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# [DBN] [$HSO_4$]-Promoted Facile and Green Synthesis of Xanthene Derivatives *via* Knoevenagel Condensation

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## ABSTRACT

A novel [DBN] [$HSO_4$] difunctionalized bronsted acidic ionic liquid-promoted Knoevenagel condensation followed by cyclization protocol has been developed for the first time by a successive reaction of aldehydes, and dimedone to afford xanthene derivatives in high to excellent yields at 80°C temperature. The ionic liquid provided the capability to allow a variability of functional groups, short reaction times, easy workup, high yields, recyclability of the catalyst and solvent-free conditions, thus providing economic and environmental advantages.

**Keywords:** [DBN] [$HSO_4$], Environmentally benign, Xanthenes, Knoevenagel condensation.

## INTRODUCTION

Xanthenes derivatives have been investigated for a wide range of pharmacologic indications such as potent antiviral, antimalarial, analgesic, antimicrobial, anticancer, anti-inflammatory, antioxidant, antiproliferative activity, urease activity, BMP-2 targeted osteogenic agents, trypanothione reductase (TryR) inhibition, selective estrogen receptor modulators selective positive allosteric modulators of the δ-opioid receptor. Additionally, some of the xanthene derivatives are used as antagonists for paralyzing the action of oxalamine, in laser technology, dyes, as bactericides in agriculture, and number of natural products accommodates the xanthenes nucleus. The structures of representative compounds (Figure 1) [1].

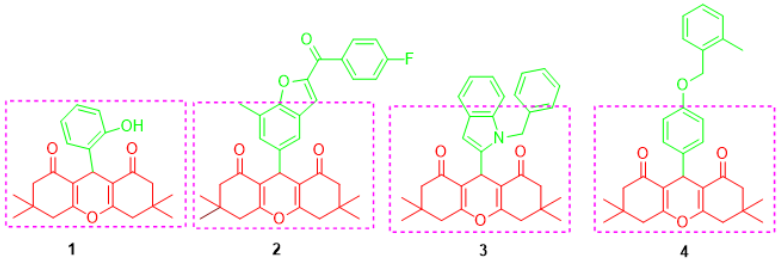



**Figure 1:** Xanthenes incorporated bioactive molecules.

Ionic liquids (ILs) have attracted interest as environmentally benign media for catalysis, synthesis, separation, adjustable physical and chemical properties. ILs includes numerous exclusive properties, such as extensive liquid range, nonvolatility, low toxicity, high thermal stability, noncombustible, excellent solubility, and recyclability. ILs act as "neoteric solvents" for a wide range of industrial and chemical processes. In recent times, ILs has been originating to be valuable as environmental friendly media for countless organic revolutions. Thus, the introduction of a dynamic, inexpensive, mild, and environmental friendly catalyst for significant cyclization reaction superior to analogues of pharmaceutical and biological prominence is in demand.

Thus, the extension of synthetic strategies for the construction of this molecule using an economical, reusable, mild, and nontoxic catalyst is of massive importance from the industrial and academic points of view. Even though various modes have been reported in the literature, these reactions can be accomplished under a variability of tentative conditions, and several improvements have been reported in recent years, such as sulfuric acid or hydrochloric acid, silica sulfuric acid, sulfamic acid, p-dodecylbenzenesulfonic acid, boric acid, pTSA, $NaHSO_4$-$SiO_2$, $TiO_2$-$SO4_2$ molecular iodine, amberlyst cyanuric chloride, core/shell $Fe_3O_4$@GA@isinglass, Feþ3 montmorillonite, $FeCl_3$/[bmim] [BF4], [Hmim]Tfa, $SmCl_3$, trimethylsilyl chloride (TMSCl), acyclic acidic ionic liquids and $InCl_3$/ionic liquid [2].

