

One-pot Multi-component Synthesis of Amidoalkyl Naphthols with Potassium Hydrogen Sulfate as Catalyst under Solvent-free Condition

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Abstract

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

Keywords: Amidoalkyl naphthol, Multicomponent reaction, Potassium hydrogen sulfate

1. Introduction

The multicomponent reactions are responsible for this higher efficiency (Bienaymè, H. C. et. al 2000), not only because of intrinsic aspects of the reaction such as superior atom economy (Trost, B. M., 1991, Trost, B. M. 1995, Trost, B. M. 2002), 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 (Mitchell, M. C. et. al 2001, Jähnisch, K. et. al 2004), 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 (Szatmári, I.; et. al 2004, Shen, A. Y. et. al 1999, Shaterian, H. R. et. al 2008).

Amidoalkyl naphthols can be prepared by multicomponent condensation of aldehydes, β -naphthols and acetonitrile or different amides in the presence of Lewis or Brösted acids such as Iodine (Das, B. et al 2007, Nagawade R. R. et. al 2007), $\text{FeCl}_3 \cdot \text{SiO}_2$ (Shaterian, H. R. et. al 2008), $\text{K}_5\text{CoW}_{12}\text{O}_{40} \cdot 3\text{H}_2\text{O}$ (Nagarapu, L. et. al 2007), $\text{HClO}_4\text{-SiO}_2$ (Mahdavinia, G. H. et. al 2008), Brösted acidic ionic liquid (Hajipour, A. R. et. al 2009), P_2O_5 (Nandi, G. C. et. al 2009), cyanuric chloride (Mahdavinia, G. H. et. al 2009), montmorillonite K10 (Kantevari, S. et. al 2007), sulfamic acid (Patil, S. B. et. al 2007), thiamine hydrochloride (Min L. et. al 2009), $\text{Sr}(\text{OTf})_2$ (Su, W. K. et. al 2008), silica sulfuric acid (Srihari, G. et. al 2007), $\text{Yb}(\text{OTf})_3$ (Kumar, A. et. al 2009), $\text{Ce}(\text{SO}_4)_2$ (Selvam, N. P. et. al 2006), etc. However, some of the reported protocols suffer from certain drawbacks such as prolonged reaction time, use of dichloromethane like 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.

Potassium hydrogen sulfate is a cheap and efficient catalyst for the condensation reactions (Huang, Z. Y. et. al 2005, Shi, F. et. al 2007, Tu, S. J. et. al 2004, CaiP, X. –H. et. al 2006). 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) under solvent-free conditions at 100 °C has been reported (Figure 1).

Benzaldehyde was selected as a representative aldehyde along with of β -naphthol, acetamide and KHSO_4 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 and gave the crude product, which was purified by crystallization from 30% ethanol to obtain **4a** 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, halide), electron releasing groups (such as, methyl or methoxy groups) and acetamide was carried out in the presence of KHSO_4 as a catalyst. In all cases, clean and the complete conversion leading to the corresponding amidoalkyl naphthols 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.

2. Experimental

General procedure: KHSO_4 (0.15 mmol) was added into a mixture of aldehyde (1 mmol), β -naphthol (1 mmol) and acetamide or urea (1.1 mmol), then the reaction mixture was heated to 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, which was purified by recrystallization from EtOH/ H_2O .

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); ES-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). ES-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.

3. 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 KHSO_4 under solvent-free conditions is reported. This method offers significant advantages, such as, high conversions, easy handling and shorter reaction times, which makes it a useful and attractive process for the rapid synthesis of substituted amidoalkyl naphthols.

References

- Bienaymè, H. C., Hulme, G., Odon, P. (2000). Schmitt. Maximizing synthetic efficiency: multi- component transformations lead the way, *Chem. Eur. J.*, 6: 3321-3329.
- CaiP, X. –H., Xie, B., PGuoP, H. (2006). Synthesis of α,α' -bis(*R*-benzylidene) cycloalkanones catalyzed by potassium hydrogen sulfate under solvent-free conditions. *Chem. Pap.*, 60: 318-320.
- Das, B., Laxminarayana, K., Ravikanth, B., Rao, R. (2007). Iodine catalyzed preparation of amidoalkyl naphthols in solution and under solvent-free conditions. *J. Mol. Catal. A: Chem.*, 261: 180-183.
- Hajipour, A. R., Ghayeb, Y., Sheikhan, N., Ruoho, A. E. (2009). Brønsted acidic ionic liquid as an efficient and reusable catalyst for one-pot synthesis of 1-amidoalkyl 2-naphthols under solvent-free conditions. *Tetrahedron Lett.*, 50: 5649-5651.
- Huang, Z. Y., Zhang, M., Wang, Y., Qin, Y. (2005). KHSO_4 -mediated condensation reactions of tert-butanefulfonamide with aldehydes. preparation of tert-butanefulfinyl aldimines, *Synlett*, 1334-1336.
- Jähnisch, K., Hessel, V., Löwe, H. (2004). Baerns, M. Chemie in mikrostrukturreaktoren. *Angew. Chem.*, 116:

