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## Green and Efficient Synthesis of Xanthene Derivatives using 1-Butyl-3-methylimidazolium Bromide under Solvent Free Condition

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### ABSTRACT

A multicomponent condensation of aromatic aldehydes,  $\beta$ -naphthols and dimidone in 1-butyl-3-methylimidazolium bromide as a green catalyst produces xanthene derivatives in good to excellent yield. Using 1-butyl-3-methylimidazolium bromide as a very efficient, convenient, economical, recyclable, green catalyst for the synthesis under solvent free condition has been developed. This method is environmental benign and advantageous compared to conventional methods because reusability of the ionic liquids, simple work-up and high yields of products.

### KEYWORDS

$\beta$ -Naphthols, Xanthene, 1-Butyl-3-methylimidazolium bromide, Ionic liquid, Solvent-free condition.

### INTRODUCTION

Xanthene has paying substantial attention because they shows a number of biological activities such as antibacterial [1], anti-inflammatory [2], antiviral [3] also their pH sensitive fluorescent property used for the image of biomolecular assemblies [4], dyes [5,6], in laser technology [7,8]. Hence, synthesis of xanthene derivatives are of a huge importance in biological and pharmacological studies.

It is well known that multicomponent reactions plays a significance role in modern organic synthesis. In multicomponent reactions three or more reactants are reacted in one pot to form a desired product without separation of intermediates and change of the reaction conditions. 1-Butyl-3-methylimidazolium bromide [Bmim]Br, have been employed as a promoter for environmentally benign alternative and ecological green catalyst in various organic transformations.

In recent years few methods have been developed for the synthesis of xanthene derivatives using  $I_2$  [9], chlorosulphonic acid [10], CA-SiO<sub>2</sub> [11], HClO<sub>4</sub>-SiO<sub>2</sub> [12], PWA [13], TCT [14], InCl<sub>3</sub> [15], strontium triflate [16], surfactant [17], SaSA [18], tungstosilicic acid [19]. However, these reported methods suffered from several drawbacks such as, prolonged reaction time, stoichiometric amounts of reagents, use of toxic solvents, low yields and difficulties in isolation of final products.

[Bmim]Br is a acidic ionic liquid and has been used for various organic transformations as catalyst, so the acidic nature

of [Bmim]Br makes significant attraction towards the synthesis of xanthene derivatives from the one pot condensation of various substituted aromatic aldehydes, dimidone and  $\beta$ -naphthols, respectively under solvent free condition.

## EXPERIMENTAL

All the chemicals were purchased from Sigma Aldrich and Spectrochem. Melting points were measured in open capillaries on melting-point apparatus and are uncorrected.  $^1\text{H NMR}$  was recorded at room temperature on a Bruker Avance II 400 MHz Spectrometer (SAIF, Punjab University, Chandigarh) in  $\text{CDCl}_3$  using TMS as internal standard. IR spectra (KBr pellets) were obtained with a Perkin Elmer Spectrum RX FTIR (SAIF, Punjab University, Chandigarh, India). The reactions were monitored on TLC using pre-coated plates (silica gel on aluminum, Merck).

**General method for synthesis of 9,10-dihydro-9,9-dimethyl-12-phenyl-8H-benzo[*a*]xanthen-11(12H)-one derivative:** In 50 mL round bottom flask, a mixture of  $\beta$ -naphthol (1 mmol), dimidone (1 mmol), benzaldehyde (1 mmol) in [Bmim]Br (1 g) was refluxed for the appropriate time. After the completion of reaction, the reaction mixture was cooled and extracted with diethyl ether ( $3 \times 10$  mL). The combined organic extracts were then washed with brine ( $2 \times 10$  mL) and dried over  $\text{MgSO}_4$ . Then, after evaporation of solvent, it gives pure product without any more purification or if needed the crude products were recrystallized from ethanol (96 %) to afford the pure product. After separation of the product, diethyl ether which left behind in ionic liquid was evaporated (**Scheme-I**).

