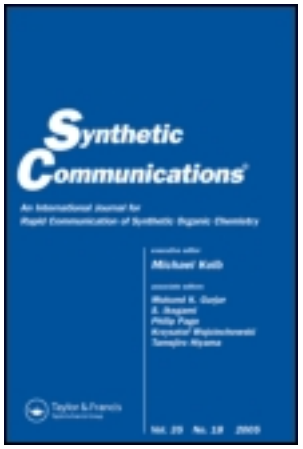

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Ionic Liquid : An Efficient and Recyclable Catalyst for the Synthesis of 1-Amidoalkyl-2-naphthols and 1-Carbamatoalkyl-2-naphthols Under Solvent-Free Conditions

Krishna M. Deshmukh [a] , Ziyauddin S. Qureshi [a] , Yogesh P. Patil [a] & Bhalchandra M. Bhanage [a]

[a] Department of Chemistry, Institute of Chemical Technology, Mumbai, India

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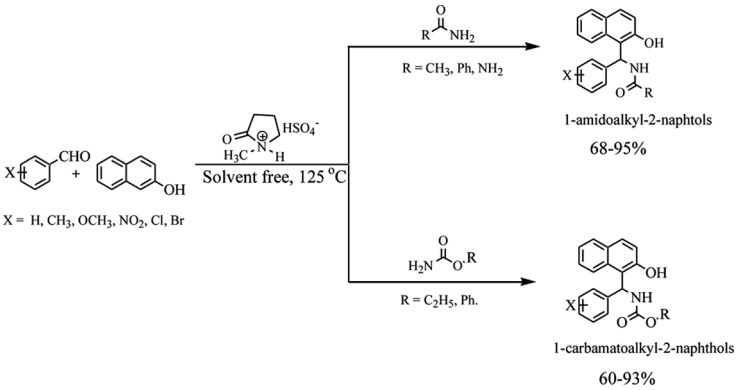
IONIC LIQUID $[NMP]^+HSO_4^-$: AN EFFICIENT AND RECYCLABLE CATALYST FOR THE SYNTHESIS OF 1-AMIDOALKYL-2-NAPHTHOLS AND 1-CARBAMATOALKYL-2-NAPHTHOLS UNDER SOLVENT-FREE CONDITIONS

Krishna M. Deshmukh, Ziyauddin S. Qureshi, Yogesh P. Patil, and Bhalchandra M. Bhanage

Department of Chemistry, Institute of Chemical Technology, Mumbai, India

GRAPHICAL ABSTRACT



Abstract *A simple and efficient protocol for the one-pot synthesis of 1-amidoalkyl-2-naphthols and novel 1-carbamatoalkyl-2-naphthols has been described under solvent-free conditions, using* N*-methyl-2-pyrrolidone hydrogen sulfate* $(NMP^+HSO_4^-)$ *as a reusable Brønsted acidic ionic liquid. This methodology has several advantages such as use of a halogen-free ionic liquid* $NMP^+HSO_4^-$*, excellent yields, short reaction time, easy workup procedure, and reusable catalyst.*

Keywords Aldehyde; amides; ionic liquids; multicomponent reaction; solvent free

INTRODUCTION

The 1,3-amino oxygenated functional motifs are widely used in many natural products, potent drugs, and HIV protease inhibitors.[1] Traditionally, these

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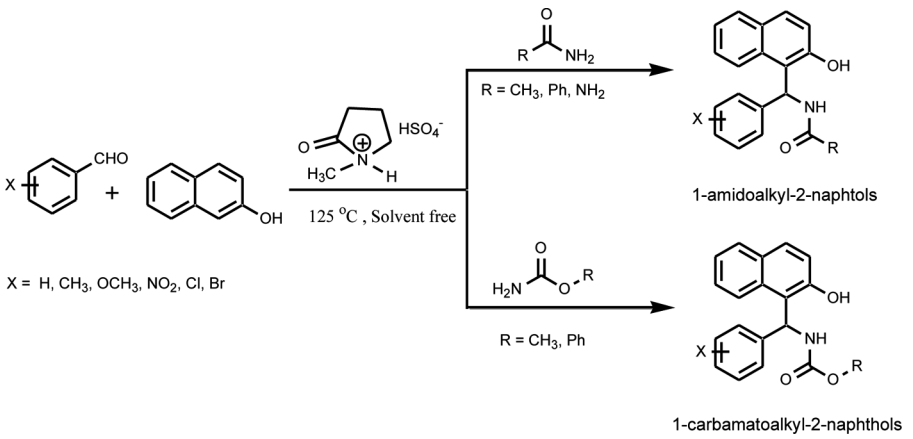
Address correspondence to Bhalchandra M. Bhanage, Department of Chemistry, Institute of Chemical Technology, N. Parekh Marg, Matunga, Mumbai 400 019, India. E-mail: bhalchandra_bhanage@yahoo.com



