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The one-pot synthesis of 14-alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes catalyzed by task-specific ionic liquid

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A Brønsted-acidic task-specific ionic liquid, 1-methyl-3-propane sulfonic-imidazolium hydrosulfate ([MIMPS]HSO_4), was employed as a catalyst for the synthesis of 14-alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes via the one-pot condensation of β-naphthol with aliphatic or aromatic aldehydes. Various aliphatic and aromatic aldehydes were used in the reaction and in all cases the desired products were synthesized successfully. The novel synthesis method offers the advantages of high yields, short reaction times, simplicity and easy workup compared to the conventional method of syntheses. The catalyst could be recycled and reused five times without a noticeably decrease in its activity.

1. Introduction

The synthesis of xanthenes, especially benzoxanthenes, has received significant attention in recent years because of their wide range of biological and pharmaceutical properties such as antiviral [1], antibacterial [2], and anti-inflammatory [3] activities as well as efficacy in photodynamic therapy [4] and antagonists for the paralyzing acting of zoxazolamine [5]. Furthermore, these compounds can be used as dyes [6], pH-sensitive fluorescent materials for visualization of biomolecules [7] and utilized in laser technologies [8]. Thus, the synthesis of xanthene derivatives currently is of much importance. Various methods have been reported for the synthesis of these compounds, including the reaction of β-naphthol with 2-naphthol-1-methanol [9], the cyclocondensation reaction of 2-hydroxyaromatic aldehydes with 2-tetralone [10], the reaction of benzaldehydes with acetophenones [11], palladium-catalyzed cyclization of polycyclic aryltriflate esters [12] and the intermolecular trapping of benzynes by phenols [13]. Recently, the synthesis of benzoxanthenes has been achieved by the reaction of aldehydes with β-naphthol by dehydration in the presence of a catalyst, such as AcOH–H_2SO_4 [14], *p*TSA [15,16], sulfamic acid [17], molecular iodine [18,19], heteropoly acid [20,21], silica sulfuric acid [22,23], Amberlyst-15 [24], and wet cyanuric chloride [25]. However, these methods suffer from one or more disadvantages such as a long reaction time, low yield, use of toxic solvents, requirement of excess of reagents/catalysts, laborious workup procedures, and hash reaction conditions. Thus, the development of an environmentally benign methodology for the synthesis of benzoxanthene derivatives is in great demand.

In recent years, ionic liquids have received recognition as green media in organic synthesis due to their favorable properties, such as good solvating capability, wide liquid range, negligible vapour pressure, tunable polarity, high thermal stability, and ease of recyclability [26–28]. Although ionic liquids were initially introduced as an alternative green reaction medium, today they have marched far beyond this border, showing their significant role in controlling the reaction as catalysts [29–31]. So, the development and application of so-called "task-specific" ionic liquids are desirable. Brønsted-acidic task-specific ionic liquids (TSILs) are one of the successful examples that task-specific ionic liquids used as reaction medium and catalysts in organic synthesis [32–34]. Some Brønsted-acidic TSILs, which possess the advantageous characteristics of solid acids and mineral acids, have been successfully used as catalysts for Mannich reaction [35], Biginelli reaction [36], the protection of carbonyl groups [37] and the synthesis of quinoxaline derivatives [38] in our foregoing reports. In continuation of our work on the development of efficient and environmentally benign procedures using Brønsted-acidic TSILs, we use a novel Brønsted-acidic ionic liquid [MIMPS]HSO_4 as catalyst for the synthesis of benzoxanthene derivatives. To the best of our knowledge in the open literature, one-pot synthesis of benzoxanthene derivatives catalyzed by [MIMPS]HSO_4 has not been reported. Herein we report

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a simple and fast reaction of various aldehydes with β-naphthol to afford corresponding 14-alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes catalyzed by [MIMPS]HSO_4 (Scheme 1).

2. Experimental

2.1. General

All the products are known and were characterized by comparing their IR spectra, ^1H NMR spectra and melting points with those reported in literature. IR spectra were recorded on a Nicolete spectrometer in KBr. ^1H NMR spectra were obtained from solution in $CDCl_3$ with TMS as internal standard using a Bruker DRX 300 (300 MHz) spectrometer. Melting points were measured on a WRS-1B melting point apparatus and were uncorrected.

The synthesis of the Brønsted-acidic task-specific ionic liquids and neutral ionic liquid 1-butyl-3-methyl-imidazolium tetrafluoroborate ([BMIM]BF_4) has been reported in our previous reports [39,40]. All other chemical and reagents were of analytical grade and used as-obtained.

