One-Pot Synthesis of Amidoalkyl Naphthols Using $POCl_3/Na_2B_4O_7$ as a Heterogeneous Catalyst

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Abstract: A convenient and efficient procedure for the synthesis of 1-amidoalkyl-2-naphthols by condensation of β-naphthol, aldehydes and amid/urea in the presence of $POCl_3$/ $Na_2B_4O_7$ is described. This method offers several advantages including low cost and easy availability of the catalyst, environmentally friendly procedure and easy work-up under solvent-free conditions.

Keywords: 1-Amidoalkyl-2-naphthols, borax, multicomponent reactions, $POCl_3$.

INTRODUCTION

The multicomponent reactions (MCRs) [1] are attracting the interest of organic chemists and other researchers due to their significant potential for converting more than two adducts directly into respective products in quantitative yields in a one-pot reaction as compared to conventional strategies used in multi-step synthesis of various biologically active organic compounds. MCRs are particularly useful to generate diverse chemical libraries of 'druglike' molecules for biological screening [2, 3]. One of these MCRs is the preparation of amidoalkyl naphthols. 1-amidoalkyl-2-naphthols and their derivatives have attracted considerable interest in recent years due to biologically important antibacterial, natural products and potent drugs including a number of nucleoside antibiotics and HIV protease inhibitors, such as ritonavir and lipinavir [4, 5].

The preparation of 1-amidoalkyl-2-naphthols can be carried out by multi-component condensation of aryl aldehydes, 2-naphthol amide/urea in the presence of catalysts such as PPA-SiO_2, Iodine, $K_5CoW_{12}O_{40}.3H_2O$, cation-exchange resins, $HClO_4$-SiO_2, $Ce(SO_4)_2$, $Yb(OTF)_3$ and Indium(III) Chloride [6-8]. However, many of these methodologies suffer from the drawback of green chemistry and have been associated with several shortcomings such as long reaction times, expensive reagents and low product yields. Therefore, to overcome these limitations, the search for a new, easily available catalyst with high catalytic activity for the preparation of amidoalkyl naphthols is strongly desirable.

The use of catalysts and reagents on solid supports has been developed because such reagents not only simplify purification processes but also help to prevent the release of reaction residue into the environment [9]. In continuation of our interest in the use of $POCl_3/Na_2B_4O_7$ (BPO) [10, 11] as a supported catalyst, we wish to report the synthesis of 1-amidoalkyl-2-naphthols **4** by condensation of aryl aldehydes,2-naphthol and amide/urea in the presence of $POCl_3$/ $Na_2B_4O_7$ at 120 °C under solvent-free conditions (Scheme **1**).

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RESULTS AND DISCUSSION

To study the feasibility of the BPO catalyzed in this reaction, the reaction of benzaldehyde (10 mmol) **2**, β-naphthol (10 mmol) **1** and acetamide (12 mmol) **3** was selected as a model under solvent-free conditions. We first studied the model reaction catalyzed by 0.1 g BPO at different temperatures. The reaction rate was increased as the reaction temperature was raised. When it was carried out at 120 ˚C, the maximum yield was obtained in a short reaction period. Next, to evaluate the effect of catalyst concentration, the model reaction was carried out in the presence of different amounts of catalyst (0.05, 0.08, 0.1 and 0.12 g) at 120 ˚C. The result showed, that for the model reaction 0.1 g of catalyst was sufficient to achieve a fairly high yield (Table **1**).

With the optimized condition established above, we then attempted to extend the process to β-naphthol, various types of aromatic aldehydes and different amides including acetamide, urea and benzamide under solvent-free conditions at 120 °C. The results have been summarized in Table **2**. In all cases, 1-amidoalkyl-2-naphthols **4** were obtained in high to excellent yields without formation of any side products such as di-benzoxanthenes, which are normally observed under the influence of strong acids. Although as it can be seen from the results of Table **2**, this reaction is affected by electronic and steric factors. Aldehydes with electron-withdrawing groups, give higher yields than aldehydes with electron-donating groups. Aliphatic aldehyde like propionaldehyde was also examined, but the yields were low as compared to aromatic aldehyde (Table **2**, entry 15).

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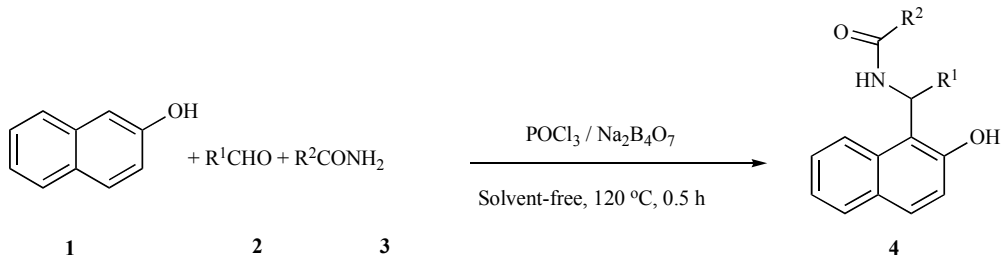

1 **2** **3** **4**

Scheme 1.

