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Contributed Paper

Efficient Solvent-free Synthesis of 14*H*-Dibenzo[*a,j*] xanthenes Catalyzed by 2-Hydroxy-5-sulfobenzoic Acid

Hamzeh Kiyani* and Hassan Darbandi
School of Chemistry, Damghan University, 36715-364 Damghan, Iran.
*Author for correspondence; e-mail: hkiyani@du.ac.ir

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ABSTRACT

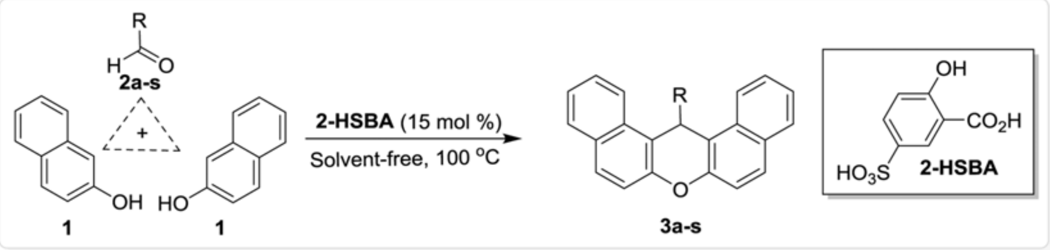
The use of 2-hydroxy-5-sulfobenzoic acid (2-HSBA) to demonstrate the catalyze one-pot condensation of 2-naphthol with various aldehydes under solvent-free conditions is described. This method can be implemented with a wide variety of readily accessible reagents to provide 14*H*-dibenzo[*a,j*]xanthenes as the dye candidates. A significant feature for the present method to the synthesis of 14*H*-dibenzo[*a,j*]xanthenes is that the reactions were performed in the absence of solvent and give products in good to high yields. This approach is reasonably priced, and commercially available of the catalyst is also valuable point for the presented procedure.

Keywords: 2-hydroxy-5-sulfobenzoic acid, 2-naphthol, 14*H*-dibenzo[*a,j*]xanthene, solvent-free, condensation

1. INTRODUCTION

The benzoxanthenes constitute an important category of fused oxygen-containing heterocyclic compounds, which appears in many biological and pharmacological molecules and is of great interest in several fields. They are eligible activities, including cytotoxic [1], anti-proliferative [2], antiviral [3], and antibacterial [4]. Besides, some synthetic compounds of this class have found practical use as dyes in lasers [5], solar cells [6], fluorescent materials for sensing of biomolecules [7], as well as drug delivery in photodynamic therapy [8]. The most popular method for the synthesis of 14*H*-dibenzo[*a,j*]xanthenes, is the reaction of 2-naphthol with numerous aldehydes. Consideration of the importance of benzoxanthenes specifically 14*H*-dibenzo[*a,j*]xanthenes, much effort has been devoted to development of methods to facilitate the synthesis of these dye candidates. There are literature precedents for the preparation of these interesting compounds using a number of catalysts including, $CuSO_4.5H_2O$ [9], boric acid [10], silica sulfuric acid [11], iodine [12], methanesulfonic acid [13], camphor-10-sulfonic acid [14], PEG-SO_3H [15], cellulose sulfuric acid [16], polyvinylsulfonic acid [17], $NH_4H_2PO_4/SiO_2$ [18], and $NbCl_5$ [19]. In addition, nanomaterials [20, 21] and ionic liquids [22, 23] have been used toward synthesis of these heterocycles. Diatomite-SO_3H [24] and fluoroboric acid adsorbed on silica gel (HBF_4-SiO_2) [25] are the other reagents for the catalyzing condensation of aldehydes with 2-naphthol. Some of aforementioned methods suffer from several drawbacks like the usage of hazardous organic solvents, prolonged reaction times, relatively low yields, the use of microwave heating and ultrasonic waves. Consequently, development of an efficient, simple, and green procedure for the environmentally benign synthesis of the 14*H*-dibenzo[*a,j*]xanthenes remains a challenging task.

We recently reported the efficient synthesis of 1-amidoalkyl-2-naphthols, 3,4-disubstituted isoxazol-5(4*H*)-ones [26] and 3,3′ -(arylmethylene)-bis-(4-hydroxycoumarins) [27] using 2-HSBA as the useful catalyst. This report describes the use of 2-HSBA to catalyze the reaction between 2-naphthol (**1**) and a wide range of aldehydes (**2a**-**s**) in order to the synthesis of the 14*H*-dibenzo[*a,j*]xanthene derivatives (**3a**-**s**) (Scheme 1).



