

An efficient procedure for protection of carbonyls in Brønsted acidic ionic liquid [Hmim]BF₄

Hai-Hong Wu, Fan Yang, Peng Cui, Jie Tang* and Ming-Yuan He

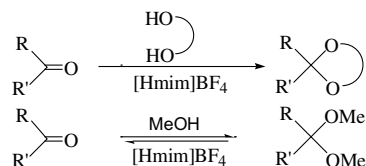
Center for the Chemistry of Ionic Liquids, Department of Chemistry, East China Normal University, Shanghai 200062, China

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Abstract—Protection of carbonyls as acetals or ketals using Brønsted acidic ionic liquid [Hmim]BF₄ as catalyst as well as solvent was investigated. Satisfactory results were obtained for the protection of carbonyls as cycloacetals or ketals with diols. The product can be separated conveniently from the reaction system, and the ionic liquid can be reused after removal of water.
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Protection of carbonyl groups plays an important role in organic synthesis. Acid-catalyzed formation of acetals and ketals is the most practical choice for protection of aldehydes or ketones.^{1,2} The shortcomings of methods currently used are: use of a large excess amount of alcohols, poor chemical selectivity, and tedious work-up processes. Alternative catalysts, including organometallic reagents,³ silyl reagents,⁴ and inorganic compounds (FeCl₃, TiCl₄, Bi(NO₃)₃),⁵ have recently been reported for the protection of carbonyls as acetals or ketals, and the search for a new catalyst is still being actively pursued due to problems such as difficulty in handling the reagents and limited examples.⁶

In recent years, ionic liquids have attracted intensive interests as a possible replacement of traditional solvents for organic reactions, particularly in the area of green chemistry, due to their advantageous properties, including negligible vapor pressure and high thermal and chemical stability.⁷ An ever-increasing interest has focused on ionic liquids as media for catalytic reactions where the catalyst is in one phase and the product in another, which makes product-isolation easy and catalyst-reuse convenient. We have recently reported a practical and efficient procedure for esterification of carboxylic acids with alcohols in Brønsted acidic ionic liquid, *N*-methylimidazolium tetrafluoroborate



Scheme 1.

([Hmim]BF₄).⁸ We further report here a practical procedure for protection of various carbonyl compounds by the formation of acetals or ketals in [Hmim]BF₄ as depicted in Scheme 1.

In the protection of a variety of aldehydes and ketones with neopentyl glycol, ethylene glycol or methanol, Brønsted acidic ionic liquid [Hmim]BF₄ acted as catalyst as well as medium. Various carbonyls have been investigated and the results are summarized in Table 1.

The results in Table 1 clearly demonstrate that the method of protecting carbonyls with neopentyl glycol is efficient, with almost quantitative conversions and selectivities in most cases. The molar ratio of aldehyde or ketone to neopentyl glycol is 1:1. *n*-Hexanal was converted in 3 h with 98% conversion and 100% selectivity (Table 1, entry 1). Aromatic aldehydes, such as benzaldehyde and *o*-nitrobenzaldehyde, also gave satisfactory results with 93% and 100% conversions (Table 1, entries 5 and 6). The protection of ketones was also investigated. Cyclohexanone and cyclopentanone were converted into the corresponding ketal with high

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* Corresponding author. Fax: +86-21-62232100; e-mail: jtang@chem.ecnu.edu.cn

Table 1. Results of protection for different aldehydes and ketones with alcohols in ionic liquid [Hmim]BF₄^a