410-451.

Kantevari, S., Vuppapapati, S. V. N., Nagarapu, L. (2007). Montmorillonite K10 catalyzed efficient synthesis of amidoalkyl naphthols under solvent free conditions. *Catal. Commun.*, 8: 1857-1862.

Kumar, A., Rao, M. S., Ahmad, I., Khungar, B. (2009). A simple and facile synthesis of amidoalkyl naphthols catalyzed by Yb(OTf)₃ in ionic liquids. *Can. J. Chem.*, 87: 714-719.

Lei, M., Ma, L., Hu, L. H. (2009). Thiamine hydrochloride as a efficient catalyst for the synthesis of amidoalkyl naphthols. *Tetrahedron Lett.*, 50: 6393-6397.

Mahdavinia, G. H., Bigdeli, M. A. (2009). Wet cyanuric chloride promoted efficient synthesis of amidoalkyl naphthols under solvent-free conditions. *Chin. Chem. Lett.*, 20: 383-386.

Mahdavinia, G. H., Bigdeli, M. A., Heravi, M. M. (2008). Silica supported perchloric acid (HClO₄-SiO₂): A mild, reusable and highly efficient heterogeneous catalyst for the synthesis of amidoalkyl naphthols. *Chin. Chem. Lett.*, 19: 1171-1174.

Mitchell, M. C., Spikmans, V., Manz, A., de Mello, A. (2001). Microchip-based synthesis and total analysis systems (μSYNTAS): chemical microprocessing for generation and analysis of compound libraries. *J. Chem. Soc. Perkin Trans., 1*: 514-518.

Nagarapu, L., Baseeruddin, M., Apuri, S., Kantevari, S. (2007). Potassium dodecatungstocobaltate trihydrate (K₅CoW₁₂O₄₀ · 3H₂O): A mild and efficient reusable catalyst for the synthesis of amidoalkyl naphthols in solution and under solvent-free conditions. *Catal. Commun.*, 8: 1729-1734.

Nagawade R. R. and Shinde. D. B. (2007). Synthesis of amidoalkyl naphthols by an iodine-catalyzed multicomponent reaction of β-naphthol. *Mendeleev Commun.*, 17: 299-300.

Nandi, G. C., Samai, S., Kumar, R., Singh, M. S. (2009). Atom-efficient and environment-friendly multicomponent synthesis of amidoalkyl naphthols catalyzed by P₂O₅. *Tetrahedron Lett.*, 50: 7220-7222.

Patil, S. B., Singh, P. R., Surpur, M. P., Samant, S. D. (2007). Ultrasound-promoted synthesis of 1-amidoalkyl-2-naphthols via a three-component condensation of 2-naphthol, ureas/amides, and aldehydes, catalyzed by sulfamic acid under ambient conditions. *Ultrason. Sonochem.*, 14: 515-518.

Selvam, N. P., Perumal, P. T. (2006). A new synthesis of acetamido phenols promoted by Ce(SO₄)₂. *Tetrahedron Lett.*, 47: 7481-7483.

Shaterian, H. R., Yarahmadi, H., Ghashang. M. (2008). An efficient, simple and expedition synthesis of 1-amidoalkyl-2-naphthols as 'drug like' molecules for biological screening. *Bioorg. Med. Chem. Lett.*, 18: 788-792.

Shaterian, H. R.; Yarahmadi, H. (2008). A modified reaction for the preparation of amidoalkyl naphthols. *Tetrahedron Lett.*, 49: 1297-1300.

Shen, A. Y., Tsai, C. T., Chen, C. L. (1999). Synthesis and cardiovascular evaluation of N-substituted aminonaphthols. *Eur. J. Med. Chem.*, 34: 877-882.

