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SHORT COMMUNICATION

SYNTHESIS OF 1-AMIDOALKYL-2-NAPHTHOLS BASED ON A THREE-COMPONENT REACTION CATALYZED BY BORIC ACID AS A SOLID HETEROGENEOUS CATALYST UNDER SOLVENT-FREE CONDITIONS

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ABSTRACT. An efficient method for the preparation of 1-amidoalkyl-2-naphthols has been described using a multi-component, one-pot condensation reaction of 2-naphthol, aldehydes and amides in the presence of boric acid under solvent-free conditions.

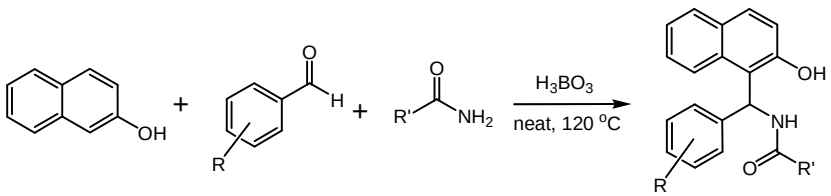
KEY WORDS: 1-Amidoalkyl-2-naphthols, Boric acid, 2-Naphthol, Solvent-free synthesis

INTRODUCTION

One-pot, multi-component processes have recently gained considerable economic and ecological interest as they have proved to be remarkably successful in generating molecular complexity in a single synthetic operation [1]. The use of heterogeneous catalysts in different areas of the organic synthesis has now reached significant levels, not only for the possibility to perform environmentally benign synthesis, but also for the good yields [2].

It is noteworthy that 1-amidomethyl-2-naphthols can be converted to important biologically active 1-aminomethyl-2-naphthol derivatives by amide hydrolysis reaction. The hypotensive and bradycardiac effects of these compounds have been evaluated [3-4]. The preparation of 1-amidoalkyl-2-naphthols can be carried out by multi-component condensation of aryl aldehydes, 2-naphthol and acetonitrile or amide in the presence of Lewis or Brønsted acid catalysts [5-16]. However, some of these catalysts suffer from the drawback of green chemistry such as prolonged reaction times, low yields and toxicity of the catalyst. Therefore, introducing clean processes and utilizing eco-friendly and green catalysts which can be simply recycled at the end of reactions have been under permanent attention. The demand for environmentally benign procedure with heterogeneous and reusable catalyst promoted us to develop a safe alternate method for the synthesis of amidoalkyl naphthols.

As a consequence of our interest in the application of solid acid catalysts in organic synthesis [17-20], herein, we describe an efficient method for the synthesis of 1-amidoalkyl-2-naphthols by one-pot condensation reaction of 2-naphthol, aldehydes and amides using catalytic amounts of boric acid under solvent-free conditions (Scheme 1).