Scheme 1. Synthesis of 1-amidoalkyl-2-naphthols and 1-carbamatoalkyl-2-naphthols.

compounds were synthesized by multicomponent condensation of aryl aldehydes, 2-naphthol, and acetonitrile or amide in the presence of Lewis or Brønsted acid catalysts such as *p*-toluenesulfonic acid (*p*-TSA),[2] $FeCl_3 \cdot SiO_2$,[3] cation exchange resin,[4] and N-(4-sulfonic acid) butyl triethyl ammonium hydrogen sulfate ([TEBSA][HSO_4].)[5] Shaterian et al. first investigated the synthesis of 1-carbamatoalkyl-2-naphthol using a three-component reaction.[6] The previous methodologies have drawbacks of long reaction time, moisture-sensitive catalysts, and poor catalyst reusability.

The use of ionic liquids has gained considerable interest in the context of green synthesis and catalysis. They are emerging as most promising alternatives for a wide variety of acid-catalyzed reactions as they have useful characteristics of both solid acids and mineral liquid acids and they can be designed to replace customary mineral liquid acids such as sulfuric acid and hydrochloric acid in chemical procedures.[7]

In continuation of our research on applications of ionic liquids in several organic transformations,[8] herein we report a halogen-free Brønsted acidic ionic liquid, *N*-methyl-2-pyrrolidone hydrogen sulfate ($NMP^+HSO_4^-$), as an efficient and reusable catalyst for preparation of both 1-amidoalkyl-2-naphthols and 1-carbamatoalkyl-2-naphthols via a three-component reaction. The synthesis of novel 1-carbamatoalkyl-2-naphthols is reported for the first time.

RESULTS AND DISCUSSION

The reaction conditions were optimized using condensation of 2-naphthol, benzaldehyde, and acetamide as a model reaction under solvent-free conditions. The reaction parameters such as different types of ionic liquids, effects of catalyst loading (i.e., ionic liquid), and temperature on the reaction yield were optimized.

First, the influence of different types of Brønsted acidic ionic liquids was investigated. The ionic liquid, $NMP^+HSO_4^-$, was found to be most effective in terms of short reaction time with excellent yield (93%) of the desired product (Table 1, entry 4). The effect of catalyst loading on the reaction yield was also investigated, and 10 mol% of the catalyst was found to be effective giving good yield within 3 min.

Table 1. Effects of various parameters on synthesis of 1-amidoalkyl-2-naphthols[a]

Entry	Ionic liquid	Loading (mol%)	Temperature (°C)	Time (min)	Yield[b] (%)
Effects of various ionic liquids					
1	$C_4MIm^+HSO_4^-$	10	125	18	78
2	C_4MIm^+ *p*-TSA	10	125	12	80
3	$HMIm^+$ Tfa^-	10	125	42	75
4	$NMP^+HSO_4^-$	10	125	3	93
5	$HMIm^+NO_3^-$	10	125	50	71
6	$HMIm^+HSO_4^-$	10	125	10	84
Effects of ionic liquid loading					
7	$NMP^+HSO_4^-$	5	125	5	82
8	$NMP^+HSO_4^-$	10	125	3	93
9	$NMP^+HSO_4^-$	15	125	3	87
10	$NMP^+HSO_4^-$	20	125	3	90
Effects of temperature					
11	$NMP^+HSO_4^-$	10	60	20	83
12	$NMP^+HSO_4^-$	10	80	7	86
13	$NMP^+HSO_4^-$	10	110	7	87

[a]Reaction conditions: 2-naphthol (2.5 mmol), benzaldehyde (2.5 mmol), acetamide (2.8 mmol), $NMP^+HSO_4^-$, temperature 125 °C.
[b]Isolated yield.

