Res Chem Intermed (2013) 39:2123–2131
DOI 10.1007/s11164-012-0744-1

# Efficient one-pot synthesis of 1-carbamatoalkyl-2-naphthols using aluminum methanesulfonate as a reusable catalyst

**Zhiguo Song · Xiaohu Sun · Lianli Liu · Yan Cui**

Received: 27 June 2012 / Accepted: 24 July 2012 / Published online: 5 August 2012

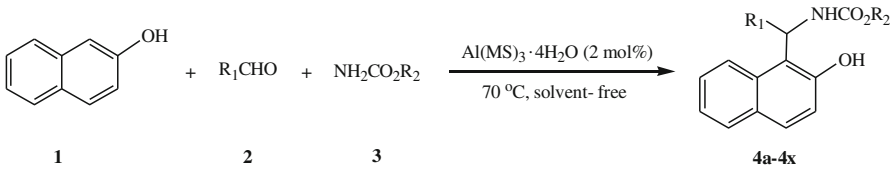

**Abstract** A wide range of 1-carbamatoalkyl-2-naphthols were synthesized via a one-pot three-component condensation of 2-naphthol, aldehydes, and carbamates in the presence of aluminum methanesulfonate at 70 °C under solvent-free conditions. The catalyst is reusable and could be recycled for several runs without any distinct decrease in its efficiency. A plausible mechanism for this three-component reaction was proposed.

**Keywords** Carbamatoalkyl naphthol · Aluminum methanesulfonate · Multicomponent reaction · Solvent-free

## Introduction

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 [1–3]. Recently, we have reported the reactions of 2-naphthol, aldehydes, and amides or urea to form amidoalkyl naphthol derivatives [4], which proceed through the in situ formation of *ortho*-quinone methides (*o*-QMs), intermediates with amide acting as a nucleophile. Carbamates instead of amides in the mentioned reaction produce carbamatoalkyl naphthols, which can be deprotected more easily than the amide group [5]. Amidoalkyl naphthols and carbamatoalkyl naphthols are all important intermediates for preparing 1-aminomethyl-2-naphthols, which exhibit important cardiovascular activity [6]. Therefore, the discovery of simple and green methods for synthesis of carmatoalkyl naphthols is of prime importance.

Z. Song (✉) · X. Sun · L. Liu · Y. Cui
Management Center for Experiment, Bohai University, Jinzhou 121000, People's Republic of China
e-mail: lnszgsky@yahoo.com.cn




**Scheme 1** $Al(MS)_3{\cdot}4H_2O$-catalyzed synthesis of 1-carmatoalkyl-2-naphthols under solvent-free conditions

To the best of our knowledge, the synthesis of carbamatoalkyl naphthols have been largely overlooked, and only a few references about their synthesis have been reported [7–17]. In these references, 1-carmatoalkyl-2-naphthols can be synthesized by a one-pot three-component reaction from 2-naphthol, aldehydes, and methyl or benzyl carbamates. Though these methods achieved good results, many of them suffer from at least one of the following disadvantages: low yields, expensive catalyst, higher reaction temperature (>100 °C), and a large excess of reagents and catalysts (10 mol%). Now, during our continuous study on green and efficient multicomponent reactions, we report here a one-pot three-component synthesis of 1-carmatoalkyl-2-naphthols from equivalent 2-naphthol, aldehydes, and methyl/ethyl/benzyl carbamates in the presence of 2 mol% aluminum methanesulfonate ($Al(MS)_3{\cdot}4H_2O$) under solvent-free conditions at 70 °C (Scheme 1). Metal methanesulfonates ($M(MS)_x{\cdot}aH_2O$) as water-tolerant Lewis acids catalysts have been well documented in recent years [18–24]. For this, the new synthetic protocol enlarges the application scope of $M(MS)_x{\cdot}aH_2O$ in organic synthesis.

## Experimental

### General

Melting points were determined by using an RY-1 micromelting point apparatus. Infrared spectra were recorded on a Varian Scimitar 2000 series Fourier transform instrument. $^1H$ and $^{13}C$ NMR spectra were recorded on an Agilent 400-MR instrument in DMSO-$d_6$ using TMS as an internal standard. Mass spectra were obtained with an Agilent 1100 series LC/MSD VL ESI instrument. Elemental analyses (C, H, N) were conducted using the Elemental Analyzer EA 2400II (Perkin Elmer). Metal methanesulfonates were synthesized according to Ref. [25], and the characterized results of $Al(MS)_3{\cdot}4H_2O$ were consistent with those in Ref. [24].

