

One-Pot Multi-Component Synthesis of Amidoalkyl Naphthols with Potassium Hydrogen Sulfate as Catalyst under Solvent-Free Condition

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Received on April 26, 2010

Accepted on Jan. 10, 2011

Abstract

One-pot multicomponent condensation of β -naphthol, aromatic aldehydes, acetamide or urea in the presence of potassium hydrogen sulfate was carried out under solvent-free condition to afford amidoalkyl naphthols in 83%~96% yields.

Keywords: Amidoalkyl naphthol; Multicomponent reaction; Potassium hydrogen sulfate.

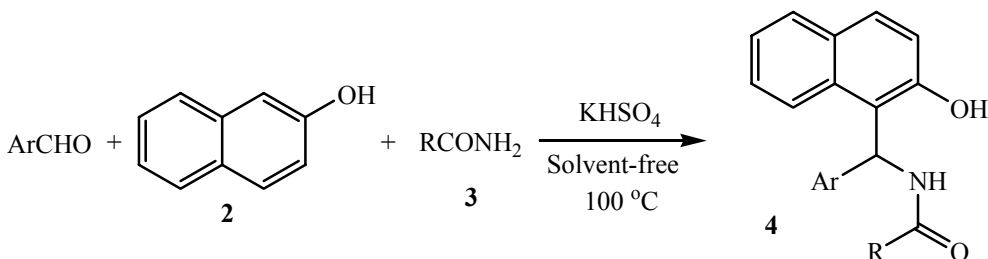
Introduction

The multicomponent reactions are responsible for this higher efficiency^[1], not only because of intrinsic aspects of the reaction such as superior atom economy^[2], atom utilization and selectivity, as well as lower level of by-products, but also because of extrinsic aspects of the processing reaction, such as simpler procedures and equipment^[3], lower costs, time, and energy, as well as more environmentally friendly criteria. It is noteworthy that 1-carbamato-alkyl-2-naphthols can be converted to important biologically active 1-aminomethyl-2-naphthol derivatives by carbamate hydrolysis. The hypotensive and bradycardiac effects of these compounds have been evaluated^[4].

Amidoalkyl naphthols can be prepared by multicomponent condensation of aldehydes, β -naphthols and acetonitrile or different amides in the presence of Lewis or Brønsted acids such as Iodine^[5], $\text{FeCl}_3 \cdot \text{SiO}_2$ ^[6], $\text{K}_5\text{CoW}_{12}\text{O}_{40} \cdot 3\text{H}_2\text{O}$ ^[7], $\text{HClO}_4\text{-SiO}_2$ ^[8], Brønsted acids ionic liquid^[9], P_2O_5 ^[10], cyanuric chloride^[11], montmorillonite K10^[12], sulfamic acid^[13], Thiamine hydrochloride^[14], $\text{Sr}(\text{OTf})_2$ ^[15], silica sulfuric acid^[16], $\text{Yb}(\text{OTf})_3$ ^[17], and $\text{Ce}(\text{SO}_4)_2$ ^[18]. However, some of the reported protocols suffer from certain drawbacks such as prolonged reaction time, use of carcinogenic solvent, unsatisfactory yield, high temperature (120~125 °C) and use of toxic, highly acidic, expensive catalysts and additional microwave or ultrasonic irradiation. Therefore, the discovery of clean procedures and the use of green and eco-friendly catalysts with high catalytic activity and short reaction times for the production of amidoalkyl naphthols have gained considerable attention.

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Potassium hydrogen sulfate is a cheap and efficient catalyst for the condensation reactions^[19]. In the present study, a simple and green procedure for the synthesis of amidoalkyl naphthols by the condensation of aldehydes with β -naphthol, acetamide or urea in the presence of potassium hydrogen sulfate (KHSO_4) at 100 °C under solvent-free conditions is reported herein (Scheme 1).



Scheme 1

Experimental

General procedure: To a solution of the particular aldehyde (1 mmol), β -naphthol (1 mmol), acetamide or urea (1.1 mmol), KHSO_4 (0.15 mmol) was added, then the reaction mixture was stirred at 100 °C and maintained for the appropriate time (Table 1). After completion of the reaction (monitored by TLC), the reaction mixture was diluted with water, and the resulting solid product was collected by filtration and was recrystallized from aqueous EtOH.

N-[(4-Fluorophenyl)(2-hydroxynaphthalen-1-yl)methyl]acetamide **4e**, ¹H NMR (400 MHz, CDCl_3 , δ ppm): 10.16 (s, 1H), 8.08 (d, $J = 8.2$ Hz, 1H), 7.88 (d, $J = 12.2$ Hz, 1H), 7.81–7.65 (m, 2H), 7.38–7.05 (m, 8H), 2.02 (s, 3H); ESI-MS, m/z : 308 (M–H, 100%); Anal. Calcd for $\text{C}_{19}\text{H}_{16}\text{FNO}_2$: C, 73.77; H, 5.21; N, 4.53; F, 6.14. Found: C, 73.72; H, 5.25; N, 4.52; F, 6.14.

