



An Efficient One-Pot Synthesis of 14-aryl or Alkyl-14-H-dibenzo[α ,j]xanthenes Catalyzed by Ionic Liquid with Multi-SO₃H Groups under Ambient Temperature

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ABSTRACT

Ionic liquid with multi-SO₃H groups was employed as a catalyst for facile preparation of 14-aryl or alky-14-*H*-dibenzo[α ,j]xanthenes via the one-pot condensation of 2-naphthol with aldehydes. Various aliphatic and aromatic aldehydes were utilized in the reaction and in all situations the desired product were synthesized successfully. The described novel synthesis method propose several advantages of safety, mild condition, short reaction times, high yields, simplicity and easy workup compared to the traditional method of syntheses.

Key words: Ionic liquid with multi-SO₃H groups, Xanthene, 2-Naphthol, Aldehyde, Chemoselective.

INTRODUCTION

Xanthenes and benzoxanthenes derivatives are important biologically active heterocycles which has drawn great attention in medicinal chemistry as well as organic chemistry in recent years. These compounds have been reported to possess a variety of biological and pharmaceutical properties such as antiviral,¹ antibacterial,² and anti-inflammatory³ activities along with antagonists for paralyzing the action of

zoxazolamine.⁴ Xanthene-based compounds have also depict agricultural and bactericide activity and efficacy in photodynamic therapy.⁵ Furthermore, because of their wonderful spectroscopic properties, these heterocycles have found applications in the production of fluorescent dyes, including rhodamine, fluorescein, and the eosins,⁶ pH-sensitive fluorescent materials for visualization of biomolecules assemblies⁷ and utility in laser technologies.⁸ Thus, vast application of this oxygen heterocycles lead to further research in this aspect

of organic chemistry which currently is of great interest.

Literature reveals a number of xanthenes-based compounds which are available from natural sources⁹ Various methods have been described to the synthesis of 14-*H*-dibenzo[*a,j*]xanthenes including the reaction of 2-naphthol with 2-naphthol-1-methanol,¹⁰ aldehydes and cyclic 1,3-dicarbonyl compounds,¹¹ formamide¹² and carbon monoxide,¹³ cyclodehydrations¹⁴ the cyclocondensation reaction of 2-hydroxyaromatic aldehydes with 2-tetralone,¹⁵ the reaction of benzaldehydes with acetophenones,¹⁶ palladium-catalyzed cyclization of polycyclic aryltriflate esters¹⁷ and the intermolecular trapping of benzynes by phenols.¹⁸ The reaction of 2-naphthol with aldehydes or acetals under acidic conditions such as sulfamic acid,¹⁹ Amberlyst-15,²⁰ AcOH-H₂SO₄,²¹ *p*-TSA²² and silica sulfuric acid²³ have also been reported.²⁴ However, many of these traditional procedures suffer from one or more disadvantages including prolonged reaction times, low yield,²⁶ harsh reaction conditions, a requirement of excess of reagents and catalysts, use of toxic solvents or special apparatus and laborious workup.

As mentioned above, considering the importance of xanthenes derivatives in pharmaceutical and industrial chemistry as well as taking into account the disadvantages associated with earlier reported protocols necessitate the development of simple, well-organized, and eco-friendly synthetic methods for the efficient preparation of 14-aryl or alky-14-*H*-dibenzo[*a,j*]xanthenes.

In recent years, ionic liquids have attracted much attention as a new class of green solvent and catalyst.²⁶ These aqueous media is utilized for organic synthesis due to their astonishingly properties, such as wide liquid range, favorable solvating capability, requirement low temperature, tunable polarity, high thermal stability, and ease of recyclability.²⁷⁻²⁹ Ionic liquids have also negligible vapor pressure, which facilitates product separation by distillation. Moreover, they are cheapest and environmentally friendly solvents, because water exhibits unique reactivity and selectivity, which is differ from those in conventional organic solvents. So, the appropriate property of ionic liquids lead to

the development and application of so-called "task-specific" ionic liquids to synthesize the desirable products.

Recently, Jianguo *et al.*³⁰ introduced a new ionic liquid with multi-SO₃H groups (scheme 1) which have much higher activity than other reported catalysts with the additional advantage of reusability.

