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Brønsted acidic ionic liquid as an efficient and reusable catalyst for one-pot synthesis of 1-amidoalkyl 2-naphthols under solvent-free conditions

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ABSTRACT

A mild and efficient method has been developed for the preparation of amidoalkyl naphthols from condensation of aldehydes with amides or urea and 2-naphthol in the presence of a catalytic amount of Brønsted acidic ionic liquid ([TEBSA][HSO_4]) under thermal solvent-free conditions. High yields, short reaction time, easy work-up and reusability of the catalyst are advantages of this procedure.

Multicomponent reactions (MCRs) are very important and attractive subjects in organic synthesis due to formation of carbon–carbon and carbon–hetero atom bonds in one pot.[1–4] Simple procedures, high bond forming efficiency, time and energy saving and low expenditures are advantages of these reactions.[5] Therefore, researchers have made great efforts to find and develop new MCRs.

Compounds containing 1,3-amino-oxygenated functional groups are frequently found in biologically active natural products and potent drugs such as nucleoside antibiotics and HIV protease inhibitors.[6–9] Furthermore, 1-amidoalkyl 2-naphthols can be converted to useful and important biological building blocks and to 1-amino methyl 2-naphthols by an amide hydrolysis reaction, since compounds exhibit depressor and bradycardia effects in humans.[10,11] 1-Amidoalkyl 2-naphthols can be prepared by multicomponent condensation of aldehydes, 2-naphthols and acetonitrile or different amides in the presence of Lewis or Brønsted acids such as *p*-TSA,[12] montmorillonite K10,[13] $Ce(SO_4)_2$,[14] Iodine,[15] $Fe(HSO_4)_3$,[16] $Sr(OTf)_2$,[17] $K_5CoW_{12}O_{40}.3H_2O$,[18] sulfamic acid,[19,20] molybdophosphoric acid,[21] cation-exchange resins[22] and silica sulfuric acid.[23] However some of the reported methods suffer from disadvantages such as prolonged reaction time, low yield of products, toxic and corrosive reagents and the use of additional microwave or ultrasonic irradiation. Therefore, the discovery of clean procedures and the use of green and eco-friendly catalysts with high catalytic activity and short reaction times for the production of 1-amidoalkyl 2-naphthols have gained considerable attention.

Ionic liquids (ILs) have attracted extensive research interest as environmentally benign solvents due to their specific properties such as undetectable vapour pressure, non-inflammability, wide liquid range, reusability and high thermal stability.[24,25] Ionic liquids have been widely applied in many reactions as catalysts or dual catalyst-solvents including the Mannich reaction[26] and esterification.[27]

Brønsted acidic ionic liquids consist of the useful characteristics of solid acids and mineral liquid acids and are designed to replace traditional mineral liquid acids such as sulfuric acid and hydrochloric acid in chemical procedures.[28,29] *N*-(4-sulfonic acid) butyl triethyl ammonium hydrogen sulfate ([TEBSA][HSO_4]) has been synthesized and used as an efficient and reusable catalyst for nitration of aromatic compounds[30] and esterification of various alcohols by different acids.[31] In a continuation of our investigations on the development of new synthetic methodologies,[32–35] herein we report a new, convenient, mild and efficient procedure for one-pot three-component synthesis of amidoalkyl naphthol derivatives from various aryl aldehydes, 2-naphthol and different amides (acetamide, benzamide and urea) in the presence of [TEBSA][HSO_4] as an effective and recoverable catalyst under solvent-free conditions (Scheme 1).[36,37]

Initially to optimize the amount of ionic liquid, the reaction of 2-naphthol (1 mmol), 4-chloro benzaldehyde (1 mmol) and acetamide (1.2 mmol) was performed under solvent-free conditions

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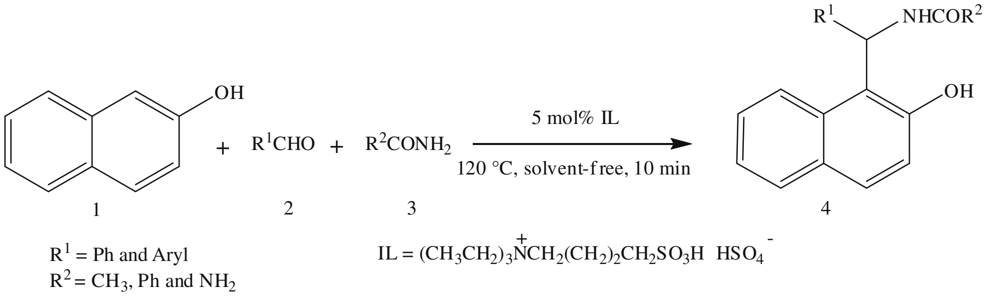


Scheme 1.