Shi, F., Jia, R. H., Zhang, X. J., Tu, S. J., Yan, S., Zhang, Y., Jiang, B., Zhang, J. Y., Yao, C. S. (2007). Extension of the Biginelli-type reaction: one-pot synthesis of pyrimido-pyrimidines and spirobi [pyrimidine]s using potassium hydrogen sulfate as a catalyst, *Synthesis*, 2782-2790.

Srihari, G.; Nagaraju, M.; Murthy, M. M. (2007). Solvent-free one-pot synthesis of amidoalkyl naphthols catalyzed by silica sulfuric acid. *Helv. Chim. Acta.*, 90: 1497-1504.

Su, W. K., Tang, W. Y., Li, J. J. (2008). Strontium(II) triflate catalysed condensation of β-naphthol, aldehyde and urea or amides: a facile synthesis of amidoalkyl naphthols. *Chem. Res.*, 123-128.

Szatmári, I., Fülöp, F. (2004). Syntheses and Transformations of 1-(α-Aminobenzyl)-2-naphthol Derivatives. *Curr. Org. Synth.*, 1: 155-165.

Trost, B. M. (1991). The atom economy: a search for synthetic efficiency. *Science*, 254: 1471-1477.

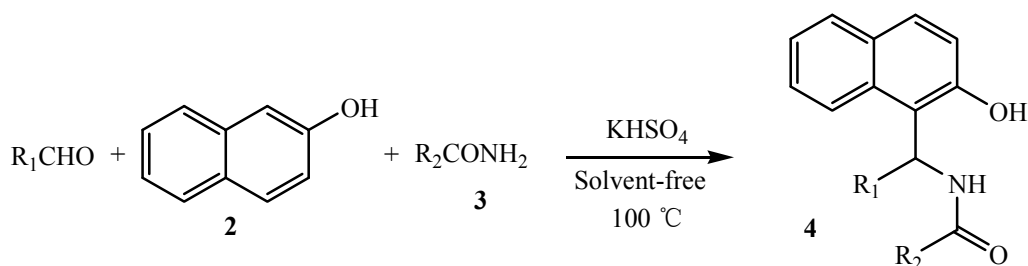
Trost, B. M. (1995). Atom economy-a challenge for organic synthesis: homogeneous catalysis leads the way. *Angew. Chem.*, 107: 285-307.

Trost, B. M. (2002). On inventing reactions for atom economy. *Acc. Chem. Res.*, 35: 695-705.

Tu, S. J., Fang, F., Zhu, S. L., Li, T. J., Zhang, X. J., and Zhuang, Q. Y. (2004). A new Biginelli reaction procedure using potassium hydrogen sulfate as the promoter for an efficient synthesis of 3,4-dihydropyrimidin-2(1H)-one. *Synlett*, 537-539.

Table 1. Synthesis of Amidoalkyl Naphthols with Potassium Hydrogen Sulfate as Catalyst under Solvent-free Condition

Product ^a	R ₁	R ₂	Time (h)	Yield ^b (100%)	Mp (°C)
4a	C ₆ H ₅	CH ₃	1.0	90	232-233
4b	4-MeC ₆ H ₅	CH ₃	1.0	91	223-224
4c	4-ClC ₆ H ₅	CH ₃	0.5	95	233-234
4d	4-MeOC ₆ H ₅	CH ₃	1.0	94	172-174
4e	4-FC ₆ H ₅	CH ₃	0.5	95	205-207
4f	4-NO ₂ C ₆ H ₅	CH ₃	0.5	96	239-240
4g	3-NO ₂ C ₆ H ₅	CH ₃	0.5	93	238-240
4h	4-BrC ₆ H ₅	CH ₃	0.5	92	230-231
4i	2-ClC ₆ H ₅	CH ₃	0.5	93	194-195
4j	3-MeOC ₆ H ₅	CH ₃	1.0	88	192-194
4k	2-Furyl	CH ₃	1.5	83	218-220
4l	C ₆ H ₅	NH ₂	1.0	90	173-174
4m	4-ClC ₆ H ₅	NH ₂	0.5	94	170-171
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
4p	4-BrC ₆ H ₅	NH ₂	1.0	92	173-175
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.Figure 1. Synthesis of amidoalkyl naphthols by the condensation of aldehydes with β-naphthol, acetamide or urea in the presence of (KHSO₄) under solvent-free conditions