In continuation of our investigations on the development of new synthetic methodologies,³¹ we herein report a new, convenient, mild and efficient procedure for the synthesis of 14-aryl or alkyl-14-*H*-dibenzo[*a,j*]xanthenes from one-pot condensation of various aldehydes with 2-naphthol using this non-volatile ionic liquid with multi-SO₃H groups under ambient temperature.

EXPERIMENTAL

A mixture of 2-naphthol (2.0 mmol), aldehyde (1.0 mmol) and ionic liquid (1mol%) in ethanol (2mL) was stirred at room temperature for an appropriate time. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was extracted with CH₂Cl₂. The organic layer was separated, dried over Na₂SO₄, and concentrated under reduced pressure. The crude product recrystallized from ethanol to obtain pure product. The physical data (mp, NMR, IR) of these known compounds were found to be identical with those reported in the literature.

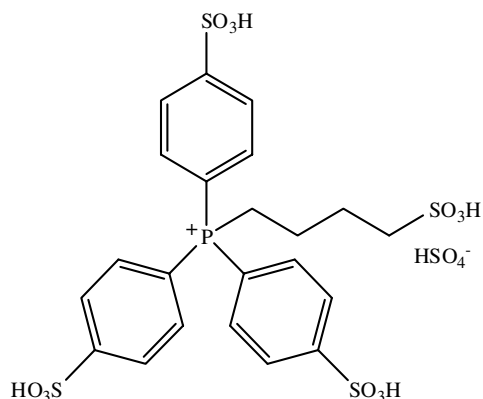
The spectral data for selected products

14-Phenyl-14*H*-dibenzo[*a,j*]xanthene (1): Colorless solid, m.p. 180–182 °C. ¹H NMR (CDCl₃, 400 MHz) δ: 6.45 (s, 1H), 6.96 (t, *J* = 7.2 Hz, 1H), 7.12 (t, *J* = 7.2 Hz, 2H), 7.37–7.58 (m, 8H), 7.74–7.81 (m, 4H), 8.34 (d, 2H); IR (KBr) ν: 1080, 1250, 1445, 1585, 3070 cm⁻¹.

14-(2-Chlorophenyl)-14*H*-dibenzo[*a,j*]xanthene (2): White solid, m.p. 215–216 °C. ¹H NMR (CDCl₃, 400 MHz) δ: 6.80 (s, 1H), 6.87–7.13 (m, 2H), 7.42–7.67 (m, 8H), 7.79–7.86 (m, 4H), 8.73 (d, *J* = 8.5 Hz, 2H); IR (KBr) ν: 1240, 1459, 1515, 1592, 2998, 3058 cm⁻¹.

14-(4-Chlorophenyl)-14*H*-dibenzo[*a,j*]xanthene (3): Yellow solid, m.p. 287–288

°C. $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ : 6.46 (s, 1H), 6.96 (d, $J = 7.3$ Hz, 2H), 7.38 (t, $J = 7.5$ Hz, 2H), 7.42–7.76 (m, 10 H), 8.39 (d, $J = 8.6$ Hz, 2H); IR (KBr) ν : 1140, 1209, 1237, 1245, 1397, 1456, 1514, 1590, 1622, 2922, 3066 cm^{-1} .



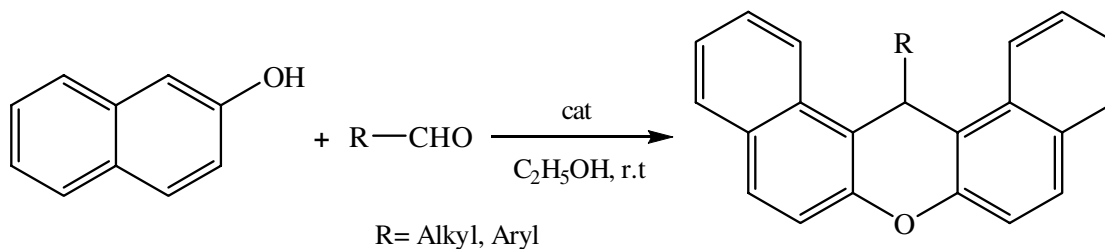
Scheme 1: ILs with multi SO_3H groups

14-(4-Nitrophenyl)-14H-dibenzo[a,j]xanthene (7): Yellow solid, m.p. 311–313 °C. $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ : 6.59 (s, 1H), 7.03 (t, $J = 7.8$ Hz, 2H), 7.40–7.56 (m, 6H), 7.66–7.72 (m, 4H), 8.30–8.46 (m, 4H); IR (KBr) ν : 1145, 1236, 1335, 1516, 1590, 2925 cm^{-1} .