### Spectral data of some selected compounds

**9,9-Dimethyl-9,10-dihydro-12-(3-nitrophenyl)-8H-benzo[*a*]xanthen-11(12H)-one (4b):**  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.20 (s, 6H), 2.29 (s, 2H), 2.51 (s, 2H), 5.62 (s, 1H), 7.47-7.59 (m, 4H), 7.78-7.92 (m, 4H), 8.02-8.09 (m, 2H).  $^{13}\text{C NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  27.2, 30.5, 37.0, 43.2, 52.1, 110.2, 113.9, 118.2, 122.2, 123.5, 124.2, 125.9, 127.7, 128.8, 129.7, 130.6, 131.2, 133.2, 136.0, 145.4, 146.8, 149.2, 163.8, 196.0. Mass (GC/MS):  $m/z$  399 ( $\text{M}^+$ ). Elemental analysis (%) for  $\text{C}_{25}\text{H}_{21}\text{NO}_4$ : C, 75.17; H, 5.30; N, 3.51. Found: C, 75.26; H, 5.41; N, 3.66.

**9,9-Dimethyl-9,10-dihydro-12-(4-methoxyphenyl)-8H-benzo[*a*]xanthen-11(12H)-one (4e):**  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 1.22 (s, 6H), 1.98 (s, 2H), 2.72 (s, 2H), 3.53 (s, 3H), 5.63 (s, 1H), 6.70 (d, 2H), 7.20-7.52 (m, 6H), 7.68-7.72 (m, 2H).  $^{13}\text{C NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  27.6, 30.7, 33.2, 41.1, 49.9, 54.5, 112.8, 114.2, 116.8, 120.4, 123.2, 125.0, 126.2, 127.8, 128.5, 130.4, 133.6, 136.2, 145.1, 154.2, 164.0, 192.4. Mass (GC/MS):  $m/z$  385 ( $\text{M}^+$ ). Elemental analysis (%) for  $\text{C}_{26}\text{H}_{24}\text{O}_3$ : C, 81.22; H, 6.29; Found: C, 81.28; H, 6.21.

**12-(4-Fluorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[*a*]xanthen-11-one (4k):**  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.24 (s, 6H), 2.18 (s, 2H), 2.78 (s, 2H), 5.75 (s, 1H), 6.30 (m, 2H), 7.27-7.43 (m, 6H), 7.75 (m, 2H).  $^{13}\text{C NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  27.8, 32.9, 37.2, 41.5, 52.4, 112.4, 114.9, 116.4, 118.8, 119.6, 122.8, 125.2, 127.8, 128.8, 129.8, 130.7, 131.5, 134.2, 144.3, 148.8, 165.1, 194.6. Mass (GC/MS):  $m/z$  372 ( $\text{M}^+$ ). Elemental analysis (%) for  $\text{C}_{25}\text{H}_{21}\text{O}_2\text{F}$ : C, 80.62; H, 5.68. Found: C, 80.45; H, 5.82.

## RESULTS AND DISCUSSION

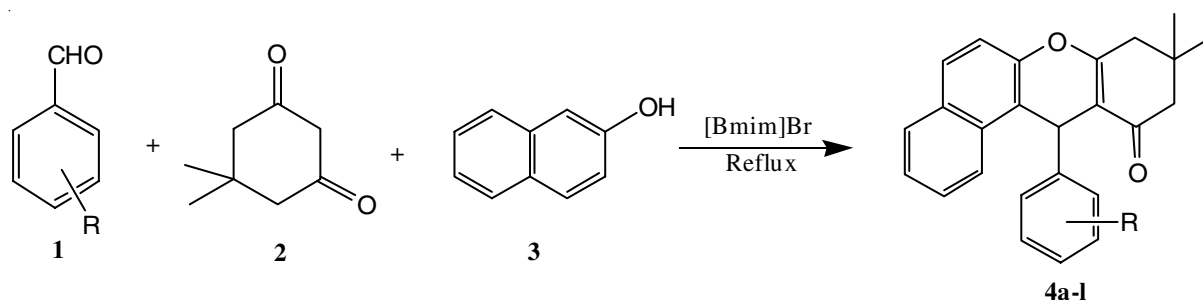
Recently, literature survey showed that solvent free reactions play significant role and have several unique benefits in organic synthesis. Also, ionic liquid mediated reactions have received considerable attention in organic synthesis due to inherent features and environmentally benign nature. These properties of ionic liquids encouraged us to study the synthesis of xanthene derivatives in [Bmim]Br, at solvent free and reflux condition.