However, numerous of these testified methods become infected with several disadvantages such as strong acidic conditions, use of hazardous or costly reagents, long reaction times, low yields of products, and sophisticated treatment. Moreover, many of these schemes utilize organic solvents as the reaction medium. Hence, the further innovation toward contemporary reaction with easy isolation of product, reusability of catalyst, perhaps with minimal or no waste is highly attractive. Recently, DBN was widely used as catalysts in different research area. The combination of DBN with cation to give the formation of novel ionic liquids. The large number of functionalized ILs has been considered for diverse purposes. ILs have been deemed as environment friendly substitutes and recyclable for volatile organic solvents attributing to their good-looking thermal and chemical stability, negligible vapour pressure, high ionic conductance and non-flammability. Due to this wide range of applications, they are used as a suitable solvent for wide array of synthetic protocols. The synthesis of this ionic liquid *via* assembling the zwitterionic precursors to these functionalized acidic -SO3H ionic liquid.

As per our investigation, the existential of this work is to begin a rapid and efficient synthetic protocol for obtaining xanthene derivatives under ecofriendly conditions. As an extension of emerging economic and efficient strategy to develop pharmaceutically and biologically significant molecules, herein, we reported synthesis of library of xanthene derivatives promoted by synergistic effect of ionic liquid without any added catalyst in good to excellent yields [3].

## EXPERIMENTAL SECTION

### *Materials and methods*

All of the reagents used were of laboratory grade. Melting points of all of the synthesized analogues were resolute in an open capillary tube and are uncorrected. The progress of the reaction was monitored by thin-layer chromatography on Merck's silica plates, and imagining was accomplished by iodine/ultraviolet light. 1H NMR spectra were recorded with a Bruker AvIII HD-400 MHz spectrometer operating at 400 MHz using DMSO solvent and tetramethylsilane (TMS) as the internal standard and chemical shift in δ ppm. Mass spectra were recorded on a Waters UPLCTQD (ESI-MS and APCI-MS) instrument, and elemental analysis was recorded on the CHNS auto-analyzer (Thermo Fischer EA1112 SERIES). Chemical shifts (δ) are reported in parts per million using TMS as an internal standard. The splitting pattern abbreviations are designed as singlet (s); doublet (d); double doublet (dd); bs (broad singlet), triplet (t); quartet (q); and multiplets (m) [4].

### *Preparation of [DBN] [$HSO_4$]*

General Procedure for the Synthesis of [DBN] [$HSO_4$] is given in supporting information.

### *General procedure for synthesis of xanthene derivatives*

A mixture of aldehyde (1a) (1 mmol) and dimedone (1 mmol) in [DBN] [$HSO_4$] 20 mol% was stirred at 80$^{o}$C; the evolution of reaction was

supervised by thin-layer chromatography [ethyl acetate/n-hexane (3:7)] as a solvent after a stirring reaction mixture was cooled for 15 min and a poured on crushed ice. Thus, acquired solid was filtered, dried, and purified by crystallization using ethanol as a solvent. The synthesis compound is confirmed by MP, $^{1}$H NMR and $^{13}$C NMR spectra [5].

***3,3,6,6-tetramethyl-9-phenyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3a)***

The compound 3a was synthesized from condensation reaction 1a and 2 as white solid;

Mp: 204-205$^{o}$C; Yield: 93%; $^{1}$H NMR (500 MHz, cdcl$_3$) δ 11.94 (s, 1H), 7.28 (t, *J*=7.6 Hz, 2H), 7.22-7.10 (m, 3H), 5.63 (d, *J*=60.1 Hz, 1H), 2.66-2.12 (m, 9H), 1.16 (dd, *J*=64.4, 29.0 Hz, 12H); $^{13}$C NMR (101 MHz, cdcl$_3$) δ 196.66, 165.08, 144.17, 136.06, 130.50, 128.52, 120.85, 51.42, 43.24, 33.44, 32.35, 30.57 and 30.34 [6].

***3,3,6,6-tetramethyl-9-(m-tolyl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3b)***

The compound 3b was synthesized from condensation reaction 1b and 2 as white solid;

Mp: 207-208$^{o}$C; Yield: 89%; $^{1}$H NMR (400 MHz, cdcl$_3$) δ 7.10 (s, 1H), 7.05-6.99 (m, 2H), 6.86 (d, *J*=6.7 Hz, 1H), 4.68 (s, 1H), 2.44 (s, 4H), 2.24 (s, 3H), 2.14 (t, *J*=13.9 Hz, 4H), 1.05 (s, 6H), 0.95 (s, 6H); $^{13}$C NMR (101 MHz, cdcl$_3$) δ 196.31, 162.23, 144.01, 137.26, 129.38, 127.84, 127.13, 125.21, 115.67, 50.76, 40.84, 32.17, 31.68, 29.24, 27.30 and 21.48 [7].