Table 1. Different Reaction Conditions for the Condensation of β-naphthol (10 mmol), Benzaldehyde (10 mmol) and Acetamide (12 mmol) in the Presence of BPO

Entry	BPO (gr)	Time (h)	Temperature (° C)	Yield (%)[a]
1	0.1	5	r.t	15
2	0.1	5	60	48
3	0.1	5	90	65
4	0.1	0.5	120	92
5	0.1	0.5	130	94
6	0.05	0.5	120	65
7	0.08	0.5	120	78
8	0.12	0.5	120	93

[a]Isolated yield.

Table 2. Preparation of 1-amidoalkyl-2-naphthols

Entry	R^1	R^2	Yield (%)[a]	Product	M.p (°C)	
					Found	Reported
1	Ph	CH_3	92	**4a**	240-242	242-244 [6]
2	4-MePh	CH_3	88	**4b**	220-223	220-222 [6]
3	4-ClPh	CH_3	92	**4c**	227-229	228-229 [6]
4	2-ClPh	CH_3	89	**4d**	193-195	194-196 [7]
5	4-MeOPh	CH_3	85	**4e**	183-186	184-186 [6]
6	3-NO_2Ph	CH_3	94	**4f**	213-215	212-215 [6]
7	Ph	NH_2	86	**4g**	171-172	171-173 [6]
8	4-ClPh	NH_2	92	**4h**	211-213	210-212 [6]
9	2-ClPh	NH_2	85	**4i**	150-152	150-153 [8]
10	3-NO_2Ph	NH_2	92	**4j**	185-188	186-188 [6]
11	Ph	Ph	90	**4k**	232-235	234-236 [7]
12	4-MePh	Ph	82	**4l**	191-193	192-193 [7]
13	4-ClPh	Ph	94	**4m**	176-179	177-178 [7]
14	3-NO_2Ph	Ph	93	**4n**	215-218	216-217 [7]
15	CH_3CH_2	CH_3	-	**4o**	-	-

[a]Isolated yield.

CONCLUSION

$POCl_3$/Borax is an inexpensive, easily available, non-corrosive and environmentally benign compound. A convenient and efficient procedure for the preparation of 1-amidoalkyl-2-naphthols under solvent-free conditions was reported in this work. This thermal solvent-free green procedure not only affords the products in high to excellent yields but also avoids the problems associated with catalyst cost, handling and work-up procedure. Furthermore, the easy

removal of the catalyst makes this method a better choice for chemical industries.

EXPERIMENTAL SECTION

$POCl_3$/Borax (BPO) was prepared according to the previous work [10]. All the products were known compounds, which were characterized by IR and ^{1}H-NMR spectral data and their m.p's compared with literature reports.

General Procedure for the Synthesis of 1-amidoalkyl-2-naphthols

To a mixture of β-naphthol (10 mmol), aldehydes (10 mmol), and amid or urea (12 mmol), BPO (0.1 g) was added and the reaction mixture was heated at 120 ˚C for 0.5 h. Then the mixture was washed thoroughly with water to remove the catalyst. The resulting precipitate was recrystalylied from ethanol:water (1:3) to afford pure amidoalkyls.

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REFERENCES

[1] Ivar, U. Recent progress in the chemistry of multicomponent reactions. *Appl. Chem*., **2001**, *73*, 187-191.

[2] Weber, L. Multi-component reactions and evolutionary chemistry. *Drug Disc. Tod*., **2002**, *7*, 143-147.

[3] Domling, A. Recent advances in isocyanidebased multicomponent chemistry. *Curr. Opin. Chem. Biol*., **2002**, *6*, 306-313.

[4] Knapp, S. Synthesis of complex nucleoside antibiotics. *Chem. Rev*., **1995**, *95*, 1859-1876; (b) Wang, Y.; Izawa, T.; Kobayashi, S.; Ohno, M. Stereocontrolled synthesis of (+)-negamycin from an acyclic homoallylamine by 1,3-asymmetric induction. *J. Am. Chem. Soc*., **1982**, *104*, 6465-6466.

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

[6] Shaterian, H. R.; Hosseinian, A.; Ghashang, M. PPA-SiO_2-Catalyzed Multicomponent Synthesis of Amidoalkyl Naphthols. *Synth. Commun*., **2008**, *38*, 3375-3389. And references cited therein.

[7] Wang, L. M.; Xia, J.; Qin, F.; Qian, C.; Sun, J. Yb(OTf)3-Catalyzed One-Pot Synthesis of Quinazolin-4(3H)-ones from Anthranilic Acid, Amines and Ortho Esters (or Formic Acid) in Solvent-Free Conditions. *Synthesis,* **2003**, 1241-1247.

[8] Chavan, N. L.; Naik, P. N.; Nayak, S. K.; Kusurkar, R. S. Indium(III) Chloride: An Efficient Catalyst for the Synthesis of Amidoalkyl Naphthols. *Synth. Commun*. **2010**, *40*, 2941-2947.

[9] Clark, J. H. Catalysis of organic reactions by supported inorganic reagents. New York: VCH; **1994**.

[10] Gholivand, Kh. Jafari, H.; Adibi, H. Simple and new method for the synthesis of β-Acetamido ketones on a solid surface. *Synth. Commun.,* **2011**, *41*, 1786-1793.

[11] Gholivand, Kh.; Zare, K.; Jafari, H.; Adibi, H. A New and Efficient Procedure for Synthesis of 1,5-Benzodiazepine Derivatives in Solution and under Solvent-Free Conditions. *Chin. J. Chem*., **2011**, *29*, 2421-2424.