

[Et₃NH][HSO₄] catalyzed one-pot synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes under solvent-free conditions

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ABSTRACT

A simple and environmentally benign procedure for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes by a one-pot condensation of 2-naphthol with aromatic aldehyde in the presence of [Et₃NH][HSO₄] as an acidic ionic liquid catalyst under solvent-free conditions has been developed. The reaction work-up is very simple and the catalyst can be easily separated from the reaction mixture and reused several times in subsequent reactions.

Keywords: 14-Aryl-14H-dibenzo[a,j]xanthenes, [Et₃NH][HSO₄], Solvent-free conditions, 2-Naphthol, Aldehyde.

1. Introduction

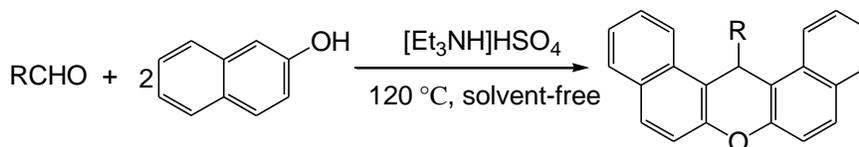
The synthesis of xanthenes, especially benzoxanthenes has attracted great interest in recent years because of their wide range of biological and pharmaceutical properties such as antibacterial [1], antiviral [2] and anti-inflammatory [3] activities. Furthermore, these heterocyclic compounds can be used as dyes [4], pH-sensitive fluorescent materials for visualization of biomolecules [5] and in laser technology [6]. Recently, the synthesis of benzoxanthenes has been achieved by the reaction of aldehydes with 2-naphthol by dehydration in the presence of a catalyst, such as AcOH-H₂SO₄ [7], P₂O₅ or InCl₃ [8], BSA or o-TSA [9], silica gel-supported polyphosphoric acid [10], molecular iodine [11], silica sulfuric acid [12], cellulose sulfuric acid [13], succinimide-N-sulfonic acid [14], methanesulfonic acid [15], Yb(OTf)₃ [16], In(OTf)₃ [17], K₅CoW₁₂O₄₀·3H₂O [18], NH₄H₂PO₄/SiO₂ [19], P₂O₅/Al₂O₃ [20], poly(4-vinylpyridinium)hydrogen sulfate [21], zinc oxide nanoparticle [22], sulfonic acid functionalized silica [23], polyvinylpyrrolidone-supported boron trifluoride [24], sulfonyl-functionalized ionic liquids [25-29], tungsto-divanado-phosphoric acid [30], sulfonated single-walled carbon nanotubes [31] and N-sulfonic acid poly(4-vinylpyridinium) chloride [32]. However, some of these methods suffer from certain disadvantages such as long

reaction time, use of toxic catalysts and organic solvents, the requirement of special apparatus, and difficulty in recovery and reusability of the catalysts. Thus, the development of clean, efficient, and facile processes to synthesize xanthene derivatives is of current interest. Acidic ionic liquids have emerged as promising acid catalysts in replacement of conventional homogeneous and heterogeneous acidic catalysts because they are flexible, nonvolatile, noncorrosive, low toxicity, immiscible with many organic solvents, and reusable [33]. Although sulfonyl-functionalized ionic liquids show satisfactory behavior [25-29], they are relatively expensive, which hinders their industrial applications. We now report a clean and efficient method for the synthesis of 14-aryl-14H-dibenzo[a,j] xanthenes by a one-pot condensation reaction of 2-naphthol with aromatic aldehydes using easily available and cheap ionic liquid [Et₃NH][HSO₄] as a acid catalyst under solvent-free conditions (Scheme 1).

2. Experimental

Melting points were determined on a X-4 micro melting point apparatus and were uncorrected. FT-IR spectra were obtained on a Nexus 470 spectrophotometer. ¹H NMR spectra were recorded on a Bruker Avance III 400 with TMS as internal standard. All chemicals were commercially available and were used as received. All of the products are known, and physical data were found to be identical with those reported in the literature.

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Scheme 1. $[\text{Et}_3\text{NH}][\text{HSO}_4]$ catalyzed synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes.

2.1. Preparation of $[\text{Et}_3\text{NH}][\text{HSO}_4]$

Sulfuric acid (19.6 g, 0.2 mol) 98% solution in water was dropped into the triethylamine (20.2 g, 0.2 mol) under stirring at 60 °C in 1 hour. After the addition, the reaction mixture was stirred for an additional period of 1 hour at 70 °C to ensure the reaction had proceeded to completion. Then, the trace of water was removed by heating the residue at 80 °C in high vacuum until the weight of the residue remained constant [34].