### General procedure for preparation of 1-carmatoalkyl-2-naphthols catalyzed by $Al(MS)_3{\cdot}4H_2O$

A mixture of 2-naphthol **1** (0.721 g, 5 mmol), aldehydes **2** (5 mmol), carbamates **3** (5 mmol), and $Al(MS)_3{\cdot}4H_2O$ (0.038 g, 0.1 mmol) was magnetically stirred at 70 °C in a water bath and the reaction was followed by TLC. After completion, the mixture was cooled to room temperature, washed with cold water, and recrystallized

from aqueous EtOH (60 %, v). The filtrate containing the catalyst was evaporated under reduced pressure to give the recovered catalyst, which could be reused without further treatment. The products were characterized by IR, $^1$H NMR, $^{13}$C NMR, LC/MS, and elemental analysis. Spectral data for some new compounds are given below:

Methyl ((2-chlorophenyl)(2-hydroxynaphthalen-1-yl)methyl) carbamate (**4e**): white solid, IR (KBr): 3,431, 3,220, 1,690, 1,527, 1,341, 1,051, 819, 753, 706 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 9.96 (s, 1H, OH), 8.04 (d, 1H, $J = 8.2$ Hz, NH), 7.86 (d, 1H, $J = 7.1$ Hz, ArH), 7.77 (q, 2H, $J = 8.6$ Hz, ArH), 7.52 (d, 1H, $J = 4.6$ Hz, ArH), 7.40 (dd, 2H, $J = 12.3$, 6.8 Hz, ArH), 7.26 (d, 3H, $J = 13.9$ Hz, ArH), 7.16 (d, 1H, $J = 8.6$ Hz, ArH), 6.91 (d, 1H, $J = 7.8$ Hz, CH), 3.54 (s, 3H, $OCH_3$); $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ 156.5, 153.9, 139.8, 133.0, 132.9, 130.3, 129.9, 129.7, 129.0, 128.8, 128.7, 126.9, 126.7, 123.3, 122.7, 119.0, 117.4, 51.9, 50.1; MS (ESI): *m/z* (%) 340 $(M–H)^-$; Anal. calcd. for $C_{19}H_{16}NO_3Cl$: C, 66.77; H, 4.72; N, 4.10. Found: C, 66.58; H, 4.83; N, 4.02.

Methyl ((2,4-dichlorophenyl)(2-hydroxynaphthalen-1-yl)methyl) carbamate (**4g**): white solid, IR (KBr): 3,403, 3,260, 1,678, 1,519, 1,061, 874, 753, 718 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 9.97 (s, 1H, OH), 8.02 (d, 1H, $J = 8.5$ Hz, NH), 7.96 (d, 1H, $J = 7.8$ Hz, ArH), 7.78 (q, 2H, $J = 8.7$ Hz, ArH), 7.57-7.38 (m, 4H, ArH), 7.28 (t, 1H, $J = 7.3$ Hz, ArH), 7.14 (d, 1H, $J = 8.7$ Hz, ArH), 6.85 (d, 1H, $J = 8.0$ Hz, CH), 3.55 (s, 3H, $OCH_3$); $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ 156.6, 154.0, 139.3, 133.5, 133.0, 132.3, 131.6, 130.1, 129.0, 128.9, 128.6, 127.0, 126.9, 123.0, 122.8, 119.0, 116.7, 52.0, 49.8; MS (ESI): *m/z* (%) 375 $(M–H)^-$; Anal. calcd. for $C_{19}H_{15}NO_3Cl_2$: C, 60.66; H, 4.02; N, 3.72. Found: C, 60.82; H, 3.94; N, 3.75.

Ethyl ((2-nitrophenyl)(2-hydroxynaphthalen-1-yl)methyl) carbamate (**4l**): white solid, IR (KBr): 3,402, 3,277, 1,686, 1,531, 1,334, 1,038, 813, 744, 697 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 9.79 (s, 1H, OH), 7.92 (d, 1H, $J = 8.6$ Hz, NH), 7.81–7.72 (m, 4H, ArH), 7.61 (q, 2H, $J = 7.5$ Hz, ArH), 7.44 (dt, 2H, $J = 7.5$, 6.5 Hz, ArH), 7.29–7.26 (m, 2H, ArH), 7.05 (d, 1H, $J = 8.7$ Hz, CH), 4.04 (q, 2H, $J = 7.0$ Hz, $CH_2$), 1.15 (t, 3H, $J = 7.0$ Hz, $CH_3$); $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ 156.4, 154.0, 149.0, 136.9, 133.3, 132.5, 130.3, 129.3, 128.8, 128.5, 128.1, 127.0, 124.4, 123.0, 122.8, 118.8, 116.5, 60.5, 48.1, 15.0; MS (ESI): *m/z* (%) 365 $(M–H)^-$; Anal. calcd. for $C_{20}H_{18}N_2O_5$: C, 65.57; H, 4.95; N, 7.65. Found: C, 65.43; H, 5.02; N, 7.58.