(Table 1, entry 8). We have also tested the effects of temperature on the reaction yield, for which we carried out the reaction at various temperatures (60, 80, 110, and 125 °C). It was observed that reaction at 125 °C gives the best yield of the desired product (Table 1, entry 4).

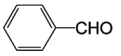
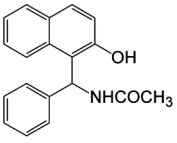
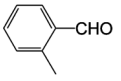
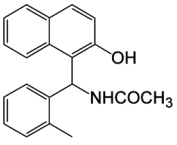
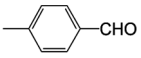
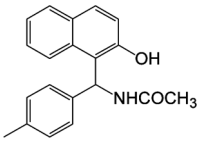
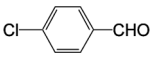
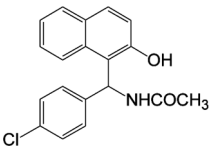
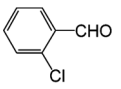
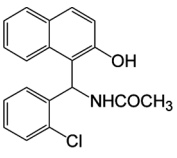
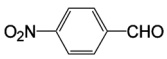
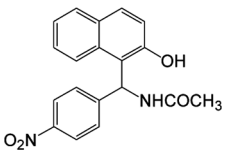
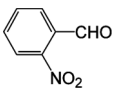
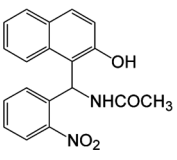
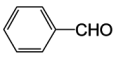
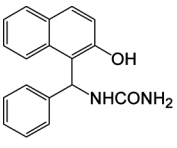
Using these optimized reaction conditions a wide range of 1-amidoalkyl-2-naphthols were prepared (Table 2). It has been observed that the aromatic aldehydes with activating group (-CH_3) at the *para* position react faster than those with it at the *ortho* position (Table 2, entries 2 and 3). Aromatic aldehydes with deactivating groups (like -NO_2, -Cl, -Br) require longer reaction time for completion of the reaction (Table 2, entries 4–7, 9, and 14). Sterically hindered aromatic aldehydes such as 2-CH_3, 2-NO_2, 2-Cl, and 2-Br provide moderate to good yields of the desired product in short reaction times (Table 2 entries 3, 5, 7, and 14). Further, we have also varied the nucleophiles such as urea and benzamide (Table 2, entries 8–14).

Under these optimized reaction conditions, we explored the scope of ionic liquid for the synthesis of 1-carbamatoalkyl-2-naphthols (Table 3). Aldehydes with an electron donating group (-OCH_3) react smoothly with urethane and phenyl carbamate to give a good yield of the product (Table 3, entries 2 and 4). On the other hand, electron-withdrawing groups like (-NO_2, -COOH) underwent the reaction at a faster rate to yield the desired product (Table 3, entries 3, 5, and 6). Urethane shows trends in reactivity similar to those of amides.

CONCLUSION

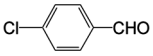
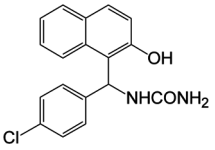
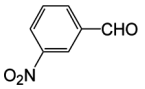
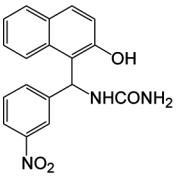
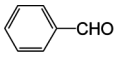
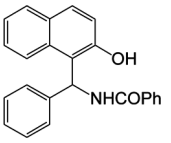
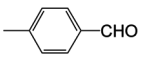
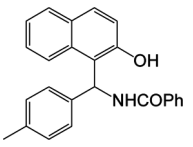
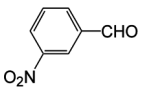
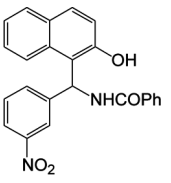
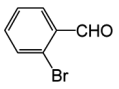
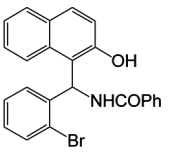
In conclusion, the synthesis of a wide range of 1-amidoalkyl-2-naphthols and new 1-carbamato-alkyl-2-naphthol under mild operating conditions has been carried

