmol) in the absence or presence of CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H. A summary of the optimization experiments is provided in Table 1. No significant yield of the product **3c** was obtained in the absence of the catalyst (entry 1) under solvent-free conditions at high temperature, indicating that the catalyst is necessary for the reaction. Next, the reaction was performed in the presence CuFe$_2$O$_4$@SiO$_2$-OP$_2$O$_5$H in different solvents as well as under solvent-free conditions. Among the solvents tested, those being MeOH, EtOH, CH$_2$Cl$_2$, and CHCl$_3$, and also solvent-free conditions, the reaction proceeded most readily to give the highest yield of the product **3c** under solvent-free conditions. As can be seen from Table 1, 0.04 g of the catalyst under solvent-free conditions at 130 °C has been found to be the choice of reaction conditions (entry 10). The higher amounts of the catalyst or temperature had no significant effect on the yield and reaction time. All subsequent reactions were carried out under these optimized conditions.

Having optimized the experimental conditions, we next explored the scope and generality of reaction. Therefore, a range of 14-aryl-14*H*-dibenzo[*a,j*]xanthene derivatives were prepared using various substituted aromatic aldehydes under optimized reaction conditions. All aromatic aldehydes having substituted electron-donating or electron-withdrawing groups and or none reacted successfully and gave the expected products **3a-j** in high yields and short reaction times. The results are shown in Table 2.

Table 1. Screening of reaction parameters for the formation of compound **3c** catalyzed by $CuFe_2O_4@SiO_2-OP_2O_5H$ MNPs[a]

Entry	Catalyst (g)	Solvent	T (°C)	Time (min)	Isolated Yield (%)
1	-----	-----	130	90	-----
2	0.02	-----	90	30	59
3	0.02	-----	110	20	70
4	0.02	-----	130	15	78
5	0.03	-----	90	25	63
6	0.03	-----	110	15	75
7	0.03	-----	130	12	81
8	0.04	-----	90	20	65
9	0.04	-----	110	15	87
10	0.04	-----	130	4	91
11	0.04	-----	150	4	90
12	0.06	-----	130	4	91
13	0.04	MeOH	Reflux	60	78
14	0.04	EtOH	Reflux	45	85
15	0.04	CH_2Cl_2	Reflux	70	62
16	0.04	$CHCl_3$	Reflux	55	64

[a]Reaction conditions: *β*-naphthol **1** (2 mmol), and 4-chlorobenzaldehyde **2c** (1 mmol).

Table 2. Synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes **3a-j** catalyzed by $CuFe_2O_4@SiO_2-OP_2O_5H$ MNPs[a]

Entry	Ar	Product	Time (min)	Isolated Yield (%)	m.p. (°C)	
					Found	Reported
1	C_6H_5	**3a**	6	88	185-188	184-186 [xl]
2	$2-ClC_6H_4$	**3b**	4	90	216-218	217-220 [xli]
3	$4-ClC_6H_4$	**3c**	4	91	290-292	293-295 [xli]
4	$3-BrC_6H_4$	**3d**	6	89	193-195	190-192 [xl]
5	$2-O_2NC_6H_4$	**3e**	5	93	210-212	213-214 [xl]
6	$3-O_2NC_6H_4$	**3f**	15	93	213-125	210-212 [xl]
7	$4-O_2NC_6H_4$	**3g**	1	95	312-313	310-311 [xl]
8	$4-MeOC_6H_4$	**3h**	15	85	205-207	208-211 [xli]
9	$4-MeC_6H_4$	**3i**	4	90	231-234	235-237 [xli]
10	$4-HOC_6H_4$	**3j**	20	83	145-147	147-150 [xli]

[a]Reaction conditions: *β*-naphthol **1** (2 mmol), aromatic aldehyde **2a-j** (1 mmol), $CuFe_2O_4@SiO_2-OP_2O_5H$ (0.04 g), 130 °C, solvent-free.

We also investigated recycling of the catalyst under solvent-free conditions using the model reaction. After completion of the reaction, the reaction mixture was cooled to room temperature, and hot acetone was added. The catalyst was readily recycled by simple magnetic decantation, washed with ethyl acetate, dried under vacuum at 60 °C for 1 h, and then used for the subsequent catalytic runs. The recovered catalyst worked well for up to four catalytic runs without substantial reduction of its activity (91, 89, 88, 86 in first to fourth use, respectively).

To show the catalyst's role, a plausible mechanism for this reaction may proceed as depicted in Scheme 3. It is proposed that the reaction occurs *via* initial formation of the ortho-quinone methide (*o*-QM) intermediate (**II**), prepared by condensation of *β*-naphthol **1** with aromatic aldehydes **2a-j**. Subsequent Michael addition of second molecule of *β*-naphthol **1** to the *o*-QM intermediate (**II**) followed by addition of the phenolic hydroxyl moiety in intermediate (**III**) to the carbonyl group provides cyclic hemiketal intermediate (**IV**), which on dehydration affords final products **3a-j**. As shown in Scheme 3, we propose that the catalyst $CuFe_2O_4@SiO_2$-OP_2O_5H activates the aldehyde and the intermediates in this reaction. Under these conditions, however, attempts to isolate the intermediates failed even after careful monitoring of the reactions.
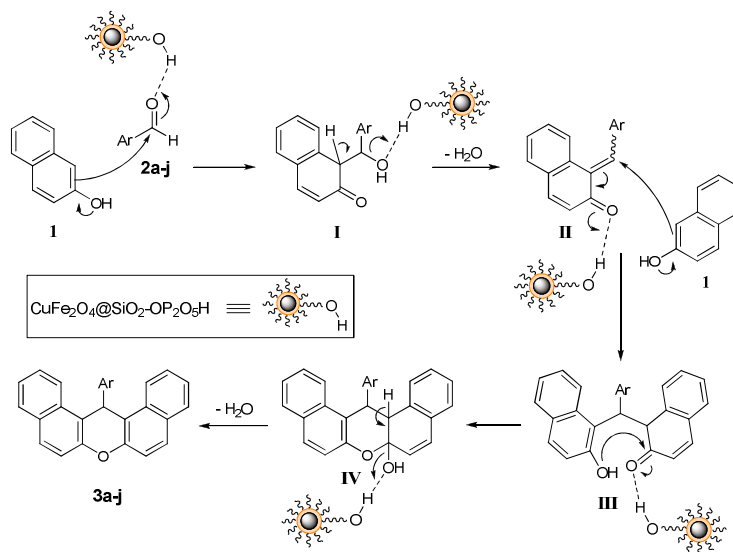
Scheme 3. Plausible mechanism for the formation of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes catalyzed by $CuFe_2O_4@SiO_2$-OP_2O_5H MNPs

Conclusion

In conclusion, we showed that newly synthesized $CuFe_2O_4@SiO_2$-OP_2O_5H MNPs, efficiently catalyze the synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes by reaction of *β*-naphthol and aryl aldehydes under solvent-free conditions. The process was characterized by easy catalyst separation by simple magnetic decantation, short reaction time, high yield, absence of hazardous organic solvents, and reusability of the catalyst.

Acknowledgement

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Received on January 28, 2018.