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$Yb(OTf)_3$ catalyzed condensation reaction of β-naphthol and aldehyde in ionic liquids: a green synthesis of aryl-14*H*-dibenzo[*a*,*j*]xanthenes

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Abstract

A facile, efficient and green synthesis of aryl-14*H*-dibenzo[*a*,*j*]xanthenes has been developed by one-pot condensation of β-naphthol and substituted benzaldehydes in the presence of ytterbium triflates in ionic liquids.

The synthesis of xanthenes, especially benzoxanthenes, has been of considerable interest to chemists because their oxygen heterocycles may contribute to potential antibacterial,[1] antiviral,[2] and anti-inflammatory activities.[3] Furthermore, these compounds can be used as dyes,[4] in laser technology,[5] and pH-sensitive fluorescent materials for the visualization of biomolecular assemblies[6] (Fig. 1).

For the synthesis of benzoxanthenes, various methods have been reported including the reaction of β-naphthol with formamide,[7] 2-naphthol-1-methanol,[8] and carbon monoxide.[9] However, these methods have drawbacks such as poor yields, prolonged reaction time, using of toxic organic solvents, excess reagents/catalysts, and harsh reaction conditions. Due to these disadvantages, several reactions have been improved by the condensation of β-naphthol with aldehydes in the presence of a catalyst, such as *p*-TSA,[10] sulfamic acid,[11] $AcOH/H_2SO_4$,[12] iodine,[13,14] $K_5CoW_{12}O_{40}·3H_2O$,[15] cyanuric chloride,[16] LiBr.[17] However, searching another environmentally friendly catalyst and green solvents is still highly desirable.

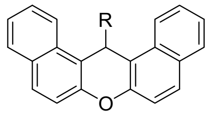

Fig. 1. Benzoxanthenes.

The use of lanthanide triflates has given many advantages in organic synthesis. Lanthanide triflates are mild and selective catalysts, which have been used widely in C–C and C–X bond-forming reactions, including Friedel–Crafts,[18] Baylis–Hilman,[19] aromatic nitration,[20] and Diels–Alder reactions.[21] In contrast to classical Lewis acids, which often are required in stoichiometric quantities, lanthanide triflates readily promote a range of reactions in catalytic quantities. Furthermore, lanthanide triflates can be recovered and reused without the loss of activity.

Ionic liquids (ILs) are liquid salts at low temperature (<100 °C), which represent a new class of solvents. They offer the probability of organic reactions with easy isolation and recovery of catalysts. Moreover, Ionic liquids have no vapor pressure, which facilitates product separation by distillation.[22]

Recently, our group has reported the wide use of metal triflates as excellent catalysts in organic synthesis.[23] As a result of our ongoing interest in green chemistry and Lewis

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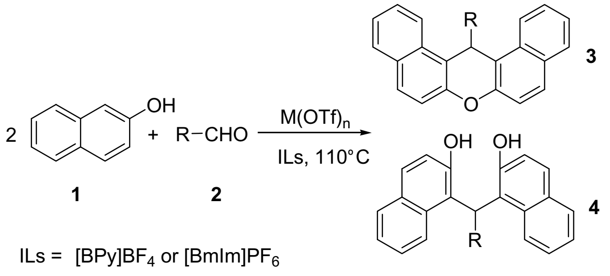


Scheme 1. Reactions of aromatic aldehydes with β-naphthol in ILs.

acid catalyzed organic reactions, we wish to report a novel catalyst for the preparation of benzoxanthenes by the condensation reaction of aromatic aldehydes with β-naphthol in ILs system. To the best of our knowledge, metal triflates have not been used in the synthesis of aryl-14*H*-dibenzo[*a*,*j*]xanthene (Scheme 1).

In our initial research, the condensation reaction of 2-naphthol (2 mmol) with 4-chlorobenzaldehyde (1 mmol) was carried out in different solvents in the presence of $Yb(OTf)_3$. Comparing with other organic solvents, $[BPy]BF_4$ and $[BmIm]PF_6$ were the most effective reaction media (Table 1, entries 1 and 2). It was confirmed that **3** was the only product in the presence of $Yb(OTf)_3$.