Scheme 1. The 2-HSBA-catalyzed synthesis of 14*H*-dibenzo[*a,j*]xanthenes (**3a**-**s**) under solvent-free conditions.

2. MATERIALS AND METHODS

2.1 Instruments and Characterization

All the reagents were obtained from commercial sources and used without further purification. Melting points were measured on a Büchi 510 melting point apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded at ambient temperature on a BRUKER AVANCE DRX-500 MHz spectrophotometer using $CDCl_3$ as the solvent. Elemental microanalyses were performed on an Elementar Vario EL III analyzer. The progress of the reactions was monitored by thin layer chromatography (TLC) analysis on Merck pre-coated silica gel 60 F_{254} aluminum sheets, visualized by UV light.

2.2 General Procedure for the Synthesis of 14*H*-dibenzo[*a,j*]xanthenes (3a-s)

A mixture of 2-naphthol (**1**, 2 mmol), aldehyde (**2**, 1 mmol), and 2-HSBA (15 mol%) was heated on the oil bath at 100 °C and the progress of the reaction was monitored by TLC analysis (ethyl acetate: *n*-hexane; 1:3). After completion of the reaction, the mixture was cooled to room temperature (RT); hot ethyl acetate was added to it and then was allowed to cool to RT. The resulting solid product was filtered off, washed with distilled water, and dried to afford the corresponding compounds (**3a**-**s**). The desired products were found to be pure and no additional purification was required. The catalyst was recovered by the evaporation of solvent from the filtrate, washed with the small amounts of ethyl acetate, dried, and then used for the subsequent reactions. The desired pure products were characterized by comparison of their physical and spectral data with those of known reported compounds. The spectral data and elemental microanalyses for selected examples are listed as follows:

*14-(3-Nitrophenyl)-14H-dibenzo[a.j]xanthene) (**3c**)*

IR (KBr, cm^{-1}): 3081, 2900, 1625, 1593, 1529, 1347, 1459, 1384, 1252, 1081, 825, 808, 744; ^{1}H NMR (CDCl$_3$, 500 MHz): δ 8.47 (s, 1H), 8.33 (d, J = 8.5 Hz, 2H), 7.88-7.84 (m, 6H), 7.65 (t, J = 7.8 Hz, 2H), 7.55 (d, J = 8.9 Hz, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.30 (t, J = 7.8 Hz, 1H), 6.60 (s, 1H); ^{13}C NMR (CDCl$_3$, 125 MHz): δ 149.2, 148.6, 147.4, 134.7, 131.5, 131.4, 130.0, 129.9, 129.5, 127.7, 125.0, 123.1, 122.5, 122.1, 118.5, 116.3, 38.1; Anal. Calcd. for $C_{27}H_{17}NO_3$: C, 80.38; H, 4.25; N, 3.47; found C, 80.35; H, 4.28; N, 3.45.

*14-(4-Methylphenyl)-14H-dibenzo[a,j]xanthene (**3i**)*

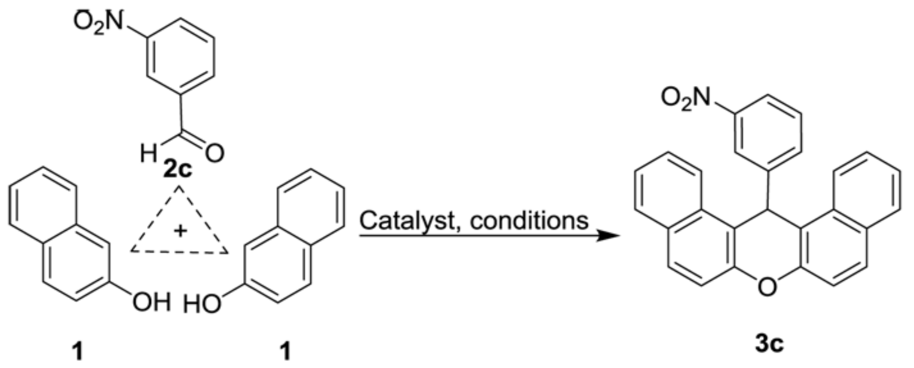
IR (KBr, cm^{-1}): 3072, 2919, 1620, 1592, 1513, 1457, 1429, 1398, 1246, 1139, 1080, 836, 812, 742; ^{1}HNMR (500 MHz, CDCl$_3$): δ 8.55 (d, J = 8.6 Hz, 2H), 7.84 (d, J = 8.1 Hz, 2H), 7.81 (d, J = 8.8 Hz, 2H), 7.61 (t, J = 8.2 Hz, 2H), 7.54 (d, J = 8.8 Hz, 2H), 7.47-7.43 (m, 4H), 6.92 (d, J = 7.9 Hz, 2H), 6.58 (s, 1H), 2.16 (s, 3H); ^{13}CNMR (125 MHz, CDCl$_3$): δ 148.8, 141.9, 136.1, 131.6, 131.4 129.7, 129.4, 129.2, 128.3, 127.3, 125.1, 123.2, 117.8, 116.9, 37.2, 21.1; Anal. Calcd. for $C_{28}H_{20}O$: C, 90.29; H, 5.41, Found: C, 90.33; H, 5.45.

