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Trityl chloride as an efficient organic catalyst for the synthesis of 1-amidoalkyl-2-naphtols in neutral media at room temperature

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ABSTRACT

A highly efficient and simple procedure for the preparation of 1-amidoalkyl-2-naphthols *via* one-pot three-component condensation reaction of 2-naphthol, arylaldehydes and acetonitrile (Ritter type reaction) in the presence of catalytic amount of trityl chloride at room temperature is described. The reactions proceed in high yields and in relatively short reaction times.

1. Introduction

1-Amidoalkyl-2-naphthol derivatives are significant as they can be easily converted to 1-aminoalkyl-2-naphthols as an important class of bioactive compounds, by amide hydrolysis reaction. 1-Aminoalkyl-2-naphthols have been frequently applied as hypotensive and bradycardiac agents [1–3]. 1-Amidoalkyl-2-naphthols can be also converted to 1,3-oxazine derivatives [4]. 1,3-Oxazines have potentially different biological activities including antibiotic [5–7], antitumor [8–10], analgesic [11,12], anticonvulsant [13], antipsychotic [14], antimalarial [15], antianginal [16], antihypertensive [17], and antirheumatic properties [18]. One-pot three-component condensation of 2-naphthol, arylaldehydes and amide derivatives or acetonitrile has been used as a practical synthetic route toward 1-amidoalkyl-2-naphthols [19–28]. Several Lewis and Brønsted acidic catalysts have been used for this transformation, including $Ce(SO_4)_2$ [19], *p*-toluenesulfonic acid [20], iodine [21], cation-exchanged resins [22], $Fe(HSO_4)_3$ [23], sulfamic acid/ultrasound [24], silica-supported perchloric acid [25], $NaHSO_4{\cdot}H_2O$ [26], $K_5CoW_{12}O_{40}{\cdot}3H_2O$ [27], $H_3PW_{12}O_{40}$ [28], $FeCl_3{\cdot}SiO_2$ [29], and triflic acid [30]. However, many of the reported methods are associated with one or more of the following drawbacks: (i) low yield, (ii) long reaction time, (iii) harsh reaction conditions, (iv) the use of toxic, corrosive, expensive or non-reusable catalysts, (v) the use of large amount of catalyst, (vi) application of large amount of acetonitrile (as reactant and solvent), and (vii) because of the use of acidic catalysts in most of the reported methods, application of aldehydes bearing basic groups or acid-sensitive aldehydes in the reaction is not possible. In addition, there are only very few methods for the synthesis of 1-aminoalkyl-2-naphthols at room temperature or mild conditions [21,24]. The preparation of these compounds *via* the condensation of 2-naphthol, arylaldehydes and acetonitrile (Ritter type reaction) has been also scarcely studied [19,23,25,26,29,30]. Thus, search for finding an efficient, extremely mild and non-acidic catalyst for the synthesis of 1-aminoalkyl-2-naphthols by Ritter type reaction is still of practical importance.

The use of organic catalysts instead of inorganic Lewis and Brønsted acidic catalysts have some advantages including (i) the possibility to perform reactions for acid-sensitive substrates, (ii) performing reactions in milder reaction conditions, (iii) selectivity, and (iv) the substrates bearing basic functional groups or electron-donating substituents prone to capture the acidic catalyst do not affect reaction results [31–36]. While carbocations are Lewis acids, their inherent instability has precluded up to now their use in catalysis with decent turnover numbers. Nevertheless, recently, tri-

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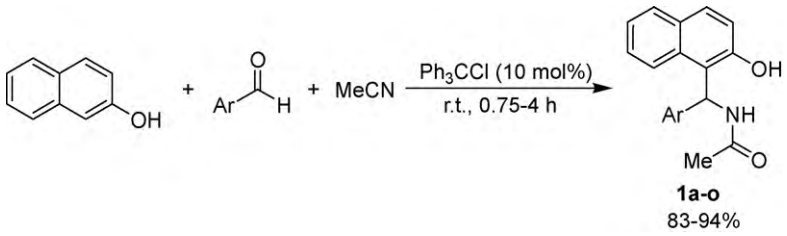


Scheme 1. The synthesis of 1-amidoalkyl-2-naphthols.

arylmethyl chlorides (Ar_3CCl) have been successfully employed as novel organic catalysts for the synthesis of bis(indolyl)methanes [31] and *N*-sulfonyl imines [32] in which triarylmethyl cation has acted as catalyst. Triarylmethyl chlorides are inexpensive and can be obtained commercially or easily prepared by the known procedure [37]. These compounds have been also extensively studied as bulky protective groups for amino and primary hydroxyl functional groups in multi-step organic synthesis [38]. Furthermore, triarylmethyl chlorides in combination with metal salts particularly $SnCl_2$ have been used in a few organic transformations [39]. Nevertheless, the use of these compounds in the absence of co-catalysts is really attractive.

Considering the above subjects, we wish to introduce trityl chloride as a highly efficient and homogeneous organic catalyst for the synthesis of 1-amidoalkyl-2-naphthol derivatives by the one-pot three-component condensation of 2-naphthol with aromatic aldehydes and acetonitrile under extremely mild conditions in neutral media (Scheme 1).

2. Results and discussion

First of all, to optimize the reaction conditions, the reaction of 2-naphthol (2 mmol), 4-chlorobenzaldehyde (2 mmol) and acetonitrile (2.5 mmol) was selected as a model reaction, and its behavior was studied in the presence of 10 mol% of trityl chloride (TrCl), monomethoxytrityl chloride ($Ph_2(p\text{-}MeOC_6H_4)CCl$, MMTCl) and dimethoxytrityl chloride ($Ph(p\text{-}MeOC_6H_4)_2CCl$) at room temperature. The results are summarized in Table 1. As it is shown in Table 1, higher yield and shorter reaction time were obtained using trityl chloride. Furthermore, we calculated turn over numbers (TON) and turn over frequencies (TOF) states on the effectiveness of these catalysts for the synthesis of 1-amidoalkyl-2-naphthols (Table 1). The TON and TOF values showed that TrCl is more effective than MMTCl and DMTCl. Thus, TrCl was chosen as catalyst for the synthesis of 1-amidoalkyl-2-naphthols.

In another study, the condensation of 2-naphthol, 4-chlorobenzaldehyde and acetonitrile was examined in the presence of different quantities of trityl chloride at room temperature (Table 2). As Table 2 indicates, the reasonable results were obtained when the reaction was performed using 10 mol% of trityl chloride (entry 3). No improvement in the reaction results was observed by increasing the amount of trityl chloride to 15 mol% (entries 4 and 5).