***3,3,6,6-tetramethyl-9-(p-tolyl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3c)***

The compound 3c was synthesized from condensation reaction 1c and 2 as yellow solid;

Mp: 232-233$^{o}$C; Yield: 92%; $^{1}$H NMR (400 MHz, cdcl$_3$) δ 7.15 (d, *J*=7.8 Hz, 2H), 6.99 (d, *J*=7.6 Hz, 2H), 4.69 (s, 1H), 2.44 (s, 4H), 2.21 (s, 3H), 2.18-2.08 (m, 4H), 1.07 (s, 6H), 0.96 (s, 6H); $^{13}$C NMR (101 MHz, cdcl$_3$) δ 197.37, 163.18, 142.22, 136.62, 129.72, 129.21, 116.68, 78.34, 77.86, 51.76, 41.82, 33.14, 32.41, 30.24, 28.32 and 22.03 [8].

***9-(3-methoxyphenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3d)***

The compound 3d was synthesized from condensation reaction 1d and 2 as yellow solid;

Mp: 162-163$^{o}$C; Yield: 88%; $^{1}$H NMR (400 MHz, cdcl$_3$) δ 7.04 (t, J=8.3 Hz, 1H), 6.80 (d, J=6.8 Hz, 2H), 6.57 (d, J=7.2 Hz, 1H), 4.68 (s, 1H), 3.67 (s, 3H), 2.41 (s, 4H), 2.12 (q, J=16.4 Hz, 4H), 1.02 (s, 6H), 0.92 (s, 6H); $^{13}$C NMR (101 MHz, cdcl$_3$) δ 197.27, 163.34, 160.27, 146.69, 129.78, 121.73, 116.43, 115.27, 112.79, 56.02, 51.71, 41.76, 33.10, 32.74, 30.20, 28.30 [9].

***9-(4-methoxyphenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3e)***

The compound 3e was synthesized from condensation reaction 1e and 2 as yellow solid;

Mp: 250-251$^{o}$C; Yield: 93%; $^{1}$H NMR (400 MHz, cdcl$_3$) δ 7.24-7.10 (m, 2H), 6.71 (dd, J=5.9, 2.7 Hz, 2H), 4.66 (s, 1H), 3.69 (d, J=4.8 Hz, 3H), 2.43 (s, 4H), 2.24 – 2.09 (m, 4H), 1.06 (s, 6H), 0.95 (s, 6H); $^{13}$C NMR (101 MHz, cdcl$_3$) δ 197.41, 163.06, 158.91, 137.48, 130.26, 116.73, 114.42, 56.06, 51.75, 41.82, 33.15, 31.93, 30.24 and 28.30.

***9-(3,4-dimethoxyphenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3f)***

The compound 3f was synthesized from condensation reaction 1f and 2 as yellow solid;

Mp: 201-202$^{o}$C; Yield: 90%; $^{1}$H NMR (400 MHz, cdcl$_3$) δ 6.89 (s, 1H), 6.72 (td, J=8.3, 4.4 Hz, 2H), 4.69 (s, 1H), 3.84 (d, J=1.7 Hz, 3H), 3.78 (d, J=1.8 Hz, 3H), 2.45 (s, 4H), 2.28 – 2.10 (m, 4H), 1.09 (s, 6H), 0.99 (s, 6H); $^{13}$C NMR (101 MHz, cdcl$_3$) δ191.86, 169.54, 155.65, 153.88, 142.69, 133.63, 128.25, 127.62, 121.81, 56.49, 55.62, 51.17, 43.14, 33.88, 31.97, 30.30 and 28.14 [10].

