



ORIGINAL ARTICLE

Amberlite IR-120 catalyzed, microwave-assisted rapid synthesis of 1-amidoalkyl-2-naphthols



Mehdi Forouzani ^{a,*}, Hassan Ghasemnejad-Bosra ^b

^a Department of Chemistry, Payamenoor University, 19395-4697 Tehran, Islamic Republic of Iran

^b Islamic Azad University-Babol Branch, School of Science, P.O. Box 755, Babol, Islamic Republic of Iran

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Abstract An expeditious synthesis of 1-amidoalkyl-2-naphthols by the condensation of 2-naphthol with various arylaldehydes and acetamide is described. This greener protocol is catalyzed by amberlite IR-120, and proceeds efficiently in the absence of any organic solvent under microwave irradiation within 3–6 min.

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1. Introduction

Microwave technology has become very important in organic synthesis, and there are very few areas of synthetic organic chemistry, which have not been covered by this technology. It has been noted that microwave chemistry can provide access to synthetic transformations, which may otherwise be time consuming or low yielding using conventional heating (De La Hoz et al., 2004). 1-Amidoalkyl-2-naphthols can be converted to useful and important biological building blocks and to 1-aminomethyl-2-naphthols by an amide hydrolysis reaction, since compounds exhibit depressor and bradycardia effects in humans (Szatmari and Fulop, 2004; Shen et al., 1999). 1-Amidoalkyl-2-naphthols can be prepared by multi-component condensation of aldehydes, 2-naphthols and aceto-

nitrile or different amides in the presence of Lewis or Brønsted acids such as *p*-TSA (Khodaei et al., 2006), montmorillonite K10 (Kantevari et al., 2007), Ce(SO₄)₂ (Selvam and Perumal, 2006), Iodine (Das et al., 2007), Fe(HSO₄)₃ (Shaterian et al., 2008), Sr(OTf)₂ (Su et al., 2008), K₅CoW₁₂O₄₀·3H₂O (Nagarapu et al., 2007), sulfamic acid (Nagawade and Shinde, 2007; Patil et al., 2007a,b), molybdophosphoric acid (Jiang et al., 2008), cation-exchange resins (Patil et al., 2007a,b) and silica sulfuric acid (Srihari et al., 2007). However, many of the reported methods are associated with one or more of the following drawbacks: (i) low yield, (ii) long reaction time, (iii) harsh reaction conditions, (iv) the use of toxic, corrosive, expensive, or non-reusable catalysts, (v) the use of large amount of catalyst, (vi) application of large amount of acetamide (as reactant), and (vii) because of the use of acidic catalysts in most of the reported methods, application of aldehydes bearing basic groups or acid-sensitive aldehydes in the reaction is not possible. In addition, there are only very few methods for the synthesis of 1-aminoalkyl-2-naphthols at room temperature or mild conditions (Patil et al., 2007a,b; Das et al., 2007). Recently, the use of solid acidic catalysts has gained importance in organic synthesis because of several advantages, such as operational simplicity, non-toxicity, reusability, low cost, and ease of separation after

* Corresponding author. Tel.: +98 111 3279746.

E-mail address: forouzanimehdi@yahoo.com (M. Forouzani).

