

Knoevenagel Condensation Reaction Using Brønsted-Acidic Ionic Liquids as Green and Reusable Catalysts

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Knoevenagel condensation reaction of aromatic aldehydes with malononitrile proceeded efficiently in water using Brønsted-acidic ionic liquids as catalyst. The experimental results show that these ionic liquids have good catalytic activities to the Knoevenagel condensation. The reactions are carried out in a few minutes with high yields. The products could simply be separated from the catalyst/water and the catalyst could be recycled without noticeably decreasing the catalytic activity.

Key Words: Brønsted-acidic ionic liquids, Knoevenagel condensation, Aromatic aldehydes, Malononitrile.

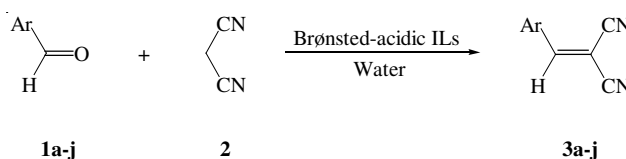
INTRODUCTION

Knoevenagel condensation is one of the most useful and widely employed methods for the formation of C=C bond in organic synthesis^{1,2}. Normally, it carried out in the presence of harmful organic solvent³ and catalysts such as $\text{AlPO}_4\text{-Al}_2\text{O}_3$ ⁴, ZnCl_2 ⁵ and K_2PO_4 ⁶. Additionally, this reaction could also performed by microwave irradiation⁷ or infrared⁸, but it requires special reaction instruments and conditions. In recent years, ionic liquids have been known as effective catalysts in the context of green synthesis in organic chemistry. Ionic liquids have interesting advantages such as extremely low vapour pressure, excellent thermal stability, ready to dissolve many organic and inorganic substrates⁹. These compounds have been widely applied in many reaction as catalysts such as alkylation, esterification, Micheal addition, oligomerization and rearrangement¹⁰⁻¹³. However, the study of Knoevenagel reaction using ionic liquids as catalyst are scanty¹⁴⁻¹⁶. It might be due to the limitation of the traditional ionic liquids that either are water unstable¹⁷ or just have very week acidities¹⁸, therefore making it hard to obtain good catalytic reactions in the Knoevenagel reaction using ionic liquids as catalyst. The introduction of Brønsted-acidic functional groups into cations or anions of the ionic liquids, especially the SO_3H -functional groups, obviously enhanced their acidities and water solubilities¹⁹⁻²¹. Therefore, Brønsted-acidic ionic liquids can be used as highly efficient acid catalysts in aqueous media. To the best of our knowledge, there are no examples of the use of Brønsted-

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acidic ionic liquids as catalyst in aqueous media for the Knoevenagel condensation reaction.

In continuation of our previous works on the applications of reusable acid catalysts in the synthesis of organic compounds²²⁻²⁴ here we wish to report a simple method for the Knoevenagel condensation of aromatic aldehydes with malononitrile in high yields using Brønsted-acidic ionic liquids (**Scheme-I**).



Scheme-I: Knoevenagel condensation

EXPERIMENTAL

All compounds were known and their physical and spectroscopic data were compared with those of authentic samples and found to be identical. Melting points were recorded on an electrothermal type 9100 melting point apparatus. The IR spectra were obtained on a 4300 Shimadzu spectrophotometer as KBr disks. The ¹H NMR (500 MHz) spectra were recorded on Bruker DRX500 spectrometer.

General procedure for the Knoevenagel condensation of aromatic aldehydes with malononitrile using Brønsted-acidic ionic liquids: A mixture of aromatic aldehyde (1 mmol), malononitrile (1 mmol) and the Brønsted-acidic IL (0.12 mmol of ionic liquid-1 or 0.10 mmol of ionic liquid-2) in water (3 mL) was heated on the oil bath at 70 °C for a few minutes. The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature. The precipitate was filtered off and recrystallized from ethanol to give compounds **3a-j** in high yields (Table-3).

Recycling of the catalyst: The catalysts are soluble in water and therefore could be recycled of the filtrate. The catalysts were recovered by evaporation of the water, washed with diethyl ether and dried at 50 °C under vacuum for 1 h.

RESULTS AND DISCUSSION

For present investigations, two Brønsted-acidic ionic liquids, 3-methyl-1-(4-sulphonic acid)butylimidazolium hydrogen sulphate [(CH₂)₄SO₃HMIM][HSO₄] (ionic liquid-1) (Fig. 1) and N-(4-sulphonic acid)butylpyridinium hydrogen sulphate [(CH₂)₄SO₃HPY][HSO₄] (ionic liquid-2) (Fig. 2) were prepared according to the literature procedure^{25,26}.

