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## Research Paper

### One-pot Synthesis of Benzoxanthenes in Solvent Free Condition Using $ZrCl_4$ as Catalyst

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**Abstract:** A simple, highly efficient and eco-friendly procedure has been developed for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes by one-pot condensation reaction of  $\beta$ -naphthol with various benzaldehydes in the presence of a catalytic amount of  $ZrCl_4$  under thermal and solvent free conditions. The major advantages of the present method are less reaction time, solvent-free condition, high yields, easy work up and simple purification of the products.

## Introduction

Xanthenes are an important class of heterocyclic compounds which have attracted considerable attention due to their various pharmaceutical properties. The natural xanthenes and their synthetic analogues have been reported to possess a wide range of pharmacological and biological activities including antibacterial [1], anti-proliferative [2], anti-inflammatory [3] and antiviral activities [4]. These molecules are also useful in photodynamic therapy [5], laser technologies [6] and as pH-sensitive fluorescent materials for bio-molecular visualization [7]. The unique biological profile of xanthenes has made this scaffold as a prime synthetic molecule.

Therefore, a number of methods have been developed for the synthesis of xanthenes. Among them, the general method includes condensation of aldehydes with  $\beta$ -naphthol in the presence of acid catalysts, such as  $AcOH-H_2SO_4$  [8], *p*-TSA [9], sulfamic acid [10], molecular iodine [11], tungsten heteropoly acid [12], silica sulfuric acid [13], amberlyst-15 [14],  $K_5CoW_{12}O_{40} \cdot 3H_2O$  [15], boric acid [16], SWCNT- $SO_3H$ , [17], Zinc oxide nanoparticles, [18], Chloroaluminate Ionic Liquids [19] polymeric N-sulfonic acid poly(4-vinylpyridinium) chloride [20]. However, most of these reported methods suffer from some limitations such as long reaction times, harsh reaction conditions, low yields and tedious workup. Thus, there is always a need to develop an improved and environmentally benign method for the synthesis of these types of compounds.

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The green processes generally involve the use of efficient, cost-effective and biodegradable catalysts, non-toxic and non-inflammable media such as water, ionic liquids and the reactions under solvent-free conditions. Although, a variety of Lewis acid catalyst have been used for the synthesis of xanthenes but most of them suffer from air or moisture sensitive conditions.  $ZrCl_4$  is a readily available Lewis acid catalyst that is air and moisture tolerant, easy and safe to handle. It has also been used as a catalyst for various other organic transformations resulting good efficacy [21–23]. These salient features along with the strong coordinating ability of  $Zr^{4+}$ , makes it a potential Lewis acid catalyst [21, 22]. Because of the large use of toxic reagents, chemicals, and volatile, flammable organic solvents, the solvent free conditions are more advantageous over the solvent mediated reactions [24]. The solvent free methods reduce the use of organic solvents and minimize the burden of other wastes. Thus solvent free reactions are of great interest in order to modernize classical procedures making them more clean, safe, and easy to perform.

In the present work we have studied catalytic effect of the  $ZrCl_4$  for the one-pot synthesis of 14-aryl-14H-dibenzo [a,j]xanthenes under solvent free and thermal conditions.

## Results and discussions

In the search of a convenient, economical and efficient catalyst for the one-pot synthesis of 14-aryl-14-H-dibenzo [a,j]xanthenes, a model reaction was carried out by using  $\beta$ -naphthol and benzaldehyde as substrates in the presence of  $ZrCl_4$ . The results of this reaction were summarized in table 1. Among all the solvents screened, the

best result was observed under solvent free condition.

The reaction was carried out with varying amount of  $ZrCl_4$  by keeping the amount of reactants constant (table 2). In the absence of catalyst, no product formation was observed even after 1 h. At lower amount of catalyst (entry 2, and 3, table 2) low yield of product was observed. As the amount of catalyst was increased from 0.025 mmol to 0.05 mmol, a significant increase in yield was observed (entry 4, table 2). Further increasing the amount of catalyst no change in the yield of the product (entry 5 and 6, table 2). Thus the optimum condition was obtained at 0.05 mmol of  $ZrCl_4$  for 1 mmol of benzaldehyde and 2 mmol of  $\beta$ -naphthol (entry 4, table 2).

The scope and generality of this method was investigated in the reaction of  $\beta$ -naphthol with various types of aromatic aldehydes with both electron-donating and electron-withdrawing substituents. The corresponding dibenzoxanthene were obtained in the 80–95% yields (table 3).

