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Evaluation of Catalytic Activity of Two Newly Prepared Functionalized Sulfonic Acids Ionic Liquids in the Synthesis of Carbamatoalkyl Naphthols under Mild Conditions[1]

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Abstract—Catalytic activity of two newly prepared functionalized sulfonic acids ionic liquids, [MPyrrSO_3H]Cl (IL_1) and [MMorSO_3H]Cl (IL_2), is studied in one-pot three-component synthesis of carbamatoalkyl naphthols by the reaction of β-naphthol with aromatic aldehydes and methyl or benzyl carbamate. The efficiently catalyzed reaction proceeded under solvent-free conditions. The synthesis was characterized by easy work-up, absence of volatile and hazardous organic solvents, and recyclability of the catalysts.

Keywords: sulfonic acid functionalized ionic liquids, carbamatoalkyl naphthols, solvent-free synthesis

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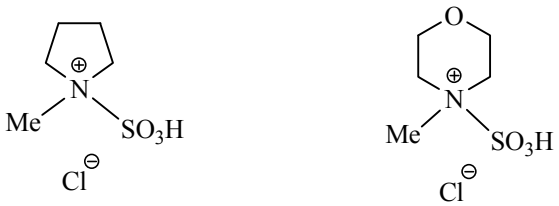
INTRODUCTION

Carbamatoalkyl naphthols can be synthesized by a multi-component reaction (MCR) [1–5] and converted further to biologically active 1-aminomethyl-2-naphthol derivatives by carbamate hydrolysis. The hypotensive and bradycardiac effects of the latter compounds have been evaluated [6, 7]. A number of methods has been developed for the synthesis of carbamatoalkyl naphthols [8–18] each of which possessed some advantages. Nevertheless, development of new efficient recyclable catalysts for the synthesis of carbamatoalkyl naphthols was of certain demand. Over recent years, Brønsted acidic ionic liquids (IL) [19–21] received close attention as environmentally friendly catalysts.

In conjunction with our interest in ILs, recently, two new functionalized sulfonic acids ILs, 1-methyl-1-sulfonic acid pyrrolidinium chloride [MPyrrSO_3H]Cl (IL_1) and 4-methyl-4-sulfonic acid morpholinium chloride [MMorSO_3H]Cl (IL_2) (see figure), were synthesized [22]. The new recyclable ILs demonstrated high catalytic activity in the synthesis of 1,8-dioxo-octahydroxanthenes. Following our earlier studies of new environmental friendly methods of synthesis of organic compounds based on reusable catalysts [23–26], we present application of the above ILs in the synthesis of carbamatoalkyl naphthols. The process involved one-pot three-component reaction of β-naphthol with aromatic aldehydes and methyl or benzyl carbamate under solvent-free conditions (Scheme 1).

Initially, catalytic activity of IL_1 and IL_2 was optimized in the synthesis of methyl (4-chlorophenyl)-(2-hydroxynaphthalen-1-yl)methylcarbamate **4b** via the reaction of β-naphthol (1 mmol) with 4-chloro-benzaldehyde (1 mmol) and methyl carbamate (1.1 mmol) (Table 1). A non-catalyzed reaction was tested under solvent-free conditions but without a significant yield (entry 1). On the contrary, the reaction catalyzed by IL_1 or IL_2 under solvent-free conditions demonstrated enhanced rate of formation of **4b**. The best result was achieved at 100°C in the presence of 10 mol % of IL_1 or IL_2 (entry 9). The test of various media, EtOH, MeOH, CH_2Cl_2, CH_3CN, and solvent free, in the presence of 10 mol % of IL_1 or IL_2 exhibited solvent-free conditions to be the most favorable.

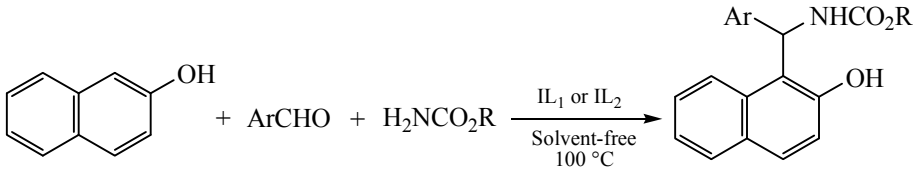


[MPyrrSO_3H]Cl (IL_1) [MMorSO_3H]Cl (IL_2)

Structures of IL_1 and IL_2.

[1] The text was submitted by the authors in English.