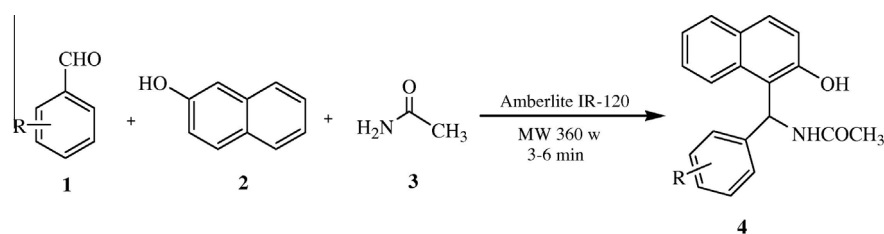
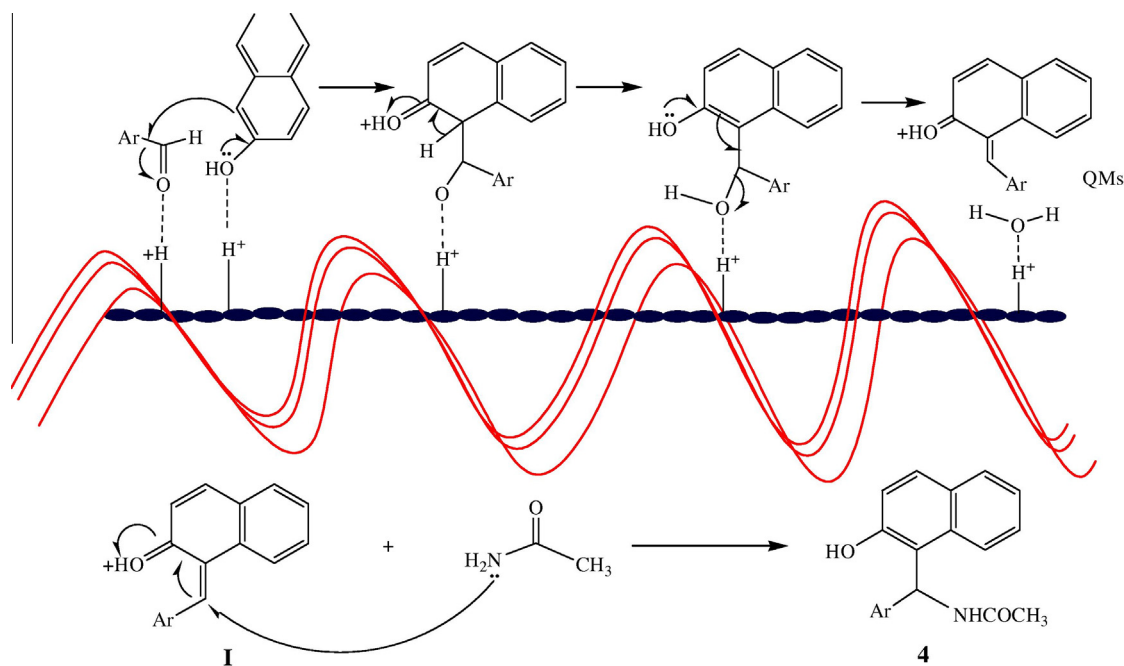
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Table 1 Synthesis of 1-amidoalkyl 2-naphthols in the presence of catalytic amount of amberlite IR-120 under solvent-free microwave irradiation.

Entry	Product ^a	R	Time (min)	Yields (%) ^b	M.p. (°C) (Lit.) ^c
1	2a	H	4	94	240–241(241–243)
2	2b	4-Me	5	95	220–222 (222–223)
3	2c	2-Me	6	94	201–203 (200–202)
4	2d	4-OMe	5	93	186–188 (184–186)
5	2e	3-OMe	6	96	202–204 (203–205)
6	2f	3,4-OMe ₂	6	90	233–235 (235–236)
7	2g	4-N(Me) ₂	5	92	126–127 (123–125)
8	2h	4-NO ₂	3	91	249–251 (248–250)
9	2i	3-NO ₂	4	92	235–237 (236–237)
10	2j	2-NO ₂	4	94	178–180 (180–182)
11	2k	4-Cl	3	95	222–224 (224–227)
12	2l	2-Cl	4	94	196–198 (194–196)
13	2m	4-Br	4	93	228–230 (227–229)
14	2n	4-F	4	96	202–203 (203–205)
15	2o	2,4-Cl ₂	3	93	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.^c Melting points of compounds are consistent with reported values (Selvam and Perumal, 2006; Shaterian et al., 2008; Patil et al., 2007a,b; Khazaei et al., 2010).**Scheme 1** The synthesis of 1-amidoalkyl-2-naphthols.**Scheme 2** A possible mechanism for the synthesis of 1-amidoalkyl-2-naphthols.

completion of the reaction (Bhattacharya and Rana, 2008; Tewari et al., 2003; Akagawa et al., 2007; Park et al., 2007).