Table 2
The condensation of 2-naphthol, 4-chlorobenzaldehyde and acetonitrile using different amounts of TrCl at room temperature.

Entry	Catalyst Amount (mol%)	Time (h)	Yield[a] (%)
1	5	4	82
2	7.5	3	90
3	10	1.25	94
4	12.5	1.25	94
5	15	1.25	94

[a] Isolated yield.

To assess the efficiency and the scope of the organic catalyst in the preparation of 1-amidoalkyl-2-naphthols, the condensation of 2-naphthol with various arylaldehydes and acetonitrile was examined in the presence of TrCl at room temperatures. The corresponding results are displayed in Table 3. As it can be seen in Table 3, the reactions were carried out efficiently within 0.75–4 h, and the desired products were produced in high to excellent yields (83–94%). Thus, TrCl is a highly efficient, general and mild organic catalyst for the preparation of 1-amidoalkyl-2-naphthols. The influence of electron-releasing substituents, electron-withdrawing substituents and halogens on the aromatic ring of arylaldehydes on the reaction results was investigated. As Table 3 indicates, electron-releasing groups slightly decreased the yields and increased the reaction times (entries 2–7); however, electron-withdrawing substituents and halogens had no significant effect on the yields, and arylaldehydes bearing these substituents were reacted faster than benzaldehyde (entries 8–15). It should be mentioned that when the reaction was examined with 4-(dimethylamino)benzaldehyde, the corresponding 1-amidoalkyl-2-naphthol (**1g**) was obtained in 86% yield, indicating that the amine function cannot affect the efficiency of the reaction *via* irreversible complexation with the catalyst (entry 7).

Interestingly, the condensation of 2-naphthol with 4-(diethoxymethyl)benzaldehyde and acetonitrile was successfully performed using trityl chloride and afforded two products **2a** and **2b** (Scheme 2). When 1 equiv. of 2-naphthol and 1 equiv. of the adehyde were reacted with 1.25 equiv. of acetonitrile in the presence of TrCl (15 mol%), bis(1-amidoalkyl-2-naphthol) **2a** and 1-amidoalkyl-2-naphthol **2b** were obtained in 25 and 39%, respectively; however, the use of 2 equiv. of 2-naphthol, 1 equiv. of 4-(diethoxymethyl)benzaldehyde and 2.5 equiv. of acetonitrile gave compounds **2a** and **2b** in 76 and 18%, correspondingly. It is worth noting that almost in none of the reported methods

Table 1
Catalytic activity of different triarylmethyl chlorides on the reaction of 2-naphthol, 4-chlorobenzaldehyde and acetonitrile at room temperature.

Entry	Catalyst	Catalyst amount (mol%)	Time (h)	TON[a]	TOF[b] (h^{-1})	Yield[c] (%)
1	TrCl	10	1.25	9.4	7.52	94
2	MMTCl	10	3	8.5	2.83	85
3	DMTCl	10	5	5.7	1.14	57

[a] Turn over number.
[b] Turn over frequency.
[c] Isolated yield.

Table 3
The synthesis of 1-aminoalkyl-2-naphthols from 2-naphthol, aromatic aldehydes and acetonitrile using TrCl at room temperature.

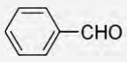
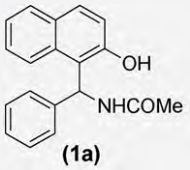
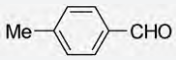
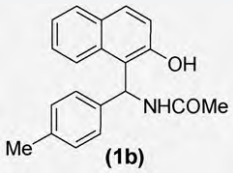
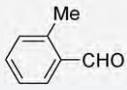
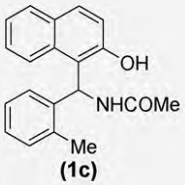
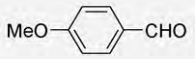
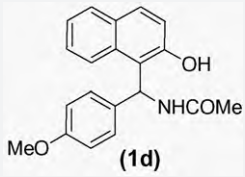
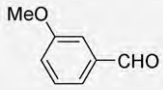
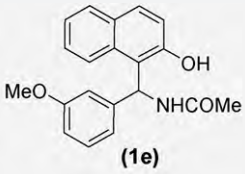
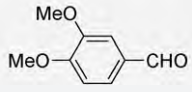
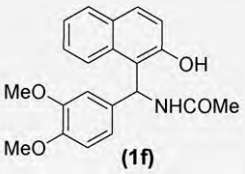
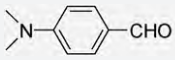
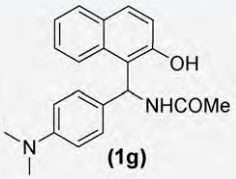
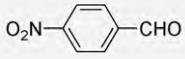
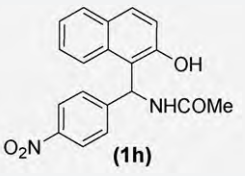
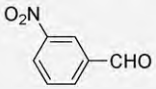
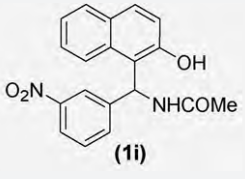
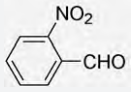
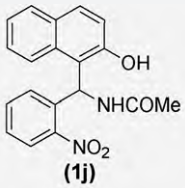
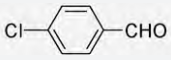
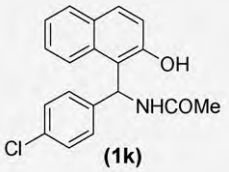
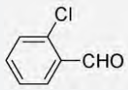
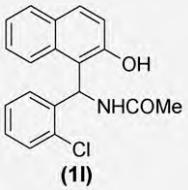
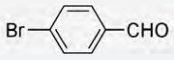
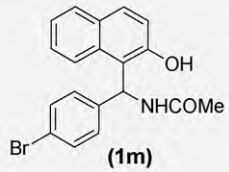
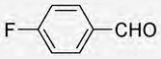
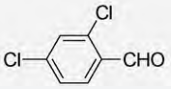
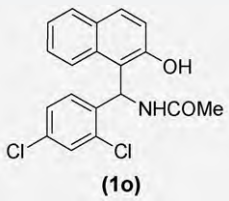
Entry	Aldehyde	Product	Time (h)	Yield[a] (%)	Mp (°C) (Lit.)
1		 (1a)	1.75	92	238–240 (241–243) [19]
2		 (1b)	2.5	89	220–222 (222–223) [23]
3		 (1c)	3	86	197–199 (200–202) [22]
4		 (1d)	3.25	87	183–185 (184–186) [23]
5		 (1e)	3.5	88	200–202 (203–205) [23]
6		 (1f)	4	83	232–234 (235–236) [23]
7		 (1g)	3	86	119–121 (123–125) [25]
8		 (1h)	1.75	93	246–248 (248–250) [28]
9		 (1i)	1.5	94	235–237 (236–237) [24]

