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ORIGINAL ARTICLE

Nano magnetite (Fe_3O_4), an efficient and robust catalyst for the one-pot synthesis of 1-(aryl(piperidin-1-yl)methyl)naphthalene-2-ol and 1-(α-amido alkyl)-2-naphthol under ultrasound irradiation

Masoud Mokhtary *, **Mogharab Torabi**

Department of Chemistry, Rasht Branch, Islamic Azad University, Rasht, Iran

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KEYWORDS

Fe_3O_4 magnetic nanoparticle;
Functionalized 2-naphthol;
Multicomponent reaction;
Ultrasound irradiation

Abstract The direct three component reaction via condensation of aldehydes, 2-naphthol and piperidine or acetamide to generate 1-(aryl(piperidin-1-yl)methyl)naphthalene-2-ol and *N*-((2-hydroxy naphthalene-1-yl)(aryl)methyl)acetamide derivatives has been carried out over Fe_3O_4 magnetic nanoparticle with high efficiency under ultrasound irradiation. These reactions were studied under different conditions. In terms of reaction time and yield, it was found that optimum results were obtained for the synthesis of 1-(aryl(piperidin-1-yl)methyl)naphthalene-2-ol under solvent free condition and for preparation of *N*-((2-hydroxynaphthalene-1-yl)(aryl)methyl)acetamide in acetic acid under ultrasound irradiation at 80 °C. Clean methodologies, easy workup procedure, and high yields are some advantages of this work.

1. Introduction

Recently, magnetic nanoparticles (MNPs) have emerged as viable alternatives to conventional materials, as robust, readily available, high surface area heterogeneous catalyst supports [1–5]. The nano-sized particles increase the exposed surface area of the active component of the catalyst, thereby enhancing the contact between reactants and catalyst dramatically. Post-synthetic surface modification of magnetic nanoparticles imparts desirable chemical functionality and enables the generation of catalytic sites on the surfaces of the resulting nano-catalyst. Their insoluble and paramagnetic natures enable trouble-free separation of these nano-catalysts from the reaction mixture using an external magnet, which eliminates the necessity of catalyst filtration. Successful application of these nanomaterials is highly dependent on their stability during the reaction as well as their particle size. These novel nano-catalysts bridge the gap between homogeneous and

* Corresponding author. Tel./fax: +98 1314223621.
E-mail address: mmokhtary@iaurasht.ac.ir (M. Mokhtary).
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heterogeneous catalysis, thus preserving the desirable attributes of both systems. Additionally, the activity and selectivity of magnetic nano-catalysts can be manipulated by their surface modification [6].

The aminonaphthol product became known in the literature as a Betti base, and the protocol as the Betti reaction [7,8]. The syntheses of a wide-ranging library of racemic and nonracemic Betti base derivatives were recently reviewed, with especial attention to the possibilities of their application as building blocks [9]. These compounds can be transformed into derivatives having antibacterial, hypotensive, and bradycardiac activities [10]. Also, 1-amidoalkyl-2-naphthols are important precursors for the synthesis of 1,3-amino oxygenated compounds frequently found in biologically important natural products and potent drugs including a number of nucleoside antibiotics and HIV protease inhibitors [11,12,13]. There are very few reports for the synthesis of 1-(aryl(piperidin-1-yl)methyl)naphthalene-2-ol derivatives using neutral non-ionic surfactant [14], nanocrystalline MgO [15] and $Cu(OTf)_2{\cdot}SiO_2$ catalyst [16]. However, some of these methods suffer from at least one of the following disadvantages: high cost and toxicity of the reagent and solvent and take longer reaction time. Fortunately, nano Fe_3O_4 as a magnetically recoverable and economically viable material has become the most promising catalyst in many important organic reactions such as oxidation of aromatic olefins to the corresponding aldehydes [17], synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones via the Biginelli reaction [18,19] and synthesis of α-aminophosphonates [20]. Herein, we wish to report the use of Fe_3O_4 magnetic nanoparticle catalyzed one-pot three component synthesis of 1-(aryl(piperidin-1-yl)methyl)naphthalene-2-ol and *N*-((2-hydroxynaphthalene-1-yl)(aryl)methyl)acetamide derivatives under ultrasound irradiation (Scheme 1).

