

1-(1-Propylsulfonic)-3-methylimidazolium chloride Brønsted acidic ionic liquid catalyzed one-pot synthesis of 14-aryl-14H-dibenzo[a,j]xanthene derivatives under solvent-free conditions

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ABSTRACT

A rapid, green and efficient method for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthene derivatives through a one-pot condensation of 2-naphthol with various aromatic aldehydes in the presences of several acidic ionic liquids including [PSMIM]Cl, [BMIM]HSO₄, [BMIM]Cl, [BMIM]Br, and [BMIM]BF₄ as organocatalysts and task-specific acidic ionic liquids (AILs) under solvent-free conditions is described. Compared with other synthetic methods, this new method has the advantages such as milder reaction conditions, good to excellent yields, short reaction times, and environmentally benign procedure. Also, 1-(1-Propylsulfonic)-3-methylimidazolium chloride [PSMIM]Cl acts as a catalyst under solvent-free conditions and can be recovered and reused six times without apparent loss of its catalytic activity.

Keywords: Ionic liquids, One-pot reaction, 2-Naphthol, Aldehydes, Reusable catalyst, Xanthenes.

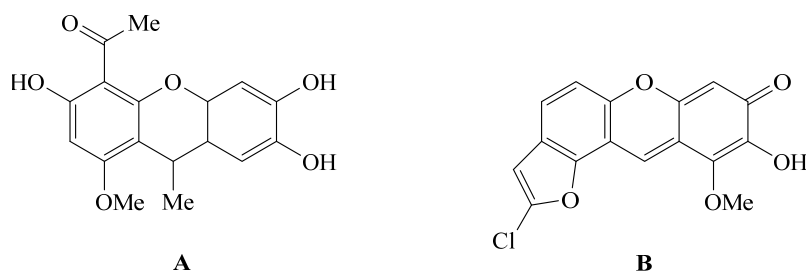
1. Introduction

Ionic liquids (ILs) are considered as an ideal alternative to volatile organic solvents in chemical industries in the future, because they are non-volatile. Ionic liquids also considered as new novel chemical agents and widely regarded as a greener alternative to many solvents. The term ILs has been used to describe salts that melt below 100°C. Whereas, the term room temperature ionic liquids (RTILs) is unusually reserved for ILs melts with melting points below room temperature. ILs have received a lot of interest recently as ion conductive matrices and reaction media because of wide liquid range, high ionic conductivity, a wide voltage window, non-volatility, and non-flammability. In addition, the ILs are readily recycled (residual reagents, reaction products and catalysts are separated by suitable procedures e.g., removal under reduced pressure or extraction), and can be designed, non-flammable and thermally stable as well (high thermal stability and liquid range up to about 300°C) [1-3].

The synthesis of xanthenes and benzoxanthenes have received much attention because of their wide range of therapeutic and biological properties such as antiviral [4], antibacterial [5], and anti-inflammatory activities [6], as well as in photodynamic therapy [7], and in the food industry as additives [8-9]. Furthermore, benzoxanthenes are used anti-proliferative properties [10], in laser technologies [11], and in fluorescent materials [12]. Also, xanthenes are rare in natural plants and have been isolated from only two plant families, Compositae and Fabaceae. Blumeaxanthene (**A**) and blumeaxanthene (**B**) have been isolated from *Blumea riparia* DC (Compositae), a Chinese medicinal herb traditionally used to treat gynecological disorders (Scheme 1) [13].

Many procedures for the synthesis of xanthenes and benzoxanthenes have been reported in the literature, including the reaction of cyclodehydration [14-16], trapping of benzyne by phenols [17], cyclocondensation of 2-hydroxy aromatic aldehydes and 2-tetralone [18], aryloxymagnesium halides with triethylorthoformate [19], intermolecular phenyl carbonyl coupling reactions of benzaldehydes and

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Scheme 1. Examples of natural xanthene.

acetophenones [20], and cyclization of polycyclic aryltriflate esters [21]. Recently, the preparation of xanthene derivatives has been achieved by the condensation of aldehydes with 2-naphthol by cyclodehydration in the presence of diverse catalysts, such as *p*-toluenesulfonic acid [22], *p*-dodecylbenzene sulphonic acid [23], triethylbenzylammonium chloride [24], diammoniumhydrogen phosphate under various conditions [25], I₂ [26], K₅CoW₁₂O₄₀·3H₂O/silica-gel/MW [27], LiBr/MW [28], and isonitriles [29]. However, some of these methods have some drawbacks, such as hazardous organic solvents, unsatisfactory yields, use of expensive catalysts, longer reaction time and tedious workup. In this study, 1-(1-Propylsulfonic)-3-methylimidazolium chloride (cat. 1) were prepared according to the literature procedure [30]. The rest of the ILs (cat. 2), (cat. 3), (cat. 4), and (cat. 5) were obtained from Sigma-Aldrich Chemicals (Scheme 2).

