

An efficient [Bmim]OH catalysed the condensations of aromatic aldehydes and diethyl malonate

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Abstract:

The rapid and green procedure for the Knoevenagel reaction between aromatic aldehydes and diethyl malonate was developed by using 1-butyl-3-methylimidazolium hydroxide, [Bmim]OH, as an efficient catalyst. The condensations showed good yields with a wide range of aromatic aldehydes in solvent-free condition and short reaction times. [Bmim]OH was easy to recover and could be reused several times without significant loss of catalytic activity.

Keywords: green catalyst, green chemistry, ionic liquids, Knoevenagel reaction.

Classification number: 2.2

Introduction

Ionic liquids are ionic compounds that are liquid below 100°C. Their unique properties include thermal stability, biodegradability and non-volatility, and they have received special attention as environmentally benign solvents for organic synthesis. Ultimately, the combinations of organic cations and anions help to design and fine-tune their physical and chemical properties [1-4]. Due to the requirement in developing the environmentally benign processes, ionic liquids have been studied intensively as green solvents in diverse fields such as chemical reactions, electrochemistry and biochemistry [3, 5-9].

The Knoevenagel condensation reaction, which occurs between aldehydes or ketones and active methylene compounds, is a classic method for carbon-carbon bond formation [2]. The α,β -unsaturated products obtained by this method has been widely used as intermediates in organic synthesis and have been found to have increasing applications in medicine, biological science, agriculture and light-emitting materials [10]. Unfortunately, this method needs to be carried out in organic solvents and requires the

Lewis base catalysts such as piperidine, pyridine, NaOH, K_2CO_3 , etc., which are not recovered and reused [11-14]. Recently, the Knoevenagel reaction using ionic liquids as catalysts has been studied extensively. The ionic liquid was one of the most efficient catalytic systems that were easily recovered and reused several times [15].

In this research, we reported the Knoevenagel condensations using a basic ionic liquid, [Bmim]OH. In terms of green chemistry in organic synthesis, we synthesised [Bmim]OH via the metathesis reaction and used it as an efficient catalyst for the condensations of aromatic aldehydes and diethyl malonate under solvent-free condition. The basic catalyst could be recycled easily by the extraction and removal of water.

Experimental section

All chemicals were purchased from Sigma-Aldrich. The solvents were supplied by Xilong Chemical. The Agilent 7890A GC-MS system was equipped with a mass selective detector Agilent 5975N and a capillary column HP-5MS (length = 30 m, inner diameter = 320 μ m, film thickness = 0.25 μ m). The 1H NMR spectra were recorded on a Bruker 500 MHz using $CDCl_3$ as solvent (Fig. 1).

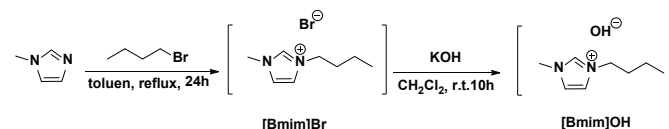


Fig. 1. Procedure for the synthesis of [Bmim]OH.

A typical procedure for the synthesis of [Bmim]Br: a round-bottomed flask (100 mL volume) was charged with a mixture of 1-methylimidazole (4.10 g, 5 mmol) and 1-bromobutane (6.85 g, 5 mmol) in toluene. Then, it was placed in an oil bath and heated at 110°C in a magnetic stirrer for 12 h. After completion the reaction, the reaction mixture was cooled down to room temperature and then washed with diethyl ether (3 x 10 mL) to obtain [Bmim]Br

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[16]. The purity and authenticity of the ionic liquids were confirmed by ^1H NMR spectroscopy.

1-butyl-3-methylimidazolium bromide [16]: a yellowish syrup. IR: ν (cm^{-1}): 3098, 2962, 2874, 1631, 1571, 1382, 1168, 1109, 760, 649. ^1H NMR (500 MHz, CDCl_3) δ 10.29 (s, 1H), 7.53 (t, $J = 2$ Hz, 1H), 7.42 (t, $J = 2$ Hz, 1H), 4.30 (t, $J = 7.5$ Hz, 2H), 4.09 (s, 3H), 1.88 (m, 2H), 1.396-1.321 (sext, $J = 7.5$ Hz, 2H), 0.93 (t, $J = 7.5$ Hz, 3H).