Table 1
The effect of different amounts of [TEBSA][HSO_4] on the reaction of 2-naphthol, acetamide and 4-chlorobenzaldehyde

Entry	[TEBSA][HSO_4] (mmol)	Time (min)	Yield of **4c**[a] (%)
1	3	45	0
2	1	40	60
3	0.5	30	65
4	0.17	10	80
5	0.09	10	84
6	0.05	10	85
7	0.03	10	75
8	0.01	10	63

[a] Isolated yields.

Table 2
The one-pot three-component reaction of 2-naphthol, urea/amides and aryl aldehydes in the presence of ionic liquid under solvent-free conditions at 120 °C and 10 min[a]

Entry	Aldehyde R^1	Urea/amide R^2	Product	Yield[b] (%)	Mp
1	C_6H_5	CH_3	**4a**	87	218–220
2	2-ClC_6H_4	CH_3	**4b**	90	192–194
3	4-ClC_6H_4	CH_3	**4c**	85	229–230
4	2,6-$Cl_2C_6H_3$	CH_3	**4d**	90	223–224
5	4-Br C_6H_4	CH_3	**4e**	87	229–231
6	3-$O_2NC_6H_4$	CH_3	**4f**	89	238–240
7	4-$O_2NC_6H_4$	CH_3	**4g**	88	222–223
8	4-MeC_6H_4	CH_3	**4h**	84	214–216
9	3-$MeOC_6H_4$	CH_3	**4i**	83	218–220
10	2,5-$(MeO)_2C_6H_3$	CH_3	**4j**	84	228–230
11	4-NCC_6H_4	CH_3	**4k**	87	232–234
12	4-$CH_3OCOC_6H_4$	CH_3	**4l**	91	225–227
13	C_6H_5	NH_2	**4m**	73	176–178
14	3-$O_2NC_6H_4$	NH_2	**4n**	76	192–193
15	C_6H_5	C_6H_5	**4o**	86	234–236
16	4-Br C_6H_4	C_6H_5	**4p**	83	182–184
17	3-$MeOC_6H_4$	C_6H_5	**4q**	87	214–216
18	4-MeC_6H_4	C_6H_5	**4r**	79	209–211
19	4-ClC_6H_4	C_6H_5	**4s**	83	180–182
20	3-$O_2NC_6H_4$	C_6H_5	**4t**	81	233–235
21	2,5-$(MeO)_2C_6H_3$	C_6H_5	**4u**	86	238–240

[a] Aldehyde/urea or amide/2-naphthol/IL = 1:1.2:1:0.05.
[b] Yields refer to isolated products and all synthesized amidoalkyl naphthols were characterized by spectral data (IR, ^1H and ^{13}C NMR) and melting points and comparison with authentic samples.

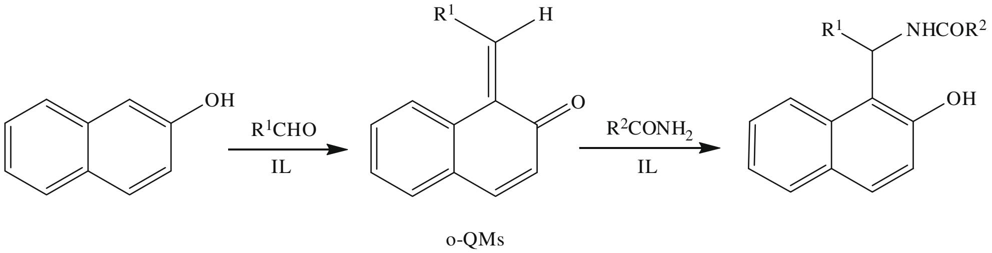
at 120 °C in the presence of different quantities of [TEBSA][HSO_4] (Table 1). As shown in Table 1, the yields of product **4c** using high amounts of [TEBSA][HSO_4] were low and the reaction time was long (Table 1, entries 1–3). No improvement in the reaction rate was observed by decreasing the amount of ionic liquid from 17 to 1 mmol but the yield of product **4c** in the presence of 0.05 mmol of [TEBSA][HSO_4] was higher than the others (Table 1, entries 4–8). Therefore 5 mol % of ionic liquid was chosen as the optimal quantity of [TEBSA][HSO_4].

Thus, we employed 5 mol % ionic liquid for one-pot synthesis of amidoalkyl naphthols from various aldehydes, amides or urea and 2-naphthol under solvent-free conditions at 120 °C (Table 2, entries 1–21). Aromatic aldehydes reacted with amides or urea and 2-naphthol to produce the corresponding 1-amidoalkyl 2-naphthols in 73–91% yields. It was shown that aromatic aldehydes with electron-donating (e.g., entries 9, 10, 17 and 20) or electron-withdrawing substituents (e.g., entries 6, 7, 11, 12, 14 and 20) were converted to amidoalkyl naphthols in 76–91% yields and in short reaction time (10 min).

As shown in Scheme 2, the reaction of 2-naphthol with aromatic aldehydes in the presence of acid catalyst is known to provide ortho-quinone methides (*o*-QMs).[12,18] The *o*-QMs were reacted with amides or urea to produce 1-amidoalkyl-2-naphthol derivatives (Scheme 2).

