

An Efficient Synthesis of [(Tosylamino)alkyl]naphthalenols by Nucleophilic Addition of Naphthalen-2-ol with *N*-Tosyl Imines Using Boron Trifluoride Etherate as Catalyst¹⁾

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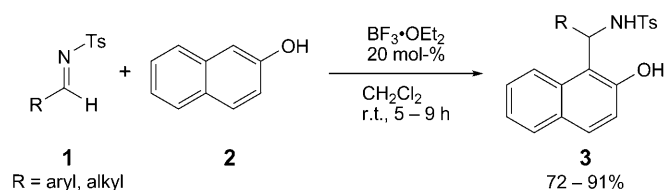
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[(Tosylamino)alkyl]naphthalenols have efficiently been synthesized by nucleophilic addition of naphthalen-2-ol with *N*-tosyl imines (derived from both aromatic and aliphatic aldehydes) in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ as a catalyst at room temperature. The products are formed within 5–9 h in high yields (72–91%).

Introduction. – Compounds possessing 1,3-amino oxygenated functional groups are found in different bioactive natural products and important drugs such as HIV protease inhibitors and nucleoside antibiotics [1]. They also exhibit biological properties including bradycardiac and hypotensive activities [2]. In addition, they have been applied as chelating agents and as catalysts [3]. Here, we report a simple method for the synthesis of 1-[(tosylamino)alkyl]naphthalen-2-ols, which contains 1,3-amino oxygenated function.

Results and Discussion. – In continuation of our work [4] on the development of useful synthetic methodologies, we have discovered that 1-[(tosylamino)alkyl]naphthalen-2-ols can be synthesized efficiently within 6–9 h by treatment of *N*-tosyl aldimines with naphthalen-2-ol in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ as catalyst at room temperature (*Scheme 1*). Recently, one method for the synthesis of these compounds (in chiral form) has been reported, the synthesis involved a dinuclear zinc complex as a catalyst, and the reaction time was 48 h [5].

Scheme 1



¹⁾ 'Studies on Novel Synthetic Methodologies', Part 207.

Initially, *N*-tosylbenzaldimine (**1a**; R = Ph) was treated with naphthalen-2-ol for 8 h using various catalysts at room temperature (Table 1). Considering the yield of the products, $\text{BF}_3 \cdot \text{OEt}_2$ was found to be most effective to catalyze the reaction. Even within 6 h, a similar yield of the product was obtained in the presence of this catalyst. Consequently, this catalyst was used to prepare a series of 1-[(tosylamino)alkyl]naphthalen-2-ols from various *N*-tosyl aldimines and naphthalen-2-ol (Table 2). The conversion was complete within 6–9 h, and the products were formed in high yields (72–91%). *N*-Tosyl aldimines were derived from both aromatic and aliphatic aldehydes. The aromatic aldehydes containing electron-donating as well as electron-withdrawing groups were used. A sterically hindered *N*-tosyl aldimine prepared from naphthalene-2-carbaldehyde also underwent the conversion smoothly. Different functional groups such as ether, halogen, nitrogen, and nitrile remained unchanged.

Table 1. Evaluation of the Activity of Different Catalysts for the Preparation of 1-[(Tosylamino)alkyl]naphthalen-2-ols^{a)}

Entry	Catalyst	Yield [%] ^{b)}
1	$\text{BF}_3 \cdot \text{Et}_2\text{O}$	91
2	$\text{Sc}(\text{OTf})_3$	81
3	$\text{Cu}(\text{OTf})_2$	79
4	InCl_3	77
5	ZnCl_2	69
6	ZrCl_4	67
7	FeCl_3	64
8	$\text{NaHSO}_4 \cdot \text{SiO}_2$	62
9	I_2	43
10	$\text{Ba}(\text{NO}_3)_2$ ^{c)}	Trace

^{a)} Reaction conditions: *N*-tosylbenzaldimine (1 mmol), naphthalen-2-ol (1 mmol), and catalyst (20 mol-%) were stirred at r.t. for 8 h. ^{b)} Yield of the isolated product. ^{c)} The mixture was stirred for 24 h.