It has been found that the nature of the functional group on the aromatic ring of the aldehyde affects the reaction time and yield. The presence of electron withdrawing group at *para*-position in comparison to the unsubstituted aromatic aldehyde shows increase of the yield while the presence of an electron donating group decreases the yield. Though *meta* and *para*-substituted aromatic aldehydes gave good results, *ortho*-substituted aromatic aldehydes such as 2-nitrobenzaldehyde gave lower yields because of the steric effects [27].

## Experimental Protocols

All the aldehydes and the catalyst  $ZrCl_4$  used were purchased from Merck and  $\beta$ -naphthol

from Fisher Scientific Chemicals. All the chemicals were of analytical grade and used without further purification. Thin layer chromatography (Merck Kiesel 60 F254, 0.2 mm thickness) was used to monitor the progress of the reactions. The  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectrum were recorded on Jeol ECX spectrosin instrument at 400 and 100 MHz, respectively using TMS as internal standard. The chemical shift values were expressed on  $\delta$  scale and the coupling constant ( $J$ ) in Hz. FT-IR of all the synthesized xanthenes were recorded on a spectrometer Perkin Elmer Spectrum BX II from range 4000- 400  $\text{cm}^{-1}$  by making sample pallets with KBr. The melting points of synthesized compounds were determined on a Thomas Hoover Unimelt capillary melting point apparatus.

### Experimental procedure

A mixture of  $\beta$ -naphthol (2 mmol), aldehyde (1 mmol) and  $\text{ZrCl}_4$  (0.05 mmol) was heated in a oil bath at  $130^\circ\text{C}$  with vigorous stirring for the time as indicated in table 3. The reaction progress was monitored by TLC (hexane: ethylacetate, 4:1). After completion of the reaction, methanol (10 mL) was added to the semisolid product and stirred for 10 minutes. The solid so obtained was filtered off. This was repeated three times to isolate the product completely. The crude product was stirred in dichloromethane and the catalyst was removed by filtration. Finally the pure product was obtained.

**14-phenyl-14H-dibenzo[a,j]xanthene (3a):** Colour: White solid; IR (KBr,  $\text{cm}^{-1}$ ): 3075, 3021, 2998, 1621, 1593, 1513, 1458, 1404, 1253, 1080, 965, 828, 803, 745;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 6.47 (s, 1H, CH), 7.10-7.14 (t,  $J = 8.24$  Hz, 2H, ArH), 7.38-7.41 (t,  $J = 8.24$  Hz, 2H, ArH), 7.45-7.56 (m, 6H), 7.76-7.81 (m, 4H, ArH), 8.36-8.39 (d,  $J = 8.70$  Hz, 2H, ArH);  $^{13}\text{C}$  NMR (100

MHz,  $\text{CDCl}_3$ )  $\delta$ : 37.9, 117.2, 117.8, 122.7, 124.0, 126.6, 128.1, 128.2, 128.7, 128.7, 130.9, 131.3, 145.6, 148.6

### 14-(4-Bromophenyl)-14H-dibenzo[a,j]

**xanthenes (3b):** Colour: White solid; IR (KBr,  $\text{cm}^{-1}$ ): 3070, 2908, 1592, 1482, 1401, 1239, 963, 806, 740;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 6.45 (s, 1H, CH), 7.26 (d,  $J = 8.1$  Hz, 2H, ArH), 7.37-7.48 (m, 8H, ArH), 7.79-7.84 (m, 4H, ArH), 8.31 (d,  $J = 8.1$  Hz, 2H, ArH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 37.4 (PhC), 117.9, 118.5, 122.3, 124.3, 126.9, 128.8, 129.0, 129.8, 131.5, 131.7, 132.0, 144.4, 149.

### 14-(2-Chlorophenyl)-14H-dibenzo[a,j]

**xanthene (3c):** Colour: White solid; IR (KBr,  $\text{cm}^{-1}$ ): 3057, 2924, 1592, 1515, 1458, 1246, 960, 809, 745;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 6.73 (s, 1H, CH), 6.8-7.18 (m, 2H, ArH), 7.35-7.53 (m, 8H, ArH), 7.70-7.75 (m, 4H, ArH), 8.67 (d,  $J = 8.0$  Hz, 2H, ArH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 34.59, 118.0, 123.4, 124.3, 126.8, 127.8, 127.9, 128.6, 129.0, 129.5, 130.8, 131.7, 143.5, 148.9.