Table 2. $NMP^{+}HSO_4^{-}$-catalyzed synthesis of 1-amidoalkyl-2-naphthol[a]

Entry	Aldehyde	Nucleophiles	Product	Time (min)	Yield[b] (%)	Mp (°C)[Ref.]
1[c]		CH_3CONH_2		3	93, 92, 90	244–245[3]
2		CH_3CONH_2		15	82	206–208[3]
3		CH_3CONH_2		4	85	215–216[3]
4		CH_3CONH_2		7	94	222–223[3]
5		CH_3CONH_2		16	92	214–216[3]
6		CH_3CONH_2		8	92	246–247[3]
7		CH_3CONH_2		22	68	203–204[3]
8		NH_2CONH_2		18	90	171–173[4]

(*Continued*)

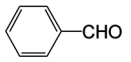
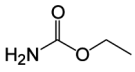
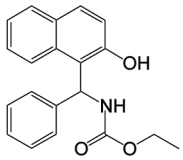
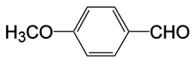
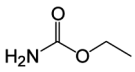
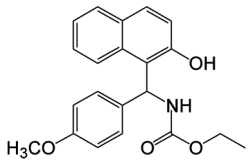
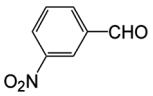
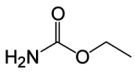
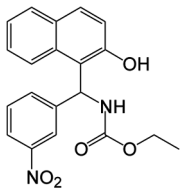
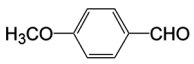
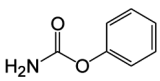
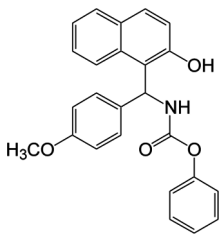
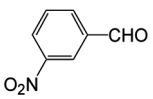
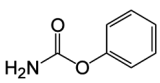
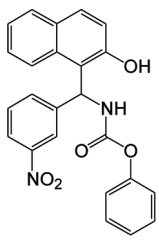
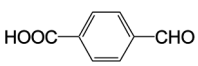
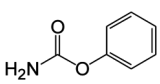
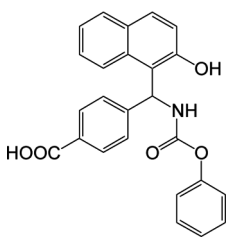
Table 2. Continued

Entry	Aldehyde	Nucleophiles	Product	Time (min)	Yield[b] (%)	Mp (°C)[Ref.]
9		NH_2CONH_2		9	93	169–170[4]
10		NH_2CONH_2		8	81	194–196[4]
11		$PhCONH_2$		5	91	231–233[4]
12		$PhCONH_2$		19	76	178–180[4]
13		$PhCONH_2$		7	95	216–218[4]
14		$PhCONH_2$		9	80	224–226[4]

[a]Reaction conditions: 2-naphthol (2.5 mmol), aldehyde (2.5 mmol), nucleophile (2.8 mmol), $NMP^+HSO_4^-$ (10 mol%), temperature 125 °C.
[b]Isolated yield.
[c]Recyclability.

out using $NMP^+HSO_4^-$ as a reusable and moisture-stable Brønsted acidic ionic liquid in an efficient manner. The system tolerates a wide range of functional groups, affording the desired products with good to excellent yields.

Table 3. $NMP^+HSO_4^-$-catalyzed synthesis of 1-carbamatoalkyl-2-naphthol[a]

Entry	Aldehyde	Nucleophiles	Product	Time (min)	Yield[b] (%)	Mp (°C)
1				6	90	195–196
2				14	79	202–204
3				9	93	215–217
4				20	60	180–182
5				9	85	178–179
6				7	82	183–185

[a]Reaction conditions: 2-naphthol (2.5 mmol), aldehyde (2.5 mmol), nucleophile (2.8 mmol), $NMP^+HSO_4^-$ (10 mol%), temperature (125 °C).
[b]Isolated yield.