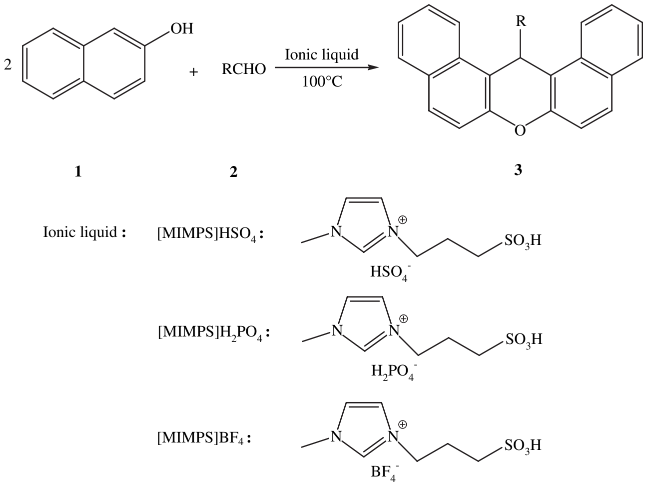
2.2. General procedure for the preparation of 14H-dibenzo[a,j] xanthene derivatives

A mixture of β-naphthol **1** (10 mmol), aldehyde **2** (5 mmol) and ionic liquid (0.25 mmol) was stirred at 100 °C for the appropriate time (monitored by TLC). After cooling to room temperature, water (10 mL) was added and the mixture was stirred for 5 min. The precipitated product was filtered and purified by crystallization from ethyl alcohol afferding **3**. The filtrate containing the ionic liquid was further vacuumed to dryness and the resulting catalyst was reused directly for the next run. The reactions using the recycled catalyst were conducted in a similar manner.

2.3. Representative spectral data

2.3.1. 14-Phenyl-14H-dibenzo[a,j]xanthene (3a)

Colorless crystals, ^1H NMR ($CDCl_3$, 300 MHz): δ 6.46 (s, 1H, CH), 6.96 (t, $J = 7.2$ Hz, 1H, ArH), 7.12 (t, $J = 7.2$ Hz, 2H, ArH), 7.36–7.58 (m, 8H, ArH), 7.74–7.81 (m, 4H, ArH), 8.37 (d, $J = 8.4$ Hz, 2H, ArH); IR (KBr, cm^{-1}): 3074, 3020, 2886, 1622, 1591, 1513, 1455, 1430, 1401, 1251, 1152, 1078, 1028, 962, 857, 827, 743, 700.



Scheme 1. Synthesis of 14-alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes.

Table 1
Different catalytic system for synthesis of **3a**

Entry	Catalysts	Time (h)	Yields (%)[a]
1[b]	–	10	–
2[c]	[BMIM]BF_4	10	20
3[c]	[MIMPS]HSO_4	0.1	93
4[c]	[MIMPS]H_2PO_4	2	76
5[c]	[MIMPS]BF_4	0.5	87

[a] Isolated yield.
[b] Reaction condition: benzaldehyde (5 mmol), β-naphthol (10 mmol), 100 °C.
[c] Reaction condition: benzaldehyde (5 mmol), β-naphthol (10 mmol), ionic liquid (0.25 mmol), 100 °C.

2.3.2. 14-(4-Methylphenyl)-14H-dibenzo[a,j]xanthene (3i)

Colorless crystals, ^1H NMR ($CDCl_3$, 300 MHz): δ 2.11 (s, 3H, CH_3), 6.43 (s, 1H, CH), 6.93 (d, $J = 7.8$ Hz, 2H, ArH), 7.22–7.36 (m, 8H, ArH), 7.42–7.81 (m, 4H, ArH), 8.37 (d, $J = 8.4$ Hz, 2H, ArH); IR (KBr, cm^{-1}): 3466, 3070, 3020, 2904, 1622, 1590, 1510, 1398, 1245, 1111, 1077, 961, 811, 778, 741.

3. Results and discussion

In the initial experiments, in order to examine the catalytic activity of different ionic liquids in this condensation reaction, reaction of benzaldehyde and β-naphthol was selected as model. It showed that nearly no product could be detected when a mixture of benzaldehyde and β-naphthol (mole rate 1:2) was heated at 100 °C for 10 h in absence of TSILs (Table 1, entry 1), which indicated that the catalysts should be absolutely necessary for this transformation. The neutral ionic liquids such as [BMIM]BF_4 gave product with low yield (Table 1, entry 2). However, among the acyclic SO_3H-functional Brønsted-acidic TSILs studied for this reaction, [MIMPS]HSO_4 was found to be the most effective catalyst for this transformation since it gave the highest yield and the shortest reaction time (Table 1, entry 3). This showed the vital role of the SO_3H-functional group and HSO_4^- of this functionalized ionic liquid in this transformation. In conclusion, [MIMPS]HSO_4 was an effective catalyst for the condensation reaction of benzaldehyde with β-naphthol.