### 14-(4-Chlorophenyl)-14H-dibenzo[a,j]

**xanthene (3d):** Colour: Yellow solid; IR (KBr,  $\text{cm}^{-1}$ ): 3068, 2915, 1622, 1592, 1514, 1458, 1354, 1247, 1239, 1141, 1065, 959, 807, 778, 741;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 6.45 (s, 1H, CH), 7.09 (d,  $J = 8.1$  Hz, 2H, ArH), 7.40-7.56 (m, 8H, ArH), 7.77-7.80 (m, 4H, ArH), 8.28 (d,  $J = 8.3$  Hz, 2H, ArH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 37.34, 116.71, 117.97, 122.36, 124.32, 126.88, 128.60, 128.87, 129.05, 131.02, 131.21, 148.66.

### 14-(4-Nitrophenyl)-14H-dibenzo[a,j]

**xanthene (3e):** Colour: Yellow solid; IR (KBr,  $\text{cm}^{-1}$ ): 2925, 1592, 1515, 1340, 1239, 827, 742;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 6.58 (s, 1H, CH), 7.42-7.49 (m, 4H, ArH),

7.58–7.67 (m, 4H, ArH), 7.83–7.65 (m, 5H, ArH) 7.97–7.99 (m, 2H, ArH), 8.25–8.27 (d,  $J = 8.2\text{Hz}$ , 2H, ArH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 37.8 (PhC), 115.2, 118.0, 121.9, 123.8, 124.5, 127.1, 128.9, 129.0, 129.5, 131.0, 158.1

#### 14-(4-Tolyl)-14H-dibenzo[a,j]xanthenes

**(3f)**: Colour: White solid; IR (KBr,  $\text{cm}^{-1}$ ): 3020, 2924, 2854, 1592, 1508 1459, 1431, 1401, 1249, 962, 808, 740, 610, 518, 488;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 2.11 (s, 3H), 6.43 (s, 1H, CH), 6.93 (d,  $J = 8.0\text{ Hz}$ , 2H, ArH), 7.37–7.46 (m, 8H, ArH), 7.74–7.80 (m, 4H, ArH), 8.38 (d,  $J = 7.2\text{ Hz}$ , 2H, ArH);  $^{13}\text{C}$  NMR (100 MHz  $\text{CDCl}_3$ )  $\delta$ : 21.6 ( $\text{CH}_3$ ), 38.3 (PhC), 117.9, 122.6, 124.1, 126.7, 128.0, 128.7, 129.1.

#### 14-(4-Fluorophenyl)-14H-dibenzo[a,j]

**xanthene (3g)**: Colour: Brown solid; IR (KBr,  $\text{cm}^{-1}$ ): 3068, 3034, 1622, 1592, 1502, 1458, 1432, 1412, 1399, 1239, 959, 743;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 6.46 (s, 1H, CH), 6.78–6.82 (t,  $J = 8.1\text{Hz}$ , 2H, ArH); 7.40–7.47(m, 8H, ArH), 7.76–7.82 (m, 4H, ArH); 8.30 (d,  $J = 8.1\text{ Hz}$ , 2H ArH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 37.1, 115.1, 115.3, 117.9, 122.4, 124.3, 126.8, 128.8, 128.9, 129.5, 129.6, 131.0, 141.2, 148.6, 159.8, 162.8.

#### 14-(3-Bromophenyl)-14H-dibenzo[a,j]

**xanthenes (3h)**: Colour: White solid; IR (KBr,  $\text{cm}^{-1}$ ): 3066, 2924, 1591, 1398, 1239, 1064, 960, 811, 746;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 6.43 (s, 1H, CH), 7.00 (t,  $J = 8.1\text{ Hz}$ , 1H, ArH), 7.12 (d,  $J = 8.2\text{Hz}$ , 1H, ArH), 7.41–7.48(m, 8H, ArH), 7.80–7.83(m, 4H, ArH), 8.30 (d,  $J = 8.2\text{ Hz}$ , 2H, ArH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 42.7(PhC), 118.2, 119.9, 122.5, 123.5, 127.3, 129.8, 130.1, 133.4, 140.1, 152.9.

#### 14-(3-Nitrophenyl)-14H-dibenzo[a,j]

**xanthene (3i)**: Colour: Pale yellow; solid IR (KBr,  $\text{cm}^{-1}$ ): 3067, 1623, 1592, 1521, 1237, 807, 744;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 6.57 (s, 1H, CH), 7.24–7.28 (t,  $J = 8.1\text{Hz}$ , 1H, ArH), 7.39–7.61 (m, 6H, ArH), 7.77–7.83 (m, 6H, ArH) 8.26 (d,  $J = 8.1$ , 2H, ArH), 8.39 (s, 1H, ArH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 37.6, (PhC) 118.0, 121.6, 121.9, 124.5, 127.1, 129.0, 129.4, 129.5, 131.0, 134.2, 146.8, 148.1, 148.7.