3. RESULTS AND DISCUSSION

At the start, the reaction parameters such as effect of catalyst loading and reaction temperature were optimized using condensation of 2-naphthol (**1**) and 3-nitrobenzaldehyde (**2c**) as a model reaction in the presence of 2-HSBA (Table 1). As illustrated in Table 1, when the reaction was implemented in the absence of catalyst at 100 °C, a trace amounts of desired 14-(3-nitrophenyl)-14*H*-dibenzo[*a,j*]xanthene (**3c**) was obtained (Table 1, entry 1). We have found that when the same reaction is conducted in the presence of 5 mol% 2-HSBA at 100 °C, the results showed that the reaction was successfully proceeded and the corresponding product (**3c**) was formed in 80% isolated yield after 40 min (Table 1, entry 2). This result indicated that participation of the catalyst is crucial for the reaction between 2-naphthol (**1**) and 3-nitrobenzaldehyde (**2c**), as shown in Table 1. To study the effect of catalyst amounts on the reaction, the model experiment was carried out in the presence of 2-HSBA at different catalyst loadings at 100 °C (Table 1, entries 3 and 4), and the results showed that an increase of the catalyst loading from 5 to 15 mol% led to an increase in the yield of reaction up to 94%. The reaction yield remained unchanged further than 15 mol% catalyst (Table 1, entry 5). Therefore, 15 mol% catalyst loading; was chosen in order to further studies. Screenings of the reaction temperature were explored using the optimum loading of catalyst (Table 1, entries 6-10). The reaction yields and reaction times were not improved at lower temperatures than 100 °C and beyond that. The effect of solvent on the model reaction was also studied using 15 mol% catalyst loading in various solvents such as ethanol, water, acetonitrile, and dichloromethane at reflux conditions for 60 min, and the desired product was isolated in 50%, 48%, 55%, and 30% yields, respectively. Compared with solvent-free conditions, the results were not promising.

Based on the above studies, the use of 15 mol% 2-HSBA loading, 100 °C as reaction temperature and solvent-free were selected as the optimized reaction conditions for the cyclocondensation of 2-naphthol (**1**) and a wide range of aldehydes (**2a**-**s**).

Table 1. Effect of 2-HSBA loading and temperature on the synthesis of 14-(3-nitrophenyl)-14*H*-dibenzo[*a,j*]xanthene (**3c**).[a]



Entry	Catalyst (mol %)	Temperature (°C)	Time (min)	Yield (%)[b]
1	-	100	120	-
2	5	100	40	80
3	10	100	24	89
4[c]	**15**	**100**	**9**	**94**
5	20	100	9	94
6	15	25	120	Trace
7	15	50	120	40
8	15	60	60	69
9	15	80	11	89
10	15	120	8	92

[a] Reaction conditions: 2-Naphthol (2 mmol), 2-nitrobenzaldehyde (1 mmol), different reaction temperatures. [b] Isolated yields. [c] Optimized reaction conditions shown in bold.

