

[A025] **One-pot three-component Mannich-type reaction catalyzed by functionalized ionic liquid**

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Abstract

Several ionic liquids used as catalyst for three-component Mannich reactions of aldehydes, amines, and naphthols at room temperature. The used ionic liquids include 1-butyl-3-methylimidazolium tetrafluoroborate ([Bmim]BF₄), 1-octyl-3-methylimidazolium tetrafluoroborate ([Omim]BF₄), 1-ethyl-3-methylimidazolium tetrafluoroborate ([Emim]BF₄), butyl dimethylimidazolium tetrafluoroborate ([Bdmim]BF₄), 1-octyl-3-methylimidazolium nitrate ([Omim]NO₃), 1-methylimidazolium sulfuric acid ([Hmim]HSO₄) and 1-methylimidazolium trifluoroacetic acid ([Hmim] Tfa). Higher yields were obtained in the presence of [Hmim] Tfa in comparison with other ionic liquids.

Introduction

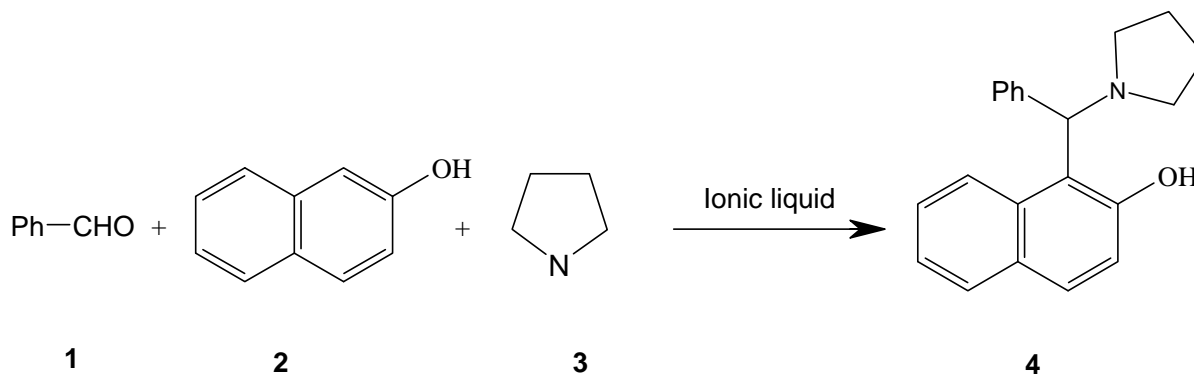
Nitrogen containing biologically active compounds are of high interests as pharmaceuticals and has been a significant branch of organic synthesis.[1-3] The Mannich reaction is one of the most basic and useful methods for the synthesis of such compounds.

Various catalyst such as Lewis acids, Lewis bases, Bronsted acids, rare metal salts or organic catalysts have been investigated in this reaction over the past decades. However, the search for the new and green catalysts is still of special interest.[4]

In recent years, ionic liquids including functionalized ones have attracted extensive attention in the framework of green synthesis.[4] These liquids are a kind of ionic solvent, which combine the advantages of both conventional organic solvents and melt salts, have been considered as new reaction media, and have found wide use in catalytic and non-catalytic reactions. Their benefit lie not only on their capability on dissolving many organic or inorganic substances, but also on the ease of their recycling. Moreover, their properties are tunable to satisfy specific chemical tasks.[5]

Result and Discussion

In this work we chose a reaction of benzaldehyde, pyrrolidine and 2-naphthol (Scheme 1) to test the catalytic activity of several ionic liquids include [Bmim]BF₄, [Omim]BF₄, [Emim]BF₄, [Bdmim]BF₄, [Hmim]Tfa, [Hmim]HSO₄ and [Omim]NO₃. The results are shown in Table 1.



Scheme 1

Table 1: The study of various ionic liquids on Mannich reaction of benzaldehyde, pyrrolidine and β -naphthol

Entry	Catalyst	Time(h)	Yeild(%)
1	[Bmim]BF ₄	24	N.R
2	[Omim]BF ₄	24	N.R
3	[Emim]BF ₄	24	N.R
4	[Omim]NO ₃	24	N.R
5	[Bdmim]BF ₄	24	N.R
6	[Omim]BF ₄ /FeCl ₃	24	N.R
7	[Omim]BF ₄ /Al ₂ O ₃	24	N.R
8	[Omim]BF ₄ /ZnCl ₂	24	N.R
9	[Omim]BF ₄ /H ₂ O	24	N.R
10	[Omim]BF ₄ /NaHCO ₃	24	N.R
11	[Omim]BF ₄ /Na ₂ CO ₃	24	N.R
12	[Hmim] Tfa/ EtOH ^a	18	>85
13	[Hmim] HSO ₄	24	N.R

as shown in Table 1, ([Hmim]Tfa) can catalyze the reaction efficiently (Entry 12). However, other ionic liquids yield no Mannich base. Morpholine as the base has afforded less yield than pyrrolidine (Table 2). Paraformaldehyde has proven to be more active than benzaldehyde (Table 3).

Table 2: The reaction between benzaldehyde, 2-naphthol and pyrrolidine or morpholine in the presence of [Hmim]Tfa

Aldehyde	Naphthol	Amine	Product	Time(h)	Yeild(%)
Benzaldehyde	2-naphthol	Pyrrolidine (3a)	4a	15	>85
Benzaldehyde	2-naphthol	Morpholine (3b)	4b	22	>70

Table 3: The reaction between Paraformaldehyde, naphthols and a secondary amine in the presence of ([Omim]BF₄)

Aldehyde	Naphthol	Amine	Product	Time(h)	Yeild(%)
1a	2-naphthol	3a	4a	1	85
1a	1-naphthol	3a	4b	1	60
1a	2-naphthol	3b	4c	1.5	60
1a	2-naphthol	diethylamine (3c)	4d	2	99
1a	2-naphthol	piperidine (3d)	4e	1	>95

Experimental

In this study, several ILs were synthesized according to the procedures described in the literature.[5] 1-Methylimidazole was placed in a two-necked flask, which was equipped with a magnetic stirrer and cooled in an ice–water bath. A small amount of water was added and then the acid (trifluoroacetic acid 1 equivalent) was added slowly with stirring. The reaction mixture was stirred for an additional period of 2 h. Then water in the crude product was evaporated with a rotary evaporator at 70 °C and thus a colorless liquid product was obtained.

General procedure for the synthesis of aminonaphthols by condensation of naphthols, benzaldehyde and a 2^o amine

Freshly distilled Benzaldehyde (1.0mmol) was added to a solution of 2-naphthol (1.0 mmol) in 2mL of 95% ethanol. To this mixture were added a 2^o amine (1.0 mmol) and 0.1g of [Hmim] Tfa. The reaction mixture was refluxed for 16-22h and brought to room temperature. The

precipitate was filtered and washed with 90% ethanol (2×5cc) to isolate the aminonaphthol as a white solid.

Conclusion

[Hmim]Tfa has been successfully used as catalyst in ethanol for Mannich reaction using aldehydes, amines and naphthols. Utilization of acidic ILs as catalyst has several advantages: (1) high yield; (2) the preparation of acidic ILs is simple; (3) the ILs can be easily recycled and reused; and (4) the environmentally benign procedure.

Acknowledgment

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