2. Result and discussion

In continuation of our work on the development of simple and environmentally friendly experimental procedures using readily available reagents and catalysts for the synthesis of biologically active molecules and heterocyclic compounds under solvent-free (Ghasemnejad-Bosra et al., 2008a,b, 2009, 2010; Azarifar et al., 2006, 2007; Azarifar and Ghasemnejad-Bosra, 2006; Ghasemnejad-bosra and Forouzani, 2011; Habibzadeh et al., 2011). We, in this article, are reporting the use of amberlite IR-120[H⁺] resin (Sharma and Konwar, 2009) as a highly efficient and homogeneous organic catalyst for the exclusive synthesis of 1-amidoalkyl-2-naphthol derivatives (**4**) from condensation of 2-naphthol with aromatic aldehydes and acetamide under solvent-free microwave irradiation. The reaction between one equivalent of 2-naphthol with aromatic one equivalent of an aldehydes and acetamide in the presence of catalytic amounts of amberlite IR-120 under solvent-free microwave irradiation is fast, clean, and high-yielding and all the reactions go to completion in 3–6 min (see Scheme 1). The highlighting feature of this protocol is: (i) the method is highly efficient and selective; (ii) the catalyst is recyclable; (iii) gives excellent yield of the products; and (iv) all the reactions go to completion within 3–6 min when compared with other reported methods. For optimizing the reaction, it was examined under three different conditions: (i) thermal solvent-free condition; (ii) reflux in acetonitrile, and (iii) under solvent-free microwave irradiation. Firstly, 2-naphthol (1 mmol), benzaldehyde (1 mmol) and acetamide (1 mmol) were taken, and 0.16 g of amberlite IR-120 was added and the mixture was heated under solvent-free for 18 min or refluxed for 79 min in acetonitrile to get 63% of product **4a** [the progress of the reaction was monitored on TLC], continuation of the reaction did not improve the yield of the product. When the same reaction was carried out under the influence of microwave irradiation in the absence of solvent, the reaction proceeded effectively affording the product in 94% yield in 4 min. After optimizing these conditions using benzaldehyde as a model aldehyde, the reactions were performed with various other arylaldehydes, and it was noticed that the reaction proceeds well with all types of arylaldehydes and the results of this study are presented in Table 1.

As shown in Table 1, the reactions occurred excellently within 3–6 min under solvent-free microwave irradiation. The experimental results indicate that the most effective conversion occurred when a 1 mmol:0.16 g substrate/amberlite IR-120 was used. Longer reaction times were required when lower amounts of amberlite IR-120 were employed. It is important to note that no 1-amidoalkyl-2-naphthols derivatives were afforded when the reactions were performed in the absence of amberlite IR-120 in the reaction mixture.

A possible mechanism of this one pot reaction under MW condition is expected to include the '*in situ*' formation of intermediate *o*-QM in the presence of solid silica chloride. It is assumed that, due to the collapse of the cavitation bubbles near the surface of the catalyst, the oxygen of the carbonyl group in step 1 may easily influence [H⁺] the catalyst amberlite IR-120[H⁺] to give the activated aldehyde which may attack 2-naphthol to give *o*-QM (**I**). Further, the *o*-QM intermediate

(**I**) may undergo a nucleophilic conjugate addition with acetamide to give 1-amidoalkyl-2-naphthol (**4**) as shown in. The first step is the rate determining step wherein the activated aldehyde reacts with a molecule of 2-naphthol to give the intermediate *o*-QM (**I**) (Scheme 2).

In conclusion, we have presented a rapid, efficient and simple protocol for the synthesis of 1-amidoalkyl-2-naphthol in excellent yields by treating equimolar amounts of 2-naphthol, araldehyde and acetamide in the presence of catalytic amount of amberlite IR-120 under microwave irradiation. The highlighting features of this protocol are its efficiency, selectivity, and reusability of the catalyst.

3. Experimental

The chemicals were obtained from either Merck or Fluka. M.p.: Büchi 530 melting-point apparatus; uncorrected. IR spectra: Shimadzu-435-U-04 spectrophotometer (KBr pellets). NMR spectra: in CDCl₃, 90-MHz JEOL-FT-NMR spectrometer.

3.1. General procedure for the synthesis of 1-amidoalkyl-2-naphthol

A mixture of 2-naphthol (1 mmol), arylaldehyde (1 mmol), acetamide (1 mmol) and amberlite IR-120 (0.16 g) was taken in a 100 ml conical flask. The mixture was mixed well and then irradiated in a microwave oven (Samsung model KE300R) at 360 W for appropriate time (see Table 1). After which dichloromethane (10 ml) was added to the mixture and left aside for a few minutes, the solid thus separated was recrystallised from methanol or subjected to silica gel column chromatography to get the pure product/s.

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