Scheme 1.



1 **2** **3** **4a–4o**

Ar = 2-ClC_6H_4, R = Me (**a**), Ar = 4-ClC_6H_4, R = Me (**b**), Ar = 3-BrC_6H_4, R = Me (**c**), Ar = 4-BrC_6H_4, R = Me (**d**), Ar = 4-MeC_6H_4, R = Me (**e**), Ar = 3-$O_2NC_6H_4$, R = Me (**f**), Ar = 3-Pyridyl, R = Me (**g**, new compound), Ar = C_6H_5, R = Me (**h**), Ar = 2-ClC_6H_4, R = $CH_2C_6H_5$ (**i**), Ar = 4-ClC_6H_4, R = $CH_2C_6H_5$ (**j**), Ar = 3-BrC_6H_4, R = $CH_2C_6H_5$ (**k**), Ar = 4-BrC_6H_4, R = $CH_2C_6H_5$ (**l**), Ar = 4-FC_6H_4, R = $CH_2C_6H_5$ (**m**), Ar = 4-$O_2NC_6H_4$, R = $CH_2C_6H_5$ (**n**), Ar = C_6H_5, R = $CH_2C_6H_5$ (**o**).

The optimized reaction conditions were applied to the reaction of various aromatic aldehydes with β-naphthol and methyl or benzyl carbamate (Table 2). In all cases the products were isolated in high yields within short reaction time. Melting points, TLC and spectroscopic data (for selected products) indicated that only one product was formed in all cases. No side-products were detected upon purification. According to the accumulated data IL_2 proved to be the better catalyst than IL_1 in terms of yield and reaction time.

Table 1. Optimization of conditions for synthesis of **4b** catalyzed by IL_1 or IL_2[a]

Entry no.	Catalyst, mol %	Solvent	*T*, °C IL_1 : IL_2	Time, min IL_1 : IL_2	Yield[b], % IL_1 : IL_2
1	–	–	100	60 : 60	Trace : Trace
2	5	–	80	7 : 5	58 : 66
3	5	–	100	4 : 3	71 : 74
4	5	–	110	6 : 5	70 : 72
5	7	–	80	6 : 5	69 : 74
6	7	–	100	4 : 3	84 : 89
7	7	–	110	4 : 2	80 : 85
8	10	–	80	7 : 6	75 : 79
9	10	–	100	3 : 2	96 : 98
10	10	–	110	4 : 2	88 : 92
11	15	–	80	8 : 6	70 : 74
12	15	–	100	6 : 3	88 : 92
13	15	–	110	7 : 4	85 : 88
14	15	EtOH	Reflux	40 : 30	52 : 69
15	15	MeOH	Reflux	45 : 30	54 : 70
16	15	CH_2Cl_2	Reflux	50 : 40	53 : 58
17	15	CH_3CN	Reflux	40 : 30	63 : 70

[a] Reaction conditions: β-naphthol (1 mmol), 4-chlorobenzaldehyde (1 mmol) , and methyl carbamate (1.1 mmol). [b] Isolated yields.

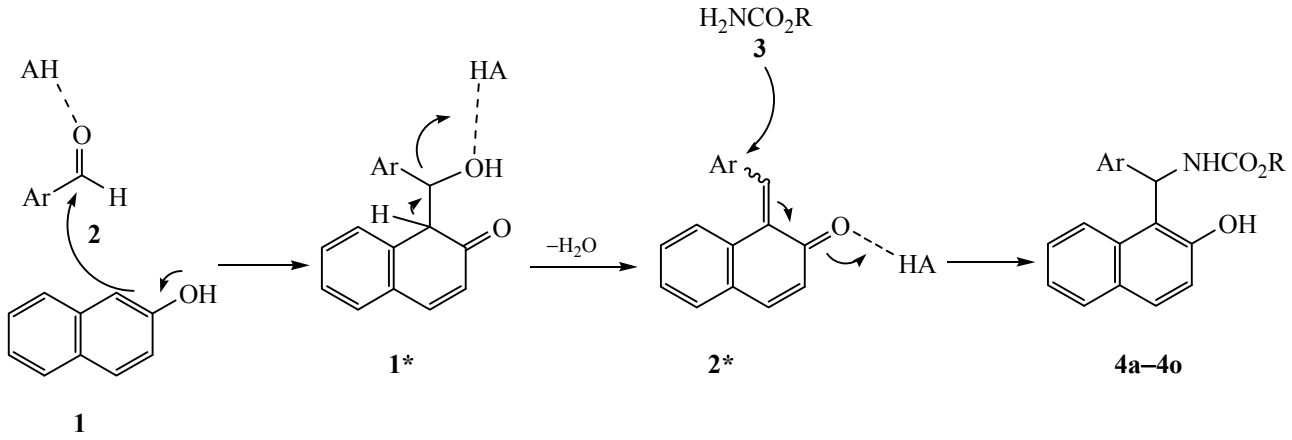
ILs could be recovered from the reaction mixtures by cooling to room temperature, adding warm distilled water, filtration and evaporation of water from the filtrate. The residual ionic liquid was repeatedly washed with diethyl ether and dried under vacuum at 60°C. The recycled catalyst could be used in four cycles to follow (IL_1 : IL_2 catalysts, yields, %: 96 : 98, 96 : 97, 94 : 95, 93 : 93 and 92 : 93).