Ethyl ((3-nitrophenyl)(2-hydroxynaphthalen-1-yl)methyl) carbamate (**4m**): white solid, IR (KBr): 3,395, 3,277, 1,678, 1,527, 1,348, 1,045, 808, 752, 701 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.24 (s, 1H, OH), 8.13 (d, 1H, $J = 8.2$ Hz, NH), 8.07 (d, 1H, $J = 8.1$ Hz, ArH), 7.98 (d, 1H, $J = 7.8$ Hz, ArH), 7.82 (t, 3H, $J = 8.4$ Hz, ArH), 7.64 (d, 1H, $J = 7.8$ Hz, ArH), 7.56 (t, 1H, $J = 8.0$ Hz, ArH), 7.44 (t, 1H, $J = 7.5$ Hz, ArH), 7.31 (t, 1H, $J = 7.5$ Hz, ArH), 7.23 (d, 1H, $J = 8.8$ Hz, ArH), 6.97 (d, 1H, $J = 7.8$ Hz, CH), 4.08 (q, 2H, $J = 6.8$ Hz, $CH_2$), 1.18 (t, 3H, $J = 6.8$ Hz, $CH_3$); $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ 156.7, 153.5, 148.1, 145.5, 133.2, 132.3, 130.3, 130.1, 129.1, 128.7, 127.3, 123.5, 123.1, 121.9, 120.9, 118.8, 118.3, 60.7, 50.3, 15.0; MS (ESI): *m/z* (%) 365 $(M–H)^-$; Anal. calcd. for $C_{20}H_{18}N_2O_5$: C, 65.57; H, 4.95; N, 7.65. Found: C, 65.70; H, 5.04; N, 7.59.

Ethyl ((4-nitrophenyl)(2-hydroxynaphthalen-1-yl)methyl) carbamate (**4n**): white solid, IR (KBr): 3,430, 3,185, 1,685, 1,518, 1,351, 1,049, 821, 739, 708 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.21 (s, 1H, OH), 8.15 (d, 2H, $J = 8.8$ Hz, NH and ArH), 7.94–7.73 (m, 4H, ArH), 7.49 (d, 2H, $J = 8.6$ Hz, ArH), 7.43 (t, 1H, $J = 7.5$ Hz, ArH), 7.30 (t, 1H, $J = 7.5$ Hz, ArH), 7.23 (d, 1H, $J = 8.8$ Hz, ArH), 6.97 (d, 1H, $J = 7.7$ Hz, CH), 4.07 (q, 2H, $J = 6.7$ Hz, $CH_2$), 1.17 (t, 3H, $J = 6.7$ Hz, $CH_3$); $^{13}C$ NMR (125 MHz, DMSO-$d_6$): $\delta$ 156.7, 153.5, 151.1, 146.4, 132.3, 130.3, 129.0, 128.7, 127.5, 127.2, 123.7, 123.2, 123.0, 118.8, 118.4, 60.7, 50.5, 15.0; MS (ESI): *m/z* (%) 365 $(M–H)^-$; Anal. calcd. for $C_{20}H_{18}N_2O_5$: C, 65.57; H, 4.95; N, 7.65. Found: C, 65.72; H, 5.04; N, 7.53.

Ethyl ((2-chlorophenyl)(2-hydroxynaphthalen-1-yl)methyl) carbamate (**4o**): white solid, IR (KBr): 3,420, 3,229, 1,685, 1,525, 1,337, 1,051, 821, 752, 706 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.19 (s, 1H, OH), 8.28 (d, 1H, $J = 8.5$ Hz, NH), 8.00 (q, 3H, $J = 8.5$ Hz, ArH), 7.77 (d, 1H, $J = 5.9$ Hz, ArH), 7.66–7.48 (m, 5H, ArH), 7.39 (d, 1H, $J = 8.7$ Hz, ArH), 7.15 (d, 1H, $J = 8.3$ Hz, CH), 4.22 (q, 2H, $J = 7.1$ Hz, $CH_2$), 1.36 (t, 3H, $J = 7.1$ Hz, $CH_3$); $^{13}C$ NMR (125 MHz, DMSO-$d_6$): $\delta$ 156.1, 153.9, 139.8, 133.0, 132.8, 130.3, 129.9, 129.7, 129.0, 128.8, 128.6, 126.9, 126.7, 123.3, 122.7, 119.0, 117.5, 60.4, 50.0, 15.1; MS (ESI): *m/z* (%) 354 $(M–H)^-$; Anal. calcd. for $C_{20}H_{18}NO_3Cl$: C, 67.51; H, 5.10; N, 3.94. Found: C, 67.72; H, 5.21; N, 3.87.