2.2. Typical procedure for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes

A mixture of 2-naphthol (20 mmol), benzaldehyde (10 mmol) and $[\text{Et}_3\text{NH}][\text{HSO}_4]$ (1 mmol) was stirred at 120 °C for the appropriate time (monitored by TLC). After completion of the reaction, 95% ethanol (10 mL) was added and the mixture was triturated. The precipitated product was filtered and purified by crystallization from a mixture of chloroform and methanol to afford pure product. The filtrate containing the ionic liquid was evaporated under reduced pressure and the resulting catalyst was reused directly for the next run. The reactions using the recycled catalyst were conducted in a similar manner.

Selected spectral data

14-Phenyl-14H-dibenzo[a,j]xanthene (Table 3, entry 1): ^1H NMR (400 MHz, CDCl_3 , ppm) δ : 6.49 (s, 1H), 6.97-7.16 (m, 3H), 7.39-7.59 (m, 8H), 7.78-7.83 (m, 4H), 8.39 (d, $J = 8.4$ Hz, 2H). IR (KBr, cm^{-1}): 3070, 3021, 2886, 1589, 1511, 1456, 1401, 1248, 1144, 1078, 961, 804, 743, 700.

14-(4-Fluorophenyl)-14H-dibenzo[a,j] xanthene (Table 3, entry 7): ^1H NMR (400 MHz, CDCl_3 , ppm) δ : 6.48 (s, 1H), 6.80-6.84 (m, 2H), 7.40-7.61 (m, 8H), 7.79-7.85 (m, 4H), 8.34 (d, $J = 8.4$ Hz, 2H). IR (KBr, cm^{-1}): 3069, 3024, 2928, 1594, 1503, 1458, 1430, 1398, 1241, 1155, 1091, 812, 743.

14-(3-Methoxyphenyl)-14H-dibenzo[a,j]xanthene (Table 3, entry 9): ^1H NMR (400 MHz, CDCl_3 , ppm) δ : 3.63 (s, 3H), 6.46 (s, 1H), 6.51-6.54 (m, 1H), 7.03-7.17 (m, 3H), 7.39-7.60 (m, 6H), 7.77-7.83 (m, 4H), 8.40 (d, $J = 8.8$ Hz, 2H) ppm. IR (KBr, cm^{-1}): 3068, 3015, 2933, 1587, 1483, 1454, 1431, 1400, 1247, 1137, 1049, 808, 743.

3. Results and Discussion

In the initial experiments, the effect of reaction temperature was examined using the reaction of 2-naphthol and benzaldehyde in the presence of 10 mol% of $[\text{Et}_3\text{NH}][\text{HSO}_4]$ under solvent-free conditions. As can be seen from Table 1, the optimum temperature was at 120 °C. The effect of the amount of catalyst was also examined. It was found that the use of 10 mol% of $[\text{Et}_3\text{NH}][\text{HSO}_4]$ was sufficient to progress the reaction and an increase in the amount of catalyst did not affect the reaction times and yields. After optimizing the temperature and the amount of catalyst, the reaction was carried out in solvents like tetrahydrofuran, acetonitrile, chloroform, benzene, ethanol and water. It was observed that, reactions in these solvents took more time and also the yields were low in comparison with solvent-free conditions.

From the viewpoint of green chemistry, efficient recovery and reuse of the catalyst are highly desirable. The reusability of the $[\text{Et}_3\text{NH}][\text{HSO}_4]$ catalyst was also examined. After completion of the reaction, 95% ethanol was added and the mixture was triturated. The product was separated by sucking filtration, the filtrate containing catalyst was evaporated to dryness under reduced pressure and the resulting catalyst was reused directly for the next run. As shown in Table 2, the recovered catalyst can be reused at least five additional times in subsequent reactions without any loss in product yield.

Next, we examined the scope of the reaction by condensing 2-naphthol with various aromatic aldehydes at 120°C using 10 mol% of $[\text{Et}_3\text{NH}][\text{HSO}_4]$ as a catalyst; results are summarized in Table 3. Aromatic aldehydes reacted with 2-naphthol to produce the corresponding aryl-14H-dibenzo[a,j] xanthenes in moderate to good yields. From this table, it is clear that, aldehydes containing electron-withdrawing substituents such as NO_2 , Cl, F, Br (Table 3, entries 2-8) react faster than aldehydes bearing electron-donating substituent like OCH_3 (Table 3, entry 9).

