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Thiamine hydrochloride as a efficient catalyst for the synthesis of amidoalkyl naphthols

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ABSTRACT

A simple, efficient, and practical procedure for the synthesis of amidoalkyl naphthols using thiamine hydrochloride (VB_1) as a novel catalyst is described in high yields. The salient features of the catalyst are efficiency, inexpensiveness, non-toxicity, and metal ion free.

Multicomponent reactions (MCRs) are special types of synthetically useful organic reactions in which three or more different starting materials react to give a final product in a one-pot procedure.[1] MCRs have drawn high efforts in recent years because they increase the efficiency by combining several operational steps without isolation of intermediates or changing the reaction conditions. MCRs are becoming powerful tools in the modern synthesis chemistry due to their efficiency, atom economy, and convenience in the construction of multiple new bonds in one-pot processes, which played powerful roles in approaching complex structures and promoting the 'green chemistry'.[2]

It is reported that amidoalkyl naphthols can convert to important biologically active aminoalkyl naphthol derivatives by an amide hydrolysis reaction.[3] Hence, our target compounds were amidoalkyl naphthols, which have been prepared by multicomponent condensation of aryl aldehydes, β-naphthol, and amide or urea in the presence of Lewis or Brøsted acid catalysts such as montmorillonite K-10 clay,[4] $Ce(SO_4)_2$,[5] iodine,[6] $Al(H_2PO_4)_3$,[3] $K_5CoW_{12}O_{40}{\cdot}3H_2O$,[7] *p*-TSA,[8] $HClO_4$–SiO_2,[9] sulfamic acid,[10] zirconyl(IV) chloride,[11] silica sulfuric acid,[12] and cation-exchanged resins.[13]

However, many of these reported methods suffer from one or more drawbacks such as long reaction times, low yields of products, the use of toxic organic solvents, the use of expensive metal salts as catalysts, and tedious work-up procedures.

In view of the conservation of the environment combining with economic aspects, literature demands the application of metal ion free, environmentally safe, and convenient reagents in the multicomponent reactions.[4] It is well known that thiamine hydrochloride (VB_1) is a cheap and non-toxic reagent. The structure of VB_1 contains a pyrimidine ring and a thiazole ring linked by a methylene bridge (Fig. 1). The use of VB_1 analogs as powerful catalysts for various organic transformations has been reported.[14]

In this Letter, we wish to report a facile, efficient, and practical method for the preparation of amidoalkyl naphthols in excellent yields using VB_1 as a catalyst (Scheme 1).

First, to investigate the feasibility of this synthetic methodology for amidoalkyl naphthol derivatives, the reaction was carried out simply by mixing β-naphthol **1a**, benzaldehyde **2a,** and benzamide **3a** in alcohol as solvents in the presence of 5 mol % VB_1. The mixture was stirred at 80 °C for 4 h and the corresponding product **4a** was obtained in 72% yield. Encouraged by this result, we have changed the amount of VB_1 from 0% to 20% and the results are summarized in Table 1.

As shown in Table 1, no reaction was observed when the mixture was heated to 80 °C for 4 h in the absence of VB_1 (Table 1, entry 1). Furthermore, we found that the yield of **4a** was improved as the amount of VB_1 increased from 0% to 10%, and the yield plateaued when the amount of VB_1 was further increased from 10% to 20%. Therefore, 10 mol % of VB_1 was considered to be most suitable. This study demonstrates that VB1 can be used as an efficient catalyst for the synthesis of amidoalkyl naphthol derivatives by multicomponent condensation of β-naphthol **1a**, benzaldehyde **2a,** and benzamide **3a**.

In order to study the generality of this procedure, a series of amidoalkyl naphthols were synthesized in the presence of 10 mol % VB_1 at 80 °C for 4 h (Table 2).[15]

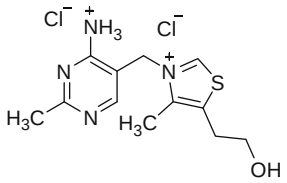

Figure 1.

