

Synthesis of Amidoalkyl Naphthols from Reaction of β -Naphthol, Acetamide and Aromatic Aldehydes in the Presence of Potassium Hydrogen Sulfate

Hassan Abd Alla Almahy

Department of Chemistry, Faculty of Science, Taif University, Alkhorma, Kingdom of Saudi Arabia

Abstract: The multicomponent condensation reaction of β -naphthol, aromatic aldehydes and acetamide in the presence of potassium hydrogen sulfate was carried out under solvent-free condition to afford amidoalkyl naphthols in 83-96% yields.

Key words: Amidoalkyl naphthol, acetamide, benzaldehyde, Potassium hydrogen sulfate, Saudi Arabia

INTRODUCTION

The multicomponent reactions are responsible for this higher efficiency (Bienayme *et al.*, 2000) not only because of intrinsic aspects of the reaction such as superior atom economy (Trost, 1991), 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 (Trost, 2002; Mitchell *et al.*, 2001), 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 (Trost, 2002).

Amidoalkyl naphthols can be prepared by multicomponent condensation of aldehydes, β -naphthols and acetonitrile or different amides in the presence of Lewis or Brosted acids such as iodine (Jahnisch *et al.*, 2004), $\text{FeCl}_3 \cdot \text{SiO}_2 \cdot \text{s}$, $\text{K}_5\text{CoW}_{12}\text{O}_{40} \cdot 3\text{H}_2\text{O}$ (Das *et al.*, 2007), $\text{HClO}_4\text{-SiO}_2$ (Das *et al.*, 2007), Brosted acids ionic liquid (Shaterian and Yarahmadi, 2008; Nagarapu *et al.*, 2007), P_2O_5 (Mahdavinia *et al.*, 2008), cyanuric chloride (Polshettiwar and Varma, 2009; Nandi *et al.*, 2009), montmorillonite K10 (Polshettiwar and Varma, 2009), sulfamic acid (Nandi *et al.*, 2009), Thiamine hydrochloride (Mahdavinia and Bigdeli, 2009; Kantevari *et al.*, 2007; Patil *et al.*, 2007), $\text{Sr}(\text{OTf})_2$ (Kantevari *et al.*, 2007), silica sulfuric acid (Patil *et al.*, 2007). Yb (Otf)₃ (Lei *et al.*, 2009) and Ce (SO₄)₂ (Srihari *et al.*, 2007; Kumar *et al.*, 2009; Nagwade and Shinde, 2007). 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, nexpensive catalysts and additional microwave or ultrasonic irradiation. Therefore,

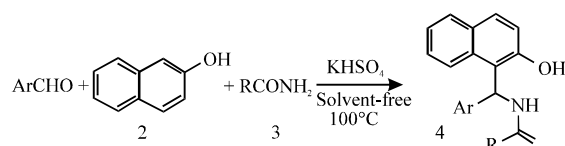


Fig. 1: A simple green procedure

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. Potassium hydrogen sulfate is a cheap and efficient catalyst for the condensation reactions (Selvam and Perumal, 2006; Huang *et al.*, 2005). 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 (KHSO₄) at 100°C under solvent-free conditions is shown in Fig. 1.

MATERIALS AND METHODS

General procedure: To a solution of the particular aldehyde (1 mmol), β -naphthol (1 mmol), acetamide (1.1 mmol), potassium hydrogen sulfate (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 thin layer chromatography), the reaction mixture was diluted with water and the resulting solid product was collected by filtration and was recrystallized from aqueous ethanol.

N-[(4-Fluorophenyl) (2-hydroxynaphthalen-1-yl) methyl] acetamide 4e, ¹H-NMR (400 MHz, CDCl₃, δ ppm): 10.16 (s, 1 H), 8.08 (d, J = 8.2 Hz, 1 H), 7.88 (d, J = 12.2 Hz, 1 H), 7.65-7.81 (m, 2 H), 7.05-7.38 (m, 8 H), 2.02 (s, 3 H); ESI-MS, m/z: 308 (M-H, 100%); Anal. Calcd for

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	Mp (°C) 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	-

^aAll known compounds were characterized by comparing their spectral data with those reported; ^bIsolated yields

C₁₉H₁₆FNO₂: 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, CDCl₃, δ ppm): 10.20 (s, 1 H), 7.08-7.67 (m, 7 H), 6.73 (s, 2 H), 6.35 (br. s, 1 H), 6.22 (m, 1 H), 6.09 (m, 1 H), 5.73 (br. s, 1 H). ESI-MS, m/z: 281 (M-H, 100%). Found (%): C, 67.89; H, 5.06; N, 9.85. Calc. for C₁₆H₁₄N₂O₃ (%): C, 67.92; H, 5.02; N, 9.89.

RESULTS AND DISCUSSION

Benzaldehyde was selected as a representative aldehyde along with β-naphthol, acetamide and potassium hydrogen sulfate 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 potassium hydrogen sulfate (0.15 mmol) was carried out at 100°C for 1 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.

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 potassium hydrogen sulfate 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 this study, 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 potassium hydrogen sulfate 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.

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