Based on the reported pathway in literature [12,13,23] and our results, the suggested mechanism of the $[\text{Et}_3\text{NH}][\text{HSO}_4]$ catalyzed transformation is shown in Scheme 2.

Table 1. Effect of different reaction conditions on xanthenes yield.^a

Entry	Solvent	Temperature (°C)	[Et ₃ NH][HSO ₄] (mol%)	Time (min)	Yield ^b (%)
1	THF	Reflux	10	60	36
2	CH ₃ CN	Reflux	10	60	3
3	CHCl ₃	Reflux	10	60	18
4	C ₆ H ₆	Reflux	10	60	51
5	EtOH	Reflux	10	60	53
6	H ₂ O	Reflux	10	60	13
7	Solvent-free	100	10	60	65
8	Solvent-free	110	10	60	69
9	Solvent-free	120	10	60	77
10	Solvent-free	120	0	60	0 [10]
11	Solvent-free	120	1	60	43
12	Solvent-free	120	5	60	74
13	Solvent-free	120	20	60	77
14	Solvent-free	130	10	60	78

^a Reaction conditions: 2-naphthol (20 mmol), benzaldehyde (10 mmol).^b Isolated yields.

Acid-base interaction between [Et₃NH][HSO₄] and aldehyde produces protonated aldehyde **1** as a reactive intermediate. The reaction of 2-naphthol with **1** forms oxonium ion **2**, aromatization-dehydration of which intermediate gives carbocation **3**. 2-Naphthol reacts with **3** to give oxonium species **4**, which undergoes cyclization-dehydration to afford the 14-aryl-14H-dibenzo[a,j]xanthenes **5**.

Our results are compared with results obtained by some other procedures for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes. Table 4 clearly shows that the presented method, using [Et₃NH][HSO₄] as the catalyst, is simple, efficient and comparable with many catalytic systems for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes derivatives.

4. Conclusions

In conclusion, we have developed a clean and efficient method for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes by the reaction of aromatic aldehydes with 2-naphthol under solvent-free

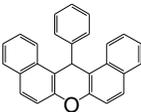
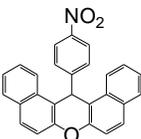
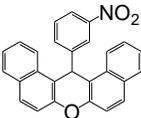
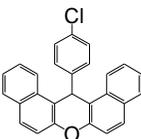
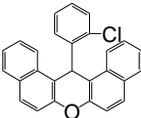
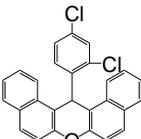
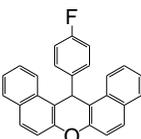
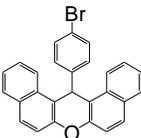
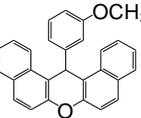
conditions using [Et₃NH][HSO₄] as an acidic ionic liquid catalyst. The operational simplicity, environmentally-benign reaction conditions, together with the use of non-toxic, inexpensive, and recyclable catalyst are remarkable features of the procedure.

Table 2. Reusability of [Et₃NH][HSO₄].^a

Run	Time (min)	Yield (%) ^b
1	60	77
2	60	77
3	60	77
4	60	78
5	60	77
6	60	75

^a Reaction conditions: 2-naphthol (20 mmol), benzaldehyde (10 mmol), [Et₃NH][HSO₄] (1 mmol) at 120 °C under solvent-free conditions.^b Isolated yields.

Table 3. Synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes with [Et₃NH][HSO₄].^a