In continuation of our work on applications of ionic liquids in organic synthesis, here we developed a green and efficient three-component reaction of  $\beta$ -naphthol (1 mmol), dimidone (1 mmol), substituted aldehyde (1 mmol) in [Bmim]Br (1 g) was taken in 50 mL round bottom flask at reflux conditions. The reaction runs smoothly to give the corresponding products in high yields and the results are summarized in Table-1.

To check the productivity and scope of solvent-free process,  $\beta$ -naphthols were treated with various substituted aromatic aldehydes. The resultant synthesized xanthene derivatives are summarized in Table-1, which shows that all reactions runs very smoothly and the desired substituted xanthene derivatives were produced at excellent yields in short reaction times. As shown in Table-1, electron withdrawing group had no major effect on the reaction time and yields of the products. However, electron donating groups slightly increased reaction time and decreased the yields of corresponding products. The reusability of ionic liquid was tested in the synthesis for xanthene derivatives. For the reaction of  $\beta$ -naphthol with benzaldehyde and dimidone (model reaction), the catalyst was recovered after each run, washed and dried in oven for 30 min before to use and tested for next reaction. The ionic liquid was tested for four runs, which shows no significant loss of the product yields (Table-2).

### Conclusion

An efficient, environmentally benign process for the one-pot synthesis of xanthene derivatives using green[Bmim]Br as a promoter under solvent-free and at reflux conditions. [Bmim]Br as commercially available ionic liquid can be used as a reaction



**Scheme-I:** Solvent free synthesis of xanthene derivatives by [Bmim]Br ionic liquid as a green catalyst

TABLE-1  
SYNTHESIS OF XANTHENE DERIVATIVES BY USING [Bmim]Br AS MEDIUM

Entry	R	Phenol	Product	Time (h) <sup>a</sup>	Yield (%)
1	C <sub>6</sub> H <sub>5</sub>	2-Naphthol	<b>4a</b>	2.0	92
2	3-NO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	2-Naphthol	<b>4b</b>	1.5	96
3	3-CH <sub>3</sub> C <sub>6</sub> H <sub>5</sub>	2-Naphthol	<b>4c</b>	2.5	80
4	3-CH <sub>3</sub> OC <sub>6</sub> H <sub>5</sub>	2-Naphthol	<b>4d</b>	3.0	79
5	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>5</sub>	2-Naphthol	<b>4e</b>	3.5	82
6	3-OH-4-OMe-C <sub>6</sub> H <sub>3</sub>	2-Naphthol	<b>4f</b>	2.5	83
7	4-CH <sub>3</sub> C <sub>6</sub> H <sub>5</sub>	2-Naphthol	<b>4g</b>	3.5	85
8	4-ClC <sub>6</sub> H <sub>5</sub>	2-Naphthol	<b>4h</b>	1.5	93
9	2,4-Cl <sub>2</sub> -C <sub>6</sub> H <sub>3</sub>	2-Naphthol	<b>4i</b>	2.0	89
10	4-NO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	2-Naphthol	<b>4j</b>	2.0	97
11	4-FC <sub>6</sub> H <sub>5</sub>	2-Naphthol	<b>4k</b>	1.5	91
12	4-OHC <sub>6</sub> H <sub>5</sub>	2-Naphthol	<b>4l</b>	2.0	91

<sup>a</sup>Yields are refer to those of pure isolated products.

TABLE-2  
SYNTHESIS OF XANTHENE (MODEL REACTION)  
DERIVATIVES BY USING RECYCLED 1-BUTYL-3-  
METHYLIMIDAZOLIUM BROMIDE

Entry	Cycle	Time (h)	Yield <sup>a</sup> (%)
1	0	5	92
2	1	5	90
3	2	5	86
4	3	5	78

<sup>a</sup>Isolated yields

medium over four runs. Furthermore, excellent yields, short reaction times, reusable ionic liquid, solvent-free condition, easy of work-up and simple procedure, will make the current method an effective and significant addition to the existing procedures for the synthesis of xanthene derivatives.

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