Initially to optimize the reaction conditions, the reaction of benzaldehyde and malononitrile was used as a model reaction. Therefore, ionic liquids and the reactions substrates, benzaldehyde and malononitrile, were mixed in water and the reaction mixture was heated on the oil bath at 70 °C for a few minutes. The efficiency of the

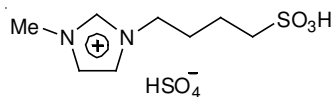
[(CH₂)₄SO₃HMIM][HSO₄]

Fig. 1. Brønsted-acidic ionic liquid-1 structure

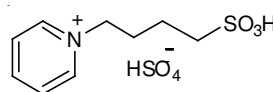
[(CH₂)₄SO₃HPY][HSO₄]

Fig. 2. Brønsted-acidic ionic liquid-2 structure

reaction is mainly affected by the amount of ionic liquids (Table-1). It showed that no product could be detected in the absence of the catalysts (entry 1), which indicated that the catalyst should be absolutely necessary for this condensation reaction. The optimal amount of ionic liquid-1 and ionic liquid-2 were 12 and 10 mol %, respectively (entries 6, 11).

TABLE-1
KNOEVENAGEL CONDENSATION OF BENZALDEHYDE
WITH MALONONITRILE IN CATALYST/H₂O^a

Entry	Catalyst	Ratio (mol %)	Time (min)	Yield (%) ^b
1	No	0	60	No reaction
2	Ionic liquid-1	2	25	86
3	Ionic liquid-1	5	16	90
4	Ionic liquid-1	8	9	93
5	Ionic liquid-1	10	7	95
6	Ionic liquid-1	12	5	97
7	Ionic liquid-1	15	5	95
8	Ionic liquid-2	2	21	88
9	Ionic liquid-2	5	71	93
10	Ionic liquid-2	8	4	95
11	Ionic liquid-2	10	1	98
12	Ionic liquid-2	12	1	98

^aReaction conditions: 1 mmol benzaldehyde, 1 mmol malononitrile and 3 mL H₂O at 70 °C.

^bIsolated yields.

All, the reaction was also carried out in various solvents (Table-2). Among the solvents tested, the reaction in water gave excellent yields of the desired product. Water is a clean and cheap solvent. It is important to carry out organic reactions in water instead of volatile solvent for the environmental and economic reasons. So in other studies all reactions carried out in water and in the presence of the optimal amount of the catalysts (12 mol % for ionic liquid-1 and 10 mol % for ionic liquid-2).

To show the generality of this method the optimized system used for the reaction of various aromatic aldehydes with malononitrile. The products obtained in high yields and at very short reaction times (Table-3).

Reusability of the catalyst was also investigated. For this purpose, the model reaction was again studied in the optimized conditions. After the completion of the reaction, the catalyst was recovered (experimental section) and reused for the similar reaction. This process was carried out over three runs without appreciable reduction in the catalytic activity of the catalyst.

TABLE-2
SYNTHESIS OF THE PRODUCTS **3a-j** IN THE PRESENCE OF
IONIC LIQUID-1 (12 mol %) IN DIFFERENT SOLVENTS

Entry	Solvent	Temperature (°C)	Time (min)	Yield (%) ^a
1	H ₂ O	70	5	97
2	CH ₃ OH	64	25	63
3	CH ₃ CN	81	20	58
4	CH ₂ Cl ₂	40	40	70
5	C ₆ H ₅ CH ₃	110	45	37
6	Solvent-free	80	30	72

^aIsolated yields.

TABLE-3
SYNTHESIS OF THE PRODUCTS **3a-j** IN THE PRESENCE OF IL₁/IL₂

Entry	Ar	Products ^a	Time (min) (IL ₁ /IL ₂)	Yield (%) ^b (IL ₁ /IL ₂)	m.p. (°C)
1	C ₆ H ₅	3a	5/1	97/98	82-85
2	2-ClC ₆ H ₄	3b	5/2	95/97	82-85
3	4-ClC ₆ H ₄	3c	5/1	91/93	158-160
4	3-MeC ₆ H ₄	3d	5/2	95/97	90-92
5	4-MeC ₆ H ₄	3e	4/1	93/95	132-134
6	4-NO ₂ C ₆ H ₄	3f	3/1	97/98	157-159
7	4-MeOC ₆ H ₄	3g	4/2	88/90	110-113
8	2-HOC ₆ H ₄	3h	6/3	89/93	180-182
9	3-HOC ₆ H ₄	3i	7/5	93/95	148-150
10	4-HOC ₆ H ₄	3j	4/1	91/92	184-185

^aAll the products were characterized by ¹H NMR and IR spectral data and comparison of their melting points with those of authentic samples. ^bIsolated yields, IL₁ = Ionic liquid-1, IL₂ = Ionic liquid-2.

Conclusion

In conclusion, we have reported a new catalytic method for the Knoevenagel condensation reaction of aromatic aldehydes with malononitrile in the presence of Brønsted-acidic ionic liquids as efficient, reusable and eco-friendly homogeneous catalysts. The catalysts can be reused after a simple work-up, with a gradual decline of its activity being observed. High yields, short reaction times, simplicity of operation and easy work-up are some advantages of this protocol. Most importantly, water has been chosen as a green solvent for these reactions.

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