Table 2. Synthesis of [(*N*-Tosylamino)alkyl]naphthalen-2-ols^{a)}

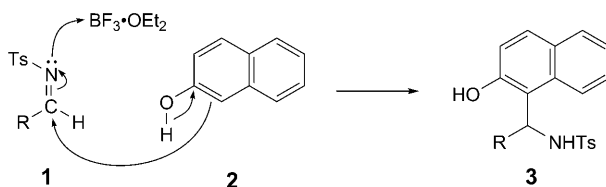
Entry	R	Time [h]	Product ^{b)}	M.p. [°] (solvent of crystallization)	Yield [%] ^{c)}
1	4-Cl-C ₆ H ₄	7	3a	168–170 (hexane/AcOEt 85 : 15)	91
2	3,4,5-(MeO) ₃ -C ₆ H ₂	9	3b	195–197 (hexane/AcOEt 80 : 20)	87
3	4-NC-C ₆ H ₄	8	3c	181–183 (hexane/AcOEt 85 : 15)	84
4	4-Me-C ₆ H ₄	5	3d	156–158 (hexane/AcOEt 90 : 10)	89
5	3-F-C ₆ H ₄	7	3e	155–157 (hexane/AcOEt 85 : 15)	90
6	Naphthalen-2-yl	6	3f	174–176 (hexane/AcOEt 90 : 10)	86
7	Ph	6	3g	171–173 (hexane/AcOEt 90 : 10)	91
8	2,3-(MeO) ₂ -C ₆ H ₃	8	3h	207–209 (hexane/AcOEt 80 : 20)	89
9	3-NO ₂ -C ₆ H ₄	9	3i	182–185 (hexane/AcOEt 80 : 20)	88
10	4-NO ₂ -C ₆ H ₄	9	3j	184–186 (hexane/AcOEt 80 : 20)	88
11	Pr	9	3k	177–179 (hexane/AcOEt 85 : 15)	72

^{a)} Reaction conditions: *N*-tosyl aldimine (1 mmol), naphthalen-2-ol (1 mmol) and $\text{BF}_3 \cdot \text{OEt}_2$ (20 mol-%) were used. ^{b)} The structures of the products were determined by their spectral analysis (IR, ¹H- and ¹³C-NMR, and ESI- and HR-ESI-MS). ^{c)} Yield of isolated product.

The structures of the products were deduced from their spectral data (IR, ^1H - and ^{13}C -NMR, and ESI-, and HR-ESI-MS).

The catalyst, $\text{BF}_3 \cdot \text{OEt}_2$ polarizes the $-\text{CH}=\text{N}-$ bond of the *N*-tosyl aldimines to facilitate the nucleophilic addition of naphthalen-2-ol (Scheme 2).

Scheme 2



The *N*-Ts group of the products can easily be removed [6] to afford the corresponding (aminoalkyl)naphthalenols, which can be utilized to prepare their various derivatives.

In conclusion, we have demonstrated a facile method for the synthesis of 1-[(tosylamino)alkyl]naphthalen-2-ols from *N*-tosyl aldimines and naphthalen-2-ol using $\text{BF}_3 \cdot \text{OEt}_2$ as catalyst. The mild reaction conditions, shorter reaction times, operational simplicity, and application of an inexpensive catalyst are the notable advantages of the present method.

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Experimental Part

General Procedure. To a soln. of *N*-tosyl aldimine (1.0 mmol) in CH_2Cl_2 (5 ml), naphthalen-2-ol (1 mmol) was added under N_2 , followed by the addition of $\text{BF}_3 \cdot \text{OEt}_2$ (0.2 mmol). The mixture was stirred at r.t., and the reaction was monitored by TLC. After completion, the mixture was concentrated, and H_2O and AcOEt (10 ml each) were added. The org. layer was separated and concentrated. The residue was subjected to column chromatography (SiO_2 ; hexane/ AcOEt) to obtain pure 1-[(tosylamino)alkyl]naphthalen-2-ol.

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