Table 3 (*Continued*)

Entry	Aldehyde	Product	Time (h)	Yield[a] (%)	Mp (°C) (Lit.)
10		 **(1j)**	0.75	92	177–179 (180–182) [23]
11		 **(1k)**	1.25	94	220–222 (224–227) [19]
12		 **(1l)**	1.5	91	197–199 (194–196) [24]
13		 **(1m)**	1	90	226–228 (227–229) [23]
14		 **(1n)**	1.25	92	201–204 (203–205) [24]
15		 **(1o)**	1	93	196–198 (198–199) [23]

[a] Isolated yield.

for the preparation of 1-amidoalkyl-2-naphthol, the synthesis of bis(1-amidoalkyl-2-naphthol)s has not been studied.

The condensation of 2-naphthol with bis-aldehydes (terephthaldehyde) and acetonitrile was also rapidly performed using TrCl at room temperature (Scheme 3). The use of 1 equiv. of 2-naphthol, 1 equiv. of terephthalaldehyde and 1.25 equiv. of acetonitrile in the reaction afforded bis(1-amidoalkyl-2-naphthol) **2a** and monomer **2c** in 28 and 35%, respectively. However, the condensation of 2 equiv. of 2-naphthol with 1 equiv. of the aldehyde and 2.5 equiv. of acetonitrile gave compounds **2a** and **2c** in 84 and 15%, correspondingly.

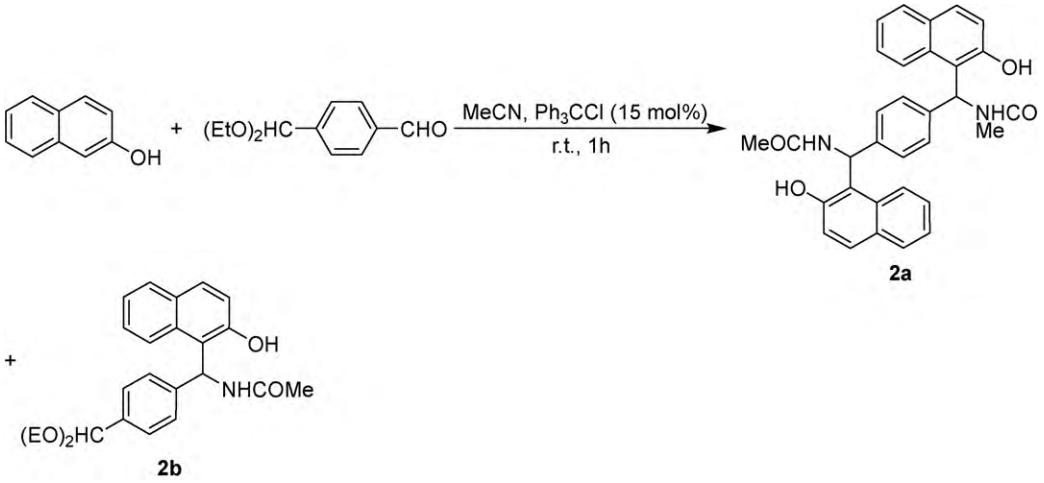
In a proposed reaction mechanism, we suggest that aldehyde and trityl chloride produce complexes of intermediates **I** and **II** in a reversible reaction (Scheme 4) [31,32]. To prove the formation of **I** and **II**, benzaldehyde was reacted with trityl chloride at room temperature, and then IR, ^{1}H and ^{13}C NMR spectra of the aldehydic functional group in the reaction mixture was compared with those in benzaldehyde as follows:

IR (nujol): ν_{max} (cm^{-1}) of C=O in benzaldehyde (1705) decreased to 1700 in the reaction mixture.

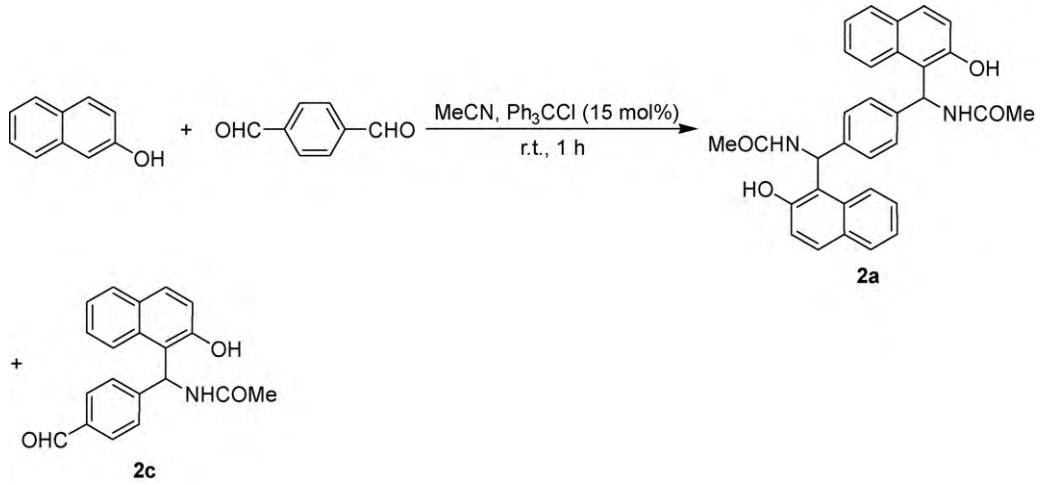
^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) of the aldehydic hydrogen (9.78) increased to 10.04 in the reaction mixture.

^{13}C NMR (300 MHz, $CDCl_3$): δ (ppm) of the carbonyl carbon (191.8) increased to 195.2 in the reaction mixture.

These results confirm that intermediates **I** and **II** are present in the reversible reaction media. Moreover, the cationic intermediates **I** and **II** have been introduced by Oikawa et al. for the first time [40]. These complexes act as activated carbonyl compound and then react with 2-naphthol providing **III**, which converts to **IV** by proton transfer. Afterward, **IV** reacts with acetonitrile to obtain **V** in a Ritter type reaction [19,26,29]. Hydrolysis of intermediate **V**, by very few absorbed water from environment, produces **VI**, and this intermediate together with previously produced Ph_3COH



Scheme 2. The condensation of 2-naphthol with 4-(diethoxymethyl)benzaldehyde and acetonitrile.