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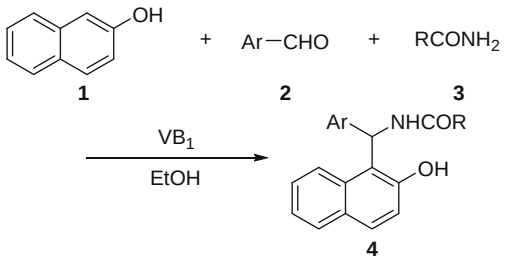


Scheme 1.

Table 1
Optimization of the amount of catalyst[a]

Entry	Catalyst (mol %)	Yield of **4a**[b] (%)
1	0	0
2	5	72
3	10	93
4	15	92
5	20	92

[a] Conditions: β-naphthol **1a** (5 mmol), benzaldehyde **2a** (5 mmol), benzamide **3a** (5.5 mmol), 80 °C.
[b] Isolated yields after recrystallization.

In all cases, aromatic aldehydes carrying either electron-donating or electron-withdrawing substituents reacted efficiently giving excellent yields. Furthermore, aliphatic and α,β-unsaturated aldehydes were also examined (Table 2, entries 5–7), but no target products were observed when the mixture were stirred under similar conditions.

To demonstrate the scope and limitations of the procedure, the condensation of β-naphthol **1**, aromatic aldehydes **2,** and different amides **3** including benzamide, acetamide, acrylamide, and N-substituted amides, such as *N*-methyl benzamide and caprolactam, were carried out in the presence of VB_1 in alcohol at 80 °C for 4 h. Different amides such as benzamide, acetamide, and acrylamide worked equally (Table 2). However, the condensation was unsuccessful with N-substituted amides. As shown in Table 2 entries 17 and 18, the reaction could not take place when using N-substituted amides.

Besides the amides, urea was employed under similar conditions to produce the corresponding products (Table 2, entries 15 and 16) in moderate yields. The yields of the products were somewhat lower when using urea (75–80%) as a substrate than using amides (88–93%).

We propose a mechanism of the VB_1-catalyzed condensation as shown in Scheme 2.[9,12] The condensation of β-naphthol **1**, aromatic aldehydes **2,** and amides or urea **3** may occur by a mechanism of

Table 2
Synthesis of amidoalkyl naphthol in the presence of 10 mol % VB_1[a]