A typical procedure for the synthesis of [Bmim]OH: a mixture of KOH (1.2 g, 20 mmol) and [Bmim]Br (4.4 g, 20 mmol) in dry CH_2Cl_2 (20 mL) was stirred at room temperature for 10 h. After the completion of the reaction, the precipitated KBr was filtered off, and the filtrate was evaporated under vacuum to obtain the [Bmim]OH as a viscous liquid. The desired ionic liquid was washed with diethyl ether (3×20 mL) and dried at 90°C for 10 h to obtain the pure ionic liquid for use [17].

1-butyl-3-methylimidazolium hydroxide [17]: a honey-coloured syrup. IR: ν (cm^{-1}): 3452 (O-H), 3150, 3099, 2962, 2906 (C-H), 1651 (C=N); 1247, 1114, 860. ^1H NMR (500 MHz, CDCl_3) δ 10.28 (s, 1H), 7.51 (s, 1H), 7.39 (s, 1H), 4.31 (t, $J = 7.5$ Hz, 2H), 4.09 (s, 3H), 2.32 (bs, 1H), 1.91-1.85 (m, 2H), 1.37 (dt, $J = 15, 7.5$ Hz, 2H), 0.94 (t, $J = 7.5$ Hz, 3H).

A typical procedure for the condensation of benzaldehyde and diethyl malonate: benzaldehyde (1 mmol), diethyl malonate (1 mmol) and [Bmim]OH (0.3 mmol) were reacted at 100°C for 2 h. After cooling, the reaction mixture was extracted with diethyl ether (3×20 mL). Since [Bmim]OH is insoluble in diethyl ether, it is easily separated from the mixture. Then, it was washed in water, which was removed by evaporation. For the ether layer, it was decanted, washed with water and dried over Na_2SO_4 . The solvent was then removed by a rotary evaporator. The desired product was purified by column chromatography. The purity and authenticity of the product was confirmed by GC-MS and ^1H NMR spectroscopy.

Diethyl benzenelidenemalonate [8]: GC-MS (EI, 80 eV) m/z 248 (M^+). ^1H NMR (500 MHz, CDCl_3) δ 7.73 (s, 1H), 7.46-7.44 (m, 2H), 7.38-7.36 (m, 3H), 4.35-4.28 (m, 4H), 1.33 (t, $J = 7$ Hz, 3H), 1.28 (t, $J = 7$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 166.7, 164.1, 142.1, 132.9, 130.5, 129.5, 128.8, 126.4, 61.7, 61.6, 14.1, 13.8.

Results and discussion

We aim to synthesise a 'green' catalyst for the Knoevenagel condensation as well as suggest an efficient

and green process for the synthesis of some functionalised alkenes that are widely used as intermediates in organic synthesis.

Preparation and characterisation of catalyst:

[Bmim]Br was synthesised from 1-methylimidazole and 1-bromobutane. Then, [Bmim]OH was obtained by the metathesis reaction of [Bmim]Br with KOH in dry CH_2Cl_2 . [Bmim]OH was obtained in high yield and it was applied as a green basic catalyst for the Knoevenagel condensation. [Bmim]OH was characterised by FT-IR and ^1H NMR spectroscopy. In the FT-IR spectra of [Bmim]OH, the peak at 3452 cm^{-1} is a characteristic of the stretching vibration of -OH. The peaks at $2900\sim 3000\text{ cm}^{-1}$ are assigned as the saturated C-H stretching vibrations. The peaks at 1651 cm^{-1} could be assigned to the stretching vibration of C=N.

Catalytic testing: the Knoevenagel condensation of benzaldehyde and dimethyl malonate is used as a model reaction to investigate reaction conditions in which the functionalised alkene was obtained in the highest yield and purity (Fig. 2). All reactions were carried out in an IKA RET BASIC (USA) heating magnetic stirrer, which is equipped with an electronic temperature controller.

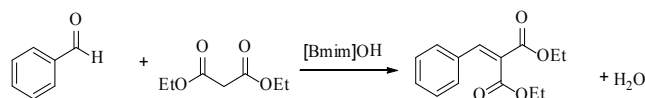


Fig. 2. Knoevenagel condensation of benzaldehyde and dimethyl malonate.

Table 1. The effect of temperature on reaction under magnetic stirring.