2. Results and discussion

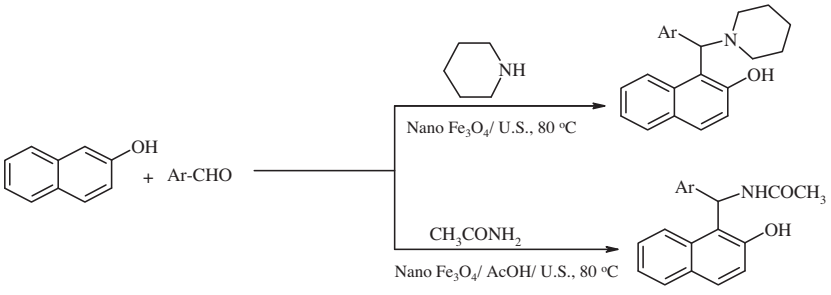
After a series of studies, we achieved excellent yields in shorter time at milder condition. Our studies indicated that solvent-free technique, due to high concentration of the reactant leads to a significant decrease in reaction time and easier workup procedure for the synthesis of 1-(aryl(piperidin-1-yl)methyl)naphthalene-2-ol derivatives. Therefore, this reaction proceeds with a catalytic amount of Fe_3O_4 nanoparticle with short reaction time, increased yields and easy workup condition. A variety of functionalized 2-naphthols was prepared from aldehydes, *2*-naphthol and piperidine in the presence of Fe_3O_4 nanoparticle under ultrasound irradiation and solvent free condition at 80 °C in excellent yields (Table 1, entries 1–7). Also, this reaction performed with 2,7-naphthalendiol and the corresponding product was achieved in very good yields under similar conditions (Table 1, entries 8–10). In a plausible mechanism, it is assumed that, the reaction may proceed through Lewis acid property of the ferrous or ferric ion due to coordination with the carbonyl group to facilitate the formation of iminium ion from arylaldehyde and piperidine followed by the nucleophilic attack of 2-naphthol carbon on iminium carbon, subsequent shifting of hydrogen atom leads to the formation of 1-(aryl(piperidin-1-yl)methyl)naphthalene-2-ol derivatives (Scheme 2).

Next, we studied this reaction with acetamide. In all cases, the corresponding product was obtained in excellent yields in the presence of Fe_3O_4 nanoparticle in acetic acid under ultrasound irradiation at 80 °C (Table 1, entries 11–16). It is worth mentioning that the corresponding functionalized 2-naphthols were isolated by crystallization from the crude filtrate. In addition, the reactions worked well with almost all the aldehydes with different substituents at ortho, meta, or para positions. However, in the absence of nano-iron oxide, the reaction proceeds with a low yield after a long reaction time (12 h). All products were characterized by comparison of their mp, FT-IR, ^{1}H NMR and ^{13}C NMR with those reported for the authentic samples [14,15,16,21]. It is noteworthy to highlight that the catalyst could be magnetically recovered by an external magnet and reused without a significant loss of activity. The recovered catalysts were dried and weighed. Afterward, according to the amount of catalyst the required amounts of fresh 2-naphthol, piperidine or acetamide, and arylaldehyde were added. The result showed that the catalyst can be reused six consecutive times with only a slight loss its activity (Table 2).

The proposed mechanism for the synthesis of *N*-((2-hydroxynaphthalene-1-yl)(aryl)methyl)acetamide is shown in Scheme 3. We supposed that the reaction may proceed via the ortho-quinone methide (*o*-QM) intermediate, which was formed by the nucleophilic addition of 2-naphthol to arylaldehyde catalyzed by Fe_3O_4 nanoparticle. Subsequent Michael addition of the *o*-QM with the acetamide afforded the expected amidoalkyl naphthol (Scheme 3).

