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N-bromosuccinimide (NBS) catalyzed, microwave-assisted rapid synthesis of 1-amidoalkyl-2-naphthols under solvent-free conditions

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ABSTRACT

An efficient and direct procedure has been developed for the preparation of 1-amidoalkyl-2-naphthols by a one-pot condensation of aryl aldehydes, naphtalen-2-ol and acetamide, in the presence of *N*-bromosuccinimide (NBS) as a catalyst. The reactions were carried out under thermal condition and microwave irradiation in high yields. The present methodology offers several advantages such as excellent yields, simple procedure and eco-friendly reaction condition.

KEYWORDS

N-bromosuccinimide (NBS);
Multicomponent reactions;
Microwave irradiation;
Solvent free.

INTRODUCTION

Multicomponent reactions (MCRs) have been proven to be a very elegant and rapid way to access complex structures in a single synthetic operation from simple building blocks, and show high atom-economy, high selectivity and procedural simplicity due to the formation of carbon–carbon and carbon–heteroatom bonds in one-pot[1]. As a one-pot reaction, MCRs generally afford good yields and are fundamentally different from the two-component reactions in several aspects[2] and permitted rapid access to combinatorial libraries of organic molecules for an efficient lead structure identification and optimization in drug discovery[3, 4]. In addition, the implementation of several transformations in a single manipulation is highly compatible with the goals of sustainable and green chemistry[5]. Compounds having 1,3-amino-oxygenated functional groups are present in variety of biologically important natural products and potent drugs including a number of nucleoside antibiotics and HIV protease inhibitors, such as ritonavir and lipinavir[6]. Moreover, 1-amidoalkyl-2-naphthol can be easily hydrolyzed to 1-aminoalkyl naphthol, which shows biological activities like hypotensive and bradycardiac effect[7]. This 1-aminoalkyl alcohol-type ligandhas been used for asymmetric synthesis and also as a catalyst[8]. Several alternative and efficient methods have been developed for the synthesis of amidoalkyl naphthols by multicomponent reaction of aphtalen-2-ol, aldehyde and amide in the presence of different acid catalysts such as montmorillonite K10 clay[9], $Ce(SO_4)_2$[10], iodine[11], $K_5CoW_{12}O_{40}.3H_2O$[17], *p*-TSA[12], sulfamic acid[13], $HClO_4$–SiO_2[14], molten tetrae-thylammonium chloride[15], silica sulfuric acid[16], cation-exchanged resins[17], $Al(H_2PO_4)_3$[18a], $Fe(HSO_4)_3$[18b], $Yb(OTf)_3$[18c], wet cyanuric chloride[18d, e], polymer-supported sulfonic acid[18f] and $FeCl_3$–SiO_2[18g]. Hajipour et al[19]. Have reported the synthesis of amidoalkyl naphthol in ionic liquid at higher temperature (120 °C). However, some of these protocols suffer from certain drawbacks such as prolonged reaction time, use of dichloromethane like carcinogenic solvent, unsatisfactory yield, high tempera-

ture (120–125 °C) and use of toxic, highly acidic and expensive catalysts.

MATREIAL AND METHODS

All the reactions were carried out using a conventional (unmodified) household microwave oven (LG, 230 V, ~50 Hz). Reactions were monitored on TLC by comparison with the samples prepared by known procedures. The IR spectra were recorded using a Shimadzu 435-U-04 spectrophotometer (KBr pellets) and the NMR spectra were obtained in using a 90 MHz JEOL FT NMR spectrometer. All melting points were determined on a Büchi 530 melting point apparatus and are reported uncorrected.

General procedure for the preparation of amidoalkyl naphthols

Method A

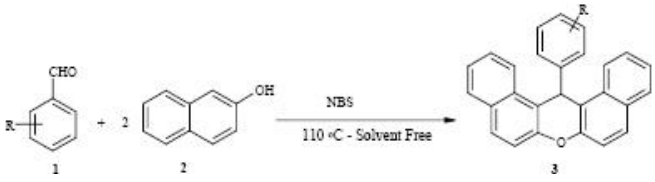
A mixture of aldehyde (1 mmol), naphtalen-2-ol (1 mmol), acetamide (1.2 mmol) and NBS (0.12 mmol, 0.27 mg) was stirred at 100 °C in oil bath. The completion of the reaction was monitored through TLC (ethyl acetate/cyclohexane, 1:3), after the reaction was compeleted, water (10 mL) was added and the product was filtered and then recrystallized from ethyl alcohol (TABLE 1).