Entry	Temperature ($^\circ\text{C}$)	Yield (%)
1	r.t	13
2	50	54
3	80	76
4	100	95
5	120	99

The condensation between aldehyde and activated methylene is preferred at high temperature (Table 1). The temperature of 100°C was chosen as the optimal temperature. When the temperature was 120°C , the yield of the reaction slightly increased (Table 1, entries 4-5).

Table 2. The effect of the reaction time.

Entry	Time (h)	GC Yield (%)
1	0.5	43
2	1.0	61
3	1.5	84
4	2.0	95

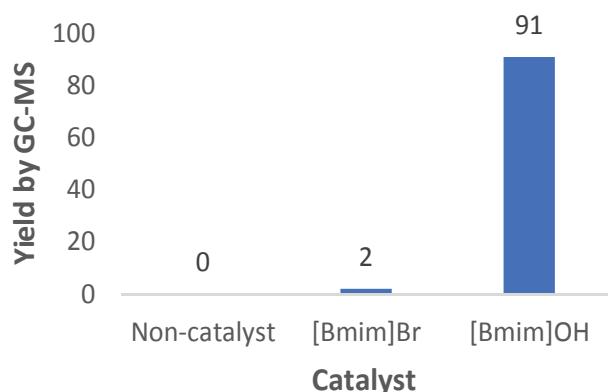
As the reaction time prolonged, there was a significant increase in the conversion of benzaldehyde. The desired product was obtained in quantity (95%) for 2 h (Table 2, entry 4).

Table 3. The effect of the amount of catalyst.

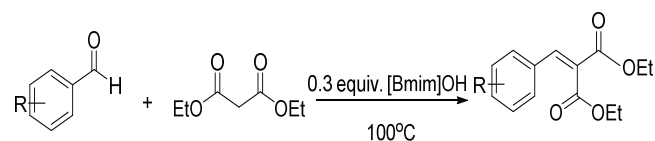
Entry	Catalyst (mol%)	Yield (%)
1	0	0
2	5	29
3	20	78
4	30	91
5	40	92
6	50	95

The effect of the catalyst was investigated on the Knoevenagel condensation under the current method. The optimal amount of the catalyst was only 0.3 equiv. (Table 3).

As a result, the optimal condition was using 0.3 equiv of [Bmim]OH and magnetic stirring at 100°C for 2 h. Additionally, we carried out the control experiments (Fig. 3). No desired product was obtained in the absence of [Bmim]OH. In addition, [Bmim]Br was not reactive in the current method because [Bmim]Br is a neutral ionic liquid.

**Fig. 3. Control experiments.**

We applied the optimal conditions for the Knoevenagel condensation between some benzaldehyde derivatives and diethyl malonate to study the effects of the structural effect of benzaldehyde derivatives. The results are shown in Table 4.

Table 4. The Knoevenagel reaction of different substrates using [Bmim]OH under solvent-free.

Entry	Substrate	Time (h)	Product	Isolated yield (%)
1		2		90
2		3		83
3		3		87
4		3		67
5		3		75

It is evident that aromatic aldehyde with an electron-donating group such as 4-methylbenzaldehyde and 4-methoxybenzaldehyde was less reactive than benzaldehyde, by 83% and 77%, respectively (Table 4, entries 2, 3). The desired products were obtained in lower yields with nitrobenzaldehydes because these substrates were less soluble in the reaction mixture (Table 4, entries 4, 5). In addition, 2-nitrobenzaldehyde reacted at lower conversion (Table 4, entry 4) due to the increased steric hindrance of *ortho*-substitution.

The [Bmim]OH catalyst was easily recovered and reused without any loss of catalytic activity. Since [Bmim]OH is insoluble in diethyl ether, it is easily separated from the mixture. Then, it was washed and dried under vacuum.

The recovered [Bmim]OH was reactive in the Knoevenagel condensation of benzaldehyde, and dimethyl malonate produced the desired product in 89% isolated yield.

Conclusions

To conclude, the basic ionic liquid [Bmim]OH is an efficient catalyst for the Knoevenagel condensation. The ionic liquid is known as green solvent/catalyst for many organic transformations. These condensations of aromatic aldehydes and diethyl malonate were efficiently catalysed by a small amount of [Bmim]OH under a solvent-free condition with high reaction yields in short reaction times.

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