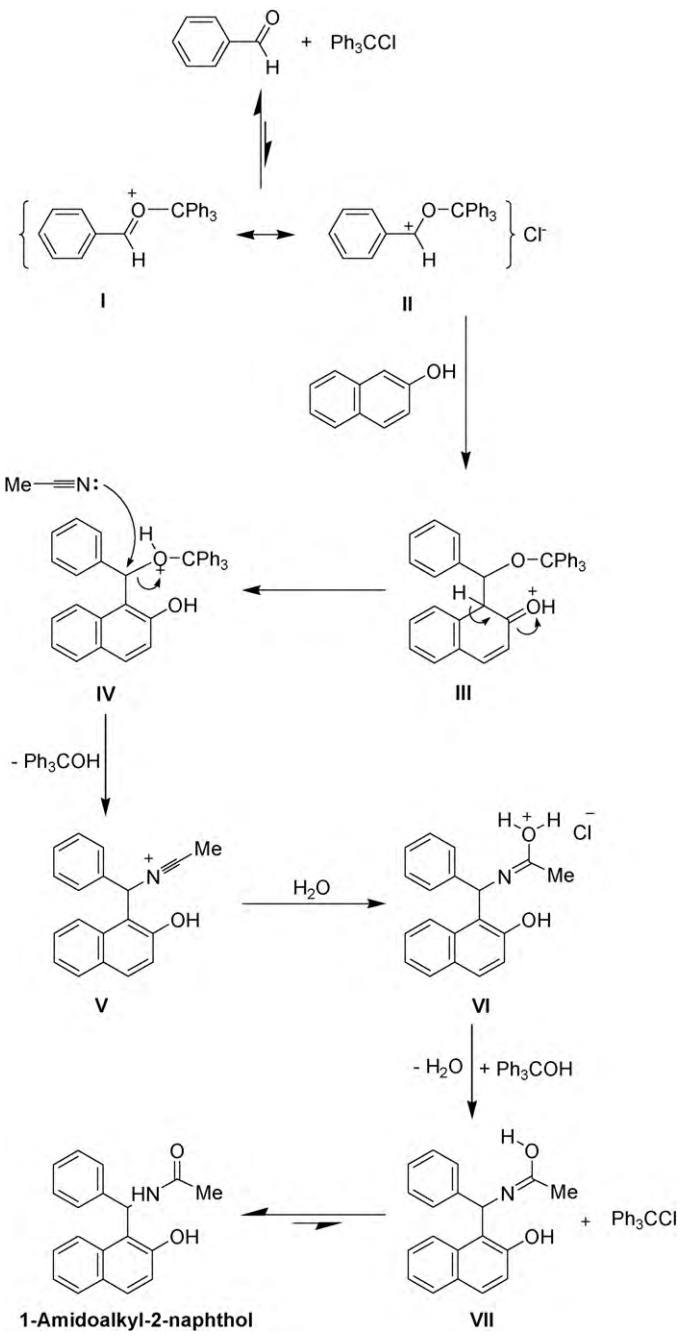
Scheme 3. The condensation of 2-naphthol with terephthaldehyde and acetonitrile.

afford **VII**, H_2O and TrCl. This *in situ* produced H_2O can convert **V** to **VI**; thus, there is no need to absorb H_2O from environment except the few amount absorbed for starting the conversion of **V** to **VI**. To verify this subject, the condensation of 2-naphthol with 4-chlorobenzaldehyde and acetonitrile was tested using TrCl in the presence of different amounts of water at room temperature. The results are summarized in Table 4. As Table 4 shows, increment the amount of water decreased the yield and enhanced the reaction time. This can be attributed to the hydrolysis of TrCl to TrOH in the presence of stoichiometric or larger amount of water. It should be mentioned that because of high reactivity of intermediate **V**, the gradually produced water in the reaction media absorb very fast by this intermediate and cannot hydrolyze TrCl. Therefore, the very few water in the reaction media absorbed from environment accompanied with the water produced gradually in the conversion of intermediate **VI** to **VII** is sufficient to hydrolyze **V** to **VI**, and there is no need to add water to the reaction mixture. Furthermore, in the papers cited in Refs. [19,23,25,26,29,30], the reaction has been performed without addition of water. Finally, intermediate **VII** converts to the corresponding 1-amidoalkyl-2-naphthol by tautomerization [19,26,29]. The suggested mechanism is confirmed based on Refs. [19,26,29,31,32,40], and also by the fact that the catalyst was completely recovered unchanged and triarylmethanol could not be identified after the completion of the reaction as it could be observed on TLC by comparison with pure authentic samples. In another study, to confirm that TrCl cannot convert to TrOH and HCl by very few water presented in the reaction medium from environment, and consequently HCl is not the real catalyst of the process, the reaction of 2-naphthol, 4-chlorobenzaldehyde and acetonitrile was examined in the presence of the expected amount of HCl. In these conditions, the product was obtained in 58% yield within 2.5 h, and two by-products were produced as monitored by TLC. Moreover, the reaction was tested using a base (pyridine) in which no progress in the reaction was observed. The reaction was also examined in the presence of TrCl together with pyridine wherein the reaction was carried out suc-

Table 4
The condensation of 2-naphthol (2 mmol) with 4-chlorobenzaldehyde (2 mmol) and acetonitrile (2.5 mmol) using TrCl (0.2 mmol) in the presence of different amounts of water.

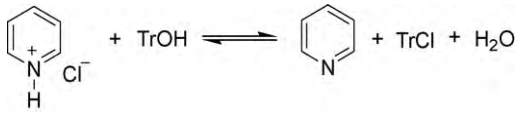
Entry	Water amount (mmol)	Time (h)	Yield[a] (%)
1	–	1.25	94
2	0.5	1.25	91
3	1	1.5	85
4	2	1.75	74
5	4	2	60
6	10	3	38
7	20	8	17

[a] Isolated yield.



