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Zirconyl triflate as an efficient and reusable catalyst for one-pot synthesis of 1-amidoalkyl-2-naphthols under solvent-free conditions

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Abstract In the present work, the preparation of 1-amidoalkyl-2-naphthols via one-pot three-component condensation of amides, aldehydes, and β -naphthol in the presence of catalytic amounts of zirconyl triflate, as a highly efficient, low toxic, stable and non-hygroscopic catalyst under solvent-free conditions is reported. This low-cost procedure offers several other advantages such as short reaction times and good to excellent yields.

Keywords β -Naphthol \cdot Zirconyl triflate \cdot Solvent-free \cdot 1-Amidoalkyl-2-naphthol

Introduction

Multicomponent reactions (MCRs) are a powerful and useful synthetic tool to produce complex molecules from simple precursors by a one-pot procedure [1]. These reactions are performed without isolation of any intermediate which reduces the reaction times and saves both energy and raw materials [2]. Therefore, the design of novel MCRs has attracted a great deal of attention in the field of medicinal chemistry, drug discovery, and materials science [3]. Biginelli [4], Ugi [5], and Manich [6] reactions are some examples of MCRs.

1-Amidoalkyl-2-naphthol derivatives are of significant importance since they have been frequently applied as hypotensive and bradycardiac agents [7–9]. 1-Amidoalkyl-2-naphthols can be converted to 1,3-oxazine derivatives [10]. 1,3-Oxazines have potentially different biological

H. Hashemi · A. R. Sardarian (⊠) Department of Chemistry, College of Sciences, Shiraz University, Shiraz 75454, Iran e-mail: sardarian@susc.ac.ir activities including antibiotic [11–13], antitumor [14–16], analgesic [17, 18], anticonvulsant [19], antipsychotic [20], antimalarial [21], antianginal [22], antihypertensive [23], and antirheumatic properties [24]. 1-Amidoalkyl 2-naphthols can be prepared by multicomponent condensation of aldehydes, 2-naphthols, and amides in the presence of different Lewis or Brønsted acids such as p-TSA [25], ZrOCl₂ [26], FeCl₃·SiO₂ [27], montmorillonite K10 [28], I_2 [29], Ce(SO₄)₂ [30], Fe(HSO₄)₃ [31], Sr(OTf)₂ [32], ([TEBSA][HSO₄]) [33], thiamine hydrochloride [34], P₂O₅ [35], Yb(OTf)₃/[Bmim]BF₄ [36], Cu_{1.5}PMo₁₂O₄₀ [37], polymer-supported sulfonic acid [38], NaHSO₄·H₂O [39], K₅CoW₁₂O₄₀·3H₂O [40], sulfamic acid [41, 42], molybdophosphoric acid [43], cation-exchange resins [44], silica sulfuric acid [45], silica gel-supported polyphosphoric acid (PPA-SiO₂) [46], oxalic acid [47], and Al(HSO₄)₃ [48], dodecylphosphonic acid [49].

Zirconium (IV) salts have recently attracted much attention because of their low cost, high catalytic activity, easy availability, and low toxicity. A variety of Zr (IV) salts have been used for several organic transformations [50].

In 2008, the synthesis of the zirconyl triflate [ZrO(OTf) 2] as a super catalyst was explored [51] and applied in trimethylsilylation of alcohols and phenols with hexamethyldisilazane (HMDS) [51], acetylation and benzoylation of alcohols, phenols, amines and thiols with acetic and benzoic anhydrides [52], aminolysis of epoxides [53], acetalization of carbonyl compounds [54], preparation of benzoxanthenes [55], and ring opening of epoxides [56].

Here, we report a novel, convenient, mild and efficient method for one-pot synthesis of 1-amidoalkyl-2-naphthol derivatives from various aldehydes, amides and β -naphthol in the presence of zirconyl triflate under solvent-free conditions (Scheme 1).

Scheme 1 Preparation of 1-amidoalkyl-2-naphthol derivatives



 R^1 =aryl or alky R^2 = CH₃, Ph

Experimental

General

All chemicals were purchased from Merck or Fluka Chemical Companies. The known products were identified by comparison of their melting points, spectral data, and CHN analysis with those reported in the literature. NMR spectra were recorded on a Bruker Avance DPX-250 (¹H NMR 250 MHz and ¹³C NMR 63 MHz), spectrometer in DMSO- d_6 , using TMS as an internal standard. IR spectra were obtained using a Shimadzu FT-IR 8300 spectrophotometer. Mass spectra were determined on a Shimadzu GCMS-QP 1000 EX instruments at 70 or 20 eV and CHN data were measured on a Flash EA instrument. Melting points were determined in open capillary tubes in a Büchi-545 circulating oil melting point apparatus. ZrO(OTf)₂ was prepared according to the reported procedure [51].