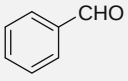
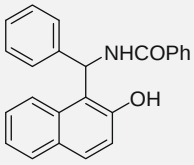
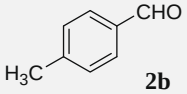
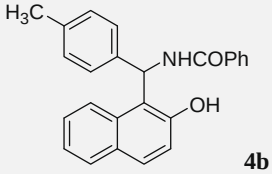
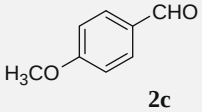
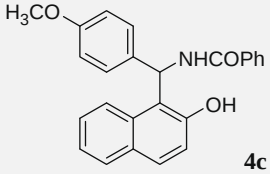
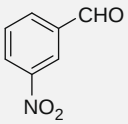
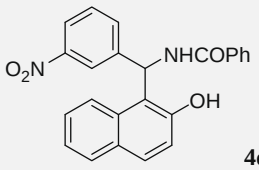
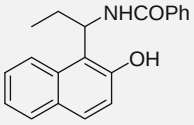
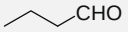
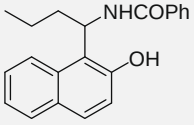
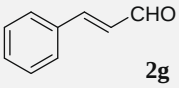
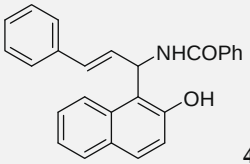
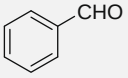
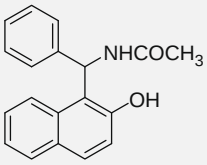
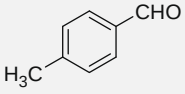
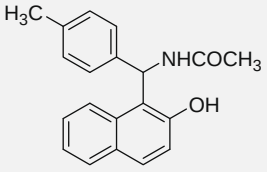
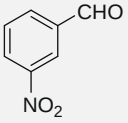
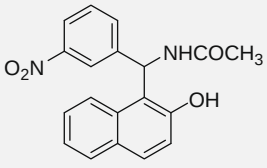
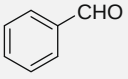
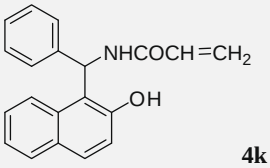
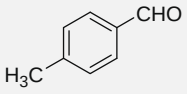
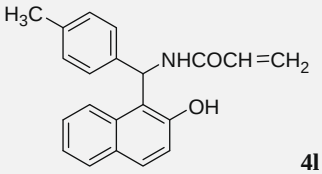
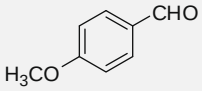
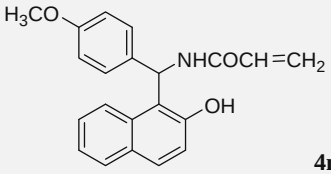
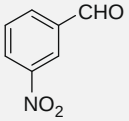
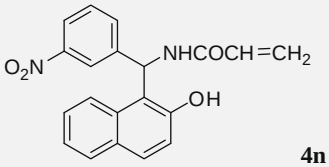
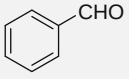
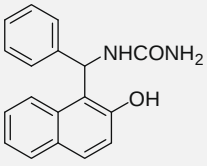
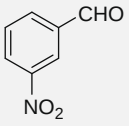
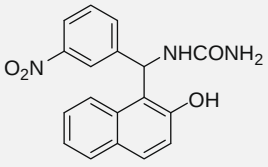
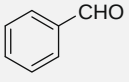
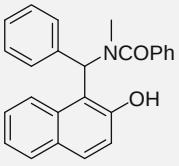
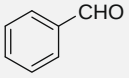
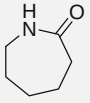
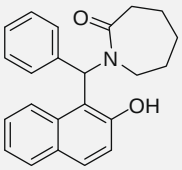
Entry	Aldehyde **2**	Amide or urea **3**	Product **4**	Yield of **4**[b] (%)
1	 **2a**	$PhCONH_2$ **3a**	 **4a**	93
2	 **2b**	$PhCONH_2$ **3a**	 **4b**	92
3	 **2c**	$PhCONH_2$ **3a**	 **4c**	90
4	 **2d**	$PhCONH_2$ **3a**	 **4d**	90

Table 2 (*continued*)

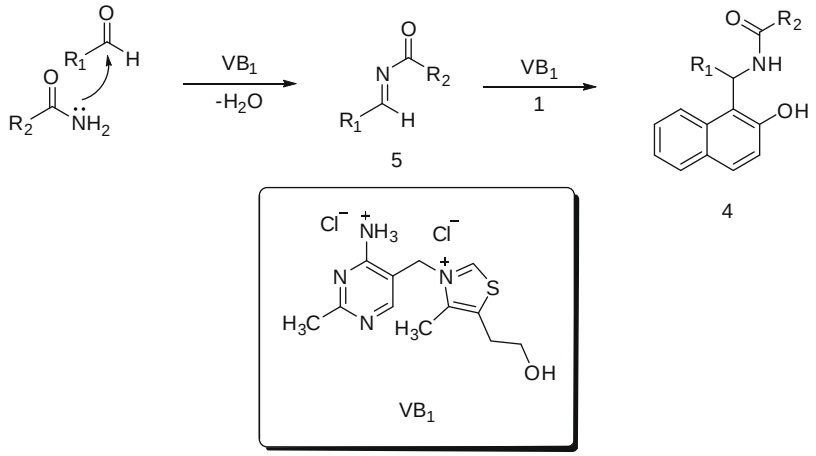
Entry	Aldehyde **2**	Amide or urea **3**	Product **4**	Yield of **4**[b] (%)
5	 **2e**	$PhCONH_2$ **3a**	 **4e**	NR[c]
6	 **2f**	$PhCONH_2$ **3a**	 **4f**	NR[c]
7	 **2g**	$PhCONH_2$ **3a**	 **4g**	NR[c]
8	 **2a**	CH_3CONH_2 **3b**	 **4h**	88
9	 **2b**	CH_3CONH_2 **3b**	 **4i**	90
10	 **2d**	CH_3CONH_2 **3b**	 **4j**	88
11	 **2a**	$CH_2{=}CHCONH_2$ **3c**	 **4k**	92

(*continued on next page*)