'Next, we examined the scope of the reaction by using various aliphatic and aromatic aldehydes, and the results are summarized in Table 2. In all the cases the corresponding benzoxanthenes were obtained in good to excellent yields. However, when aromatic aldehydes with electron-withdrawing groups (such as nitro-) are

Table 2
Synthesis of 14-alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes catalyzed by [MIMPS]HSO_4[a]

Entry	R	Time (min)	Compound	Yields (%)[b]	Mp (°C)/(lit.)
1	C_6H_5	7	**3a**	93	184–185 (181–183) [19]
2	2-ClC_6H_5	12	**3b**	92	214–215 (215) [15]
3	4-ClC_6H_5	6	**3c**	96	287–288 (289) [15]
4	2,4-ClC_6H_5	8	**3d**	95	227–228 (227) [22]
5	4-FC_6H_5	5	**3e**	96	239–240 (239) [15]
6	2-$NO_2C_6H_5$	10	**3f**	88	214–215 (214) [19]
7	3-$NO_2C_6H_5$	8	**3g**	90	210–211 (211) [15]
8	4-$NO_2C_6H_5$	6	**3h**	94	310–311 (310) [19]
9	4-$CH_3C_6H_5$	9	**3i**	91	227–228 (229) [15]
10	4-$CH_3OC_6H_5$	30	**3j**	85	202–203 (204) [15]
11	CH_3CH_2	40	**3k**	92	149–150 (152) [15]
12	CH_3CHCH_2	60	**3l**	80	152–152 (151–153) [16]
13	$(CH_3)_2CH$	60	**3m**	75	152–153 (153–154) [16]
14	$(CH_3)_2CHCH_2$	60	**3n**	78	112–113 (113) [15]

[a] Reaction condition: aldehyde (5 mmol), β-naphthol (10 mmol), [MIMPS]HSO_4 (0.25 mmol), 100 °C.
[b] Isolated yield.

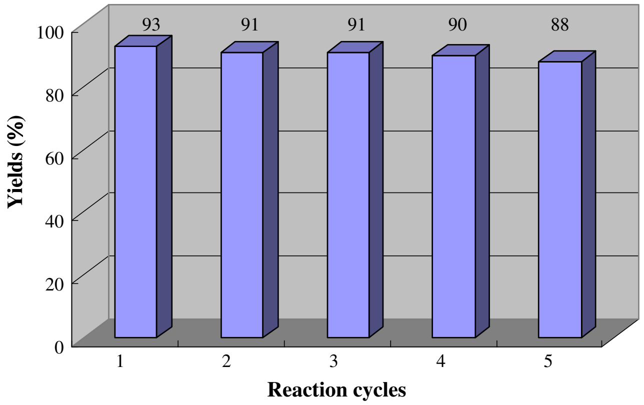


Fig. 1. Reusability of [MIMPS]HSO_4 for synthesis of **3a**.

reactants, the reaction time is shorter than that with electron-donating groups (such as methoxy-). Though *meta*- and *para*-substituted aromatic aldehydes gave good results, *ortho*-substituted aromatic aldehydes (such as 2-nitrobenzadehyde) gave lower yields because of the steric effects. These good results were also obtained in the case of the aliphatic aldehydes (Table 2, entries 11–14).

Compared with traditional solvents and catalysts, it is easy for ionic liquids to be reused, which is prior to the conventional solvents and catalysts [41]. Hence, we decided to study the catalytic activity of recycled Brønsted-acidic TSIL [MIMPS]HSO_4 for the synthesis of **3a**. After the separation of product, the filtrate containing catalyst was vacuumed to remove water and the resulting catalyst was reused directly for the next run. As shown in Fig. 1, the Brønsted-acidic TSIL [MIMPS]HSO_4 can be recycled at least five times without significant decrease in catalytic activity, the yields ranged from 93% to 88%.

4. Conclusions

In summary, a novel and highly efficient method for the synthesis of 14-alkyl- or aryl-14*H*-dibenzo[*a,j*]xanthenes by condensation reaction of β-naphthol with aliphatic or aromatic aldehydes catalyzed by the Brønsted-acidic TSIL [MIMPS]HSO_4 has been described. The attractive features of this protocol are simple procedure, short reaction time, the reuse of catalyst, and its adaptability for synthesis of a diverse set of benzoxanthene derivatives. This approach could make a valuable contribution to the existing processes in the field of benzoxanthene syntheses.

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