Although the reaction mechanism was not studied, the speculative one may be presented (Scheme 2). O*rtho*-quinone methide (*o*-QM) intermediate [II] readily forms in situ by the Knoevenagel condensation of β-naphthol **1** and an aromatic aldehyde **2** via the intermediate **2***. The subsequent Michael addition of methyl or benzyl carbamate to the *o*-QM intermediate **2*** can lead to the final products **4**. We believe that the catalysts, IL_1 and IL_2 ≡ HA, could act as Brønsted acids and promote the reaction by increasing the electrophilic character of the carbonyl groups in aldehydes and *o*-QM intermediate **2***. However, under the reaction conditions used, the intermediates were not detected.

EXPERIMENTAL

IL_1 and IL_2 were synthesized according to the earlier method [22]. All chemicals were purchased from Merck and Aldrich and used without purification. Melting points were measured on a Stuart SMP3 melting point apparatus. IR spectra were recorded on a Tensor 27 Bruker spectrophotometer in KBr disks. ^1H and ^{13}C NMR spectra were measured on a Bruker 300

Scheme 2.



FT spectrometer in DMSO-d_6 using TMS as the internal standard.

General procedure for the synthesis of carbamatoalkyl naphthols 4a-o catalyzed by IL_1 and IL_2. To a mixture of β-naphthol (1 mmol), an aromatic aldehyde (1 mmol) and methyl or benzyl carbamate (1.1 mmol), IL_1 or IL_2 (10 mol % based on aromatic aldehyde) was added. The mixture was heated on the oil bath at 100°C for 2–5 min. The reaction was monitored by TLC. Upon completion, the reaction mixture was cooled down to room temperature and warm distilled water was added. The product was filtered off, washed repeatedly with warm distilled water and recrystallized from ethanol to give carbamatoalkyl naphthols **4a–4o**. The previously known products were

Table 2. Synthesis of carbamatoalkyl naphthols **4a–4o** using IL_1 or IL_2 as catalysts[a]

Comp. no	Ar	R	Time, min IL_1 : IL_2	Yield[b], % IL_1 : IL_2	mp, °C	
					found	calculated
4a	2-ClC_6H_4	Me	5 : 4	85 : 89	183–185	181–183 [15]
4b	4-ClC_6H_4	Me	3 : 2	96 : 98	202–204	203–205 [15]
4c	3-BrC_6H_4	Me	4 : 3	89 : 97	194–196	190–192 [15]
4d	4-BrC_6H_4	Me	4 : 2	87 : 90	198–200	197–199 [15]
4e	4-MeC_6H_4	Me	5 : 4	85 : 87	188–190	187–189 [15]
4f	3-$O_2NC_6H_4$	Me	3 : 2	92 : 95	248–250	249–251 [10]
4g	3-Pyridyl	Me	5 : 4	85 : 89	207–209	New
4h	C_6H_5	Me	3 : 3	94 : 97	218–220	220–222 [10]
4i	2-ClC_6H_4	$CH_2C_6H_5$	5 : 4	83 : 85	168–169	163–165 [16]
4j	4-ClC_6H_4	$CH_2C_6H_5$	4 : 3	88 : 92	183–185	178–180 [13]
4k	3-BrC_6H_4	$CH_2C_6H_5$	5 : 4	82 : 85	184–186	186–187 [16]
4l	4-BrC_6H_4	$CH_2C_6H_5$	5 : 3	84 : 88	185–187	188–190 [15]
4m	4-FC_6H_4	$CH_2C_6H_5$	5 : 4	90 : 94	187–189	185–186 [16]
4n	4-$O_2NC_6H_4$	$CH_2C_6H_5$	4 : 3	88 : 91	206–208	202–204 [13]
4o	C_6H_5	$CH_2C_6H_5$	4 : 4	94 : 95	182–183	180–182 [15]