Ethyl ((4-chlorophenyl)(2-hydroxynaphthalen-1-yl)methyl) carbamate (**4p**): white solid, IR (KBr): 3,424, 3,197, 1,676, 1,517, 1,330, 1,042, 820, 751, 711 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.15 (s, 1H, OH), 7.93 (d, 1H, $J = 8.3$ Hz, NH), 7.80 (q, 2H, $J = 8.2$ Hz, ArH), 7.58 (d, 1H, $J = 8.2$ Hz, ArH), 7.41 (t, 1H, $J = 7.3$ Hz, ArH), 7.33–7.22 (m, 6H, ArH), 6.87 (d, 1H, $J = 8.1$ Hz, CH), 4.05 (q, 2H, $J = 7.2$ Hz, $CH_2$), 1.17 (t, 3H, $J = 6.9$ Hz, $CH_3$); $^{13}C$ NMR (125 MHz, DMSO-$d_6$): $\delta$ 156.6, 153.3, 141.9, 132.3, 131.4, 129.9, 129.0, 128.7, 128.4, 128.2, 127.4, 127.1, 123.6, 123.0, 118.9, 60.7, 50.2, 15.0; MS (ESI): *m/z* (%) 354 $(M–H)^-$; Anal. calcd. for $C_{20}H_{18}NO_3Cl$: C, 67.51; H, 5.10; N, 3.94. Found: C, 67.69; H, 5.01; N, 3.85.

Ethyl [(2,4-dichlorophenyl)(2-hydroxynaphthalen-1-yl)methyl] carbamate (**4q**): white solid, IR (KBr): 3,412, 3,071, 1,683, 1,514, 1,336, 1,052, 815, 743, 721 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta$ 9.93 (s, 1H, OH), 8.04 (d, 1H, $J = 8.6$ Hz, NH), 7.78 (dd, 3H, $J = 13.8$, 8.3 Hz, ArH), 7.58 (d, 1H, $J = 8.5$ Hz, ArH), 7.49 (d, 1H, $J = 1.5$ Hz, ArH), 7.44 (t, 1H, $J = 7.5$ Hz, ArH), 7.38 (dd, 1H, $J = 6.8$, 1.8 Hz, ArH), 7.28 (t, 1H, $J = 7.4$ Hz, ArH), 7.14 (d, 1H, $J = 8.8$ Hz, ArH), 6.86 (d, 1H, $J = 8.1$ Hz, CH), 3.98 (q, 2H, $J = 6.7$ Hz, $CH_2$), 1.14 (t, 3H, $J = 6.4$ Hz, $CH_3$); $^{13}C$ NMR (125 MHz, DMSO-$d_6$): $\delta$ 156.2, 154.0, 139.3, 133.5, 132.9, 132.3, 131.6, 130.1, 129.0, 128.9, 128.6, 127.0, 126.9, 123.1, 122.8, 119.0, 116.8, 60.4, 49.7, 15.0; MS (ESI): *m/z* (%) 389 $(M–H)^-$; Anal. calcd. for $C_{20}H_{17}NO_3Cl_2$: C, 61.55; H, 4.39; N, 3.59. Found: C, 61.71; H, 4.47; N, 3.50.

Benzyl ((2-nitrophenyl)(2-hydroxynaphthalen-1-yl)methyl) carbamate (**4s**): white solid, IR (KBr): 3,424, 3,250, 1,702, 1,528, 1,334, 1,046, 834, 752, 696 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta$ 9.81 (s, 1H, OH), 8.08 (d, 1H, $J = 7.9$ Hz, NH), 7.94 (d, 1H, $J = 8.2$ Hz, ArH), 7.79 (d, 1H, $J = 8.0$ Hz, ArH), 7.74 (t, 2H, $J = 7.3$ Hz, ArH), 7.62–7.26 (m, 11H, ArH), 7.08 (d, 1H, $J = 8.5$ Hz, CH), 5.12 (d, 1H, $J = 12.8$ Hz, $CH_2$), 5.06 (d, 1H, $J = 12.8$ Hz, $CH_2$); $^{13}C$ NMR

**Table 1** Screening of metal methanesulfonates and aluminum salts for the condensation of 2-naphthol, 2-nitrobenzaldehyde, and methyl carbamate

| Entry | Catalyst | Time (h) | Yield (%) |
|---|---|---|---|
| 1 | $Al(MS)_3{\cdot}4H_2O$ | 0.5 | 93 |
| 2 | $Cu(MS)_2{\cdot}4H_2O$ | 0.8 | 77 |
| 3 | $Zn(MS)_2{\cdot}4H_2O$ | 2.0 | 58 |
| 4 | $Mg(MS)_2{\cdot}6H_2O$ | 4.0 | 55 |
| 5 | $La(MS)_3{\cdot}2H_2O$ | 6.0 | 51 |
| 6 | $Nd(MS)_3{\cdot}2H_2O$ | 3.0 | 46 |
| 7 | $Ce(MS)_3{\cdot}2H_2O$ | 5.0 | 21 |
| 8 | $AlCl_3{\cdot}6H_2O$ | 1.0 | 83 |
| 9 | $Al(NO_3)_3{\cdot}9H_2O$ | 2.0 | 61 |