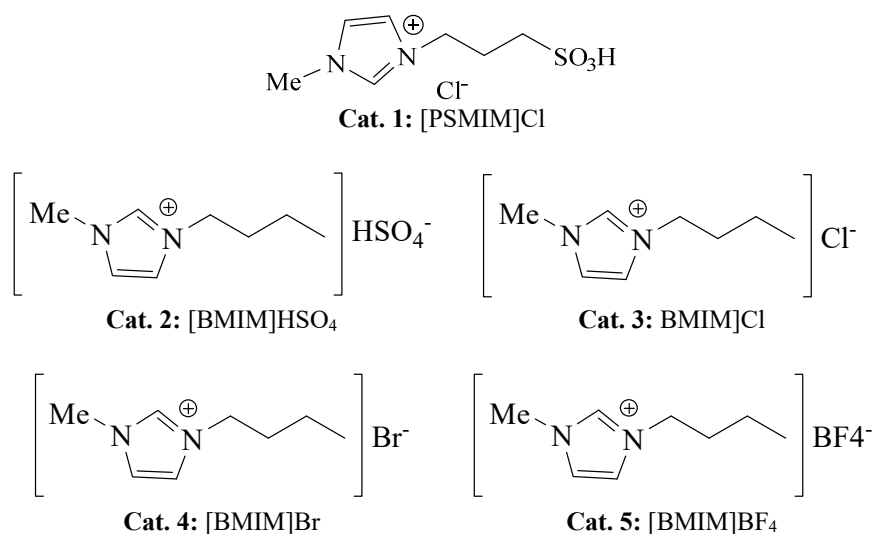
In continuation of our research using Brønsted acid catalyst for organic transformations [31-36], we herein report an efficient and green procedure for the synthesis of 14-aryl(alkyl)-14H-dibenzo[a,j]xanthenes

by cyclo condensation reaction of 2-naphthol **1** and various aromatic aldehydes **2** catalyzed by several acidic ionic liquids as an effective and organocatalyst under solvent-free conditions (Scheme 3).

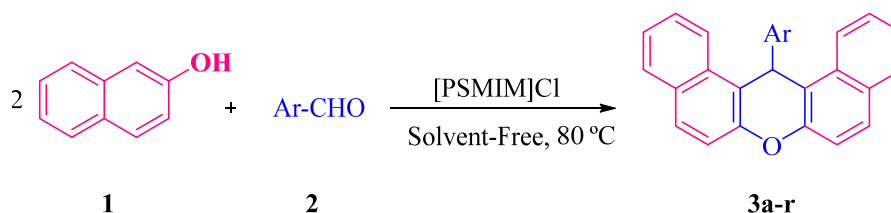
2. Experimental

2.1. General

All reagents and solvent were purchased from Sigma-Aldrich and used as supplied without further purification. NMR Chemical shifts are reported in (δ) ppm relative to tetramethylsilane (TMS) (d = 0.00) with the residual solvent as internal reference (CDCl₃, δ 7.26 ppm for ¹H NMR and δ 77.0 for ¹³C NMR). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. IR spectra of the compounds were obtained on a Perkin Elmer spectrometer version 10.03.06 using a KBr disk. The progress of reaction was followed with thin-layer chromatography (TLC) using silica gel SILG/UV 254 and 365 plates. All melting points recorded are uncorrected open capillary measurements.



Scheme 2. Acidic ILs examined in this work.



Scheme 3. [PSMIM]Cl promoted synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes.

2.2. Preparation of 1-(1-Propylsulfonic)-3-methylimidazolium chloride

1-methylimidazole, and 1,3-propanesultone were purchased from Sigma-Aldrich Chemical Co. 1-(1-Propylsulfonic)-3-methylimidazolium chloride was prepared via the condensation of 1-methylimidazole with 1,3-propanesultone and acidification of the resulting salt with concentrated HCl, according to the literature procedure [30].