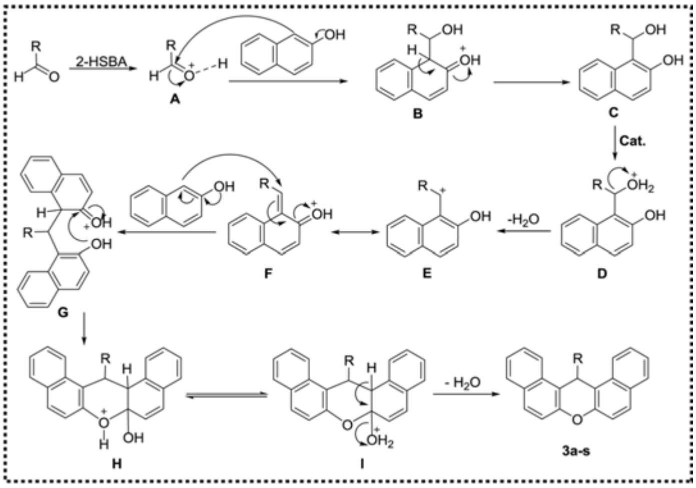
Having the optimized reaction conditions in hand, in order to extend the reaction, 2-HSBA was then tested in the reaction of 2-naphthol (**1**) with various types of aldehydes (**2a**-**s**). The results are summarized in Table 2. The reactions were conveniently performed in the presence of 2-HSBA (15 mol%) at 100 °C. The results show that the corresponding products (**3a**-**s**) were achieved in good to high yields within 8-45 min. However, when aryl aldehydes with electron-deficient substituents (such as NO_2, Cl, and F) are reactants (Table 2, entries 3, 4, 6 and 7), the reaction times is shorter and the yields are also relatively higher than that with electron-rich substituents (such as CH_3, CH_3O, and HO) (Table 2, entries 9-15). Interestingly, hindered *ortho*-substituted benzaldehydes [such as 2-nitrobenzadehyde (**2b**), 2-chlorobenzaldehyde (**2e**), and 2, 4-dichlorobenzaldehyde (**2h**)] were cyclocondensed with 2-naphthol (**1**) providing high yields of the 14*H*-dibenzo[*a,j*]xanthene products (**3b**, **3e** and **3h**) (Table 2, entries 2, 5 and 8). An aryl aldehyde containing both electron-deficient and electron-rich substituents (**2p**) was efficiently reacted with 2-naphthol (**1**) and desired product (**3p**) was formed in high yield (Table 2, entry 16). Moreover, aliphatic aldehydes gave the corresponding 14*H*-dibenzo[*a,j*]xanthenes (**3q**-**r**) in good yields (Table 2, entries 17-18). When the pyridine-2-carbaldehyde (**2s**) was used as an aldehyde precursor, the corresponding product (**3s**) was also formed with 88% isolated yield (Table 2, entry 19).

Table 2. Synthesis of various 14*H*-dibenzo[*a,j*]xanthenes (**3a**-**s**) in the presence of 2-HSBA.[a]

Entry	R	Product	Time (min)	Isolated yields (%)	Mp (°C)	
					Observed	Reported [Ref.]
1	C_6H_5, **2a**	**3a**	12	92	186-188	181-183 [20]
2	2-NO_2-C_6H_4, **2b**	**3b**	10	89	270-271	288-290 [9]
3	3-NO_2-C_6H_4, **2c**	**3c**	9	94	210-212	211-212 [20]
4	4-NO_2-C_6H_4, **2d**	**3d**	10	94	319-320	310-312 [20]
5	2-Cl-C_6H_4, **2e**	**3e**	20	90	213-215	212-213 [22]
6	4-Cl-C_6H_4, **2f**	**3f**	8	92	288-290	287-289 [20]
7	4-F-C_6H_4, **2g**	**3g**	9	90	240-242	235-238 [9]
8	2,4-di-Cl-C_6H_3, **2h**	**3h**	25	91	231-232	229-230 [22]
9	4-Me-C_6H_4, **2i**	**3i**	11	92	229-231	227-229 [20]
10	3-MeO-C_6H_4, **2j**	**3j**	27	88	173-175	172-173 [25]
11	4-MeO-C_6H_4, **2k**	**3k**	17	90	203-205	203-204 [20]
12	3-HO-C_6H_4, **2l**	**3l**	18	90	240-241	240-242 [9]
13	4-HO-C_6H_4, **2m**	**3m**	20	88	140-142	140 [8]
14	3,4-di-MeO-C_6H_3, **2n**	**3n**	35	91	201-203	194-495 [1]
15	4-HO-3-MeOC_6H_3, **2o**	**3o**	25	88	210-212	206-207 [3]
16	3-NO_2-4-HO-C_6H_3, **2p**	**3p**	18	93	267-269	268-270 [25]
17	Propyl, **2q**	**3q**	40	80	152-153	152-154 [9]
18	$PhCH_2CH_2$**, 2r**	**3r**	45	84	176-178	176-177 [24]
19	2-Pyridyl, **2s**	**3s**	30	88	180-182	179-182 [3]

[a] All reactions were implemented using 2-naphthol **1** (2 mmol), aldehyde **2** (1 mmol), 2-HSBA (15 mol%) at 100 °C under solvent-free conditions.