(125 MHz, DMSO-$d_6$): $\delta$ 156.3, 154.1, 149.0, 137.5, 136.8, 133.3, 132.5, 130.4, 129.7, 129.4, 128.9, 128.7, 128.5, 128.2, 128.1, 127.8, 127.2, 127.0, 124.5, 123.0, 122.9, 118.8, 116.4, 65.9, 48.3; MS (ESI): *m/z* (%) 427 $(M–H)^-$; Anal. calcd. for $C_{25}H_{20}N_2O_5$: C, 70.09; H, 4.71; N, 6.54. Found: C, 69.92; H, 4.82; N, 6.67.

Benzyl ((4-nitrophenyl)(2-hydroxynaphthalen-1-yl)methyl) carbamate (**4u**): white solid, IR (KBr): 3,414, 3,064, 1,686, 1,515, 1,347, 1,050, 824, 745, 695 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.21 (s, 1H, OH), 8.15 (d, 2H, $J = 8.7$ Hz, NH and ArH), 7.99 (d, 1H, $J = 6.6$ Hz, ArH), 7.93 (d, 1H, $J = 6.4$ Hz, ArH), 7.82 (t, 2H, $J = 8.7$ Hz, ArH), 7.50 (d, 2H, $J = 8.5$ Hz, ArH), 7.41–7.28 (m, 7H, ArH), 7.24 (d, 1H, $J = 8.8$ Hz, ArH), 7.01 (d, 1H, $J = 7.8$ Hz, CH), 5.14 (d, 1H, $J = 12.6$ Hz, $CH_2$), 5.08 (d, 1H, $J = 12.6$ Hz, $CH_2$); $^{13}C$ NMR (125 MHz, DMSO-$d_6$): $\delta$ 156.6, 153.5, 151.0, 146.5, 137.2, 132.3, 130.3, 129.1, 128.8, 128.7, 128.2, 127.5, 127.2, 123.7, 123.3, 123.0, 118.7, 118.3, 66.3, 50.6; MS (ESI): *m/z* (%) 427 $(M–H)^-$; Anal. calcd. for $C_{25}H_{20}N_2O_5$: C, 70.09; H, 4.71; N, 6.54. Found: C, 70.25; H, 4.65; N, 6.42.

Benzyl ((2-chlorophenyl)(2-hydroxynaphthalen-1-yl)methyl) carbamate (**4v**): white solid, IR (KBr): 3,421, 3,170, 1,700, 1,518, 1,336, 1,050, 819, 753, 694 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta$ 9.96 (s, 1H, OH), 8.04 (d, 2H, $J = 7.8$ Hz, NH and ArH), 7.80 (d, 1H, $J = 7.0$ Hz, ArH), 7.75 (d, 1H, $J = 8.0$ Hz, ArH), 7.52–7.25 (m, 10H, ArH), 7.16 (d, 2H, $J = 7.3$ Hz, ArH), 6.94 (d, 1H, $J = 5.8$ Hz, CH), 5.09 (d, 1H, $J = 12.0$ Hz, $CH_2$), 5.01 (d, 1H, $J = 12.0$ Hz, $CH_2$); $^{13}C$ NMR (125 MHz, DMSO-$d_6$): $\delta$ 156.0, 153.9, 139.7, 137.6, 133.0, 132.9, 130.3, 129.9, 129.7, 129.0, 128.9, 128.7, 128.1, 127.8, 126.9, 126.7, 123.3, 122.7, 119.0, 117.3, 65.8, 50.1; MS (ESI): *m/z* (%) 416 $(M–H)^-$; Anal. calcd. for $C_{25}H_{20}NO_3Cl$: C, 71.86; H, 4.82; N, 3.35. Found: C, 71.69; H, 4.73; N, 3.41.

Benzyl ((4-chlorophenyl)(2-hydroxynaphthalen-1-yl)methyl) carbamate (**4w**): white solid, IR (KBr): 3,402, 3,200, 1,681, 1,515, 1,321, 1,042, 812, 746, 696 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta$ 10.15 (s, 1H, OH), 7.93 (d, 1H, $J = 8.2$ Hz, NH), 7.80 (q, 3H, $J = 7.9$ Hz, ArH), 7.39–7.23 (m, 12H, ArH), 6.90 (d, 1H, $J = 8.1$ Hz, CH), 5.11 (d, 1H, $J = 12.6$ Hz, $CH_2$), 5.01 (d, 1H, $J = 12.6$ Hz, $CH_2$); $^{13}C$ NMR (125 MHz, DMSO-$d_6$): $\delta$ 156.5, 153.4, 141.8, 137.3, 132.3, 131.3, 129.9, 129.0, 128.8, 128.7, 128.4, 128.3, 128.2, 127.4, 127.0, 123.7, 123.4, 122.8, 118.9, 118.7, 66.2, 50.3; MS (ESI): *m/z* (%) 416 $(M–H)^-$; Anal. calcd. for $C_{25}H_{20}NO_3Cl$: C, 71.86; H, 4.82; N, 3.35. Found: C, 72.01; H, 4.75; N, 3.41.