Method B

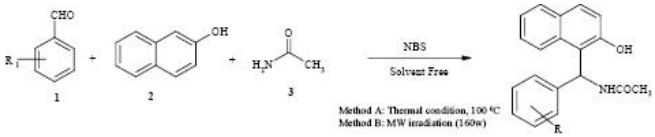
A mixture of aldehyde (1 mmol), naphtalen-2-ol (1 mmol), acetamide (1.2 mmol) and NBS (0.12 mmol, 0.27 mg) was taken in a 100 ml conical flask. The mixture was mixed well and then irradiated in a domestic microwave oven at 160 W for appropriate time (see TABLE 1). After the reaction was compeleted, water (10 mL) was added and the product was filtered and then recrystallized from ethyl alcohol (TABLE 1). The desired pure products were characterized by comparison of their physical data with those of known amidoalkyl naphtols[18, 28].

RESULTS AND DISCUSSION

In continuation of our confirming research on various transformations by halogenating agents[14-20], we reported a simple and convenient method for the synthesis of the 14-aryl-14*H*-dibenzo[*a*,*j*]xanthene derivatives by condensation of aldehydes with naphtalen-2-ol in a solvent-free media under heating conditions in the presence of *N*-bromosuccinimide (NBS)[21]. The reaction proceeds through the *in situ* formation of ortho-quinone methides and naphtalen-2-ol acted as a nucleophile (Scheme 1). We have now extended this *N*-bromosuccinimide (NBS) promoted procedure using acetamide (to work as nucleophiles) along with naphtalen-2-ol and aldehydes under thermal condition and microwave irradiation to produce the corresponding 1-amidoalkyl-2-naphthols in high yields (Scheme 2).



Scheme 1



Scheme 2

To find out the optimum quantity of *N*-bromosuccinimide (NBS), the reaction of naphtalen-2-ol, benzaldehyde and acetamide was carried out under thermal solvent-free conditions using different quantities of *N*-bromosuccinimide (NBS) (TABLE 1). As shown this TABLE, 0.12 mmole of NBS gave excellent yield in 96 as can be seen from TABLE 1. Thus, we prepared arrange of 1-amidoalkyl-2-naphthols under the optimized reaction conditions: 2-naphthol (1 mmol), aldehydes (1 mmol) and acetamide (1.2 mmol) in the presence of NBS (0.12 mmol). A series of 1-amidoalkyl 2-naphtoles were prepared in high to excellent yields by two methods (A, B) (TABLE 2).

As shown in the TABLE 2, The electron withdrawing groups (EWD) substituted on benzaldehyde in *o*-QM intermediate increase the rate of 1,4-nucleophilic addition reaction because of alkene LUMO is at lower energy in the neighbouring with-drawing groups than electron donating groups (EDG)[27].

We proposed a mechanism for these reactions four steps as shown in Scheme 3. Thus, the reaction likely proceeds via initial formation of intermediate ortho-quinone methides (*o*-QMs) 5. The same *o*-QMs, generated in-situ, have been reacted with acetamide to form

TABLE 1 : The effect of amount of NBS on the reaction of naphtalen-2-ol, benzaldehyd and acetamide under thermal solvent free conditions.

Entry	NBS	Time [min]	Yield [%][a])
1	1.2	20	88
2	1	25	90
3	0.5	40	89
4	0.12	22	94
5	0.08	70	80
6	0.0	100	-

[a]Yields refer to the pure isolated products.