Run	Aldehydes (ketones)	Alcohols	Molar ratio	Conv. ^b (%)	Select. ^{b,c} (%)	T (°C)	Time (h)
1	<i>n</i> -Hexanal	Neopentyl glycol	1:1	98	100	90	3
2	Butanone	Neopentyl glycol	1:1	100	100	90	3.5
3	Cyclohexanone	Neopentyl glycol	1:1	93	100	90	6
4	Cyclopentanone	Neopentyl glycol	1:1	76	100	90	6
5	Benzaldehyde	Neopentyl glycol	1:1	93	100	90	6
6	<i>o</i> -Nitrobenzaldehyde	Neopentyl glycol	1:1	100	100	90	6
7	<i>n</i> -Hexanal	Ethylene glycol	1:1	97	100	90	6
8	Butanone	Ethylene glycol	1:1	94	100	90	6
9	Cyclohexanone	Ethylene glycol	1:1	92	100	90	3
10	Cyclopentanone	Ethylene glycol	1:2	100	100	90	3
11	Benzaldehyde	Ethylene glycol	1:2	60	100	90	6
12	<i>o</i> -Nitrobenzaldehyde	Ethylene glycol	1:2	100	100	90	6
13	<i>p</i> -Nitrobenzaldehyde	Ethylene glycol	1:2	100	100	90	6
14	<i>p</i> -Chlorobenzaldehyde	Ethylene glycol	1:2	53	100	90	6
15	<i>n</i> -Hexanal	Methanol	1:6	100	100	65	3
16	Cyclohexanone	Methanol	1:10	50	100	65	3

^a Ketones or aldehydes (27 mmol), alcohols (27 mmol), [Hmim]BF₄ (4 mL).

^b Detected by GC-MS. Conversions based on the starting carbonyls.

^c Condensation by-products were detected.

selectivity (Table 1, entries 3 and 4). However, the conversion of cyclopentanone was difficult.

When ethylene glycol was used, reaction rates slightly decreased for straight chain carbonyls (Table 1, entries 7–14) under identical reaction conditions. For *n*-hexanal, the reaction time required for similar conversions and selectivities was longer than when neopentyl glycol was used (Table 1, entry 7). Similarly, butanone reached 94% conversion after 6 h (Table 1, entry 8). However, treatment of cyclopentanone with 2 equiv of ethylene glycol gave quantitative conversion and selectivity (Table 1, entry 10). The conversion of *o*-nitrobenzaldehyde and *p*-nitrobenzaldehyde into corresponding protected compounds produced higher yields than that of benzaldehyde (Table 1, entries 11–13). This is consistent with reports that showed electron-withdrawing substituents enhanced the rate of acetal formation.⁹

The protection of *n*-hexanal and cyclohexanone with methanol was also examined (Table 1, entries 15 and 16). *n*-Hexanal can be protected smoothly using a higher proportion of methanol (molar ratio 1:6), while ketone gave only about 50% conversion even when the molar ratio of methanol was increased to 1:10. In this case, large amount of excess methanol partially acted as the solvent, and [Hmim]BF₄ mainly played the role of an acidic catalyst.

There was no need to remove the water produced during the reaction, because [Hmim]BF₄ was miscible with water while the acetals and ketals were immiscible with [Hmim]BF₄. Therefore, the products could be separated conveniently by decanting. The ionic liquid [Hmim]BF₄ could be easily recycled. After the reaction, [Hmim]BF₄ was readily separated and reused upon drying in vacuum. The [Hmim]BF₄ was reused eight times in the protection of cyclohexanone with ethylene glycol, each time with the same conversion and selectivity (Table 2).

Table 2. Recycling of [Hmim]BF₄^a

Run	Conversion (%)	Selectivity (%)
1	92	100
2	92	100
3	94	100
4	94	100
5	95	100
6	94	100
7	95	100
8	94	100

^a Reaction of cyclohexanone with ethylene glycol (molar ratio 1:1) at 90 °C for 3 h.

In conclusion, aldehydes or ketones were efficiently converted to corresponding acetals or ketals using Brønsted acidic ionic liquid [Hmim]BF₄ as catalyst as well as medium. The products can be separated conveniently from the reaction system, and the ionic liquid can be reused after removal of water. The merit of this methodology is that it is simple, mild, and efficient.¹⁰ Further studies on its applicability are currently under investigation.

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10. General procedure for the protection of carbonyl groups: The ionic liquid [Hmim]BF₄ (4 mL) was mixed with *n*-pentanal (2.9 mL, 27 mmol) and ethylene glycol (1.5 mL, 27 mmol). The mixture was heated in oil bath at designed temperature. After the reaction, the organic layer was separated from the ionic liquid by decanting, and the product was detected by GC–MS. The ionic liquid [Hmim]BF₄ was reused after removal of water under vacuum.