General procedure for the preparation of 1-amidoalkyl-2- naphthols under solvent-free

Zirconyl triflate (5 mol %) was added to a mixture of β -naphthol (1 mmol), aldehyde (1 mmol), and amide (1.2 mmol). The mixture was stirred at 80 °C for the corresponding time and the reaction was followed by TLC. After completion of the reaction, the reaction mixture was washed with water (3 × 5 mL) and the residue was recrystallized from EtOH–H₂O to give pure product in 65–98 % yield.

Results and discussion

For optimization of the reaction parameters, the reaction of 2-naphthol (1 mmol) with benzaldehyde (1 mmol) and benzamide (1.2 mmol) was chosen, as model, in the presence of $ZrO(OTf)_2$ (5 mol %) under solvent-free conditions at room temperature. TLC monitoring showed no progress in the reaction even after 2 h. The model reaction was also carried out under solvent-free conditions at 60, 80, and 90 °C and the corresponding 1-amidoalkyl-2-naphthol was formed in 78, 98, and 98 % after 5, 2, and 2 min, respectively, in the presence of 5 mol % of $ZrO(OTf)_2$

(Table 1, entries 2–4). Running the same reaction using lesser amount of the catalyst, 2 mol %, led to lower yield, 80 %, and higher amount of the catalyst, 10 mol %, did not show pronounced effect on the efficiency of the reaction (Table 1, entries 10 and 11). Therefore, 5 mol % of $ZrO(OTf)_2$ was chosen as the most efficient amount of catalyst in the rest of study.

For studying the effect of solvent, the reaction was examined in petroleum ether, ethyl acetate, toluene, ethanol, and water under reflux conditions.

According to the results shown in Table 1 (Entries 5–9),we decided to examine generality and versatility of $ZrO(OTf)_2$ as a catalyst in the synthesis of 1-amidoalkyl-2-naphthols from various benzaldehydes, benzamide and 2-naphthol under solvent-free conditions at 85 °C. In these reactions, the corresponding 1-amidoalkyl-2-naphthols were produced in 65–98 % yields (Table 2, entries 1–12). As can be seen from Table 2, aromatic and aliphatic aldehydes were converted to the corresponding 1-amidoalkyl-2-naphthols in good to excellent yields. In the case of aromatic aldehydes, the nature of substituents (electron-donating and electron-withdrawing) has no significant effect on the yields and reaction times. Polyaromatic aldehydes, including phenanthrene-9-carbaldehyde and pyrene-1-carbaldehyde, were

Table 1 Optimization of reaction parameters for preparation of
1-amidoalkyl-2- naphthols using of ZrO(OTf) $_2$ as a catalyst

Entry	Catalyst (mol %)	Solvent	Temp. (°C)	Time (min)	Yield (%)
1	5	Solvent-free	R.T	120	_
2	5	Solvent-free	60	5	78
3	5	Solvent-free	80	2	98
4	5	Solvent-free	90	2	98
5	5	Petroleum ether	Reflux	60	50
6	5	Ethyl acetate	Reflux	60	50
7	5	Toluene	Reflux	60	70
8	5	EtOH	Reflux	60	20
9	5	H_2O	Reflux	60	20
10	2	Solvent-free	80	5	80
11	10	Solvent-free	80	5	98

Table 2 Synthesis of 1-amidoalkyl-2-naphthols in the presence of catalytic amounts of ZrO(OTf)2 under solvent-free conditions

Entry	Aldehyde	Amide	Product	Time (min)	Yield (%) ^a	M.p (°C) (Lit.)	Ref.
1	O ₂ N H	PhCONH ₂	O ₂ N NHCOPh OH	3	98	240–241 (239–241)	[42]
2	0 ₂ N H	PhCONH ₂	NO ₂ NHCOPh	3	98	239–241 (240–242)	[43]
3	H O	PhCONH ₂	NHCOPh OH	2	98	234–235 (235–237)	[20]
4	H ₃ CO	PhCONH ₂	H ₃ CO NHCOPh OH	5	85	196–198 (197–199)	[38]
5	H H O	PhCONH ₂	NHCOPh OH	2	95	210–211 (210)	[49]
6	H Br	PhCONH ₂	Br NHCOPh OH	1.5	90	229–231 (228–230)	[37]
7	H U U	PhCONH ₂	NHCOPh	3	65 ^b	157–159 (158)	[49]
8	H H	PhCONH ₂	NHCOPh	7	70 ^b	233–234 (234)	[49]
9	O H	PhCONH ₂	NHCOPh OH	10	85 ^b	251–253 (251)	[49]