[(Furan-2-yl)(2-hydroxynaphthalen-1-yl)methyl]urea **4q**: ¹H NMR (400 MHz, CDCl_3 , δ ppm): 10.20 (s, 1H), 7.67–7.08 (m, 7H), 6.73 (s, 2H), 6.35 (br. s, 1H), 6.22 (m, 1H), 6.09 (m, 1H), 5.73 (br. s, 1H). ESI-MS, m/z : 281 (M–H, 100%). Found (%): C, 67.89; H, 5.06; N, 9.85. Calc. for $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}_3$ (%): C, 67.92; H, 5.02; N, 9.89.

Result and Discussion

Benzaldehyde was selected as a representative aldehyde along with β -naphthol, acetamide and KHSO_4 which were reacted under solvent-free conditions at 100 °C in order to optimize the reaction conditions. The condensation of mixture of benzaldehyde **1a** (1 mmol) with β -naphthol **2** (1 mmol) and acetamide **3** (1.1 mmol) in the presence of KHSO_4 (0.15 mmol) was carried out at 100 °C for 1.0 h under solvent free conditions. The reaction proceeded smoothly and gave the corresponding amidoalkyl naphthol **4a** as the sole product in 90% isolated yield (Table 1). Water was added to the reaction mixture and simply filtering the mixture to obtain the crude product, which was purified by crystallization from 30% aqueous ethanol as white solid.

Table 1 Synthesis of Amidoalkyl Naphthols with Potassium Hydrogen Sulfate as Catalyst under solvent-free condition

Product ^a	Ar	R	Time (h)	Yield ^b (%)	Mp (°C)	
					Found	Reported
4a	C ₆ H ₅	CH ₃	1.0	90	232-233	229-230 ^[13]
4b	4-MeC ₆ H ₅	CH ₃	1.0	91	223-224	224-225 ^[10]
4c	4-ClC ₆ H ₅	CH ₃	0.5	95	233-234	237-238 ^[10]
4d	4-MeOC ₆ H ₅	CH ₃	1.0	94	172-174	163-164 ^[10]
4e	4-FC ₆ H ₅	CH ₃	0.5	95	205-207	203-205 ^[13]
4f	4-NO ₂ C ₆ H ₅	CH ₃	0.5	96	239-240	237-238 ^[10]
4g	3-NO ₂ C ₆ H ₅	CH ₃	0.5	93	238-240	236-247 ^[13]
4h	4-BrC ₆ H ₅	CH ₃	0.5	92	230-231	229-231 ^[9]
4i	2-ClC ₆ H ₅	CH ₃	0.5	93	194-195	194-196 ^[13]
4j	3-MeOC ₆ H ₅	CH ₃	1.0	88	192-194	202-204 ^[11]
4k	2-Furyl	CH ₃	1.5	83	218-220	220 dec ^[13]
4l	C ₆ H ₅	NH ₂	1.0	90	173-174	172-174 ^[13]
4m	4-ClC ₆ H ₅	NH ₂	0.5	94	170-171	168-169 ^[13]
4n	4-NO ₂ C ₆ H ₅	NH ₂	0.5	96	181-183	--
4o	3-NO ₂ C ₆ H ₅	NH ₂	1.0	95	186-188	184-186 ^[13]
4p	4-BrC ₆ H ₅	NH ₂	1.0	92	173-175	170-172 ^[13]
4q	2-Furyl	NH ₂	1.5	85	162-163	--

^a All known compounds were characterized by comparing their spectral data with those reported

^b Isolated yields.

In order to demonstrate the generality of the process, some examples illustrating the present method for the synthesis of amidoalkyl naphthols **4** was studied (Table 1). The reaction of β -naphthol **2** with various aromatic aldehydes bearing electron withdrawing groups (such as nitro, halo), electron releasing groups (such as, methyl or methoxy groups) and acetamide was carried out in the presence of KHSO₄ as a catalyst. In all cases, clean and complete conversion leading to the corresponding amidoalkyl naphthols (**4a~4k**) as observed in shorter reaction times (0.5~1.5 h). Aromatic aldehydes with electron-withdrawing groups reacted faster than aromatic aldehydes with electron-donating groups, as would be expected. Similar results were obtained under the same conditions when urea was used in place of acetamide to give the respective compounds (**4l~4q**).

Conclusion

In conclusion, a novel and highly efficient methodology for the synthesis of amidoalkyl naphthols by condensation reaction of aldehydes, β -naphthol and acetamide or urea in the presence of catalytic amounts of KHSO₄ under solvent-free conditions is reported. This method offers significant advantages such as, high conversions, easy handling and shorter reaction times, which collectively makes it a useful and attractive process for the rapid synthesis of substituted amidoalkyl naphthols.

Acknowledgement

We thank the National Natural Science Foundation of China (20962006) and the Science Foundation of the Guizhou Province Education Department (20090021) for financial support.

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