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Preparation of methyl/benzyl(2-hydroxynaphthalen-1-yl)(aryl)methylcarbamate derivatives using magnesium hydrogen sulfate

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Abstract A new approach to the synthesis of methyl/benzyl(2-hydroxynaphthalen-1-yl)(aryl)methylcarbamate derivatives based on the reaction of aldehydes, 2-naphthol and methyl/benzyl carbamate, using a catalytic amount of magnesium hydrogen sulfate [$Mg(HSO_4)_2$] as an efficient heterogeneous catalyst under solvent-free conditions has been developed.

Keywords Magnesium hydrogen sulfate [$Mg(HSO_4)_2$] · Metal hydrogen sulfate · Carbamate · 1-Carbamatoalkyl-2-naphthol · Methyl/benzyl(2-hydroxynaphthalen-1-yl)(aryl)methylcarbamate

Introduction

Finding methods for the synthesis of carbamate derivatives is an immensely important part of organic synthesis due to the role of these functional groups as a privileged building block in a myriad of pharmacologically active compounds as well as natural products [1–5]. These functional groups are ubiquitous due to their wide-ranging potential for synthetic applications [6–9]. They are present in a variety of natural products and are versatile precursors for the synthesis of pharmaceuticals such as mitomycin [10, 11], saxitoxin [12], and bleomycin [13]. In addition, carbamates are intermediates of the Curtius degradation route to amines [14]. They abound as nitrogen- or oxygen-protecting groups [14]. Therefore, as a consequence of their valuable biological activities, great interest has been shown in the preparation of carbamate derivatives [15–17].

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Three-component condensation of aldehydes, 2-naphthol, and methyl/benzyl carbamate is a useful strategy for the preparation of carbamates leading to the synthesis of methyl/benzyl(2-hydroxynaphthalen-1-yl)(aryl)methylcarbamate derivatives, and has been carried out using various precursors, such as PPA–SiO_2 [18], *p*-Toluenesulfonic acid (*P*-TSA) [19], Brønsted acidic ionic liquids [20], SiO_2–$NaHSO_4$ [21], zwitterionic-type molten salt [22], $HClO_4$–SiO_2 [23], silica-supported preyssler nano-particles [24], magnesium (II) 2,2,2-trifluoroacetate [25], [$NMP^+HSO_4^-$] [26], triethyl amine-bonded sulfonic acid [27], aluminum methanesulfonate [28], and 1,3-disulfonic acid imidazolium hydrogen sulfate [29] . Although these procedures have some advantages such as good to excellent yields, in the field of modern organic chemistry the discovery of new synthetic methodologies to facilitate the preparation of organic compounds is a demand point of research activity.

The present work concentrates on the three-component condensation of 2-naphthol, aromatic aldehydes and methyl/benzyl carbamate in the presence of magnesium hydrogen sulfate, $Mg(HSO_4)_2$ [30, 31] as a catalyst under thermal, solvent-free conditions (Scheme 1).

Results and discussions

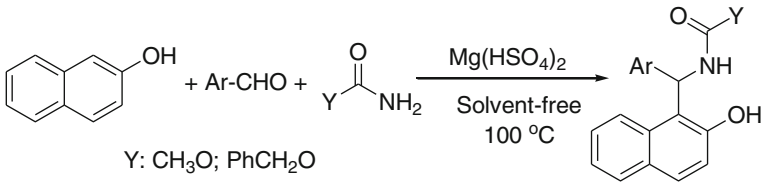
Initially, the condensation reaction of benzaldehyde, 2-naphthol and methyl carbamate was chosen as a model and the influence of $Mg(HSO_4)_2$ as a catalyst was examined to find the optimal reaction conditions (Scheme 2).

To optimize the reaction conditions, the reaction was carried out by using different solvents (Table 1, entries 1–6) or solvent-free condition (Table 1, entry 7). It was observed that the solvent-free condition was the best reaction media in terms of reaction times and yields (Table 1, entry 7).

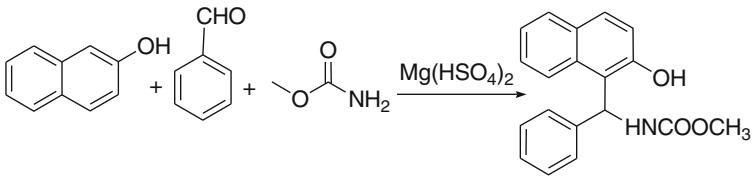
To find an optimized amount of $Mg(HSO_4)_2$ and the reaction temperature, the reaction was carried out by varying the amount of the catalyst and at different reaction temperatures (Table 1, entries 8–14). Maximum yield was obtained when 0.2 mmol of the catalyst was used at 100 °C (Table 1, entry 14). The results are summarized in Table 1.

Next, the scope and efficiency of this procedure was explored for the synthesis of a wide variety of substituted 1-carbamatoalkyl-2-naphthol (Scheme 1; Table 2).