#### 14-(3-Fluorophenyl)-14H-dibenzo[a,j]

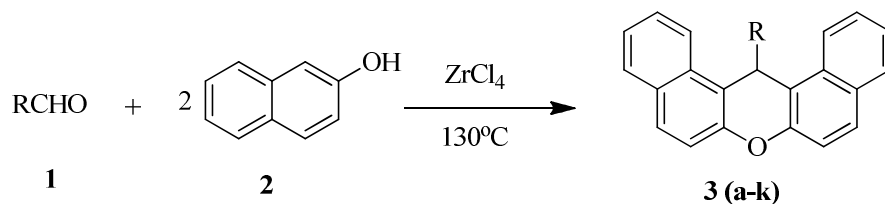
**xanthene (3j)**: Colour: Brown solid; IR (KBr,  $\text{cm}^{-1}$ ): 3053, 1593, 1403, 1244, 1081, 810, 745;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 6.47 (s, 1H, CH) 7.40–7.57(m, 10H, ArH), 7.78–7.83 (m, 4H, ArH), 8.33(d,  $J = 8.1\text{Hz}$ , 2H, ArH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 37.6, 115.3, 116.6, 118, 122.4, 123.7, 124.3, 126.8, 128.8, 129.0, 129.6, 130.9, 131.2, 147.3, 148.7.

#### 14-(4-Ethylphenyl)-14H-dibenzo[a,j]

**xanthenes(3k)**: Colour: White solid; IR (KBr,  $\text{cm}^{-1}$ ): 3043, 2964, 1622, 1591, 1509, 1458, 1431, 1399, 1240, 1066, 961, 833, 802, 737, 695, 506;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 1.03 (t,  $J = 8.1\text{ Hz}$ , 3H), 2.40 (m, 2H), 6.44 (s, 1H, CH), 6.93(d,  $J = 8.2$ , 2H, ArH) 7.38–7.47 (m, 8H, ArH), 7.75–7.77 (m, 4H, ArH), 8.37 (d,  $J = 8.2\text{ Hz}$ , 2H, ArH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 15.1, 28.18, 37.54, 117.47, 117.97, 122.68, 124.14, 126.69, 127.89, 128.67, 128.71, 131.40, 142.03, 148.66.

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**Scheme 1:** Preparation of 14-aryl-14-H-dibenzo [a,j]xanthenes

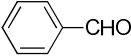
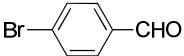
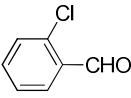
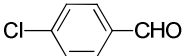
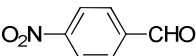
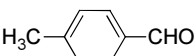
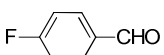
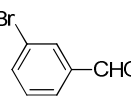
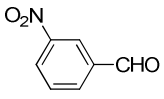
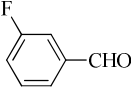

**Table 1:** Effect of different solvents on the reaction time and yields obtained using benzaldehyde

Entry	Solvents	Time	Yield
1	H <sub>2</sub> O	24 h	5
2	MeOH	24 h	36
3	CHCl <sub>3</sub>	24 h	55
4	CH <sub>2</sub> Cl <sub>2</sub>	24 h	58
5	EtOH	24 h	40
6	Solvent free	30 min	91

**Table 2:** Effect of catalyst towards % yield for benzaldehyde (1 mmol) and β-naphthol (2 mmol) at 130 °C for 30 min

Entry	Catalyst (mmol)	Time (min)	Yield (%)
1	0	60	0
2	0.01	30	40
3	0.025	30	75
4	0.05	15	93
5	0.1	15	92
6	0.2	15	93

**Table 3:** ZrCl<sub>4</sub> catalysed synthesis of 14-aryl-14H-dibenzo [a,j]xanthenes.

S. No.	Aromatic Aldehyde	Time (min)	Yield (%)	Mp (°C)	
				Found	Lit.
1		30	91	182	185 <sup>25</sup>
2		40	92	295	297 <sup>25</sup>
3		60	87	214	215 <sup>25</sup>
4		30	95	288	289 <sup>25</sup>
5		45	94	312	310 <sup>25</sup>
6		35	83	227	229 <sup>25</sup>
7		35	93	237	239 <sup>25</sup>
8		45	90	190	190 <sup>25</sup>
9		35	91	212	211 <sup>25</sup>
10		40	90	260	259 <sup>26</sup>
11		35	80	151	152 <sup>11</sup>

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