Simultaneously, the reaction of 4-chlorobenzaldehyde with β-naphthol was also performed in the presence of different catalysts (0.01 equiv) such as $AlCl_3$, $Zn(OTf)_2$, $Bi(OTf)_3$, $Yb(OTf)_3$, $Yb(OTf)_3{\cdot}xH_2O$, $Sc(OTf)_3$, $Y(OTf)_3$, $La(OTf)_3$, $Sr(OTf)_2$ in $[BPy]BF_4$ (Table 2). Data showed that $AlCl_3$ did not catalyze the reaction, but $Yb(OTf)_3$ and $Yb(OTf)_3{\cdot}xH_2O$ were the most effective catalysts in the terms of yields of the only product **3** (95%, 93%, respectively). Unexpectedly, when $Sr(OTf)_2$, $Sc(OTf)_3$, $Y(OTf)_3$ or $La(OTf)_3$ was used to promote the reaction at 110 °C for 5 h in $[BPy]BF_4$, **4** was also formed (Table 2, entries 6–9) due to the uncompleted cyclization. However, $Zn(OTf)_2$ and $Bi(OTf)_3$ only gave the desired product **3** in moderate yields, and none of **4** was detected.

Table 1
Solvent effect on the reaction of 2-naphthol (2 mmol) with 4-chlorobenzaldehyde (1 mmol)catalyzed by $Yb(OTf)_3$ (0.01 mmol)[a]

Entry	Solvent	Time (h)	Yield of **3**[b] (%)
1	$[BPy]BF_4$	5	95, 92[c]
2	$[BmIm]PF_6$	5	93
3	[BPy]Br	10	55
4	[EPy]Br	10	0
5	[BmIm]Cl	10	0
6	CH_3CN	10	0
7	$CHCl_3$	10	60
8	$ClCH_2CH_2Cl$	10	60
9	CH_3CH_2OH	10	15
10	THF	10	0

[a] Reactions carried out at 110 °C or refluxing.
[b] Yield of isolated product based on 4-chloro-benzaldehyde.
[c] $[BPy]BF_4$ was reused.

Table 2
Reaction of β-naphthol (2 mmol) with 4-chloro-benzaldehyde (1 mmol) in the presence of various catalysts (0.01 mmol) in $[BPy]BF_4$

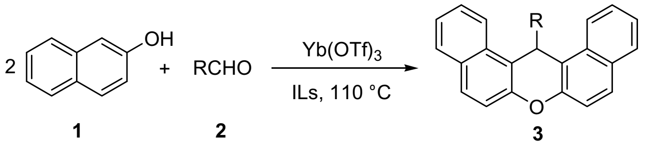
Entry	Catalyst	Temperature (°C)	Time (h)	Yields[a] (%)	
				3	4
1	$AlCl_3$[b]	125	10	0	0
2	$Yb(OTf)_3$	110	5	95	0
3	$Yb(OTf)_3{\cdot}xH_2O$	110	5	93, 92[c]	0
4	$Bi(OTf)_3$	110	5	60	0
5	$Zn(OTf)_2$	110	5	80	0
6	$Sr(OTf)_2$	110	5	35	30
7	$Sc(OTf)_3$	110	5	75	17
8	$Y(OTf)_3$	110	5	25	30
9	$La(OTf)_3$	110	5	10	55

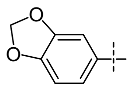
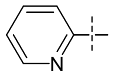
[a] Yield of isolated product based on 4-chloro-benzaldehyde.
[b] 1 mmol of anhydrous $AlCl_3$ was used.
[c] $Yb(OTf)_3/[BPy]BF_4$ was recovered and reused.

With these results in hand, we turned our attention to the scope of the aromatic aldehydes in the reaction. The results are summarized in Table 3.