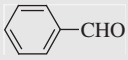
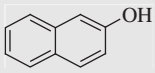
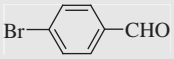
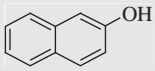
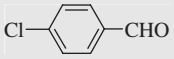
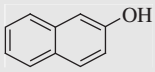
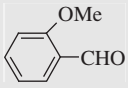
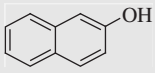
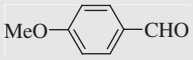
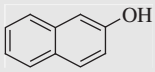
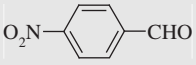
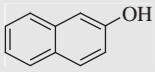
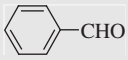
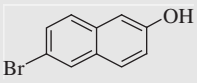
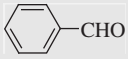
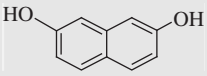
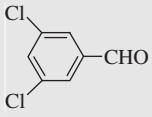
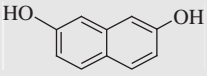
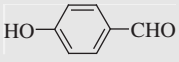
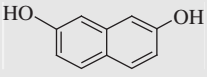
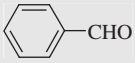
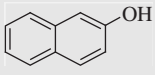
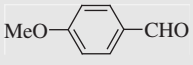
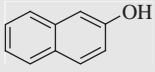
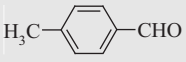
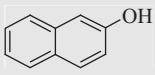
3. Experimental

The spherical Fe_3O_4 MNPs with an average size of 30 nm were purchased from Tecnan Spanish Company. For mixing chemicals, a universal Ultrasonic DSA100-SK2 was used. Melting points were recorded on an electro thermal melting point apparatus. The NMR spectra were recorded in $CDCl_3$ with TMS as an internal standard on a Bruker Avance DRX 400 MHz spectrometer. FT-IR spectra were determined on an SP-1100, P-UV-Com instrument. Products were separated



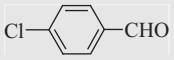
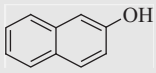
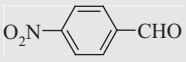
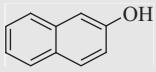
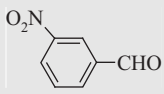
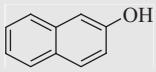
Scheme 1 Fe_3O_4 nanoparticle catalyzed synthesis of functionalized 2-naphthols.

Table 1 Synthesis of functionalized 2-naphthols using of Fe_3O_4 MNPs.[a]

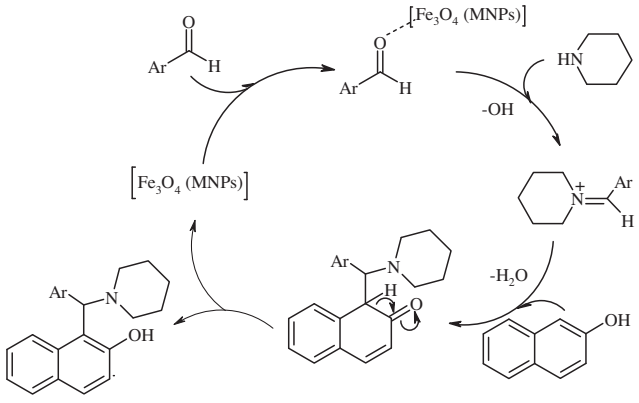
Entry	Aldehyde	Amine	2-naphthol	Time (min)	Yield%[b]
1				25	90
2				22	94
3				23	95
4				20	94
5				23	96
6				20	97
7				22	92
8				25	94 [c]
9				20	96 [c]
10				22	94 [c]
11		CH_3CONH_2		70	95[d]
12		CH_3CONH_2		80	96[d]
13		CH_3CONH_2		75	95 [d]

(*continued on next page*)

Table 1 (*continued*)

Entry	Aldehyde	Amine	2-naphthol	Time (min)	Yield%[b]
14		CH_3CONH_2		65	97[d]
15		CH_3CONH_2		60	98[d]
16		CH_3CONH_2		60	98[d]

[a] Reaction and conditions: 2-naphthol (1 mmol), aldehyde (1 mmol), piperidine (1 mmol) and nano-Fe_3O_4 (0.1 g) under ultrasound irradiation and solvent-free condition at 80 °C.
[b] All yields refer to isolated products.
[c] Reaction and conditions: 2,7-naphtalendiol (1 mmol), aldehyde (1 mmol), piperidine (1 mmol).
[d] Reaction and conditions: 2-naphthol (1 mmol), aldehyde (1 mmol), acetamide (1.1 mmol) and nano-Fe_3O_4 (0.1 g) under ultrasound irradiation in acetic acid (2 mL) at 80 °C.