***3,3,6,6-tetramethyl-9-(3-nitrophenyl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3g)***

The compound 3g was synthesized from condensation reaction 1g and 2 as red solid;

Mp: 170-171$^{o}$C; Yield: 84%; $^{1}$H NMR (400 MHz, cdcl$_3$) δ 8.07 –7.91 (m, 2H), 7.79 (d, J=6.7 Hz, 1H), 7.40 (d, J=7.8 Hz, 1H), 4.82 (s, 1H), 2.50 (s, 4H), 2.20 (q, J=16.4 Hz, 4H), 1.10 (s, 6H), 0.98 (s, 6H), $^{13}$C NMR (101 MHz, cdcl$_3$) δ 198.43, 168.97, 148.57, 142.41, 132.54, 129.55, 128.29, 126.83, 121.69, 52.95, 42.61, 33.98, 32.26, 30.52 and 28.15.

***9-(3-iodophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3h)***

The compound 3h was synthesized from condensation reaction 1h and 2 as pale yellow solid;

Mp: 275-276°C; Yield: 85%; $^{1}$H NMR (400 MHz, cdcl$_3$) δ 7.54 (s, 1H), 7.42 (d, J=7.7 Hz, 1H), 7.32 (d, J=7.8 Hz, 1H), 6.95 (t, J=7.8 Hz, 1H), 4.66 (s, 1H), 2.46 (s, 4H), 2.30 – 2.10 (m, 4H), 1.09 (s, 6H), 1.00 (s, 6H); $^{13}$C NMR (101 MHz, cdcl$_3$) δ 192.02, 166.84, 141.47, 133.58, 130.03, 128.62, 128.37, 124.88, 113.50, 51.46, 42.60, 34.02, 31.97, 30.21 and 28.43 [11].

***9-(4-bromophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3i)***

The compound 3i was synthesized from condensation reaction 1i and 2 as red solid;

Mp: 259-260°C; Yield: 87%; $^{1}$H NMR (400 MHz, cdcl$_3$) δ 7.34 (d, J=6.8 Hz, 2H), 7.18 (d, J=6.8 Hz, 2H), 4.70 (s, 1H), 2.47 (s, 4H), 2.21 (q, J=16.5 Hz, 4H), 1.11 (s, 6H), 0.99 (s, 6H). $^{13}$C NMR (101 MHz, cdcl$_3$) δ 197.27, 163.42, 144.19, 132.10, 131.12, 121.19, 116.15, 78.33, 78.01, 77.69, 51.66, 41.82, 33.16, 32.53, 30.22 and 28.27.

***9-(4-chlorophenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3j)***

The compound 3j was synthesized from condensation reaction 1 and 2j as yellow solid;

Mp: 234-235°C; Yield: 91%; $^{1}$H NMR (400 MHz, cdcl$_3$) δ 7.25 (d, J=8.5 Hz, 2H), 7.22 – 7.15 (m, 2H), 4.72 (s, 1H), 2.48 (s, 4H), 2.20 (q, J=16.4 Hz, 4H), 1.11 (s, 6H), 0.99 (s, 6H). $^{13}$C NMR (101 MHz, cdcl$_3$) δ 197.29, 163.45, 143.71, 132.94, 130.75, 129.14, 116.19, 78.38, 78.06, 77.74, 51.67, 41.80, 33.15, 32.44, 30.22 and 28.25.

***9-(4-hydroxyphenyl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3k)***

The compound 3k was synthesized from condensation reaction 1k and 2 as red solid;

Mp: 244-245°C; Yield: 85%; $^{1}$H NMR (400 MHz, cdcl$_3$) δ 7.32 (s, 1H), 7.07 (d, J=7.9 Hz, 2H), 6.55 (d, J=7.9 Hz, 2H), 4.67 (s, 1H), 2.47 (s, 4H), 2.22 (q, J=16.4 Hz, 4H), 1.09 (s, 6H), 1.00 (s, 6H). $^{13}$C NMR (101 MHz, cdcl$_3$) δ 198.31, 163.46, 155.71, 136.48, 130.30, 116.86, 116.24, 51.73, 41.82, 33.24, 31.94, 30.12 and 28.36 [12].