Based on the mechanisms reported in literature [9, 11, 16, 22, 24], a plausible reaction mechanism for the 2-HSBA-catalyzed transformation can be proposed as shown in Scheme 2. The reaction is likely proceeds through the initial activation of aldehydes by acidic catalyst, and then nucleophilic attack of the 2-naphthol (**1**) on the carbonyl group of the activated aldehydes (**A**) to make the intermediate **B**. In the next steps, intermediate **B** is converted to carbocation intermediate **E**. The oxonium species **G** is formed on the reaction with the second molecule of 2-naphthol (**1**) *via* the Michael-type addition. Then **G** undergoes cyclization to the cyclic intermediate **H**. Finally, proton exchange and dehydration occurs to afford the desired products (**3a**-**s**).



Scheme 2. A plausible reaction mechanism for the synthesis of 14*H*-dibenzo[*a,j*]xanthenes (**3a**-**s**).

Evaluation of the reusability and recovery of the catalyst was investigated using the model reaction. It was found that the catalyst could be recovered and reused up to four runs and the product was obtained in reasonable yields (Table 3).

Table 3. The recycling of 2-HSBA in the synthesis of **3c**.

Run	Fresh	1	2	3	4
Time (min)	9	9	11	15	20
Isolated yields (%)	94	91	89	84	75

To demonstrate the efficiency of this catalyst in the production of 14*H*-dibenzo[*a,j*]xanthenes and compared with other methods, some results for the synthesis of **3c** are summarized in Table 4. It is comparable in terms of yields and reaction times and not requires any solvent or inert atmosphere. It also does not require the use of some organic solvents such as toluene and dichloromethane. This method can also avoid the synthesis of catalyst and the use of special devices such as microwave and ultrasound.

Table 4. Comparison of the catalytic efficiency of 2-HSBA with some reported catalysts in the synthesis of **3c**.

Entry	Catalyst (mol%) [mg]/conditions	Time (min)	Yield (%)	References
1	SSA[a][18]/SF[b], 125 °C	70	85	[11]
2	H_3BO_3 (20)/SF, 120 °C	90	88	[10]
3	$CuSO_4.5H_2O$ (10)/SF, 80 °C	330	90	[9]
4	Nano-AgI (20)/SF, 140 °C	45	88	[20]
5	I_2 (10)/SF, MW[c], 60-70 °C	15	92	[12]
6	CSA[d][80]/SF, 110-115 °C	120	90	[16]
7	$NH_4H_2PO_4$-SiO_2[100]/US[e], 40 °C	40	88	[18]
8	$NbCl_5$ (25)/CH_2Cl_2, RT[f], N_2 atmosphere	1440	97	[19]
9	HBF_4-SiO_2 (10)/SF, 120 °C	60	90	[25]
10	2-HSBA (15)/SF, 100 °C	9	94	[This work]

[a] Silica sulfuric acid. [b] Solvent-free. [c] Microwave. [d] Cellulose sulfuric acid. [e] Ultrasound. [f] Room temperature.

4. CONCLUSIONS

In summary, the condensation reaction of 2-naphthol with a wide range of aldehydes in the presence of 2-HSBA as an solid acidic organocatalyst provided 14*H*-dibenzo[*a,j*]xanthenes. This efficient approach has the following advantages: implementation of the reaction in the absence of solvent, high catalytic activity under solvent-free reaction conditions, no need to the synthesis of a catalyst, reusability of the catalyst, cost-effective, simple, green, as well as acceptable reaction times (typically 8-45 min).

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REFERENCES

[1] Bhattacharya A.K., Rana K.C., Mujahid M., Sehar I. and Saxena A.K., *Bioorg. Med. Chem. Lett.*, 2009; **19**: 5590-5593. DOI 10.1016/j.bmcl.2009.08.033.

[2] Kumar A., Sharma S., Maurya R.A. and Sarkar J., *J. Comb. Chem.*, 2010; **12**: 20-24. DOI 10.1021/cc900143h.

[3] Naidu K.R.M., Krishna B.S., Kumar M.A., Arulselvan P., Khalivulla S.I. and Lasekan O., *Molecules*, 2012; **17**: 7543-7555. DOI 10.3390/molecules 17067543.

[4] Fareghi-Alamdari F., Golestanzadeh M. and Zekri N., *J. Chin. Chem. Soc.*, 2014; **12**: 1341-1350. DOI 10.1002/jccs.201400148.