Scheme 1

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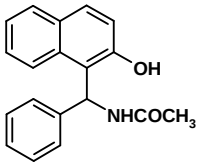
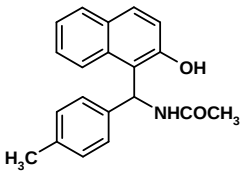
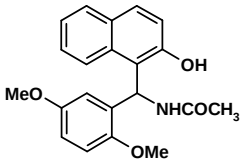
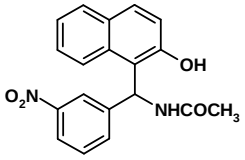
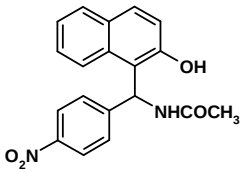
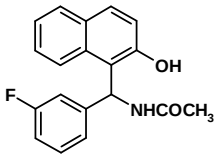
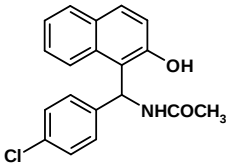
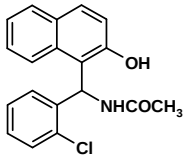
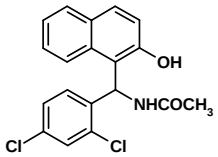
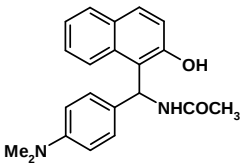
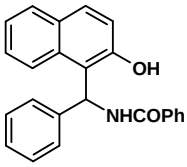
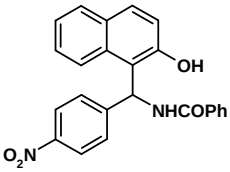
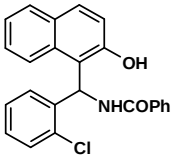
Boric acid (H_3BO_3) is a useful and environmentally benign catalyst which has been successfully utilized in numerous reactions [21-29], for example, the aza Michael addition [26], the Biginelli reaction [27], transesterification of ethyl acetoacetate [28], the Mannich reaction [29] and by our group in the synthesis of dibenzoxanthenes [17], α-aminophosphonates [18], dihydroquinazolinones [19] and benzimidazoles [20]. It offers milder conditions relative to common mineral acids. Boric acid is a readily available and inexpensive reagent and can conveniently be handled and removed from the reaction mixture. Thus, the remarkable catalytic activities together with its operational simplicity make it the most suitable catalyst for the synthesis of 1-amidoalkyl 2-naphthols.

RESULTS AND DISCUSSION

To optimize the reaction conditions, the reaction of 2-naphthol, benzaldehyde and acetamide was used as a model reaction. Reactions at different conditions and various molar ratios of substrates in the presence of boric acid revealed that the best conditions were solvent-free at 120 ^{o}C. After completion of the reaction, the catalyst (boric acid) can be separated from the reaction mixture by washing the product with water.

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

Entry	R	R′	Product	Yield (%)	m.p. (^{o}C)
1	H	CH_3		73	244-245
2	4-CH_3	CH_3		71	221-222
3	2,5-$(OMe)_2$	CH_3		71	251-256
4	3-NO_2	CH_3		76	241-243
5	4-NO_2	CH_3		75	248-249

Entry	R	R′	Product	Yield (%)	m.p. (°C)
6	3-F	CH_3		72	248-249
7	4-Cl	CH_3		72	223-225
8	2-Cl	CH_3		71	214-215
9	2,4-Cl_2	CH_3		73	199-201
10	4-NMe_2	CH_3		68	124-126
11	H	Ph		75	234-236
12	4-NO_2	Ph		76	238-240
13	2-Cl	Ph		72	285-286

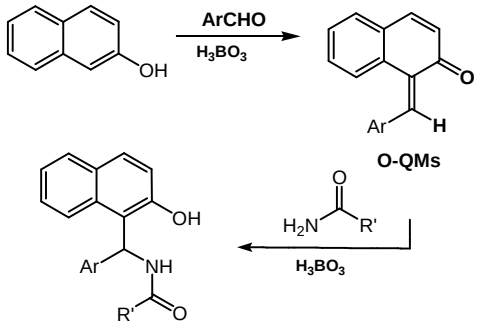
To show the generality of this method the optimized system was used for the synthesis of other amidoalkyl naphthol derivatives. The results are summarized in Table 1. Various

functionalities present in the aryl aldehydes, such as chloro, flouro, methyl and methoxy groups were tolerated under these conditions at 120 ^{o}C (Table 1).

However, the reactions of aliphatic aldehydes would fail to give the desired products as well as the known catalysts, such as montmorillonite K10 [5], $K_5CoW_{12}O_{40}.3H_2O$ [8], and $Fe(HSO_4)_3$ [9].

The reaction can also proceed with benzamide instead of acetamide (Table 1, entries 11-13). In all these cases, the corresponding 1-amidoalkyl-2-naphthols were obtained in good yields at 120 °C without formation of any side products such as dibenzoxanthenes, which are normally observed under the influence of strong acids. It is important to note that the synthesis of 1-amidoalkyl-2-naphthols could not be achieved in the absence of catalyst (boric acid).