***9-cyclohexyl-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (3l)***

The compound 3l was synthesized from condensation reaction 1l and 2 as white solid;

Mp: 178-179°C; Yield: 85%; $^{1}$H NMR (400 MHz, cdcl$_3$) δ 7.68 (s, 2H), 5.47 (s, 1H), 3.32 (s, 2H), 2.51 (s, 4H), 2.24 (s, 4H), 1.23 (s, 1H), 1.04 (d, J=18.0 Hz, 12H); $^{13}$C NMR (101 MHz, cdcl$_3$) δ 194.31, 166.55, 112.78, 51.44, 41.72, 35.52, 34.02, 32.26, 30.21, 28.43, 26.94, 25.53, 24.22, 24.16 and 24.08.

## RESULTS AND DISCUSSION

### *Chemistry*

To achieve optimized conditions protocol based on the reaction of benzaldehyde (1a) (1 mmol), and dimedone (2) (1 mmol) as model reaction, we checked temperatures and solvents, catalyst loading and the results of this study (Figure 2).


**Figure 2:** Model reaction.

Firstly, the model reaction was performed using 20 mol% of catalyst under reflux condition in different solvents. The model reaction carried out in MeOH and EtOH (Table 1, entry 1, and 2) was completed in 45 min with the yield of 62 and 55%, respectively. Whereas, in tert-BuOH (Table 1, entry 3), a better yield (68%) was obtained in 45 min. In $H_2O$ and THF, decreased yields (40 and 42%) of the product 3a

were obtained (Table 1, entries 4-5). Conducting the reaction in Toluene, $CH_3CN$ and DMF (Table 1, entries 6-8), does not improve the yield of the product. However, when the model reaction was carried out under a solvent-free condition with 20 mol% [DBN] [$HSO_4$], a significant increase in the yield was observed (Table 1). Therefore it proved that the solvent-free condition is best suited for the transformation. Therefore, it can be thought that [DBN] [$HSO_4$] is green and a superior solvent and catalyst compared to the other shown in Table 1.

| Entry | Solvent | Temp (°C) | Yield[b] (%) |
|---|---|---|---|
| 1 | MeOH | Reflux | 62 |
| 2 | EtOH | Reflux | 55 |
| 3 | Tert-BuOH | Reflux | 68 |
| 4 | $H_2O$ | Reflux | 40 |
| 5 | THF | Reflux | 42 |
| 6 | Toluene | Reflux | 48 |
| 7 | DMF | Reflux | 44 |
| 8 | $CH_3CN$ | Reflux | 56 |
| 9 | Solvent-free | 80 | 95 |

**Table 1:** [a] Reaction conditions: aldehyde 1a (1 mmol), dimedone 2 (1 mmol), [DBN] [$HSO_4$] (20 mol%) stirred at 80ºC. bIsolated yields. Bold values are for highlighting the good result.

In the next step we examine the efficiency of ionic liquid [DBN] [$HSO_4$] for the synthesis of xanthene derivatives. When change in concentration of [DBN] [$HSO_4$] on model reaction suggest that much more effect on yield of final product. The catalyst loading study suggest that 20 mol% of [DBN] [$HSO_4$] catalyst is best for the synthesis of final product in 95% yields (Table 2).

| Entry | Catalyst (mol%) | Time (min) | Yield[b] (%) |
|---|---|---|---|
| 1 | 5 | 90 | 62 |
| 2 | 10 | 70 | 72 |
| 3 | 15 | 60 | 82 |
| 4 | 20 | 45 | 95 |
| 5 | 25 | 45 | 95 |

**Table 2:** Reaction conditions: 1a (2 mmol), 2 (1 mmol) and [DBN] [$HSO_4$] at 80$^o$C. [b] Isolated yield.

Furthermore, we also studied the effect of temperature on the model reaction at different temperatures. According to this study better results of the desired product when reaction carried at 80$^o$C (Table 3 and entry 3). Detailed reaction conditions are shown in Table 3.

| Entry | Temp $^{o}$C | Time [b] (min) | Yield [c] |
|---|---|---|---|
| 1 | 60 | 120 | 68 |
| 2 | 70 | 90 | 85 |
| 3 | 80 | 45 | 95 |
| 4 | 90 | 45 | 95 |

**Table 3:** Reaction conditions: 1[a] (2 mmol) and 2 (1 mmol) in the presence of [DBN] [$HSO_4$] 20 mol% at 80$^{o}$C. [b] Reaction progress monitored by TLC [c] Isolated yield.