[a] Reaction conditions: β-naphthol (1 mmol), an aromatic aldehyde (1 mmol), methyl or benzyl carbamate (1.1 mmol), IL_1 or IL_2 (10 mol %), 100°C, solvent-free. [b] Isolated yields.

characterized by comparison of their melting points with those of authentic samples and in some cases by IR and ^{1}H NMR spectra. Structure of the new product **4g** was also confirmed by ^{13}C NMR spectrum.

Methyl (2-chlorophenyl)(2-hydroxynaphthalen-1-yl)methylcarbamate (4a). IR spectrum, ν_{max}, cm^{-1}: 3430 (NH), 3210 (OH), 1691 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.54 s (3H, OCH_3), 6.88 d (1H, J = 8.1 Hz, CH), 7.14 d (1H, J = 8.7 Hz, H_{arom}), 7.25–7.90 m (9H, H_{arom}, NH), 8.02 d (1H, J = 8.7 Hz, H_{arom}), 9.94 s (1H, OH).

Methyl (4-chlorophenyl)(2-hydroxynaphthalen-1-yl)methylcarbamate (4b). IR spectrum, ν_{max}, cm^{-1}: 3421 (NH), 3310 (OH), 1711 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.59 s (3H, OCH_3), 6.84 d (1H, J = 8.1 Hz, CH), 7.23 d (2H, J = 8.4 Hz, H_{arom}), 7.26–7.37 m (3H, H_{arom}), 7.41 t (1H, J = 7.8 Hz, H_{arom}), 7.70–7.85 m (4H, H_{arom}, NH), 7.90 d (1H, J = 8.1 Hz, H_{arom}), 10.16 s (1H, OH).

Methyl (4-bromophenyl)(2-hydroxynaphthalen-1-yl)methylcarbamate (4d). IR spectrum, ν_{max}, cm^{-1}: 3419 (NH), 3198 (OH), 1683 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.58 s (3H, OCH_3), 6.82 d (1H, J = 8.7 Hz, CH), 7.16 d (2H, J = 8.4 Hz, H_{arom}), 7.22 d (1H, J = 9.0 Hz, H_{arom}), 7.29 t (1H, J = 7.2 Hz, H_{arom}), 7.41 t (1H, J = 7.8 Hz, H_{arom}), 7.47 d (2H, J = 8.4 Hz, H_{arom}), 7.70–7.92 m (4H, H_{arom}, NH), 10.15 s (1H, OH).

Methyl (2-hydroxynaphthalen-1-yl)(3-nitrophenyl)-methylcarbamate (4f). IR spectrum, ν_{max}, cm^{-1}: 3422 (NH), 3227 (OH), 1687 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.61 s (3H, OCH_3), 6.96 s (1H, CH), 7.23 d (1H, J = 9.0 Hz, H_{arom}), 7.31 t (1H, J = 7.2 Hz, H_{arom}), 7.44 t (1H, J = 7.5 Hz, H_{arom}), 7.57 t (1H, J = 7.8 Hz, H_{arom}), 7.64 d (1H, J = 7.8 Hz, H_{arom}), 7.84 t (2H, J = 8.7 Hz, H_{arom}), 7.93–8.00 m (2H, H_{arom}, NH), 8.08 d (1H, J = 8.4 Hz, H_{arom}), 8.12 s (1H, H_{arom}), 10.28 s (1H, OH).

Methyl (2-hydroxynaphthalen-1-yl)(pyridin-3-yl)methylcarbamate (4g). IR spectrum, ν_{max}, cm^{-1}: 3428 (NH, OH, overlapped), 1724 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.59 s (3H, OCH_3), 6.91 d (1H, J = 8.4 Hz, CH), 7.23 d (1H, J = 8.7 Hz, H_{arom}), 7.27–7.34 m (2H, H_{arom}), 7.43 t (1H, J = 7.5 Hz, H_{arom}), 7.62 d (1H, J = 8.1 Hz, H_{arom}), 7.78–7.88 m (3H, H_{arom}, NH), 7.98 d (1H, J = 8.4 Hz, H_{arom}), 8.40 d.d (1H, J = 4.6, 0.9 Hz, H_{arom}), 8.46 d (1H, J = 1.8 Hz, H_{arom}), 10.22 s (1H, OH). ^{13}C NMR spectrum, δ, ppm: 49.2, 52.2, 118.4, 118.7, 123.1, 123.2, 123.7, 127.2, 128.8, 129.1, 130.2, 132.3, 134.2, 138.2, 148.0, 153.5, 157.0.