In comparison with other catalysts employed for the synthesis of *N*-[(3-nitro phenyl)-(2-hydroxy-naphthalen-1-yl)-methyl]-acetamide from 3-nitro benzaldehyde, acetamide and 2-naphthol at different conditions, [TEBSA][HSO_4] showed more catalytic reactivity than the others in terms of short reaction time and simplified conditions (Table 3, entries 1–9).

The reusability of the [TEBSA][HSO_4] was also determined. After each run, water was added to the reaction mixture and the product was filtered and the containing ionic liquid was extracted with CH_2Cl_2 (3 × 10 ml) to remove non-ionic organic impurities. Then the water was evaporated and the catalyst was dried at 65 °C under reduced pressure for 2 h and reused in the reaction of 3-nitro benzaldehyde, acetamide and 2-naphthol under solvent-free conditions at 120 °C (Table 3, entries 9–12). The results show that the catalyst can be employed four times, although the activity of the catalyst gradually decreased. This



Scheme 2.

Table 3
Acid-catalyzed synthesis of *N*-[(3-nitro phenyl)-(2-hydroxy-naphthalen-1-yl)-methyl]-acetamide via reaction of 3-nitro benzaldehyde (1 mmol), 2-naphthol (1 mmol) and acetamide (1.2 mmol) under different conditions

Entry	Catalyst (mol %)	Solvent	Conditions	Time	Yield (%)	References
1	$Fe(HSO_4)_3$ (5)	—	85 °C	25 min	97	16
2	Sulfamic acid (0.05 g)	DCE	)))) 28–30 °C	90 min	93	20
3	Montmorillonite K10 (0.1 g)	—	125 °C	30 min	96	13
4	$K_5CoW_{12}O_{40}\cdot 3H_2O$ (1)	—	125 °C	3 h	78	18
5	$K_5CoW_{12}O_{40}\cdot 3H_2O$ (1)	DCE	rt	12 h	89	18
6	Iodine (5)	DCE	rt	10 h	85	15
7	Iodine (5)	—	125 °C	5 h	81	15
8	Sulfamic acid (10)	DCE	rt	7 h	82	19
9	[TEBSA][HSO_4] (5) (first run)	—	120 °C	10 min	89	—
10	[TEBSA][HSO_4] (5) (2nd run)	—	120 °C	10 min	87	—
11	[TEBSA][HSO_4] (5) (3nd run)	—	120 °C	10 min	85	—
12	[TEBSA][HSO_4] (5) (4nd run)	—	120 °C	10 min	80	—

indicates that the Brønsted acidic ionic liquid ([TEBSA][HSO_4]) as a catalyst for the preparation of amidoalkyl naphthols was recyclable.

In conclusion, we have developed a facile, convenient and solvent-free method for the one-pot synthesis of amidoalkyl naphthols derivatives by coupling various aromatic aldehydes with amides or urea and 2-naphthol using *N*-(4-sulfonic acid) butyl triethyl ammonium hydrogen sulfate ([TEBSA][HSO_4]) as an efficient catalyst. The advantages of this method, in which a relatively non-toxic (halogen-free) and reusable Brønsted acidic ionic liquid is employed as an effective catalyst, are high catalytic efficiency, short reaction time, high yields, a straightforward work-up and environmental benignancy.

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Supplementary data

Supplementary data (^{1}H and ^{13}C NMR, EMS and IR of compounds) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.07.116.

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36. *Preparation of ionic liquid:* 1,4-butane sultone (10 mmol, 1.0 mL), triethyl amine (10 mmol, 1.4 mL) and acetonitrile (5 mL) were charged in a 100 mL round-bottomed flask. Then, the mixture was refluxed for 10 h. The white solid zwitterions were filtered and washed with ethyl acetate to remove non-ionic residues and were dried in vacuum (2.0 g, 85% yield). Then, a stoichiometric amount of concentrated sulfuric acid (96%, 0.5 mL) was added dropwise to zwitterions and the mixture was stirred for 6 h at 80 °C to produce the Brønsted acidic ionic liquid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.16 (br s, 9H), 1.59–1.73 (m, 4H), 2.53 (t, J = 7.6 Hz, 2H), 3.09–3.25 (m, 8H), 6.46 (S, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 7.60, 20.27, 22.23, 50.67, 52.48, 56.15.
37. *General procedure for the preparation of amidoalkyl naphthols:* a mixture of aldehyde (1 mmol), 2-naphthol (1 mmol), urea or amide (1.2 mmol) and [TEBSA][HSO_4] (0.05 mmol) was stirred at 120 °C in oil bath. The completion of the reaction was monitored through TLC (ethyl acetate/cyclohexane, 1:3), after 10 min, water (10 mL) was added and the product was filtered and then recrystallized from ethyl alcohol. The products were characterized by spectral data (IR, ^{1}H NMR and ^{13}C NMR) and comparison of their physical data with the literature data.