2.3. General procedure for one-pot synthesis of 14-aryl-14H-dibenzo[a,j]xanthene derivatives

In a 50 mL round-bottom flask, a mixture of aldehyde (1 mmol), 2-naphthol (2 mmol) and [PSMIM]Cl (10 mol%) was added and the mixture was kept in an oil bath at 80 °C for a certain time (Table 3). After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature, and extracted by CHCl_3 (20 mL) to separate the catalyst (the product is soluble in CHCl_3). CHCl_3 was removed and the crude product was recrystallized from aqueous ethanol to afford the pure compound corresponding to 14-aryl-14H-dibenzo[a,j]xanthene derivatives (**3a-q**). The recovered catalyst was washed with CHCl_3 (2×20 mL), dried and reused for the next run. The 14-aryl-14H-dibenzo[a,j]xanthene derivatives of the following various aldehydes show ^1H NMR, ^{13}C NMR, Mass, and IR (KBr) spectra as mentioned below.

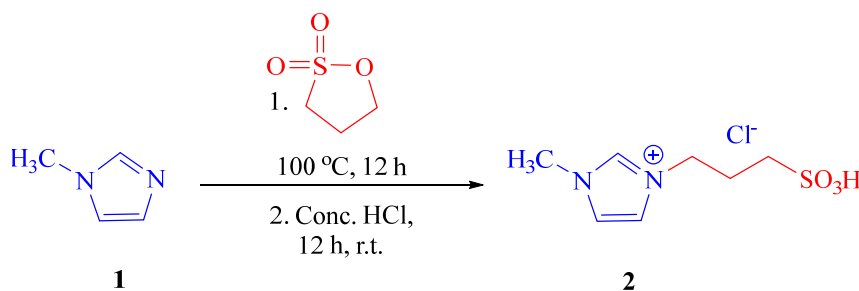
3. Results and Discussion

The 1-(1-Propylsulfonic)-3-methylimidazolium chloride [PSMIM]Cl as a reusable Brønsted acidic ionic liquid catalyst were prepared by condensation of

methyl imidazole with 1,3-propane sultone and acidification of the zwitterion with concentrated HCl as shown in Scheme 4 [30].

The preparation of 14-Phenyl-14H-dibenzo[a,j]xanthenes **3a-3q** from reaction between 2-naphthol **1** (2 mmol) with benzaldehyde **2** (1 mmol) as a model reaction using diverse ionic liquid catalysts such as [PSMIM]Cl, [BMIM]HSO₄, [BMIM]Cl, [BMIM]Br, and [BMIM]BF₄ was studied (Table 1). We found that [PSMIM]Cl, is the most effective catalyst for this condensation reaction (Table 1, entry 1-5). It can be seen that this reaction was strongly influenced by the amount of catalyst. The best results were obtained using 10 mol% of [PSMIM]Cl, in 88% in 35 min (Table 1, entry 4). Higher percentages of catalyst loading (15 mol%) neither increased the yield nor lowered the conversion time (Table 1, entry 5). Reaction with 1 and 3 mol% of the [PSMIM]Cl, required a longer reaction time and low yield (Table 1, entry 2 and 3). Also, reaction with 5 mol% of [PSMIM]Cl, produced only 76% yield of the product after 45 min (Table 1, entry 3). Accordingly, 10 mol% of [PSMIM]Cl, was selected for use in these reactions due to its low concentration, which resulted in good yields.

In the next study, to select the best temperature for the reaction, the synthesis of xanthene **3a** was examined in the presence of 10 mol% of [PSMIM]Cl in different temperature (Table 2). Higher yields and shorter reaction times were obtained when the reaction was carried out in 80°C. Therefore, this reaction was developed with other aldehydes, and the results are summarized in Table 3.



Scheme 4. Preparation of 1-(1-propylsulfonic)-3-methylimidazolium chloride.

Table 1. Catalytic efficacy of ILs for the synthesis of 14H-dibenzo[a,j]xanthenes^a.

Entry	Catalyst	Amount of catalyst (mol%)	Time (min)	Yield (%) ^b
1	[PSMIM]Cl	1	60	55
2	[PSMIM]Cl	3	60	68
3	[PSMIM]Cl	5	45	76
4	[PSMIM]Cl	10	35	88
5	[PSMIM]Cl	15	35	81
6	[BMIM]HSO ₄	10	35	75
7	[BMIM]Cl	10	50	79
8	[BMIM]Br	10	50	75
9	[BMIM]BF ₄	10	50	56

^aReaction conditions: 2-naphthol (2 mmol), benzaldehyde (1 mmol) and several ILs under solvent-free conditions at room temperature.

^bYields refer to the isolated pure products.

After optimization of the reaction conditions, a variety of 14-aryl-14H-dibenzo [a,j]xanthenes was prepared from aldehydes and 2-naphthol in the presence of [PSMIM]Cl under solvent-free conditions at 80°C (Table 3, entries 1-177). Benzaldehydes bearing 4-substituents (Table 3, entries 4 and 8) slightly afford the better product yields. This slight difference is also seen in 2-substituted benzaldehydes (Table 3, entries 2 and 9). In general, the results given in Table 3 show that good to excellent yields and short reaction times were obtained using aromatic aldehydes carrying electron-donating or electron-withdrawing substituents.