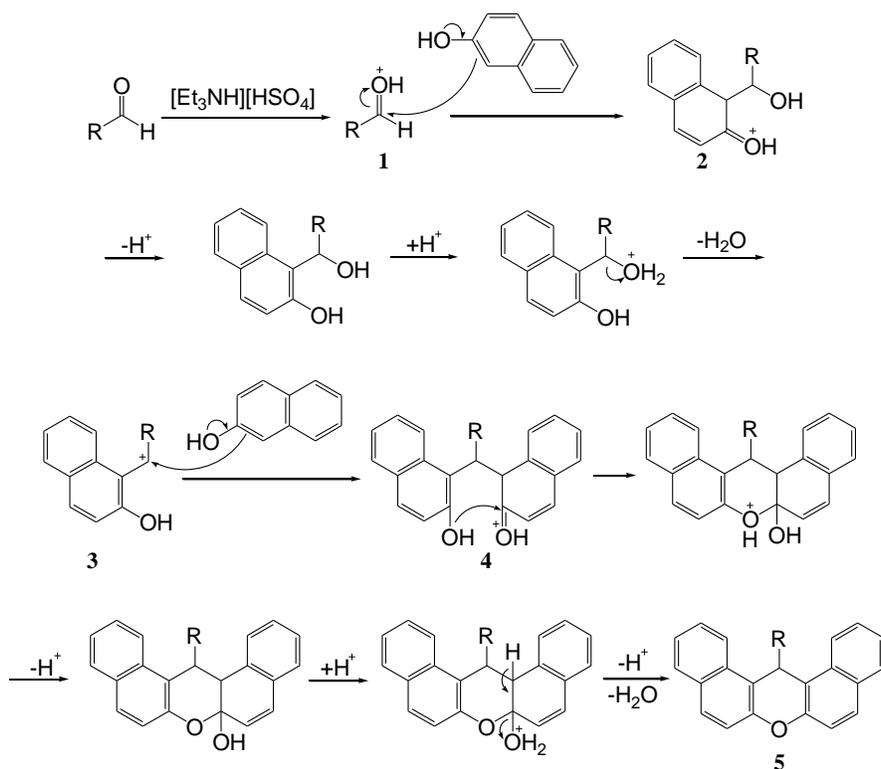
Entry	R	Product	Time (min)	Yield (%) ^b	m.p. (°C)	
					Found	Reported [Ref]
1	C ₆ H ₅		60	77	186-188	185-187 [9]
2	4-NO ₂ C ₆ H ₄		30	93	312-313	310-312 [22]
3	3-NO ₂ C ₆ H ₄		40	81	226-228	224-226 [11]
4	4-ClC ₆ H ₄		50	78	288-289	289-291 [15]
5	2-ClC ₆ H ₄		50	88	213-214	214-216 [21]
6	2,4-Cl ₂ C ₆ H ₃		45	85	252-253	253-255 [18]
7	4-FC ₆ H ₄		50	80	242-243	240-242 [22]
8	4-BrC ₆ H ₄		20	86	295-296	295-296 [8]
9	3-CH ₃ OC ₆ H ₄		120	87	179-181	179-180 [21]

^a Reaction conditions: 2-naphthol (10 mmol), aromatic aldehyde (5 mmol), [Et₃NH][HSO₄] (0.5 mmol), at 120 °C under solvent-free conditions.

^b Isolated yields.

Table 4. Comparisons of some other reported procedures with the present method for the synthesis of 14-(4-nitrophenyl)-14H-dibenzo[a,j]xanthene.

Entry	Catalyst	Conditions	Time (min)	Yield (%)	Recycle of catalyst	Ref.
1	AcOH-H ₂ SO ₄	AcOH, 0 °C for 72h then 70-80 °C for 1h	73h	60	No	[7]
2	InCl ₃	Solvent-free, 80 °C	60	94	No	[8]
3	Iodine	Chloroform, 60-70 °C	840	91	No	[11]
4	Silica sulfuric acid	Solvent-free, 125 °C	80	87	Yes	[12]
5	Cellulose sulfuric acid	Solvent-free, 110 °C	120	90	Yes	[13]
6	Yb(OTf) ₃	[BPy]BF ₄ , 110 °C	180	91	Yes	[16]
7	In(OTf) ₃	H ₂ O, 110 °C	300	88	No	[17]
8	K ₅ CoW ₁₂ O ₄₀ ·3H ₂ O	Solvent-free, 125 °C	60	97	Yes	[18]
9	NH ₄ H ₂ PO ₄ /SiO ₂	H ₂ O, 40 °C, ultrasonic irradiation	40	94	Yes	[19]
10	P ₂ O ₅ /Al ₂ O ₃	Solvent-free, microwave irradiation	10	95	No	[20]
11	P(4-VPH)HSO ₄	Solvent-free, 100 °C	70	96	Yes	[21]
12	ZnO nanoparticle	Solvent-free, 120 °C	55	86	Yes	[22]
13	SiO ₂ -Pr-SO ₃ H	Solvent-free, 125 °C	40	98	Yes	[23]
14	PVPP-BF ₃	Solvent-free, 120 °C	120	96	Yes	[24]
15	[Et ₃ NH][HSO ₄]	Solvent-free, 120 °C	30	93	Yes	This work

**Scheme 2.** Plausible mechanism for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes catalyzed by [Et₃NH][HSO₄].

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