Scheme 4. The proposed mechanism for the TrCl-catalyzed condensation of 2-naphthol with aldehydes and acetonitrile.

cessfully and the product was obtained in 94% within 1.25 h. In these conditions, pyridine firstly absorbs one H^+ from intermediate **VI** and produce pyridinium chloride. Afterward, pyridinium chloride with TrOH (produced in the conversion of intermediate **IV** to **V**) can form TrCl in a reversible reaction (Scheme 5) (to prove this, in a separate reaction, pyridinium chloride was reacted with TrOH at room temperature in which TrCl was obtained, and some



Scheme 5. The production of TrCl from pyridinium chloride and TrOH.

starting materials remained). Furthermore, the condensation of 2-naphthol, 4-chlorobenzaldehyde and acetonitrile was checked in the presence of only pyridinium chloride wherein the product was produced in 36% yield after 12 h. These experiments confirm that TrCl do not convert to TrOH and HCl in the reaction conditions; thus, HCl is not the catalyst of our reaction, and TrCl really has catalyzed the reaction.

To compare the applicability and the efficiency of trityl chloride with the reported catalysts for the synthesis of 1-amidoalkyl-2-naphthols *via* Ritter type reaction, we have tabulated turn over frequency (TOF) of these catalysts to perform the condensation of 2-naphthol, 4-chlorobenzaldehyde and acetonitrile, in Table 5. As it is shown in Table 5, trityl chloride is superior to the previously reported catalysts in term of TOF.

3. Experimental

All chemicals were purchased from Merck or Fluka Chemical Companies. The known products were identified by comparison of their melting points and spectral data with those reported in the literature. The ^{1}H NMR (250 or 300 MHz) and ^{13}C NMR (62.5 or 75 MHz) were run on a Bruker Avance DPX-250 FT-NMR spectrometer (δ in ppm). Microanalyses were performed on a Perkin-Elmer 240-B microanalyzer. Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes.

3.1. General procedure for the synthesis of 1-amidoalkyl-2-naphthols **1a–1o**

To a mixture of 2-naphthol (0.288 g, 2 mmol), aldehyde (2 mmol) and acetonitrile (0.103 g, 2.5 mmol) in a test tube, was added TrCl (0.056 g, 0.2 mmol), sealed with a stopper, and the resulting mixture was stirred at room temperature for the times reported in Table 3. Afterward, petroleum ether (20 mL) was added to the reaction mixture, refluxed and stirred for 3 min, and filtered (trityl chloride is soluble in petroleum ether; however, the products are insoluble in this solvent). The filtrate containing the catalyst was washed two times with 20 mL of 40% (w/v) solution of $NaHSO_3$ in H_2O/EtOH (4/1) to extract the unreacted aldehyde dissolved in the petroleum ether. The organic layer was separated and dried with $CaCl_2$; the solvent was evaporated to give pure recycled TrCl. The resulting precipitate from previous step (crude product) was introduced to a column chromatography on silica gel, and eluted with EtOAc/*n*-hexane (1/1) to give pure 1-amidoalkyl-2-naphthols.

3.2. General procedure for the preparation of bis(1-amidoalkyl-2-naphthol) **2a**, and 1-amidoalkyl-2-naphthols **2b** and **2c**

To a mixture of 2-naphthol (0.576 g, 4 mmol), terephthalaldehyde (0.268 g, 2 mmol) and acetonitrile (0.206 g, 5 mmol) in a in a test tube, was added TrCl (0.084 g, 0.3 mmol, 15 mol%), sealed with a stopper, and the resulting mixture was stirred at room temperature for 1 h. Afterward, petroleum ether (30 mL) was added to the reaction mixture, refluxed and stirred for 3 min, and filtered. The filtrate was washed two times with 30 mL of 40% (w/v) solution of $NaHSO_3$ in H_2O/EtOH (4/1). The organic layer was separated and dried with $CaCl_2$; the solvent was evaporated to give pure recycled TrCl. Afterward, warm aqueous ethanol (15%, 30 mL) was added to the resulting precipitate from previous step (crude products), and stirred for 3 min (1-amidoalkyl-2-naphthol **2b** is soluble in warm aqueous ethanol; however, bis(1-amidoalkyl-2-naphthol) **2a** is insoluble in this solvent). During this time, the crude 1-amidoalkyl-2-naphthol **2b** was dissolved in the aqueous ethanol, and the pure bis(1-amidoalkyl-2-naphthol) **2a** was remained; thus, two products were easily separated by filtration. Then, the solvent of the

Table 5
Comparison of the results of the reaction of 2-naphthol, 4-chlorobenzaldehyde and acetonitrile catalyzed by trityl chloride with those obtained by the reported catalysts.

Catalyst/conditions	Catalyst amount (mol%)	Time (h)	Yield (%)	TOF[a] (h^{-1})	Ref.
TrCl/MeCN, r.t.	10	1.25	94	7.52	–[b]
$Ce(SO_4)_2$/MeCN, reflux	100	24	74	0.03	[19]
$Fe(HSO_4)_3$/MeCN, reflux	5	20	63	0.63	[23]
$HClO_4/SiO_2$/MeCN, reflux	0.6	20	82	6.83	[25]
$NaHSO_4{\cdot}H_2O$/MeCN, reflux	33.3	20	79	0.11	[26]
$FeCl_3{\cdot}SiO_2$/MeCN, reflux	2.5	20	79	1.58	[29]

[a] Turn over frequency.
[b] Our work.

filtrate was evaporated and the crude 1-amidoalkyl-2-naphthol **2b** was purified by column chromatography on silica gel eluted with EtOAc/*n*-hexane (1/1).

3.3. Selected spectral data of the products

3.3.1. N-[(2-Hydroxynaphthalen-1-yl)(phenyl)methyl]acetamide (**1a**)

White solid; mp 238–240 °C (lit. [19] mp 241–243 °C); ^{1}H NMR (250 MHz, DMSO-d_6): δ (ppm) 2.06 (s, 3H), 7.01–7.20 (m, 9H), 7.65–7.73 (m, 3H), 8.11 (d, J = 7.7 Hz, 1H), 9.69 (s, 1H); ^{13}C NMR (62.5 MHz, DMSO-d_6): δ (ppm) 23.5, 41.3, 118.8, 120.2, 122.0, 123.9, 124.9, 125.7, 127.6, 128.1, 128.3, 128.5, 128.6, 134.2, 144.0, 152.6, 169.6; Anal. calcd. for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88; N, 4.81. Found: C, 78.52; H, 5.97; N, 4.93.

3.3.2. N-[(2-Hydroxynaphthalen-1-yl)(4-methylphenyl)methyl]acetamide (**1b**)

White solid; mp 220–222 °C (lit. [23] mp 222–223 °C); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 2.08 (s, 3H), 2.29 (s, 3H), 7.08–7.19 (m, 6H), 7.32–7.38 (m, 2H), 7.63 (d, J = 8.4 Hz, 1H), 7.81–7.88 (m, 2H), 8.41 (d, J = 8.0 Hz, 1H), 9.78 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 21.3, 24.7, 46.7, 117.1, 118.8, 121.9, 124.2, 125.6, 127.0, 128.6, 128.7, 129.2, 131.2, 136.1, 138.9, 145.0, 152.1, 169.3.