Good reusability of the catalyst is an important aspect of green chemistry so the potential for recovery of [PSMIM]Cl was investigated. For this purpose, the reaction of 2-naphthol (1 mmol) with benzaldehyde (1 mmol) was performed in the presence of [PSMIM]Cl (10 mol%) at 80 °C. After completion of the reaction, as monitored by TLC, the reaction mixture was cooled to room temperature, extracted with CHCl₃ to separate the catalyst (the product is soluble in CHCl₃). CHCl₃ was removed, and the recovered catalyst was washed

with CHCl₃, dried and reused for the synthesis of 14-Phenyl-14H-dibenzo[a,j]xanthene according to the mentioned procedure. The recovered [PSMIM]Cl could be directly reused in six successive runs without significant loss of activity. After six runs, a minor decline contributing ca. 8% is observed. The decrease in the activity could be mainly attributed to unavoidable loss of the catalyst during the process of collection and washing.

The advantages of [PSMIM]Cl were compared with those of other reported catalysts for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes, and the results are represented in Table 4. Reported using sulfamic acid (Table 4, entry 5), Yb(OTf)₃ (Table 4, entry 6), and alum (Table 4, entry 7) as catalyst for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes derivatives, which require long reaction times and high temperatures to complete the reaction, and product yields are low. Reported using Fe(HSO₄)₃ (Table 4, entries 1-3), as a catalyst for the preparation of 14-aryl-14H-dibenzo[a,j]xanthenes.

Table 2. Optimization of temperature in the reaction of benzaldehyde and 2-naphthol under solvent-free conditions using [PSMIM]Cl (10 mol%).

Entry	Temp. (°C)	Time (min)	Yield (%) ^a
1	60	15	65
2	80	8	96
3	100	30	81
4	120	45	40

^aYields refer to the isolated pure products.

Table 3. Preparation of 14H-dibenzo[a,j]xanthenes derivatives.

Entry	Ar	Product	Time (min)	Yield (%) ^a	m.p. (°C)		Ref.
					Found	Reported	
1	C ₆ H ₅	3a	8	96	189-191	190	[37]
2	2-ClC ₆ H ₄	3b	15	92	218-219	220	[37]
3	3-ClC ₆ H ₄	3c	10	93	197-199	200	[37]
4	4-ClC ₆ H ₄	3d	10	95	291-293	295	[37]
5	3-MeC ₆ H ₄	3e	15	93	197-199	201	[37]
6	4-MeC ₆ H ₄	3f	10	91	220-221	233	[37]
7	3-MeOC ₆ H ₄	3g	15	92	178-180	182	[37]
8	4-MeOC ₆ H ₄	3h	8	96	200-203	201	[37]
9	2-BrC ₆ H ₄	3i	15	89	214-216	215	[37]
10	3-BrC ₆ H ₄	3j	12	90	194-196	195	[37]
11	4-BrC ₆ H ₄	3k	10	89	300-301	300	[37]
12	3-FC ₆ H ₄	3l	9	91	219-222	222	[37]
13	4-FC ₆ H ₄	3m	10	93	245-246	247	[37]
14	2-O ₂ NC ₆ H ₄	3n	12	91	290-291	293	[38]
15	3-O ₂ NC ₆ H ₄	3o	12	91	226-227	225	[37]
16	4-O ₂ NC ₆ H ₄	3p	8	93	329-330	329	[37]
17	4-HOC ₆ H ₄	3q	9	89	136-138	140	[38]

^aYields refer to the isolated pure products.**Table 4.** Comparison of efficiency of various catalysts in synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes.

Entry	Catalyst	Reaction conditions	Time (h)	Yield (%) ^e	Ref.
1	Fe(HSO ₄) ₃	Solvent-free/ 120°C	5-18 ^d	81-98	[39]
2	Fe(HSO ₄) ₃	Solvent-free/ 450 W	3-11 ^d	70-93	[39]
3	Fe(HSO ₄) ₃	H ₂ O/ Reflux	1.5-3	70-94	[39]
4	H ₂ SO ₄	AcOH/ 80°C	73	60-90	[40]
5	Sulfamic acid	Solvent-free/ 125°C	6-12	90-95	[41]
6	Yb(OTf) ₃	[BPy]BF ₄ / 110°C	5-7	80-95	[42]
7	Alum	Water/ 100°C	3-4	82-91	[43]
8	Cellulose sulfuric acid	Solvent-free/ 110°C	1.5-3	81-97	[44]
9	SiO ₂ -Pr-SO ₃ H	Solvent-free/ 125°C	20-40 ^d	97-99	[45]
10	NaHSO ₄	Solvent-free/ 90°C	0.5-1	74-91	[46]
11	PFPAT ^a	Toluene/ 25-30°C	3-5	85-97	[47]
12	PSA ^b	Solvent-free/ 80°C	15-35 ^d	74-86	[48]
13	[PSMIM]Cl ^c	Solvent-free/ 80°C	8-15 ^d	88-96	This work