Most substituted benzaldehydes reacted with β-naphthol completely and afforded the corresponding products (**3**) in high yields. Since electron-donating group can stabilize the carbocation formed in the reaction, the reaction is mild and the yield is high. In contrast, aldehydes with electron-withdrawing group were more reactive and the

Table 3
$Yb(OTf)_3$ Catalyzed synthesis of 14-substitued-14*H*-dibenzo[*a*,*j*]xanthenes in $[BPy]BF_4$[24]



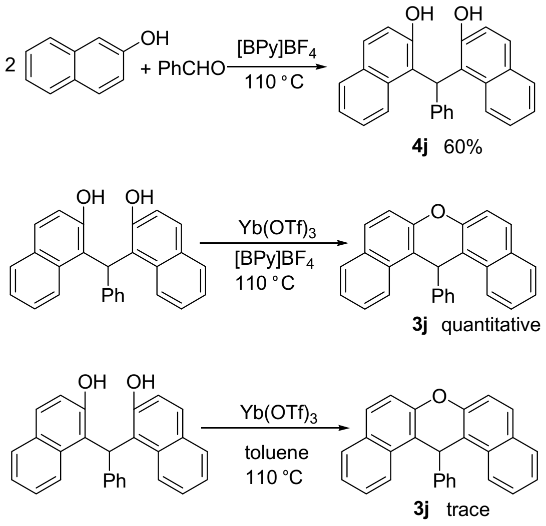
Entry	Aldehyde (R)	Time (h)	Catalyst[c] (mol %)	Product	ILs	Yield[a] (%)
1	$3\text{-Cl–}C_6H_4$	5	1	3a	$[BPy]BF_4$	87
2	$4\text{-Cl–}C_6H_4$	5	1	3b	$[BPy]BF_4$	89
3	$3\text{-Br–}C_6H_4$	5	1	3c	$[BPy]BF_4$	90
4	$4\text{-Br–}C_6H_4$	5	1	3d	$[BPy]BF_4$	91
5	$3\text{-F–}C_6H_4$	5	1	3e	$[BPy]BF_4$	88
6	$4\text{-F–}C_6H_4$	5	1	3f	$[BPy]BF_4$	90
7	$3\text{-}NO_2\text{–}C_6H_4$	3	1	3g	$[BPy]BF_4$	89
8	$4\text{-}NO_2\text{–}C_6H_4$	3	1	3h	$[BPy]BF_4$	91
9	$4\text{-CN–}C_6H_4$	3	1	3i	$[BPy]BF_4$	92
10	C_6H_5	7	1	3j	$[BPy]BF_4$	89
11	$4\text{-Me–}C_6H_4$	6	1	3k	$[BPy]BF_4$	93
12	$4\text{-MeO–}C_6H_4$	6	1	3l	$[BPy]BF_4$	95
13		6	1	3m	$[BPy]BF_4$	94
14		7	1 10	3n	$[BPy]BF_4$ $[BmIm]PF_6$	80 82[b]

[a] Yield of isolated product based on aldehydes.
[b] Reaction carried out in $[BmIm]PF_6$ with 10 mol % of $Yb(OTf)_3$.
[c] Mol based on aldehydes.

reaction with β-naphthol was faster. Thus, the aromatic aldehydes bearing both electron-donating and electron-withdrawing groups are desirable substrates for this reaction. When picolinaldehyde (**2n**) was used, the reaction proceeded relatively slowly and the yield was lower than others. It should be pointed out that hindered benzaldehydes such as 2,6-dimethoxy benzaldehyde did not react with β-naphthol under the present reaction condition even for 8 h. On the other hand, we found that phenol cannot react with substituted benzaldehydes.

In addition, when the reaction was carried out in [BPy]BF$_4$ in the absence of Yb(OTf)$_3$, condensation adduct (**4j**) was the only product, **3j** was not detected. However, **4j** could be converted into **3j** smoothly in quantitative yield in Yb(OTf)$_3$/[BPy]BF$_4$ system. But this conversion was difficult to proceed in conventional organic solvents such as toluene, nitrobenzene, and nitromethane. at high temperature even in the presence of more (20 mol %) Yb(OTf)$_3$ (Scheme 2).