Benzyl (2-chlorophenyl)(2-hydroxynaphthalen-1-yl)methylcarbamate (4i). IR spectrum, ν_{max}, cm^{-1}: 3420 (NH), 3169 (OH), 1700 (C=O). ^{1}H NMR spectrum, δ, ppm: 5.05 AB_q (2H, Δν = 25.3 Hz, J_{AB} = 12.9 Hz, CH_2), 6.93 d (1H, J = 8.1 Hz, CH), 7.16 d (1H, J = 9.0 Hz, H_{arom}), 7.22–7.57 m (11H, H_{arom}), 7.77 d (1H, J = 8.7 Hz, H_{arom}), 7.82 d (1H, J = 7.8 Hz, H_{arom}), 8.01 br.s (1H, NH), 8.04 d (1H, J = 8.4 Hz, H_{arom}), 9.94 s (1H, OH).

Benzyl (4-chlorophenyl)(2-hydroxynaphthalen-1-yl)methylcarbamate (4j). IR spectrum, ν_{max}, cm^{-1}: 3425 (NH), 3170 (OH), 1678 (C=O). ^{1}H NMR spectrum, δ, ppm: 5.09 AB_q (2H, Δν = 19.5 Hz, J_{AB} = 12.6 Hz, CH_2), 6.91 d (1H, J = 8.7 Hz, CH), 7.22–7.45 m (12H, H_{arom}), 7.77–7.95 m (4H, H_{arom}, NH), 10.19 s (1H, OH).

Benzyl (4-bromophenyl)(2-hydroxynaphthalen-1-yl)methylcarbamate (4l). IR spectrum, ν_{max}, cm^{-1}: 3423 (NH), 3169 (OH), 1680 (C=O). ^{1}H NMR spectrum, δ, ppm: 5.08 AB_q (2H, Δν = 19.2 Hz, J_{AB} = 12.6 Hz, CH_2), 6.88 d (1H, J = 8.7 Hz, CH), 7.15–7.50 m (12H, H_{arom}), 7.77–7.97 m (4H, H_{arom}, NH), 10.17 s (1H, OH).

Benzyl (2-hydroxynaphthalen-1-yl)(4-nitrophenyl)-methylcarbamate (4n). IR spectrum, ν_{max}, cm^{-1}: 3422 (NH), 3369 (OH), 1692 (C=O). ^{1}H NMR spectrum, δ, ppm: 5.10 AB_q (2H, Δν = 17.7 Hz, J_{AB} = 12.6 Hz, CH_2), 7.00 d (1H, J = 8.4 Hz, CH), 7.24 d (1H, J = 9.0 Hz, H_{arom}), 7.27–7.45 m (7H, H_{arom}), 7.49 d (2H, J = 8.7 Hz, H_{arom}), 7.80–8.10 m (4H, H_{arom}, NH), 8.16 d (2H, J = 8.7 Hz, H_{arom}), 10.25 s (1H, OH).

Benzyl (2-hydroxynaphthalen-1-yl)(phenyl)methyl-carbamate (4o). IR spectrum, ν_{max}, cm^{-1}: 3423 (NH), 3191 (OH), 1672 (C=O). ^{1}H NMR spectrum, δ, ppm: 5.10 AB_q (2H, Δν = 21.0 Hz, J_{AB} = 12.6 Hz, CH_2), 6.95 d (1H, J = 8.7 Hz, CH), 7.15–7.45 m (13H, H_{arom}), 7.77–7.87 m (3H, H_{arom}, NH), 7.95 d (1H, J = 8.1 Hz, CH), 10.17 s (1H, OH).

CONCLUSIONS

Two newly synthesized ILs acted as recyclable catalysts in one-pot three-component synthesis of carbamatoalkyl naphthols by the reaction of β-naphthol with aromatic aldehydes and methyl or benzyl carbamate under solvent-free conditions. The process was characterized by easy product separation, short reaction time, high yield, absence of hazardous organic solvents, and reusability of the catalysts.

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