3.3.3. N-[(2-Hydroxynaphthalen-1-yl)(2-methylphenyl)methyl]acetamide (**1c**)

White solid; mp 197–199 °C (lit. [22] mp 200–202 °C); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 1.96 (s, 3H), 2.23 (s, 3H), 6.97–7.23 (m, 7H), 7.61–7.78 (m, 4H), 8.39 (d, J = 8.0 Hz, 1H), 9.83 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 20.8, 23.0, 44.1, 117.4, 118.6, 120.8, 123.5, 124.9, 126.3, 127.4, 128.1, 128.3, 128.7, 129.2, 130.8, 132.7, 135.2, 142.7, 152.7, 169.1.

3.3.4. N-[(2-Hydroxynaphthalen-1-yl)(4-methoxyphenyl)methyl]acetamide (**1d**)

Pale yellow solid; mp 183–185 °C (lit. [23] mp 184–186 °C); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 2.09 (s, 3H), 3.63 (s, 3H), 6.68 (d, J = 8.0 Hz, 2H), 6.74 (s, 1H), 7.40–7.50 (m, 3H), 7.59 (t, J = 7.3 Hz, 2H), 7.78–7.85 (m, 2H), 8.39 (d, J = 8.2 Hz, 2H), 9.48 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 22.4, 39.8, 55.0, 113.9, 117.6, 118.0, 122.8, 124.3, 126.8, 128.8, 128.9, 129.2, 131.1, 131.4, 137.4, 148.7, 157.9, 167.3.

3.3.5. N-[(2-Hydroxynaphthalen-1-yl)(3-methoxyphenyl)methyl]acetamide (**1e**)

White solid; mp 200–202 °C (lit. [23] mp 203–205 °C); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 2.05 (s, 3H), 3.60 (s, 3H), 6.71 (s, 1H), 6.97–7.36 (m, 7H), 7.70–7.78 (m, 2H), 8.02–8.11 (m, 2H), 9.81 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 23.2, 42.9, 56.2, 112.4, 114.1, 117.3, 118.2, 120.5, 122.6, 123.8, 127.0, 128.4, 128.6, 129.2, 131.2, 133.5, 142.3, 150.4, 159.8, 169.1.

3.3.6. N-[(2-Hydroxynaphthalen-1-yl)(3,4-dimethoxyphenyl)methyl]acetamide (**1f**)

Pale yellow solid; mp 232–234 °C (lit. [23] mp 235–236 °C); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 2.08 (s, 3H), 3.67 (s, 3H), 6.74 (s, 3H), 6.74–6.82 (m, 2H), 7.94–8.42 (m, 7H), 7.96–8.08 (m, 2H), 9.75 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 22.6, 43.2, 56.0, 56.5, 112.9, 116.8, 117.5, 119.8, 121.3, 122.8, 124.4, 126.7, 127.6, 127.8, 128.4, 131.7, 135.3, 149.7, 151.6, 152.4, 168.7.

3.3.7. N-[(2-Hydroxynaphthalen-1-yl)(4-dimethylaminophenyl)methyl]acetamide (**1g**)

Pale yellow solid; mp 119–121 °C (lit. [25] mp 123–125 °C); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 1.97 (s, 3H), 3.02 (s, 6H), 6.63 (s, 1H), 6.70 (d, J = 8.4 Hz, 2H), 6.95–7.08 (m, 4H), 7.45–7.62 (m, 3H), 8.06 (d, J = 8.0 Hz, 1H), 8.43 (d, J = 8.3 Hz, 1H), 9.74 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 23.2, 39.3, 42.9, 113.8, 117.4, 118.7, 121.6, 123.3, 126.9, 127.8, 128.1, 128.7, 130.0, 131.7, 133.8, 148.1, 152.3, 168.7.

3.3.8. N-[(2-Hydroxynaphthalen-1-yl)(4-nitroxyphenyl)methyl]acetamide (**1h**)

Yellow solid; mp 246–248 °C (lit. [28] mp 248–250 °C); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 2.06 (s, 3H), 7.14–7.35 (m, 4H), 7.59–7.67 (m, 2H), 7.76 (d, J = 9.2, 2H), 7.95–8.06 (m, 3H), 8.52 (d, J = 8.2 Hz, 1H), 9.86 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 23.1, 48.3, 118.2, 119.4, 121.3, 122.4, 123.1, 127.2, 128.4, 128.7, 129.8, 131.5, 133.6, 145.1, 149.3, 152.1, 168.9.

3.3.9. N-[(2-Hydroxynaphthalen-1-yl)(3-nitrophenyl)methyl]-acetamide (**1i**)

Pale yellow solid; mp 235–237 °C (lit. [24] mp 236–237 °C); ^{1}H NMR (250 MHz, DMSO-d_6): δ (ppm) 2.06 (s, 3H), 7.15–7.49 (m, 6H), 7.78–8.04 (m, 5H), 8.54 (d, J = 8.1 Hz, 1H), 10.12 (s, 1H); ^{13}C NMR (62.5 MHz, DMSO-d_6): δ (ppm) 23.3, 48.1, 118.1, 118.7, 120.5, 122.3, 123.8, 125.7, 127.3, 128.4, 129.1, 129.6, 130.8, 133.1, 134.1, 144.5, 148.7, 152.9, 169.8; Anal. calcd. for $C_{19}H_{16}N_2O_4$: C, 67.85; H, 4.79; N, 8.33. Found: C, 67.62; H, 4.68; N, 8.46.

3.3.10. N-[(2-Hydroxynaphthalen-1-yl)(2-nitrophenyl)methyl]-acetamide (**1j**)

Pale yellow solid; mp 177–179 °C (lit. [23] 180–182 °C); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 2.03 (s, 3H), 7.06–7.38 (m, 5H), 7.70–7.81 (m, 4H), 7.90 (d, J = 8.2 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 8.49 (d, J = 8.1 Hz, 1H), 9.75 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 22.8, 48.0, 117.1, 118.4, 121.3, 123.4, 124.5, 126.5, 127.3, 128.2, 128.5, 129.3, 132.2, 133.0, 133.9, 140.8, 148.6, 152.4, 169.2.