An extremely superlative method to economic and greener preparation is recovery and recyclability of a ionic liquid. Therefore we have to check the efficiency of catalyst after recover from the reaction media during the work-up procedure. When reaction is completed, then reaction mass was pour on ice cold water to obtained fine crystal of final xanthene derivatives. In the last step removal $H_2O$ from filtrate using reduced pressure to give viscous liquid, which is on cooling to give pure ionic liquid. Recovered catalysts were reused for next four repeated cycles without considerable loss in catalytic efficiency (Table 4).

| Entry | Run | Time [a] (min) | Yield [b] |
|---|---|---|---|
| 1 | fresh | 45 | 95 |
| 2 | 2 | 45 | 95 |
| 3 | 3 | 45 | 85 |
| 4 | 4 | 45 | 82 |
| 5 | 5 | 45 | 80 |

**Table 4:** Elemental analysis and spectral data. Reaction progress monitored by TLC. [b] isolated yield.

***Comparison of [DBN] [$HSO_4$] (IL) catalyst with previous reported protocol***

We have proved the comparison study of the [DBN] [$HSO_4$] with other reported catalysts (Table 5).

| Entry | Catalyst | Amount of catalyst | Time (min) | Yield (%) | solvent/Condition | Ref. |
|---|---|---|---|---|---|---|
| 1 | $FeCl_3.6H_2O$ (10 mol%) | 10 mol% | 6 h | 92 | [bmim] [$BF_4$]/80°C | 50 |
| 2 | SBSSA | 30 mg | 10 h | 98 | EtOH/reflux | 51 |
| 3 | $\beta$-CD (1 mmol) | 1 mmol | 10 h | 96 | EtOH/60°C | 52 |
| 4 | Cellulose sulfonic acid | 50 mg | 5 h | 94 | Solvent free/110°C | 53 |
| 5 | Amberlyst-15 | 200 mg | 5 h | 92 | $CH_3CN$/Reflux | 54 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 6 | $Fe^{3+}$montmorillonite | 85 mg | 6 h | 94 | EtOH/reflux | 55 |
| 7 | [bmim] [$HSO_4$] (42 mol%) | 42 mol% | 3 h | 85 | Solvent free/100°C | 56 |
| 8 | ZnO-$CH_3COCl$ | 30 mol% | 5 h | 86 | $CH_3CN$/reflux | 57 |
| 9 | $Zr(DP)_2$ | 10 mol% | 24 h | 98 | EtOH/80°C | 58 |
| 10 | [DBN] [$HSO_4$] | 20 mol% | 45 min | 95 | - | Present work |

**Table 5:** Comparative catalytic performance of the [DBN] [$HSO_4$] (IL) with other previously reported catalysts.

Preparation of xanthene derivative. The comparison results proved that [DBN] [$HSO_4$] is better catalyst in terms of excellent yield and reusability with less reaction time (Table 5, entry 10). In conclusion [DBN] [$HSO_4$] is found to be a facile and environmentally benign protocol for the synthesis of xanthene derivatives [13].

The structure of the titled product 3b was confirmed by 1H NMR and 13C NMR. In 1H NMR spectra of compound 3b exhibit two singlet bands for two methyl groups at δ 0.95 and 1.05 ppm. The -CH2-C=O protons observed at δ 2.44 ppm and $CH_2$ proton are observed at δ 2.20 ppm suggest that dimedone ring in the final compound. The aliphatic -CH proton was shown at δ 4.68 ppm suggests that formation of cyclic ring. In the 13C NMR spectrum of compound 3b, distinct -C=O carbonyl group observed at δ 196.31 ppm. The CH, $CH_2$ and $CH_3$ peak observed at δ 50.76, 40.84, 32.17, 31.68, 29.24 and 27.30 ppm confirmed that formation of compound 3b (Figure 3 and Table 6).

