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Benzoin Condensation in Imidazolium Based Room-temperature Ionic Liquids

Fang Sheng JIANG, Hua YU, Ge GAO, Ru Gang XIE*

Department of Chemistry, Sichuan University, Chengdu 610064

Abstract: Benzoin condensation promoted efficiently in three imidazolium based room temperature ionic liquids [bmim]Br, [bmim]BF_4 and [Bnmim]BF_4 is reported for the first time. Benzoins were obtained in up to 91% yield within less than 30 min under mild conditions.

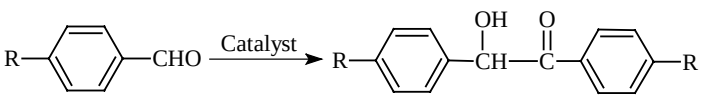
Keywords: Benzoin condensatin, imidazolium, room-temperature ionic liquid.

Benzoin condensation is one of the oldest C-C bond forming reactions in organic chemistry and has been developed for classical organic synthesis using cyanide ion and onium salts including thiazolium and imidazolium salts as catalysts[1] (**Scheme 1**). The catalytic ability of onium salts is due to onium-2-ylide generated by expulsion of C-2 hydrogen of the onium salts by base.

Recently, room-temperature ionic liquids (RTILs) have attracted growing attention because of their unique features[2] such as nonvolatility, thermal stability with a liquid range of about 300℃ and variability with respect to the choice of organic cations, anions and side-chain attached to the organic cation. As neoteric solvents instead of conventional organic solvents, RTILs have been used in many organic reactions such as Diels-Alder[3], alkylation[4], Knoevenagel[5], Friedlander[6], reduction of aldehydes[7], amination[8] and epoxidation[9] reactions *etc*., providing comparable or even better results in most cases.

Davis and co-workers reported[10] benzoin condensation was accomplished in the biphasic reaction system of ionic liquid **1** or **2** (**Scheme 2**) and toluene giving approximately 80% yield after a long reaction time of one week. Although thiazolium salts show good catalytic ability for benzoin condensation, the thiazolium ring is easily destroyed by oxygen in the presence of base.

Scheme 1



R = H, Me, OMe, Cl

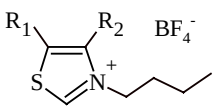
* E-mail: schemorg@mail.sc.cninfo.net

In our group, much attention has been paid for the synthesis and applications of imidazole, imidazolium and their derivatives[1h, 11]. In the previous work[1h], we used imidazolium salt **4a** (**Scheme 2**) as catalyst with 50% aqueous sodium hydroxide for benzoin condensation in refluxing tetrahydrofuran (THF), obtaining 91% yield, that is the best yield ever reported for the benzoin condensation by an imidazolium analogue as catalyst. Since imidazolium based RTILs can be obtained conveniently, imidazolium is far more stable than thiazolium and it can endure strong acids, bases and heating, we became interested in directly using RTIL as solvent and promoter for benzoin condensation.

Herein, we report the benzoin condensation promoted in three kinds of RTILs **3a** [bmim]Br, **3b** [bmim]BF_4 and **4b** [Bnmim]BF_4[12] (**Scheme 2**) for the first time. Based on our previous work[1h], we chose sodium hydroxide as base that was strong enough to remove the C-2 hydrogen of imidazolium to form the presumptive actual catalyst imidazolium-2-ylide. Firstly, benzoin condensation in RTIL **3a** [bmim]Br was investigated and four factors were considered. As shown in **Table 1**[13], lower or higher temperature resulted in decrease of yields (entries 3-6) and 65℃ was the appropriate temperature. Similarly, suitable amount of base was desired (entries 7-9, 13 and 15). Benzoin condensation did not occur without base (entry 1) and the yield decreased sharply with excess base (entry 7). The optimal amount of base used here was 0.5 equiv. that was only one eighth of that ever reported[1h]. It was found that the best ratio of RTIL to benzaldehyde (mL / mmol) was 0.1 (mL / mmol), giving 80% yield (entry 13). And no benzoin was detected when ionic liquid was absent (entry 2). This reaction showed weak dependence on the reaction time and could complete within 30 min that was much shorter than reported[10]. For RTILs **3b** and **4b**, the similar effects of temperature, base, ratio and time on the yields were observed. The difference between **3a** and **3b** (or **4b**) lay in the optimal ratio of RTIL to benzaldehyde used (entries 13, 17 and 19). For both **3b** and **4b**,optimal ratio of RTIL to benzaldehyde was 0.5 (mL / mmol), and the yield could rise up to 91% and 90%, respectively. Routinely, we recycled the ionic solvent and found no obvious decrease in condensation yields (entry 17).