As expected, this reaction proceeded smoothly and the desired products were obtained in good yields. In general, aromatic aldehydes were well tolerated in this



Scheme 1 Preparation of methyl/benzyl(2-hydroxynaphthalen-1-yl)(aryl)methylcarbamate derivatives



Scheme 2 Preparation of methyl(2-hydroxynaphthalen-1-yl)(phenyl)methylcarbamate using $Mg(HSO_4)_2$ as catalyst

Table 1 Optimization of the reaction conditions in the preparation of methyl(2-hydroxynaphthalen-1-yl)(phenyl)methylcarbamate

Entry	Catalyst (mmol)	*T* (°C)	Solvent	Time (min)	Yield (%)[a]
1	0.3	Reflux	H_2O	400	–
2	0.3	Reflux	CH_2Cl_2	400	14
3	0.3	Reflux	Methanol	400	45
4	0.3	Reflux	Ethanol	400	61
5	0.3	Reflux	*n*-Hexane	400	20
6	0.3	Reflux	Ethyl acetate	400	35
7	0.3	100	–	20	80
8	0.3	25	–	300	–
9	0.3	80	–	45	71
10	0.3	120	–	15	77
11	0.05	100	–	60	68
12	0.1	100	–	40	70
13	0.15	100	–	35	73
14	0.2	100	–	27	88

[a] Isolated yield

reaction system (Table 2, entries 1–13). Based on the obtained results, the electronic effects and the steric effects of the substituents played significant roles in the yields of products. When *ortho*-substituted aldehydes (Table 2, entries 6, 7, 11) were used in this process, the corresponding product was obtained in good yields but in longer reaction times. Electron-withdrawing groups on the aldehyde were able to facilitate the transformation by giving evidently higher yield of products and shorter reaction times than the entries using electron-donating atom-functionalized aldehydes (Table 2). In contrast to the findings of aromatic aldehydes, aliphatic aldehydes did not provide corresponding products under present conditions (Table 2, entries 22–23).

Encouraged by the results obtained with methyl carbamate, we turned our attention to benzyl carbamate (Table 2). As shown in Table 2, the reactions of 2-naphthol and aryl aldehydes with benzyl carbamate under the mentioned reaction conditions progressed smoothly and the desired products were obtained in good yields (Table 2, entries 14–21).

Table 2 Preparation of 1-carbamatoalkyl-2-naphthol derivatives using $Mg(HSO_4)_2$ as catalyst (0.2 mmol, 100 °C)

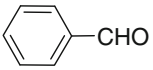
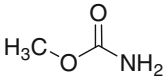
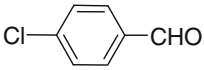
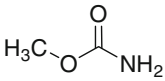
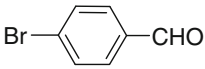
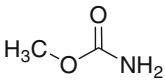
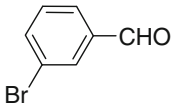
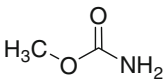
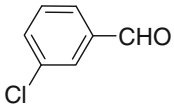
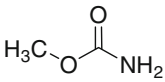
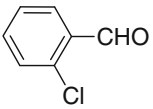
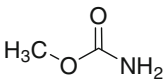
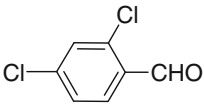
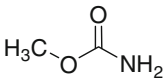
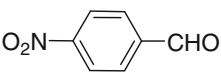
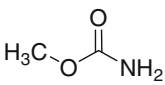
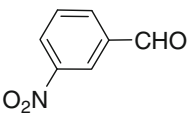
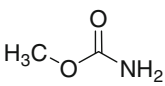
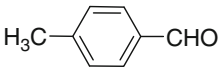
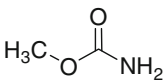
Entry	Aldehyde	Carbamate	Time (min)	Yield (%)[a]	m.p. [lit. m.p. °C] Ref.
1			27	88	211–213 [213][19]
2			21	91	203–205 [206][19]
3			20	95	197–199 [195–197][19]
4			23	90	190–192 [191–193][20]
5			25	89	200–202 [201–203][20]
6			27	84	181–183 [182–184][19]
7			25	95	189–191 [192][21]
8			15	96	205–207 [205–207][21]
9			17	95	249–251 [252][21]
10			45	75	187–189 [188][25]