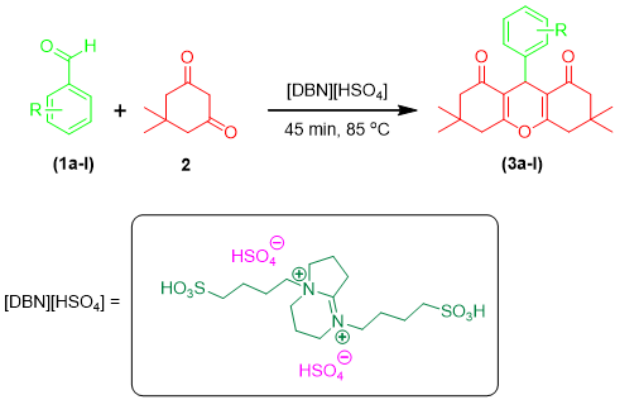
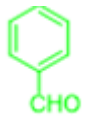
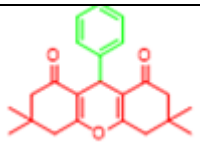
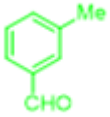
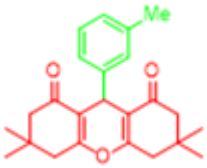
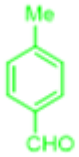
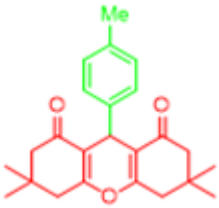
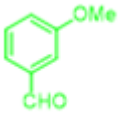
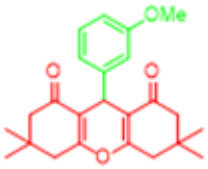
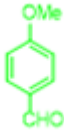
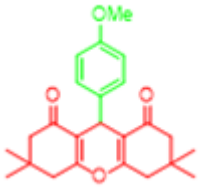
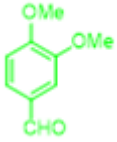
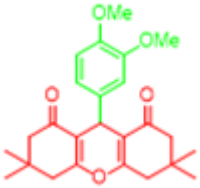
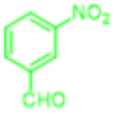
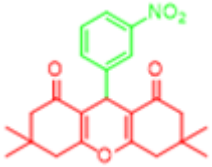
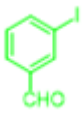
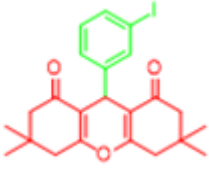



**Figure 3:** Synthesis of Xanthene derivatives (3a-l).

| Entry | Aryl aldehyde | Xanthene | Time(min) | Yield %[b] | Mp (°C)[C] | |
|---|---|---|---|---|---|---|
| | | | | | Observed | Reported |
| 1 |  |  | 45 | 95 | 204-205 | 203-205 |
| 2 |  |  | 45 | 89 | 207-208 | 206-208 |
| 3 |  |  | 45 | 92 | 232-233 | 232-234 |
| 4 |  |  | 45 | 88 | 162-163 | 162-164 |
| 5 |  |  | 45 | 93 | 250-251 | 252-254 |
| 6 |  |  | 45 | 90 | 201-202 | 202-204 |
| 7 |  |  | 45 | 84 | 170-170 | 169-171 |
| 8 |  |  | 45 | 85 | 275-276 | 276-278 |

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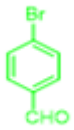
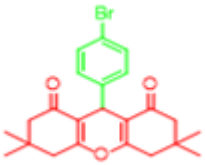
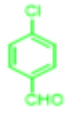
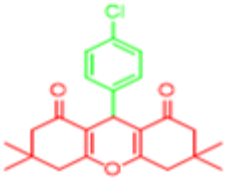
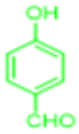
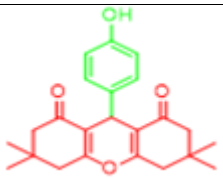
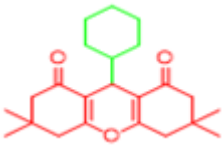
| 9 |  |  | 45 | 87 | 259-260 | 260-263 |
| 10 |  |  | 45 | 91 | 234-235 | 235-236 |
| 11 |  |  | 45 | 85 | 244-245 | 245-247 |
| 12 |  |  | 45 | 85 | 178-179 | 178-180 |

**Table 6**: [DBN] [$HSO_4$] catalyzed synthesis of xanthene derivatives.

[a]Reaction conditions: Aldehydes (1a-l) (1 mmol) and dimedone (2) (1 mmol) in [DBN] [$HSO_4$] 20 mol% stirred at 80ºC; bisolated yields, cmelting points are in good contact with those reported in the literature.