^aPentafluorophenyl ammonium triflate.^bPhospho sulfonic acid.^c1-(1-Propylsulfonic)-3-methylimidazolium chloride.^dIn minute.^eYields refer to the isolated pure products.

This method requires long reaction time and high temperature to complete the reaction, and harsh reaction conditions. Reported using H_2SO_4 (Table 4, entry 4) as a catalyst for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes, which required reaction times of almost 73 hour and gave product yields of 60-90%. In 2012, Khaksar and et al. reported the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes derivatives by using PFPAT (Table 4, entry 11) as a catalyst, the yield of the products were low and long reaction times were required, and also use of hazardous organic solvents such as toluene. As shown in Table 4, [PSMIM]Cl can act as effective catalyst with respect to reaction times, amount of the catalyst, and yields of the obtained products. Thus, the present protocol with [PSMIM]Cl catalysts is convincingly superior to some reported catalytic methods (Table 4). A possible mechanism for the condensation reaction of 2-naphthol with aryl aldehydes promoted by [PSMIM]Cl is presented in scheme 5.

4. Conclusions

In summary, we have developed a simple and an efficient method for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthene via condensation of 2-naphthol with different kinds of aromatic aldehydes in the

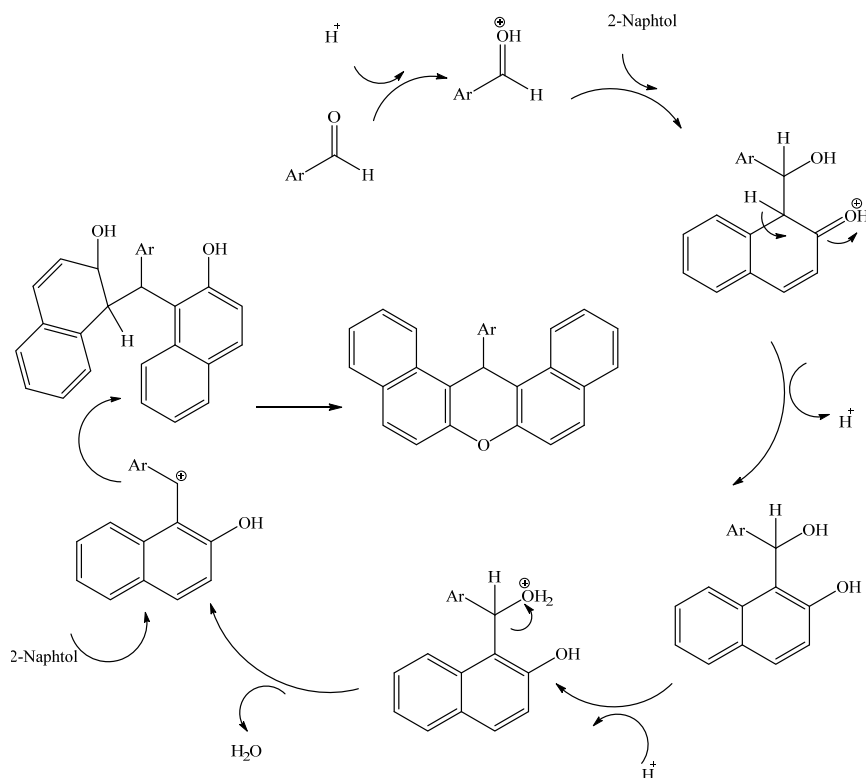
presence of the [PSMIM]Cl as a Brønsted acidic ionic liquid catalyst under solvent-free conditions. The simple experimental and work-up procedures, low-cost, high yields of the desired products and short reaction times, and application of inexpensive catalysts and compliance with the green chemistry protocols are the advantages of the present method. In addition, the catalyst can be reused in six successive runs with no considerable activity loss.

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Scheme 5. Suggested mechanism for the preparation of 14-aryl-14H-dibenzo[a,j]xanthenes derivatives.

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