Table 2 continued

Entry	Aldehyde	Amide	Product	Time (min)	Yield (%) ^a	M.p (°C) (Lit.)	Ref.
10	H C C C C	PhCONH ₂	NHCOPh OH	5	82 ^b	245–246 (246)	[49]
11		PhCONH ₂	OH	2	98	167–168 (166)	[49]
12	м Н	PhCONH ₂	NHCOPh	10	70	226–227 (226)	[49]
13	H O	CH ₃ CONH ₂	NHCOCH ₃	5	90	230–231 (228–230)	[24]
14	H H O	CH ₃ CONH ₂	NHCOCH ₃	7	72 ^b	173–175 (174–175)	[38]
15	ОН	CH ₃ CONH ₂	NHCOCH ₃	8	70 ^b	271–274 (273)	[49]
16	H O Br	CH ₃ CONH ₂	Br NHCOCH ₃ OH	8	85	203–205 (204)	[49]
17	H H	CH ₃ CONH ₂	NHCOCH ₃	5	87	110–111 (110)	[49]

^a Isolated yields

^b Isolated with column chromatography

also transformed to the desired products in good yields when treated with β -naphthol and benzamide in the presence of ZrO(OTf)₂ under solvent-free conditions in 5 min (Table 2, entries 9 and 10).

When acetamide was utilized instead of benzamide in the preparation of the title compounds, the similar results were observed although the corresponding products were formed in longer reaction times under solvent-free conditions (Table 2, entries 13–17).

The reaction of urea (1.2 mmol), in the place of benzamide, with β -naphthol (1 mmol) and benzaldehyde (1 mmol) in the presence of $ZrO(OTf)_2$ (5 mol %) under solvent-free condition did not proceed after 2 h and the starting material remained intact.

Entry	Catalyst (mol %)	Conditions	Time	Yield (%)	Ref.
1	<i>p</i> -TSA (10 %)	Solvent-free (125 °C)	6 h	89	[24]
2	Thiamine.HCl (10 %)	EtOH	4 h	88	[33]
3	ZrOCl ₂ (10 %)	ClCH ₂ CH ₂ Cl (R.T)	11 h	79	[25]
4	K ₅ CoW ₁₂ O ₄₀ .3H ₂ O (1 %)	Solvent-free (125 °C)	2 h	90	[39]
5	I ₂ (5 %)	Solvent-free (125 °C)	4.5 h	87	[28]
6	Fe (HSO ₄) ₂ (5 %)	Solvent-free (85 °C)	65 min	83	[30]
7	Dodecylphosphonic acid (10 mol %)	Solvent-free (90 °C)	20 min	88	[49]
8	ZrO(OTf) ₂ (5 %)	Solvent-free (80 °C)	2 min	98	Present work

Table 3 Comparison among of the efficiency of various acid catalysts used in the synthesis of N-[(2-hydroxynaphthalen-1-yl) (phenyl) methyl] benzamide with $ZrO(OTf)_2$

 $\label{eq:table_transform} \begin{array}{l} \mbox{Table 4} & \mbox{Reusability of } ZrO(OTf)_2 \mbox{ in solvent-free conditions for the synthesis of } N-[(2-hydroxynaphthalen-1-yl)(phenyl)methyl]benzamide \end{array}$

Entry	No. of recycles	Yield (%)
1	0	98
2	1	96
3	2	86
4	3	87
5	4	80

In order to show the effectiveness of the presented method in the preparation of 1-amidoalkyl-2-naphthols, we compared the obtained results in the reaction of benzaldehyde with 2-naphthol and benzamide catalyzed by $ZrO(OTf)_2$ with some of those reported in the literature (Table 3). The results showed that our method is superior in terms of catalyst amount, reaction time, and product yield. This superiority, especially when compared with $ZrOCl_2$, might be due to higher electron deficiency on zirconium atom because of replacement of chloride ions with OTf ions.

The reusability of a catalyst is important from economical and environmental points of view. Therefore, we decided to develop a work-up procedure for recovery and reuse of the catalyst. In this manner, the reaction of β -naphthol with benzaldehyde and benzamide was chosen as the model reaction. After completion of the reaction, water (5 mL) was added and crude product was obtained by filtration, then ZrO(OTf)₂ was recovered and regenerated by extraction with Et₂O (2 × 3 mL). The recovered catalyst was reused five consecutive times without significant loss of its activity (Table 4).

Conclusion

In summery, the present method discloses a new and simple modification of the condensation of various aldehydes, amides and β -naphthol using zirconyl triflate as a

low toxic and efficient catalyst under solvent-free conditions. This method offers several advantages such as high conversions, short reaction times, clean reaction profiles, simple experimental and work-up procedures. Finally, recovery and recyclability of $ZrO(OTf)_2$ is another advantage for this method.

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