EXPERIMENTAL

Preparation and Characterization of $NMP^+HSO_4^-$

$NMP^+HSO_4^-$ was prepared by using a reported procedure.[8] Brønsted acidity of ionic liquid was determined using pyridine as a probe molecule by monitoring the band range of 1350–1600 cm^{-1} arising from its ring vibration modes.[9] The infrared (IR) spectrum of pyridine shows a band at 1480 cm^{-1}. However, a slight shift was observed in wave number after mixing pyridine with ionic liquid. The spectrum of ionic liquids shows a band at 1550 cm^{-1}, indicating the presence of Brønsted acid sites due to the formation of pyridinium ions.

General Procedure for Synthesis of 1-Amidoalkyl-2-naphthols and 1-Carbamatoalkyl-2-naphthols

$NMP^+HSO_4^-$ (10 mol %) was added to a mixture of 2-naphthol (2.5 mmol), aldehyde (2.5 mmol), and acetamide/urea/urethane (2.8 mmol). The reaction mixture was stirred at 125 °C in a preheated oil bath for the appropriate time (Tables 1 and 2). The progress of the reaction was monitored by thin-layar chromatography (TLC). After completion of the reaction, the whole reaction mixture was added in water. The resulting precipitate was filtered off, and the residue was recrystallized from EtOH (20%).

Recyclability of Catalyst

To develop a greener and more economical protocol, a recycling experiment was conducted for applications on a larger scale (20 mmol). After completion of the reaction, the reaction mixture was added in water. The resulting white precipitate was filtered off, and the catalyst was recovered from the filtrate. The recovered catalyst was dried under vacuum using a rotavapor for 10 h and then charged for the next run. The catalyst was successfully recycled up to three times (Table 2, entry 1).

Physical and Spectral Data of Selected Compounds

Ethyl [(2-hydroxynaphthalen-1-yl)(phenyl)methyl]carbamate (Table 2, Entry 1). FT-IR (KBr): 3423, 3023, 2918, 1676, 1168, 941, 812, 740 cm^{-1}. ^1H NMR (300 MHz, DMSO) $\delta = 1.04$ (t, $J = 7$ Hz, 3 H), 4 (q, $J = 5.4$ Hz, 2 H), 6.82 (d, $J = 8.9$ Hz, 1 H), 7.38 (d, $J = 7.7$ Hz, 1 H), 7.54 (d, $J = 9.5$ Hz, 1 H), 7.15–7.38 (m, 7 H), 7.73–7.8 (m, 2 H), 7.78 (d, $J = 7.9$ Hz, 1 H), 10.1 (S, 1 H). ^{13}C NMR (75.43 MHz, DMSO) 156.1, 152.91, 142.44, 132.04, 129.25, 128.54, 128.34, 128.07, 126.55, 126.33, 125.98, 122.91, 122.5, 118.9, 118.5, 60.11, 50.32, 14.59. LC-MS (ESI) m/z: 344 ($[M^+ Na]^+$).

Ethyl [(2-hydroxynaphthalen-1-yl)(4-methoxyphenyl)methyl]carbamate (Table 2, Entry 2). FT-IR (KBr): 3417, 2956, 1673, 1510, 1176, 1041, 938, 749 cm^{-1}. ^1H NMR (300 MHz, DMSO) $\delta = 1.14$ (3 H, t, $J = 7.33$ Hz), 3.39 (s, 3 H), 4.01 (q, $J = 3.66$ Hz, 2 H), 6.79 (m, 3 H), 7.13 (d, $J = 8.43$ Hz, 1 H), 7.24 (m, 4 H), 7.38 (t, $J = 7.69$ Hz, 1 H), 7.74–7.81 (m, 2 H), 7.91 (d, $J = 8.06$ Hz, 1 H), 10.1 (S, 1 H).

^{13}C NMR (75.43 MHz, DMSO) 157.91, 156.04, 152.79, 134.32, 132.03, 129.19, 128.58, 128.40, 127.28, 126.56, 122.96, 122.56, 119.04, 118.55, 113.55, 60.11, 55.01, 50.06, 14.63. LC-MS (ESI) m/z: 374 ([M$^+$ Na]$^+$).