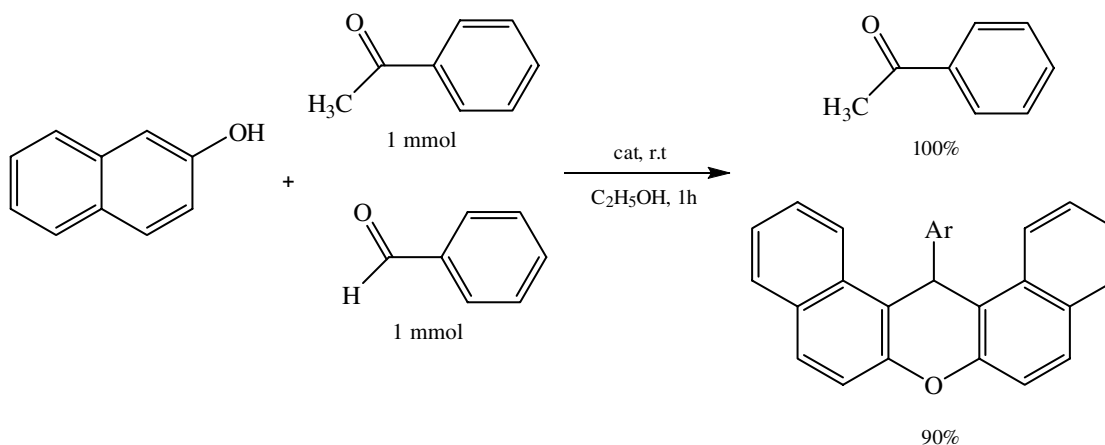
14-Propyl-14H-dibenzo[a,j]xanthene (17): White solid, m.p. 152–153 °C. $^1\text{H NMR}$ (CDCl_3 , 400 MHz) δ : 0.62 (t, $J = 7.3$ Hz, 3H), 1.01–1.08 (m, 2H), 2.03 (m, 2H), 5.58 (t, $J = 4.61$ Hz, 1H), 7.39 (d, $J = 9.2$ Hz, 2H), 7.45–7.50 (m, 2H), 7.61–7.65 (m, 2H), 7.79 (d, $J = 8.8$ Hz, 2H), 7.89 (d, $J = 8.4$ Hz, 2H), 8.26 (d, $J = 8.8$ Hz, 2H); IR (KBr) ν : 814, 1243, 1399, 1434, 1591, 2953, 3061 cm^{-1} .

RESULTS AND DISCUSSION

The catalyst was prepared according to the literature procedure.³⁰ We studied the reaction of benzaldehyde with 2-naphthol (1:2 molar ratios)



Scheme 2:



Scheme 3:

to optimize the reaction conditions with respect to temperature, time, solvent and the molar ratio of catalyst to the substrate. It was found that 1 mol% of catalyst was sufficient to obtain the desired 14-aryl or alky-14-*H*-dibenzo[*a,j*]xanthenes in 90% yield within 1 h at room temperature in ethanol using benzaldehyde.

The effect of solvent on the yield of 14-aryl or alky-14-*H*-dibenzo[*a,j*]xanthenes is given in Table 1. The reaction of 2-naphtol with benzaldehyde was chosen as a model reaction for investigating the effect of solvent. Among the solvents examined, ethanol was found to be the most effective solvent.

After finding the optimized reaction conditions, the investigation was preceded by performing the reaction between a series of aldehydes with 2-naphtol. To show the general applicability of this method, various aldehydes were efficiently reacted with two equivalents of 2-naphtol in the same conditions. These results encouraged us to investigate the scope and the generality of this new protocol for various aldehydes under optimized conditions. As shown in Table 2, a series of aromatic and aliphatic aldehydes underwent electrophilic substitution reaction with 2-naphtol to afford a wide range of substituted 14-aryl or alky-14-*H*-dibenzo[*a,j*]xanthenes in good to excellent

yields without any side products. The nature and electronic properties of the substituents on the aromatic ring effect the conversion rate, and aromatic aldehydes having electron-withdrawing groups on the aromatic ring (table 2, entries 7) react faster than electron-donating groups (table 2, entries 11). Though meta- and para substituted aromatic aldehydes gave good results, ortho-substituted aromatic aldehydes (such as 2-nitrobenzadehyde) gave lower yields because of the steric effects. On the other hand, reactions with aliphatic aldehydes provided somewhat lower yields than those with aromatic aldehydes (Table 2, entries 17-20).