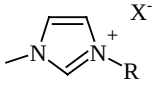
We then studied the self-condensation of a range of representative substituted benzaldehydes (**Scheme 1**, R= Me, OMe, Cl) under the best reaction conditions (65℃, 0.5 mL/mmol **3b**, 0.5 equiv. NaOH). And these aldehydes gave corresponding substituted benzoins in 53%, 51% and 68% yields, respectively.

Scheme 2



1 $R_1 = CH_3$, $R_2 = H$

2 $R_1 = H$, $R_2 = CH_3$



3a R = *n*-C_4H_9, X = Br, [bmim]Br

3b R = *n*-C_4H_9, X = BF_4, [bmim]BF_4

4a R = $PhCH_2$, X = PF_6, [bmim]PF_6

4b R = $PhCH_2$, X = BF_4, [bmim]BF_4

Table 1 Reaction conditions and results[a]

Entry	RTIL	Ratio[b]	NaOH[c]	Temp. (℃)	Yield[d] (%)
1	**3a**	1.0	-	65	0
2	-[e]	-	1.0	65	0[f]
3	**3a**	1.0	1.0	23	12
4	**3a**	1.0	1.0	65	34
5	**3a**	1.0	1.0	80	25
6	**3a**	1.0	1.0	100	25
7	**3a**	0.5	1.0	65	23
8	**3a**	0.5	0.5	65	68
9	**3a**	0.5	0.25	65	63
10	**3a**	1.0	0.5	65	55
11	**3a**	1.5	0.5	65	35
12	**3a**	0.25	0.5	65	72
13	**3a**	0.1	0.5	65	80
14	**3a**	0.05	0.5	65	74
15	**3a**	0.1	0.25	65	74
16	**3b**	0.1	0.5	65	80
17	**3b**	0.5	0.5	65	91 (89[g])
18	**3b**	1.0	0.5	65	81
19	**4b**	0.5	0.5	65	90

Notes: a. Reaction time: within 30 min; b. RTIL / benzaldehyde, mL/mmol; c. Base / benzaldehyde, mmol/mmol; d. Isolated yield; e. Using the same volume of THF instead of **3a**; f. A little of benzoic acid was formed; g. The promoter system had been twice recovered and used for a third time.

In summary, benzoin condensation proceeded smoothly and efficiently within less than 30 min using nonvolatile and recyclable room temperature ionic liquids (RTILs) **3a**, **3b** or **4b** as sole solvent and promoter. The reaction condition was rather mild and the yield of benzoins was up to 91%.

Acknowledgment

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13. A typical procedure for benzoin condensation: To a 10 mL round-bottom flask, was added 1 mL **3b** [bmim]BF_4 at 65℃. Then freshly distilled benzaldehyde (0.2 mL, 2 mmol) and pulverized sodium hydroxide (40 mg, 1 mmol) were added subsequently under vigorous stirring. After about 30 min, work-up was made. Method A: 10 mL water was added and the desired product benzoin precipitated out. The solid product was obtained by filtration, washed and dried. Method B: The reaction mixture was fully extracted with ethyl ether, combined, evaporated under reduced pressure and then purified through column chromatogram to give the desired product. Ionic liquid containing NaOH could be recovered and reused after the work-up (Method B). Benzoins obtained: m.p.: 130-131℃ (R = H), 88-89 ℃ (R=Me), 107-109℃ (R=OMe), 85-86℃ (R=Cl). The m.p., ^{1}HNMR and MS spectra of the products were identical with that of the authentic samples[1a].

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