[5] De S., Das S. and Girigoswami A., *Spectrochim. Acta Mol. Biomol. Spectrosc.*, 2005; **61**: 1821-1833. DOI 10.1016/j.saa.2004.06.054.

[6] Jhonsi M.A., Srininivasan V. and Kathiravan A., *Synth. Met.*, 2014; **196**: 131-138. DOI 10.1016/j.synthmet.2014.07.026.

[7] Ojida A., Takashima I., Kohira T., Nonaka H. and Hamachi I., *J. Am. Chem. Soc.*, 2008; **130**: 12095-12101. DOI 10.1021/ja803262w.

[8] Pellosi D.S., Estevao B.M., Semensato J., Severino D., Baptista M.S., Politi M.J., Hioka N. and Caetano W., *J. Photochem. Photobiol. Chem.*, 2012; **247**: 8-15. DOI 10.1016/j.jphotochem.2012.07.009.

[9] Behbahani F.K. and Valiallhi M., *Arab. J. Chem.*, 2013; in press, DOI 10.1016/j.arabjc.2013.06.014.

[10] Karimi-Jaberi Z. and Keshavarzi M., *Chin. Chem. Lett.*, 2010; **21**: 547-549. DOI 10.1016/j.cclet.2010.01.014.

[11] Shaterian H.R., Ghashang M. and Hassankhani A., *Dyes Pigm.*, 2008; **76**: 564-568. DOI 10.1016/j.dyepig.2006.11.004.

[12] Ding F.Q., An L.T. and Zou J.P., *Chin. J. Chem.*, 2007; **25**: 645-648. DOI 10.1002/cjoc.200790120.

[13] Bhattacharya A.K. and Rana K.C., *Mendeleev Commun.*, 2007; **17**: 247-248. DOI 10.1016/j.mencom.2007.06.023.

[14] Kundu K. and Nayak S.K., *J. Serb. Chem. Soc.*, 2014; **79**: 1051-1058. DOI 10.2298/JSC130805021K.

[15] Prasad D. and Nath M., *Catal. Sci. Technol.*, 2012; **2**: 93-96. DOI 10.1039/c1cy00407g.

[16] Madhav J.V., Reddy Y.T., Reddy P.N., Reddy M.N., Kumar S., Crooks P.A. and Rajitha B., *J. Mol. Catal. A-Chem.*, 2009; **304**: 85-87. DOI 10.1016/j.molcata.2009.01.028.

[17] Rahmatpour A., *Monatsh. Chem.*, 2011; **142**: 1259-1263. DOI 10.1007/s007 06011-0537-z.

[18] Mahdavinia G.H., Rostamizadeh S., Amani A.M. and Emdadi Z., *Ultrason. Sonochem.*, 2009; **16**: 7-10. DOI 10.1016/j.ultsonch.2008.05.010.

[19] Bartolomeu A.A., de Menezes M.L. and Filho L.C.S., *Chem. Pap.*, 2014; **68**: 1593-1600. DOI 10.2478/s11696-014-0597-8.

[20] Safaei-Ghomi J. and Ghasemzadeh M.A., *J. Saudi Chem. Soc.*, 2015; **19**: 642-649. DOI 10.1016/j.jscs.2012.05.007.

[21] Albadi J., Razeghi A., Abbaszadeh H. and Mansournezhad A., *J. Nanoparticles*, 2013; Article ID 546194, **5**: DOI 10.1155/2013/546194.

[22] Naeimi H. and Nazifi Z.S., *J. Chin. Chem. Soc.*, 2013; **60**: 1113-1117. DOI 10.1002/jccs.201300019.

[23] Shirini F., Abedini M., Seddighi M., Goli-Jolodar O., Safarpour M., Langroodi N. and Zamani S., *RSC Adv.*, 2014; **4**: 63526-63532. DOI 10.1039/C4RA12361A.

[24] Naeimi H. and Nazifi Z.S., *Appl. Catal. A: Gen.*, 2014; **477**: 132-140. DOI 10.1016/j.apcata.2014.03.012.

[25] Liu Y.H., Tao X.Y., Lei L.Q. and Zhang Z.H., *Synth. Commun.*, 2009; **39**: 580-589. DOI 10.1080/0039791080 2412842.

[26] Kiyani H., Darbandi H., Mosallanezhad A. and Ghorbani F., *Res. Chem. Intermed.*, 2015; **41**: 7561-7579. DOI 10.1007/s11164-014-1844-x.

[27] Kiyani H. and Darbandi H., *Chiang Mai J. Sci.*, 2015; Accepted for publication.