Table 2 continued

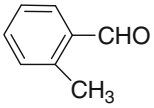
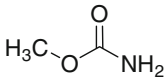
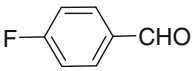
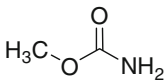
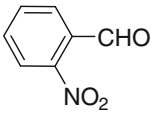
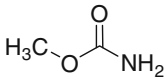
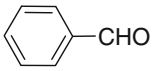
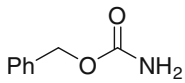
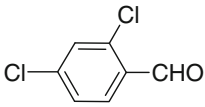
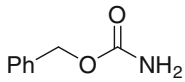
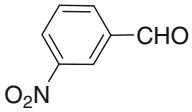
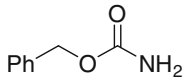
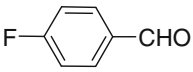
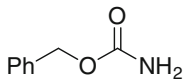
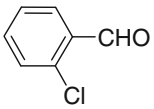
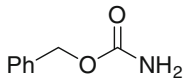
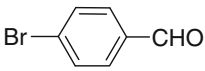
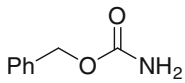
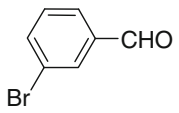
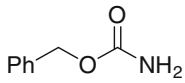
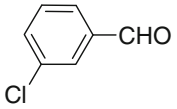
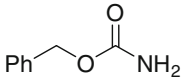
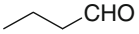
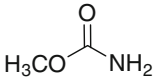
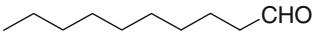
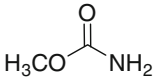
Entry	Aldehyde	Carbamate	Time (min)	Yield (%)[a]	m.p. [lit. m.p. °C] [Ref.]
11			60	70	229–231 [230–232][20]
12			20	91	203–205 [202–204][19]
13			23	83	237–239 [241–242][20]
14			28	89	180–182 [179–180][21]
15			30	94	201–203 [202][25]
16			21	91	200–202 [205–207][20]
17			25	96	187–189 [185–186][21]
18			40	87	165–167 [163–165][19]
19			30	94	188–190 [–]
20			30	93	183–185 [183–185][20]

Table 2 continued

Entry	Aldehyde	Carbamate	Time (min)	Yield (%)[a]	m.p. [lit. m.p. °C] [Ref.]
21			32	88	200–202 [203][21]
22			250	–	–
23			250	–	–

[a] Isolated yield

The work-up procedure is very clear-cut; that is, the products were isolated and purified by simple filtration and crystallization from aqueous ethanol. Our protocol avoids the use of dry media during the reaction process, making it superior to the reactions that use solvent.

Conclusion

In conclusion, a rapid and environmentally benign protocol for the preparation of methyl/benzyl(2-hydroxynaphthalen-1-yl)(aryl)methylcarbamate in a one-pot procedure has been developed. The present protocol features simple operations, short reaction time, environmental friendliness, and good yields.

Experimental

Reagents and instrumentation

All reagents were purchased from Merck and Aldrich and used without further purification. All yields refer to isolated products after purification. The NMR spectra were recorded on a Bruker Avance DPX 400 MHz instrument. The spectra were measured in DMSO-d_6 relative to TMS (0.00 ppm). IR spectra were recorded on a Perkine Elmer 781 spectrophotometer. Elemental analysis was performed on a Heraeus CHN-O-Rapid analyzer. Melting points were determined in open capillaries with a BUCHI 510 melting point apparatus. TLC was performed on silica gel polygram SIL G/UV 254 plates.

Typical procedure

To a mixture of benzaldehyde (1 mmol), 2-naphthol (1 mmol) and methyl carbamate (1.3 mmol), $Mg(HSO_4)_2$ (0.2 mmol) was added and the mixture was heated at 100 °C in an oil bath for the appropriate time (Table 2). The progress of the reaction was monitored by TLC. After completion of the reaction, the mass was cooled to 25 °C and the mixture was dissolved in pure acetone. The catalyst was removed by simple filtration. Solvent was evaporated and the solid product was purified by recrystallization from ethanol.

Benzyl (4-bromophenyl)(2-hydroxynaphthalen-1-yl)methylcarbamate (Table 2, entry 19)

^{1}H NMR (400 MHz, DMSO-d_6): $\delta = 5.03$ (d, $J = 12.6$ Hz, 1H), 5.09 (d, $J = 12.6$ Hz, 1H), 6.88 (d, $J = 7.9$ Hz, 1H), 7.16 (d, $J = 8.3$ Hz, 1H), 7.22–7.42 (m, 10H), 7.48 (d, $J = 7.3$ Hz, 2H), 7.78–7.84 (m, 2H), 7.93 (d, $J = 7.3$ Hz, 1H), 10.15 (s, 1H, OH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): 51.4, 66.5, 119.5, 121.3, 123.7, 124.6, 125.4, 127.5, 128.6, 129.0, 129.4, 129.9, 130.2, 131.6, 132.5, 133.5, 135.7, 138.5, 143.0, 154.6, 157.7 ppm; IR (KBr, cm^{-1}): 3421, 3,171, 3,021, 2,962, 1,687, 1,630, 1,572, 1,488, 1,436, 1,347, 1,267, 940, 821, 710; [Found: C, 65.07; H, 4.47; N, 3.11 $C_{25}H_{20}BrNO_3$; Requires C, 64.95; H, 4.36; N, 3.03].

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