Table 2 (*continued*)

Entry	Aldehyde **2**	Amide or urea **3**	Product **4**	Yield of **4**[b] (%)
12	 **2b**	CH_2=CHCONH$_2$ **3c**	 **4l**	93
13	 **2c**	CH_2=CHCONH$_2$ **3c**	 **4m**	93
14	 **2d**	CH_2=CHCONH$_2$ **3c**	 **4n**	90
15	 **2a**	NH_2CONH_2 **3d**	 **4o**	80
16	 **2d**	NH_2CONH_2 **3d**	 **4p**	75
17	 **2a**	$PhCONHCH_3$ **3e**	 **4q**	NR[c]
18	 **2a**	 **3f**	 **4r**	NR[c]

[a] Conditions: β-naphthol **1a** (5 mmol), aldehyde **2** (5 mmol), amide or urea **3a** (5.5 mmol), 80 °C.
[b] Isolated yields after recrystallization.
[c] No reaction was observed.



Scheme 2.

addition, dehydration, and Michael addition. Initially, this reaction may proceed via intermediate **5**, formed by the reaction of aldehyde **2** and amide or urea by the action of proton of VB_1. Then Michael addition of β-naphthol on intermediate **5** leads to the formation of amidoalkyl naphthol **4** as a product in excellent yield.

In conclusion, the present method discloses a new and simple modification of the condensation of β-naphthol **1**, aromatic aldehydes **2,** and amides or urea **3** by using VB_1 as a catalyst in alcohol. Metal ion free is one of the salient features of this method. This VB_1-catalyzed one-pot synthesis of amidoalkyl naphthols is simple, high-yielding, and environmentally friendly, which make it a useful addition to the existing methods.

Acknowledgments

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15. General procedures for one-pot preparation of amidoalkyl naphthol derivatives **4** using VB_1 as a catalyst: A mixture of β-naphthol **1** (5 mmol), aromatic aldehyde **2** (5 mmol), amide **3** (5.5 mmol), and VB_1 (0.5 mmol) in alcohol (2 mL) was heated to 80 °C under stirring for 4 h. After cooling, the reaction mixture was poured into cold water and stirred for 5 min. The solid was filtered and recrystallized from EtOH–H_2O (1:1) to afford the pure product **4**. Selected ^{1}H NMR data for compounds:
Compound **4a**: ^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.34 (s, 1H), 9.03 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 8.6 Hz, 1H), 7.87 (d, J = 7.3 Hz, 2H), 7.84 (d, J = 8.2 Hz, 1H), 7.80 (d, J = 8.8 Hz, 1H), 7.55 (t, J = 7.3 Hz, 1H), 7.45–7.50 (m, 3H), 7.18–7.34 (m, 8H). *Compound* **4c**: ^{1} H NMR (500 MHz, $CDCl_3$): δ = 8.00 (br s, 1H), 7.89 (br s, 1H), 7.84 (d, J = 7.6 Hz, 2H), 7.79 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 8.8 Hz, 1H), 7.54 (t, J = 7.0 Hz, 1H), 7.36–7.42 (m, 4H), 7.31 (t, J = 7.5 Hz, 1H), 7.22 (d, J = 8.6 Hz, 2H), 7.18 (d, J = 8.8 Hz, 1H), 6.81 (d, J = 8.6 Hz, 2H), 3.76 (s, 3H). *Compound* **4m**: ^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.02 (s, 1H), 8.69 (d, J = 8.3 Hz, 1H), 7.86 (br s, 1H), 7.80 (d, J = 8.1 Hz, 1H), 7.76 (d, J = 8.8 Hz, 1H), 7.37 (t, J = 6.8 Hz, 1H), 7.26 (t, J = 7.4 Hz, 1H), 7.23 (d, J = 8.8 Hz, 1H), 7.14 (d, J = 8.3 Hz, 1H), 7.07 (d, J = 8.3 Hz, 2H), 6.82 (d, J = 8.4 Hz, 2H), 6.58 (dd, J_1 = 10.5 Hz, J_2 = 17.1 Hz, 1H), 6.11 (d, J = 17.1 Hz, 1H), 5.60 (d, J = 10.5 Hz, 1H), 3.68 (s, 3H).