In order to show the merit of catalyst in comparison with the other catalysts used for the similar reaction, some of the results are tabulated in Table 3. According to Table 3, the required ratio for the most catalysts used for this purpose is >1 mol% and also the required reaction times are much longer (2–73 h).

The high chemoselectivity of this method had also been demonstrated by a competitive reaction between an aldehyde and a ketone with 2-naphthol, as depicted in scheme 3. The result showed that the chemoselectivity of aldehyde group in the present of a ketone can also be achieved by

Table 1 Solvent effect on the reaction between 2-naphtol and benzaldehyde^a

Entry	Solvent	Reaction time/h	Yield ^b /%
1	H ₂ O	10	18
2	CH ₃ CN	5	85
3	CHCl ₃	5	80
4	C ₂ H ₅ OH	1	90
5	CH ₃ CO ₂ Et	2.5	90

^a Reaction condition: 2-naphtol 1 mmol; PhCHO 1 mmol; catalyst 1 mol%; solvent 2 mL; r.t. ^b Isolated yield.

Table 2 Reaction of 2-naphtol with various aliphatic and aromatic aldehydes employing 1 mol% catalyst

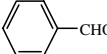
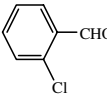

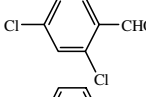
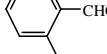
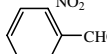
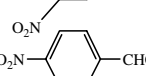


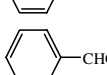


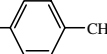
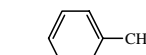
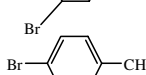
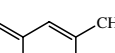
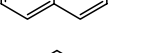
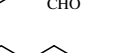
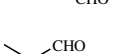
Entry	Carbonyl compound	Reaction time/h	Yield/%	Mp/ ^o C	References for the known compound
1		1	90	180-182	181-183 [34]
2		1.5	90	215-216	215 [22]
3		0.5	95	287-288	289 [22]
4		1.5	92	227-229	227 [23]
5		1.5	90	211-213	214 [34]
6		1	92	210-211	211 [22]
7		0.5	96	311-313	310 [34]
8		1.5	87	228-230	229 [22]
9		1	90	140-142	140 [25]
10		1.5	90	206-207	204 [22]
11		1.5	88	204-206	204 [22]
12		1	95	238-239	239 [22]
13		1	95	192-194	190-192 [24c]
14		1	95	297-299	297 [22]
15		1.5	90	216-218	217 [35]
16		2	87	152-153	152 [22]
17		2	87	150-151	151-153 [25]
18		2	85	154-155	153-154 [25]
19		2	85	113-115	113 [22]

Table 3 Reaction of 2-naphthol with benzaldehyde in the presence of different catalysts

Entry	Catalyst	Condition	Time/h	Yield/%	Ref.
1	IL	C ₂ H ₅ OH, r.t	1	90	—
2	<i>p</i> -toluene sulfonic acid	Solvent-free/125 °C	4	89	[32]
3	[BMIM]BF ₄	Ionic liquid/100 °C	10	20	[32]
4	[MIMPS]H ₂ PO ₄	Ionic liquid/100 °C	2	76	[32]
5	selectfour	Solvent-free/125 °C	8	93	[33]
6	I ₂	Solvent-free/90 °C	2.5	90	[34]
7	sulfamic acid	Solvent-free/125 °C	8	93	[35]
8	H ₂ SO ₄	AcOH/80 °C	73	60	[33]

using the catalyst in good yield under identical conditions because of the reactivity difference between aldehyde and ketone.

CONCLUSION

The objective of this paper is to describe green, simple and efficient ionic liquid with multi-SO₃H groups to catalyze one-pot method for the synthesis of 14-aryl or alky-14-*H*-dibenzo[*a*,*j*] xanthene derivatives. The experimental procedure for this reaction is remarkably facile and requires

no toxic organic solvents. The catalyst offers several advantages including mild reaction conditions, cleaner reactions, shorter reaction times, high yield of the products, lower catalytic loading as well as simple experimental and isolation procedures.

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