**Table 2** Optimization of various reaction conditions for the preparation of methyl [(2-nitrophenyl)(2-hydroxynaphthalen-1-yl)methyl] carbamate

| Entry | Solvent (mL) | Amount of catalyst (mol%) | Temperature (°C) | Time (h) | Yield (%) |
|---|---|---|---|---|---|
| 1 | $H_2O$ (3) | 2 | 70 | 3.0 | 0 |
| 2 | EtOH (3) | 2 | Reflux | 3.0 | 14 |
| 3 | $CH_3CN$ (3) | 2 | Reflux | 3.0 | 53 |
| 4 | Solvent-free | 2 | 70 | 0.5 | 93, 92, 90, 87[a] |
| 5 | Solvent-free | 1 | 70 | 0.5 | 83 |
| 6 | Solvent-free | 3 | 70 | 0.5 | 94 |
| 7 | Solvent-free | 2 | 60 | 1.5 | 72 |
| 8 | Solvent-free | 2 | 80 | 0.5 | 87 |
| 9 | Solvent-free | 2 | 90 | 0.5 | 81 |
| 10 | Solvent-free | 0 | 70 | 4.0 | 0 |

[a] Catalyst was reused four times

Benzyl ((2,4-dichlorophenyl)(2-hydroxynaphthalen-1-yl)methyl) carbamate (**4x**): white solid, IR (KBr): 3,416, 3,066, 1,686, 1,522, 1,341, 1,054, 819, 744, 719 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$): $\delta$ 9.92 (s, 1H, OH), 8.02 (d, 2H, $J = 8.6$ Hz, NH and ArH), 7.80 (d, 1H, $J = 8.0$ Hz, ArH), 7.75 (d, 1H, $J = 8.8$ Hz, ArH), 7.56 (d, 1H, $J = 8.4$ Hz, ArH), 7.50–7.26 (m, 9H, ArH), 7.14 (d, 1H, $J = 8.7$ Hz, ArH), 6.87 (d, 1H, $J = 6.7$ Hz, CH), 5.09 (d, 1H, $J = 12.8$ Hz, $CH_2$), 5.01 (d, 1H, $J = 12.8$ Hz, $CH_2$); $^{13}C$ NMR (125 MHz, DMSO-$d_6$): $\delta$ 156.0, 154.0, 139.2, 137.5, 133.6, 133.0, 132.3, 131.6, 130.1, 129.1, 129.0, 128.7, 128.6, 128.1, 127.9, 127.0, 126.9, 123.1, 122.8, 118.9, 116.6, 65.9, 49.9; MS (ESI): *m/z* (%) 451 $(M–H)^-$; Anal. calcd. for $C_{25}H_{19}NO_3Cl_2$: C, 66.38; H, 4.23; N, 3.10. Found: C, 66.19; H, 4.15; N, 3.14.

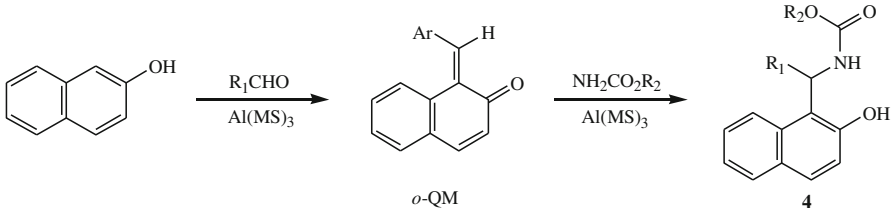
## Results and discussion

At the outset, we investigated the catalytic activity of different $M(MS)_x{\cdot}aH_2O$ (0.1 mmol) using the model reaction of 2-naphthol (5 mmol), 2-nitrobenzaldehyde (5 mmol) and methyl carbamate (5 mmol) at 70 °C under solvent-free conditions. The results are summarized in Table 1. After several trials, it was found that $Al(MS)_3{\cdot}4H_2O$ was the most efficient catalyst for this transformation, since it results in the highest conversion to the desired product in the shortest reaction time (Table 1, entry 1). Compared with conventional Lewis acids such as aluminum chloride and aluminum nitrate, $Al(MS)_3{\cdot}4H_2O$ showed excellent catalytic activity (Table 1, entries 1, 8 and 9).