Based on the experimental results, a plausible mechanism was proposed in Scheme 3. In this hypothesis, Yb(OTf)$_3$ might be served as the Lewis-acid catalyst for several stages.



Scheme 2. Conversion of **4j** to **3j** in Yb(OTf)3/ILs system.

In conclusion, ytterbium triflate is an efficient catalyst for the preparation of aryl 14*H*-dibenzo[*a*,*j*]xanthene derivatives by the condensation of β-naphthol with aromatic aldehydes. This method may be used to synthesize some useful ligands like Xantphos. Some studies are in progress in our team. In the above reaction, Yb(OTf)$_3$ showed unique catalysis in contrast to other metal triflates, and ionic liquids represented a unique class of new reaction media. Reactions using Yb(OTf)$_3$/ionic liquids as reaction media prevented uncontrolled by-products and were easy to handle. The simple experimental procedure, short reaction time, good product yields, mild reaction condition, and green standard are the advantages of this method. Yb(OTf)$_3$/ionic liquids may potentially be used as new type catalyst and solvent for a wide range of synthetic reactions.

Acknowledgment

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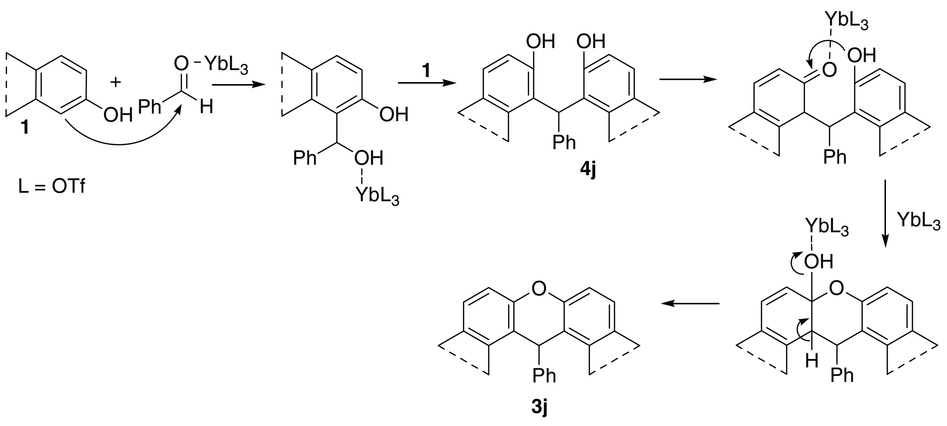

Scheme 3. Reaction mechanism of β-naphthol with benzaldehye.

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24. *Preparation of aryl-14H-dibenzo[a,j]xanthenes; general procedure*: To a mixture of aromatic aldehyde (1 mmol) and β-naphthol (2 mmol) in [BPy]$\mathrm{BF_4}$ (2 mL), ytterbium triflate (0.01 mmol, 6.2 mg) was added. The reaction mixture was stirred at 110 °C for the given time (Table 2). After completion (by TLC), the reaction mixture was cooled to room temperature, then ether (10 mL) was added to the mixture and stirred for 20 min. The above extraction was repeated, and the upper ether layers were combined and washed with brine. After dryness and condensation, the product was purified by column chromatography or TLC over silica gel (hexane/AcOEt = 1:1). The products could be easily identified by the singlet peak (about 6.4–6.6 ppm) in ^{1}H NMR spectra.