3.3.11. N-[(2-Hydroxynaphthalen-1-yl)(4-chlorophenyl)methyl]acetamide (**1k**)

Pale yellow solid; mp 220–222 °C (lit. [19] 224–227 °C); ^{1}H NMR (250 MHz, DMSO-d_6): δ (ppm) 2.07 (s, 3H), 7.06 (m, 2H), 7.14–7.24 (m, 5H), 7.68–7.77 (m, 3H), 7.98 (d, J = 7.4 Hz, 1H), 8.16 (d, J = 7.1 Hz, 1H), 9.90 (s, 1H); ^{13}C NMR (62.5 MHz, DMSO-d_6): δ (ppm) 23.2, 47.6, 118.8, 119.8, 122.1, 123.7, 125.8, 126.9, 127.4, 128.3, 128.6, 129.3,

129.9, 134.0, 143.4, 152.5, 169.8; Anal. calcd. for $C_{19}H_{16}ClNO_2$: C, 70.05; H, 4.95; N, 4.30. Found: C, 70.25; H, 4.87; N, 4.24.

*3.3.12. N-[(2-Hydroxynaphthalen-1-yl)(2-chlorophenyl)methyl]acetamide (**1l**)*

White solid; mp 197–199 °C (lit. [24] 194–196 °C); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 2.01 (s, 3H), 6.97–6.43 (m, 8H), 7.68–7.76 (m, 2H), 8.16–8.22 (m, 2H), 9.64 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 22.6, 47.3, 118.0, 118.2, 123.5, 124.5, 126.9, 127.8, 127.9, 128.6, 129.1, 129.6, 130.2, 130.9, 131.8, 131.9, 143.6, 148.9, 169.7.

*3.3.13. N-[(2-Hydroxynaphthalen-1-yl)(4-bromophenyl)methyl]acetamide (**1m**)*

White solid; mp 226–228 °C (lit. [23] 227–229 °C); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 1.98 (s, 3H), 6.98–7.34 (m, 8H), 7.61–7.67 (m, 2H), 7.86 (d, J = 10.1, 1H), 8.27 (d, J = 8.1 Hz, 1H), 9.74 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 23.7, 46.5, 117.8, 118.7, 121.2, 122.4, 123.8, 126.9, 128.4, 128.7, 129.3, 130.2, 131.0, 133.2, 139.8, 152.6, 168.4.

*3.3.14. N-[(2-Hydroxynaphthalen-1-yl)(4-fluorophenyl)methyl]acetamide (**1n**)*

White solid; mp 201–204 °C (lit. [24] 203–205 °C); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 2.05 (s, 3H), 7.11 (m, 2H), 7.18–7.35 (m, 5H), 7.65–7.78 (m, 4H), 8.46 (d, J = 7.9 Hz, 1H), 9.87 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 23.5, 47.1, 115.1, 117.9, 118.3, 121.4, 123.0, 126.1, 127.5, 128.0, 128.3, 128.9, 130.9, 137.1, 152.8, 160.1, 168.0.

*3.3.15. N-[(2-Hydroxynaphthalen-1-yl)(2,4-dichlorophenyl)methyl]acetamide (**1o**)*

White solid; mp 196–198 °C (lit. [23] 198–199 °C); ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 1.96 (s, 3H), 6.99–7.10 (m, 2H), 7.26–7.38 (m, 4H), 7.59 (d, J = 8.4 Hz, 1H), 7.73–7.79 (m, 2H), 7.95 (d, J = 8.5 Hz, 1H), 7.64 (d, J = 8.1 Hz, 1H), 9.87 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 23.1, 48.4, 117.3, 118.6, 122.8, 123.2, 127.6, 127.8, 129.4, 129.8, 130.2, 131.4, 132.5, 132.9, 133.4, 134.1, 140.7, 152.9, 168.7.

*3.3.16. N-[{4-[Acetylamino-(2-hydroxy-naphthalen-1-yl)-methyl]-phenyl}-(2-hydroxy-naphthalen-1-yl)-methyl]acetamide (**2a**)*

White solid; mp 277–279 °C; IR (KBr): 3402, 3192, 3059, 1644, 1583, 1478, 1275, 816 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 2.01 (s, 6H), 7.17–7.39 (m, 12H), 7.77–7.93 (m, 6H), 8.53 (d, J = 8.2 Hz, 2H), 10.09 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 23.1, 48.2, 118.9, 119.2, 122.8, 126.3, 126.8, 128.9, 129.0, 129.6, 132.7, 140.8, 140.9, 153.6, 169.7; MS: m/z = 504.5 (M^+); Anal. calcd. for $C_{32}H_{28}N_2O_4$: C, 76.17; H, 5.59; N, 5.55. Found: C, 76.43; H, 5.70; N, 5.47.

*3.3.17. N-[(4-Diethoxymethyl-phenyl)-(2-hydroxy-naphthalen-1-yl)-methyl]acetamide (**2b**)*

Pale yellow solid; mp 173–175 °C; IR (KBr): 3400, 3181, 3057, 1665, 1589, 1507, 1276, 812 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 1.17 (t, J = 6.9 Hz, 6H), 2.02 (s, 3H), 3.58 (q, J = 6.9 Hz, 4H), 6.96–7.46 (m, 9H), 7.73–7.85 (m, 3H), 8.26 (d, J = 8.5 Hz, 1H,), 10.22 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 19.1, 23.2, 48.5, 56.7, 111.8, 119.1, 119.6, 120.9, 122.7, 124.5, 126.2, 128.5, 129.1, 129.7, 132.9, 134.8, 139.7, 142.4, 153.3, 169.9; MS: m/z = 393.3 (M^+); Anal. calcd. for $C_{24}H_{27}NO_4$: C, 73.26; H, 6.92; N, 3.56. Found: C, 73.09; H, 7.01; N, 3.62.

*3.3.18. N-[(4-Formylphenyl)(2-hydroxynaphthalen-1-yl)methyl]acetamide (**2c**)*

Pale yellow solid; mp 237–240 °C; IR (KBr): 3390, 3207, 3057, 1700, 1628, 1607, 1278, 819 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 2.02 (s, 3H), 6.91–7.39 (m, 6H), 7.79–7.82 (m, 4H), 8.41 (d, J = 6.6 Hz, 1H), 8.56 (d, J = 7.6 Hz, 1H), 9.93 (s, 1 H), 10.10 (s, 1 H); ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 23.0, 48.4, 118.6, 118.8, 122.9, 123.5, 126.3, 127.1, 128.9, 129.1, 129.9, 130.1, 132.7, 134.9, 150.6, 153.7, 170.1, 193.1; MS: m/z = 319.2 (M^+).