Next, we examined the above reaction under different conditions (Table 2). Initially, $H_2O$, EtOH, $CH_3CN$ and solvent-free condition were investigated to optimize the reaction (Table 2, entries 1–4). It seems that solvent-free system is the best choice in terms of reaction time and product yield (Table 2, entry 4). In this

**Table 3** $Al(MS)_3{\cdot}4H_2O$-catalyzed synthesis of 1-carbamatoalkyl-2-naphthols

| Entry | $R_1$ | $R_2$ | Time (h) | Product | Yield (%) | Mp (°C) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Found | Reported |
| 1 | $C_6H_5$ | Me | 0.5 | **4a** | 90 | 224–226 | 222–224 [9] |
| 2 | 2-$NO_2C_6H_4$ | Me | 0.5 | **4b** | 93 | 245–247 | 241–242 [9] |
| 3 | 3-$NO_2C_6H_4$ | Me | 0.6 | **4c** | 94 | 243–244 | 253–255 [9] |
| 4 | 4-$NO_2C_6H_4$ | Me | 0.5 | **4d** | 90 | 212–214 | 206–208 [17] |
| 5 | 2-$ClC_6H_4$ | Me | 0.4 | **4e** | 91 | 218–220 | – |
| 6 | 4-$ClC_6H_4$ | Me | 0.5 | **4f** | 89 | 202–204 | 203–205 [9] |
| 7 | 2,4-$Cl_2C_6H_3$ | Me | 0.5 | **4g** | 90 | 210–212 | – |
| 8 | 4-$CH_3C_6H_4$ | Me | 10.0 | **4h** | 18 | 193–195 | 188 [17] |
| 9 | 4-$OCH_3C_6H_4$ | Me | 10.0 | **4i** | Trace | – | – |
| 10 | $CH_3CH_2CH_2$ | Me | 10.0 | **4j** | 0 | – | – |
| 11 | $C_6H_5$ | Et | 0.5 | **4k** | 83 | 197–199 | 195–196 [15] |
| 12 | 2-$NO_2C_6H_4$ | Et | 0.5 | **4l** | 87 | 215–216 | – |
| 13 | 3-$NO_2C_6H_4$ | Et | 0.6 | **4m** | 93 | 245–246 | – |
| 14 | 4-$NO_2C_6H_4$ | Et | 0.4 | **4n** | 89 | 229–231 | – |
| 15 | 2-$ClC_6H_4$ | Et | 0.5 | **4o** | 91 | 216–217 | – |
| 16 | 4-$ClC_6H_4$ | Et | 0.7 | **4p** | 90 | 219–221 | – |
| 17 | 2,4-$Cl_2C_6H_3$ | Et | 0.5 | **4q** | 88 | 196–197 | – |
| 18 | $C_6H_5$ | $CH_2Ph$ | 0.6 | **4r** | 85 | 185–187 | 180–182 [9] |
| 19 | 2-$NO_2C_6H_4$ | $CH_2Ph$ | 0.5 | **4s** | 90 | 208–210 | – |
| 20 | 3-$NO_2C_6H_4$ | $CH_2Ph$ | 0.6 | **4t** | 95 | 200–202 | 205–207 [9] |
| 21 | 4-$NO_2C_6H_4$ | $CH_2Ph$ | 0.5 | **4u** | 92 | 202–204 | – |
| 22 | 2-$ClC_6H_4$ | $CH_2Ph$ | 0.8 | **4v** | 91 | 211–213 | – |
| 23 | 4-$ClC_6H_4$ | $CH_2Ph$ | 1.0 | **4w** | 90 | 178–180 | – |
| 24 | 2,4-$Cl_2C_6H_3$ | $CH_2Ph$ | 0.5 | **4x** | 91 | 208–210 | – |




**Scheme 2** Proposed mechanism

case, $Al(MS)_3{\cdot}4H_2O$ could be reused four successive runs without distinct loss of activity. Then, the amount of catalyst and suitable reaction temperature were studied (Table 2, entries 4-9). The best result was obtained by carrying out the reaction using 2 mol% $Al(MS)_3{\cdot}4H_2O$ at 70 °C under solvent-free conditions (Table 2, entry 4). The product yield decreased when the reaction temperature was above 70 °C. Perhaps the reason for this is that these reactions proceed too quickly to complete

the transformations. No product was obtained in the absence of a catalyst (Table 2, entry 10).

Using the optimized reaction conditions, the scope and efficiency of the reaction were explored for the synthesis of a wide variety of substituted 1-carbamatoalkyl-2-naphthols using 2-naphthol, various aldehydes, and methyl/ethyl/benzyl carbamate. The results are summarized in Table 3. As shown in Table 3, the direct three-component reactions worked well with aromatic aldehydes carrying electron-withdrawing groups such as $NO_2$ and Cl. The position of the substituent on the aromatic ring does not show any effect on the yield of the product. Under the same conditions, the reactions proceed sluggishly with aromatic aldehydes carrying electron-donating groups (Table 3, entries 8 and 9). No product was obtained when aliphatic aldehyde such as propionaldehyde was used as the starting material (Table 3, entry 10). Beside methyl carbamate, ethyl carbamate and benzyl carbamate were also used as ammonia source, and they worked equally in the amidoalkylation reaction.