Recovering the catalytic system; general procedure: After completion of the extraction, the underlayer (ionic layer) Yb(OTf)3·*x*H2O/[BPy]$\mathrm{BF_4}$ was washed with 10 mL of ether again, then the ionic liquid was dried at 100 °C under 50 mmHg for 30 min. Then the recovered catalytic system could be reused in the next experiment. *Spectral data for selected products:*

3-Chloro-phenyl-14H-dibenzo[a,j]xanthenes (**3a**). White crystals; mp 210–211 °C; yield: 87%. ^{1}H NMR (400 MHz, $\mathrm{CDCl_3}$): $\delta = 8.32$ (d, $J = 8.4$ Hz, 2H), 7.80–7.83 (m, 4H), 7.59 (t, $J = 7.6$ Hz, 2H), 7.40–7.49 (m, 6H), 7.07 (t, $J = 8.0$ Hz, 1H), 6.96 (d, $J = 8.0$ Hz, 1H), 6.45 (s, 1H). MS (EI): *m*/*z* (%) = 394 (6, $\mathrm{M^+}$+2), 392 (17, $\mathrm{M^+}$), 281 (100).

*4-Cyano-phenyl-14H-dibenzo[a,j]xanthenes (***3i***)*.White crystals; mp 291–292 °C; yield: 91%. ^{1}H NMR (400 MHz, $\mathrm{CDCl_3}$): $\delta = 8.27$(d, $J = 8.8$ Hz, 2H), 7.85 (t, $J = 8.8$ Hz, 4H), 7.58–7.64 (m, 4H), 7.43–7.51 (m, 6H); 6.55 (s, 1H). ^{13}C NMR (100 MHz, CDCl3): $\delta = 155.1$, 147.8, 135.1, 133.9, 131.9, 130.9, 129.2, 128.1, 126.3, 124.3, 123.8, 123.2, 121.1, 117.2, 116.8, 48.9. MS (EI): *m*/*z* (%) = 383 (21, $\mathrm{M^+}$), 281 (100).

5-Benzo[d][1,3]dioxole-14H-dibenzo[a,j]xanthenes (**3m**) White crystals; mp 313–315 °C; yield: 94%. ^{1}H NMR (400 MHz, $\mathrm{CDCl_3}$): $\delta = 8.37$ (d, $J = 8.8$ Hz, 2H), 7.78–7.84 (m, 4H), 7.59 (t, $J = 7.6$ Hz, 2H), 7.40–7.48(m, 4H), 7.10 (d, $J = 7.6$ Hz, 1H), 6.87 (s, 1H), 6.61 (d, $J = 8.8$ Hz, 1H), 6.42 (s, 1H), 5.74 (s, 2H). ^{13}C NMR (100 MHz, $\mathrm{CDCl_3}$): $\delta = 148.7$, 147.8, 145.9, 139.0, 131.3, 131.1, 128.8, 126.8, 124.2, 122.6, 121.2, 118.0, 117.3, 108.8, 107.7, 100.8, 58.4, 37.6. MS (EI): *m*/*z* (%) = 402 (29, $\mathrm{M^+}$), 281 (100).

2-Pyridyl-14H-dibenzo[a,j]xanthenes (**3n**). White crystals; mp 240–242 °C; yield: 80%. ^{1}H NMR (400 MHz, $\mathrm{CDCl_3}$): $\delta = 8.67$ (2H, d, $J = 8.4$ Hz), 8.52 (d, $J = 4.8$ Hz, 1H), 7.80 (d, $J = 7.2$ Hz, 4H), 7.57 (t, $J = 8.0$ Hz, 2H), 7.47 (d, $J = 8.8$ Hz, 2H), 7.40 (t, $J = 7.6$ Hz, 2H), 7.33 (t, $J = 7.2$ Hz, 1H), 7.13 (d, $J = 8.0$ Hz, 1H), 6.90 (t, $J = 7.2$ Hz, 1H), 6.74 (s, 1H). ^{13}C NMR (100 MHz, $\mathrm{CDCl_3}$): $\delta = 164.6$, 148.2, 147.7, 137.1, 131.9, 130.9, 129.2, 128.4, 126.9, 124.3, 123.8, 123.2, 121.2, 117.9, 116.0, 41.9. MS (EI): *m*/*z* (%) = 359 (22, $\mathrm{M^+}$), 281 (100).