4. Conclusions

In conclusion, we have introduced a highly efficient and homogenous organic catalyst for the one-pot three-component Ritter type reaction of 2-naphthol, various arylaldehydes and acetonitrile. The promising points for the presented methodology are efficiency, generality, high yield, short reaction time, extremely mild reaction conditions, cleaner reaction profile and simplicity which makes it a useful and attractive process for the synthesis of 1-amidoalkyl-2-naphthoils as biologically interesting compounds.

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References

[1] T. Dingermann, D. Steinhilber, G. Folkers, Molecular Biology in Medicinal Chemistry, Wiley-VCH, Weinheim, 2004.
[2] A.Y. Shen, C.T. Tsai, C.L. Chen, Eur. J. Med. Chem. 34 (1999) 877–882.
[3] A.Y. Shen, C.L. Chen, C.I. Lin, Chin. J. Physiol. 35 (1992) 45–54.
[4] M. Damodiran, N.P. Selvam, P.T. Perumal, Tetrahedron Lett. 50 (2009) 5474–5478.
[5] T. Haneishi, T. Okazaki, T. Hata, C. Tamura, M. Nomura, A. Naito, I. Seki, M. Arai, J. Antibiot. 24 (1971) 797–799.
[6] K. Sasaki, Y. Kusakabe, S. Esumi, J. Antibiot. 25 (1972) 151–154.
[7] Y. Kusakabe, J. Nagatsu, M. Shibuya, O. Kawaguchi, C. Hirose, S. Shirato, J. Antibiot. 25 (1972) 44–47.
[8] M.C. Wani, H.L. Taylor, M.E. Wall, J. Chem. Soc., Chem. Commun. (1973) 390.
[9] P.Y. Johnson, R.B. Silver, J. Heterocycl. Chem. 10 (1973) 1029–1030.
[10] S. Remillard, L.I. Rebhun, G.A. Howie, S.M. Kupchan, Science 189 (1975) 1002–1005.
[11] T. Urbański, D. Ghrne, I. Szczerek, M. Modaski, Polish Patent, 54 (1967) 007.
[12] G.Y. Lesher, A.R. Surrey, J. Am. Chem. Soc. 77 (1955) 636–641.
[13] H.S. Mosher, M.B. Frankel, M. Gregory, J. Am. Chem. Soc. 75 (1953) 5326–5328.
[14] J.L. Peglion, J. Vian, B. Gourment, N. Despaux, V. Audinot, M. Millan, Bioorg. Med. Chem. Lett. 7 (1997) 881–886.
[15] H. Ren, S. Grady, D. Gamenara, H. Heinzen, P. Moyna, S. Croft, H. Kendrick, V. Yardley, G. Moyna, Bioorg. Med. Chem. Lett. 11 (2001) 1851–1854.
[16] F. Benedini, G. Bertolini, R. Cereda, G. Doná, G. Gromo, S. Levi, J. Mizrahi, A. Sala, J. Med. Chem. 38 (1995) 130–136.
[17] R.D. Clark, J.M. Caroon, A.F. Kluge, D.B. Repke, A.P. Roszkowski, A.M. Strosberg, S. Baker, S.M. Bitter, M.D. Okada, J. Med. Chem. 26 (1983) 657–661.
[18] H. Matsuoka, N. Ohi, M. Mihara, H. Suzuki, K. Miyamoto, N. Maruyama, K. Tsuji, N. Kato, T. Akimoto, Y. Takeda, K. Yano, T. Kuroki, J. Med. Chem. 40 (1997) 105–111.
[19] N.P. Selvam, P.T. Perumal, Tetrahedron Lett. 47 (2006) 7481–7483.
[20] M.M. Khodaei, A.R. Khosropour, H. Moghanian, Synlett (2006) 916–920.
[21] B. Das, K. Laxminarayana, B. Ravikanth, B.R. Rao, J. Mol. Catal. A: Chem. 261 (2007) 180–183.
[22] S.B. Patil, P.R. Singh, M.P. Surpur, S.D. Samant, Synth. Commun. 37 (2007) 1659–1664.
[23] H.R. Shaterian, H. Yarahmadi, M. Ghashang, Bioorg. Med. Chem. Lett. 18 (2008) 788–792.
[24] S.B. Patil, P.R. Singh, M.P. Surpur, S.D. Samant, Ultrason. Sonochem. 14 (2007) 515–518.
[25] H.R. Shaterian, H. Yarahmadi, M. Ghashang, Tetrahedron 64 (2008) 1263–1269.
[26] H.R. Shaterian, H. Yarahmadi, ARKIVOC ii (2008) 105–114.
[27] L. Nagarapu, M. Baseeruddin, S. Apuri, S. Kantevari, Catal. Commun. 8 (2007) 1729–1734.
[28] A. Dorehgiraee, H. Khabazzade, K. Saidi, ARKIVOC vii (2009) 303–310.

[29] H.R. Shaterian, H. Yarahmadi, Tetrahedron Lett. 49 (2008) 1297–1300.
[30] B. Das, K. Laxminarayana, P. Thirupathi, B. Ramarao, Synlett (2007) 3103–3106.
[31] A. Khalafi-Nezhad, A. Parhami, A. Zare, A.R. Moosavi Zare, A. Hasaninejad, F. Panahi, Synthesis (2008) 617–621.
[32] A. Khalafi-Nezhad, A. Parhami, A. Zare, A. Nasrollahi Shirazi, A.R. Moosavi Zare, A. Hasaninejad, Can. J. Chem. 86 (2008) 456–461.
[33] A. Kumar, M. Kumar, M.K. Gupta, Tetrahedron Lett. 50 (2009) 7024–7027.
[34] J. Pandey, N. Anand, R.P. Tripathi, Tetrahedron 65 (2009) 9350–9356.
[35] S. Chandrasekhar, K. Johny, C.R. Reddy, Tetrahedron: Asymmetry 20 (2009) 1742–1745.
[36] M.G. Dekamin, S. Sagheb-Asl, M.R. Naimi-Jamal, Tetrahedron Lett. 50 (2009) 4063–4066.
[37] W.E. Bachmann, Org. Synth. Coll. 3 (1955) 841–845.
[38] T.W. Green, P.G.M. Wuts, Protective Group in Organic Synthesis, 3rd ed., John Wiley and Sons, New York, 1999.
[39] T. Mukaiyama, S. Kobayashi, J. Organomet. Chem. 382 (1990) 39–52.
[40] M. Oikawa, H. Yoshizaki, S. Kusumoto, Synlett (1998) 757–760.