In conclusion, the effectiveness and better reaction time for the model reaction was observed at 80$^oC$ by using 20 mol% of [DBN] [$HSO_4$] as a catalyst. With excellent reaction conditions in hand, the adaptableness of this approach was employing the synthesis xanthene analogues (3a-l). Various substituents on aryl aldehyde including methoxy, methyl, nitro, halogen (-Cl,-Br, -I), and hydroxyl groups were used. Synthesis of compounds (3a-l) using optimized reactions conditions and results are shown in Figure 3 and Table 6. The result clearly suggests that the condensation reactions using [DBN] [$HSO_4$] catalyst shows excellent and remarkable performance irrespective to the electron withdrawing/donating groups present on the aryl aldehydes and hence this method is facile, efficient and general for the synthesis of xanthene analogues. All the synthesized final compounds 3a-l was well characterized by 1H NMR and 13C NMR spectroscopic techniques [14].

***Plausible reaction mechanism***

Reaction mechanism cycle for the preparation of xanthene analogues employing [DBN] [$HSO_4$] is catalyst. In first step benzaldehyde activated by [DBN] [$HSO_4$] results formation intermediate I. In next step [DBN] [$HSO_4$] reacts dimedone to give enol product II. In the third step intermediate I react with II afforded addition product III [15]. Further formation of alkylation product V from reaction of II and III to *via* removal of $H_2O$ molecule. In the next step intramolecular cyclization of V to give VI. In the last step elimination of $H_2O$ molecule using [DBN] [$HSO_4$] to results formation of titled xanthene analogues 3a and regeneration of catalyst. Details reaction mechanism is presented in Figure 4.

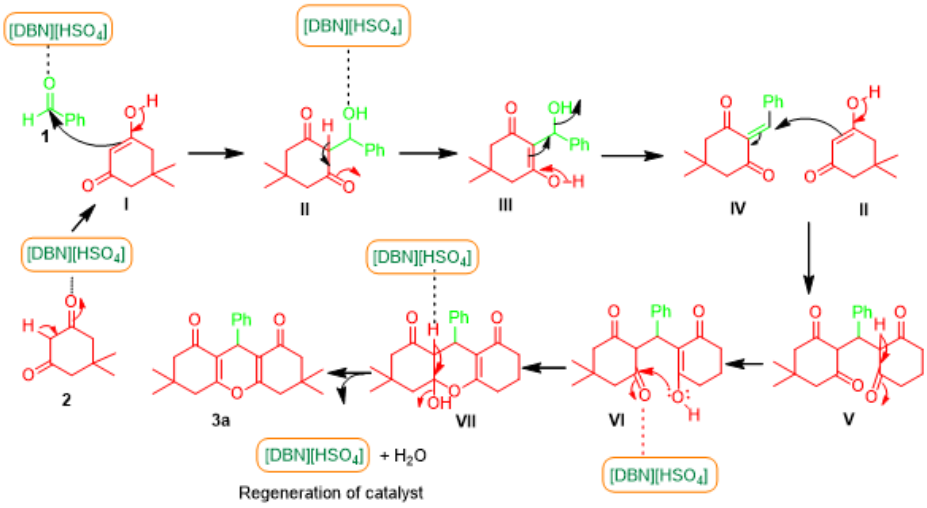



**Figure 4:** Reaction mechanism cycle for the preparation of compounds 3a.

## CONCLUSION

In conclusion, an environmentally and highly efficient green methodology has been established for the synthesis of functionalized xanthene derivatives using an inexpensive and recoverable [DBN] [$HSO_4$] catalytic solvent-free in 45 min. This, to the best of our knowledge, has no examples. This reaction scheme exposes a number of advantages, such as uniqueness, high atom efficiency, mild reaction conditions, clean reaction profiles, easy workup procedure and Eco friendliness. Furthermore, the prevention of hazardous organic solvents during the entire procedure (synthesis, ionic liquid preparation, and workup procedure) makes it a convenient and attractive method for the synthesis of these important compounds.

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