A possible mechanism for this transformation is proposed in Scheme 2. As reported in the literature [4, 26], reaction of 2-naphthol with aldehydes in the presence of an acid catalyst is known to give *o*-QMs. The *o*-QMs generated in situ reacted with carbamates to form the 1-carbamatoalkyl-2-naphthol derivatives **4**.

## Conclusions

In conclusion, we have described a new strategy for the synthesis of 1-carbamatoalkyl-2-naphthols via a one-pot three-component condensation of 2-naphthol, aldehydes, and methyl/ethyl/benzyl carbamates using the inexpensive, water-tolerant, and recyclable $Al(MS)_3{\cdot}4H_2O$ as a catalyst under solvent-free conditions. The method offers several advantages including mild reaction conditions, simple work-up, easy recovery, and reusable catalyst, and environmental friendly characteristics. Currently, studies on the extension of multicomponent reactions are ongoing in our laboratory.

**Acknowledgment** This research work was financially supported by the Education Committee of Liaoning Province of China (No. L2011198).

## References

1. S. Knapp, Chem. Rev. **95**, 1859 (1995)
2. E. Juaristi, *Enantioselective Synthesis of β-Amino Acids* (Wiley, New York, 1997)
3. T. Dingermann, D. Steinhilber, D. Folkers, *Molecular Biology in Medicinal Chemistry* (Wiley-VCH, Weinheim, 2004)
4. M. Wang, Y. Liang, T.T. Zhang, J.J. Gao, Chin. J. Chem. **29**, 1656 (2011)
5. W. Green, P.G.M. Wuts, *Protecting Groups in Organic Synthesis*, 2nd edn. (Wiley, New York, 1999)
6. A.Y. Shen, C.T. Tsai, C.L. Chen, Eur. J. Med. Chem. **34**, 877 (1999)
7. M.H. Mosslemin, M.R. Nateghi, R. Mohebat, Monatsh. Chem. **139**, 1247 (2008)
8. H.R. Shaterian, A. Hosseinian, M.A. Ghashang, Tetrahedron Lett. **49**, 5804 (2008)
9. N. Tavakoli-Hoseini, M.M. Heravi, F.F. Bamoharran, A. Davoodnia, Bull. Korean Chem. Soc. **32**, 787 (2011)
10. S.H. Reza, H. Asghar, G. Majid, Chin. J. Chem. **27**, 821 (2009)

11. M.M. Heravi, N. Tavakoli-Hoseini, F.F. Bamoharram, Green Chem. Lett. Rev. **3**, 263 (2010)
12. H.R. Shaterian, A. Hosseinian, M. Ghashang, Synth. Commun. **39**, 2560 (2009)
13. D. Kundu, A. Majee, A. Hajra, Catal. Commun. **11**, 1157 (2010)
14. F. Tamaddon, J.M. Bistgani, Synlett **20**, 2947 (2011)
15. K.M. Deshmukh, Z.S. Qureshi, Y.P. Patil, B.M. Bhanage, Synth. Commun. **42**, 93 (2012)
16. H. Yarahmadi, H.R. Shaterian, J. Chem. Res. **36**, 52–55 (2012)
17. M.R.M. Shafiee, R. Moloudi, M. Ghashang, J. Chem. Res. **35**, 622–625 (2011)
18. M. Wang, Z.C. Wang, Z.L. Sun, H. Jiang, React. Kinet. Catal. Lett. **84**, 223 (2005)
19. M. Wang, Z.C. Wang, Z.L. Sun, H. Jiang, Transition Met. Chem. **30**, 792 (2005)
20. M. Wang, H. Gong, H. Jiang, Z.C. Wang, Synth. Commun. **36**, 1953 (2006)
21. M. Wang, Z.G. Song, H. Gong, H. Jiang, Chin. Chem. Lett. **18**, 799 (2007)
22. M. Wang, Z.G. Song, H. Jiang, Org. Prep. Proced. Int. **41**, 315 (2009)
23. M. Wang, Z.G. Song, T.T. Zhang, Monatsh. Chem. **141**, 993 (2010)
24. Z.G. Song, L.L. Liu, Y. Wang, X.H. Sun, Res. Chem. Intermed. **38**, 1091 (2012)
25. M. Wang, H. Jiang, Z.C. Wang, J. Therm. Anal. Calorim. **85**, 751 (2006)
26. P. Zhang, Z.H. Zhang, Monatsh. Chem. **140**, 199 (2009)