The proposed mechanism for the boric acid catalyzed preparation of 1-amidoalkyl-2-naphthols from the reaction of 2-naphthol, aromatic aldehydes and amides is shown in Scheme 2. As has been suggested earlier [7, 10], the reaction of 2-naphthol with aromatic aldehydes in the presence of acid catalyst is known to give ortho-quinone methides (O-QMs). Further, nucleophilic conjugate addition of amide on *o*-quinone methide intermediate leads to the formation of amidoalkyl naphthol as a product.



Scheme 2

All the products were identified by ^{1}H NMR, ^{13}C NMR, IR, and mass spectroscopic methods and the results were confirmed by comparison with those available in the literature.

In conclusion, we have developed a very simple and efficient method for the high-yielding synthesis of 1-amidoalkyl-2-naphthols by one-pot three-component coupling of 2-naphthol, various aromatic aldehydes and amides using boric acid as a heterogeneous acid catalyst. This method offers some advantages in terms of simplicity of performance, low reaction times, solvent-free condition, low cost, and it follows along the line of green chemistry. The catalyst is readily available and inexpensive and can conveniently be handled and removed from the reaction mixture.

EXPERIMENTAL

Typical procedure for the preparation of 1-amidoalkyl 2-naphthols. A mixture of 2-naphthol (1 mmol), aldehyde (1 mmol), amide (1.2 mmol) and H_3BO_3 (0.05 g) at 120 ^{o}C was stirred for 15 min. The progress of reactions was monitored by TLC (ethyl acetate/n-hexane = 1/3). After completion of the reaction, the reaction mixture was diluted with water and extracted with ethylacetate, dried over Na_2SO_4, concentrated under vacuum and the crude mixture was purified by recrystalization from ethanol to afford pure products.

Spectral data for selected products

2.2.a N-[Phenyl-(2-hydroxy-naphthalen-1-yl)-methyl]-acetamide (Table 1, entry 1). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.98 (s, 3H), 7.19-1.10 (m, 4H), 7.26-7.20 (m, 4H), 7.33 (t, J = 7.5 Hz, 1H), 7.74 (d, J = 9.2 Hz, 1H,), 7.80 (d, J = 8.0 Hz, 1H), 7.84 (s, 1H), 8.45 (d, J = 8.5 Hz, 1H), 10.02 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 23.2, 40.4, 119.2, 119.4, 122.9, 123.8, 126.6, 126.9, 128.5, 128.7, 128.9, 129.1, 129.8, 132.9, 143.1, 153.7, 169.1; IR (KBr, cm^{-1}): 3399, 3246, 3062, 1640, 1582, 1514, 1372, 1337, 1060.

2.2.b N-[(2,5-Dimethoxyphenyl)-(2-hydroxynapthalen-1-yl)-methyl]-acetamide (Table 1, entry 3). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.88 (s, 3H), 3.48 (s, 3H), 3.64 (s, 3H), 6.77-6.72 (m, 2H), 7.23-7.10 (m, 4H), 7.39 (s, 1H), 7.73-7.66 (m, 2H), 8.27-8.15 (m, 2H), 9.75 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 22.5, 44.4, 55.2, 55.9, 111.1, 111.9, 115.7, 118.5, 118.9, 122.0, 123.2, 125.7, 128.1, 128.6,131.7, 132.4, 150.7, 152.7, 153.1, 168.1; IR (KBr, cm^{-1}): 3365, 3174, 3002, 2939, 1614, 1577, 1497, 1436, 1370, 1317, 1277, 1218, 1084, 1052, 819, 797, 727; MS (EI, 70 eV) m/z = 351 (M+, 18%), 308 (6%), 276 (6%), 262 (36%), 261 (100%), 218 (17%), 205 (3%), 189 (5%), 164 (4%), 144 (7%), 115 (8%), 95 (2%), 77 (2%).

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