Ethyl [(2-hydroxynaphthalen-1-yl)(3-nitrophenyl)methyl]carbamate (Table 2, Entry 3). FT-IR (KBr): 3390, 3269, 3076, 2917, 2851, 1676, 1519, 1242, 1042, 806 cm^{-1}. ^{1}H NMR (300 MHz, DMSO) $\delta = 1.16$ (t, $J = 6.48$ Hz, 3 H), 3.38 (q, $J = 6.4$ Hz, 2 H), 6.92 (d, $J = 7.5$ Hz, 1 H), 7.18–8.09 (m, 11 H), 10.2 (S, 1 H). ^{13}C NMR (75.43 MHz, DMSO) 156.24, 153.12, 147.74, 145.05, 132.8, 131.88, 129.88, 129.68, 128.66, 128.32, 126.86, 122.67, 121.47, 120.47, 118.42, 117.9, 60.31, 49.92, 14.55. LC-MS (ESI) m/z: 389 ([M$^+$ Na]$^+$).

Phenyl [(2-hydroxynaphthalen-1-yl)(4-methoxy-phenyl)methyl]carbamate (Table 2, Entry 4). FT-IR (KBr): 3317, 3004, 1695, 1510, 1334, 1246, 1037, 942, 836, 749 cm^{-1}. ^{1}H NMR (300 MHz, DMSO) $\delta = 3.68$ (S, 3 H), 6.74 (d, $J = 8.79$ Hz, 2 H), 6.89–6.96 (m, 3 H), 7.09–7.22 (m, 7 H), 7.65–7.73 (m, 3 H), 8.85 (d, $J = 8.06$ Hz, 2 H), 9.6 (S, 1 H). ^{13}C NMR (75.43 MHz, DMSO) 157.99, 154.21, 152.86, 151.02, 133.7, 131.96, 129.29, 129.19, 128.52, 128.4, 128.15, 127.33, 126.42, 124.98, 123.08, 122.47, 121.74, 118.43, 113.57, 54.98, 50.12. LC-MS (ESI) m/z: 422 ([M$^+$ Na]$^+$).

Phenyl [(2-hydroxynaphthalen-1-yl)(3-nitro-phenyl)methyl]carbamate (Table 2, Entry 5). FT-IR (KBr): 3313, 3076, 1700, 1597, 1346, 1230, 1034, 842 cm^{-1}. ^{1}H NMR (300 MHz, DMSO) $\delta = 6.99$ (d, $J = 6.59$ Hz, 1 H), 7.14–7.4 (m, 8 H), 7.54 (d, $J = 8.06$ Hz, 2 H), 7.8–7.9 (m, 3 H), 8.18 (d, $J = 8.43$ Hz, 1 H), 8.52 (S, 1 H), 10.2 (S,1 H). ^{13}C NMR (75.43 MHz, DMSO) 154.61, 153.28, 150.98, 150.21, 146.15, 131.94, 130.09, 129.29, 128.7, 128.43, 127.26, 126.83, 125.17, 123.42, 122.91, 122.69, 121.82, 118.37, 117.49, 50.4. LC-MS (ESI) m/z: 437 ([M$^+$ Na]$^+$).

Phenyl [(2-hydroxynaphthalen-1-yl)(4-carboxy-phenyl)methyl]carbamate (Table 2, Entry 6). FT-IR (KBr): 3417, 3296, 2967, 1679, 1604, 1516, 1250, 815 cm^{-1}. ^{1}H NMR (300 MHz, DMSO) $\delta = 6.99$ (d, $J = 7.69$ Hz, 1 H), 7.14–7.19 (m, 3 H), 7.22–7.31 (m, 2 H), 7.34–7.44 (m, 5 H), 7.8–7.91 (m, 5 H), 8.4 (S, 1 H), 10.2 (S, 1 H), 12.8 (S, 1 H). ^{13}C NMR (75.43 MHz, DMSO, TMS) 167.19, 154.55, 153.16, 151.04, 147.24, 132.02, 129.8, 129.35, 129.29, 129.04, 128.65, 128.46, 126.66, 126.21, 125.13, 123.15, 122.63, 121.85, 118.4, 118.01, 50.48. LC-MS (ESI) m/z: 438 ([M$^+$ Na]$^+$).

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