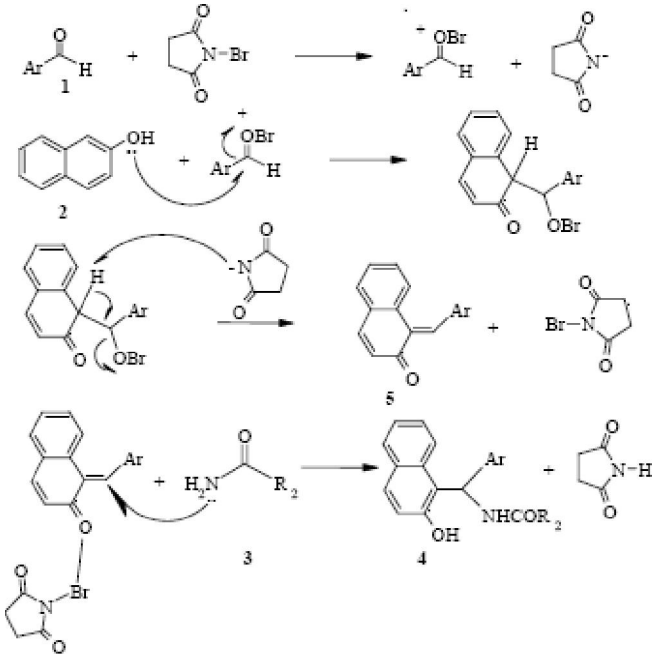
TABLE 2 : NBS catalyzed synthesis of 1-amidoalkyl-2-naphthols

Entry	Product [a]	R	Method A Time/Yields (%)[b]	Method B Time/Yields (%)[b]	M.p., °C (Lit.)[c]
1	2a	H	(22 min/96)	(5 min/93)	240-241(241-243)
2	2b	4-Me	(20 min/94)	(6 min/94)	220-222 (222-223)
3	2c	3-Me	(21 min/92)	(8 min/93)	201-203 (200-202)
4	2d	4-OMe	(20 min/93)	(5 min/90)	186-188 (184-186)
5	2e	3-OMe	(23 min/90)	(6 min/95)	202-204 (203-205)
6	2f	3,4-$(OMe)_2$	(24 min/89)	(8 min/89)	233-235 (235-236)
7	2g	4-$N(Me)_2$	(23 min/90)	(7 min/93)	126-127 (123-125)
8	2h	4-NO_2	(18 min/96)	(8 min/92)	249-251 (248-250)
9	2i	3-NO_2	(19 min/93)	(7 min/89)	235-237 (236-237)
10	2j	2-NO_2	(18 min/95)	(6 min/90)	178-180 (180-182)
11	2k	4-Cl	(17 min/96)	(5 min/94)	222-224 (224-227)
12	2l	2-Cl	(19 min/93)	(5 min/92)	196-198 (194-196)
13	2m	3-F	(18 min/93)	(6 min/93)	228-230 (224-227)
14	2n	4-F	(17 min/96)	(6 min/92)	202-203 (203-205)
15	2o	2-OH	(21 min/93)	(7 min/95)	199-201 (198-199)

a) Isolated yields. b) All the products are known, characterized by IR, NMR spectral analysis and compared with the authentic samples[12, 23]. c) Melting points of compounds are consistent with reported values[3, 12, 13, 29].

1-amidoalkyl-2-naphthol derivatives. A reasonable explanation for this result can be given by considering the nucleophilic addition to *o*-QMs intermediate favourable via conjugate addition on α,β-unsaturated carbonyl group and under the influence of NBS that aromatizes ring of this intermediate.

The advantages or the characteristic aspects of the method described in this paper in comparison with other previously reported ones are the following: the yields of products were better than the previous reported yields and in addition, the catalyst NBS is inexpensive, has no moisture sensitivity, and no special measures are required for the reaction.



Scheme 3

COCLUSION

The present methodology shows that *N*-bromosuccinimide (NBS) is an efficient catalyst in the one-pot synthesis of 1-amidoalkyl 2-naphtoles derivatives. The main advantages of the presented protocol are mild, clean and environmentally benign reaction conditions, as well as the high yields. Furthermore, this method is also expected to find application in organic synthesis due to the low cost of the reagent. It is believed that this method will be a useful addition to modern synthetic methodologies.

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