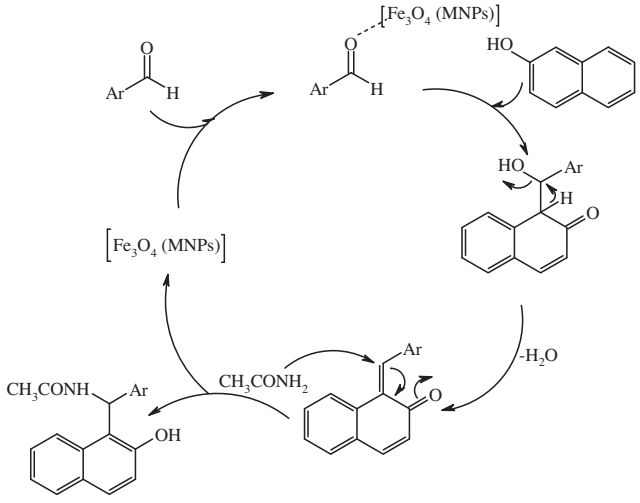


Scheme 2 A plausible mechanism for the synthesis of 1-(aryl (piperidin-1-yl)methyl) naphthalene-2-ol derivatives.

Table 2 Recycling of nano-Fe_3O_4 for the preparation of functionalized 2-naphthols.

Run	Yield[a] (%)	Yield[b] (%)
1	92	97
2	92	95
3	90	94
4	90	93
5	88	90
6	87	88

[a] Reaction and conditions: 2-naphthol (1 mmol), benzaldehyde (1 mmol), piperidine (1 mmol), nano-Fe_3O_4 (0.1 g) under ultrasound irradiation and solvent-free condition at 80 °C.
[b] Reaction and conditions: 2-naphthol (1 mmol), *p*-Cl-benzaldehyde (1 mmol), acetamide (1.1 mmol), nano-Fe_3O_4 (0.1 g) under ultrasound irradiation in acetic acid (2 mL) at 80 °C.



Scheme 3 A plausible mechanism for the synthesis of *N*-((2-hydroxynaphthalene-1-yl)(aryl)methyl)acetamide derivatives.

by simple filtration and identified by FT-IR, ^1H NMR and ^{13}C NMR spectra.

3.1. Synthesis of 1-(aryl(piperidin-1-yl)methyl)naphthalene-2-ol derivatives: general procedure

A mixture of 2–naphthol (1 mmol), aromatic aldehyde (1 mmol), piperidine (1 mmol) and Fe_3O_4 MNPs (0.1 g) was sonicated at 80 °C in an US bath having a frequency of 40 kHz and an input power of 600 W. The flask was suspended at the center of the bath for the appropriate time, as shown in Table 1, entries 1–10. After completion of the reaction, as indicated by TLC, the reaction mixture was diluted with ethyl acetate and the nanoparticles were separated with an external

magnet and then washed twice with ethyl acetate. The combined organic layers were concentrated under reduced pressure and the reaction mixture was cooled to ambient temperature, and the crude solid residue was recrystallized from ethanol to afford pure crystals of the proper 1-(aryl(piperidin-1-yl)methyl)naphthalene-2-ol derivatives in 92–98% yields.

3.1.1. Spectral data of new products are provided below

3.1.1.1. 6-Bromo-1-(phenyl (piperidin-1-yl) methyl) naphthalene-2-ol (Table 1, entry 7). White powder, yield: 92% m.p. 115–117 °C, IR: (KBr, cm^{-1}) 3446 (OH), 2933 (C–H), 2852, 1616, 1558 (C═C), 1151 (C–N), 1083 (C–Br). ^{1}H NMR (400 MHz, $CDCl_3$, ppm, δ): 1.29–2.20 (m, 10H, pipiridine-10H), 5.04 (s, 1H, CH), 7.17–7.85 (m, 10 H, ArH), 14.17 (brs, 1H, OH). ^{13}C NMR (100 MHz, δ, ppm, $CDCl_3$): 24.1 (CH_2), 26 (CH_2), 51.9 *(CH_2–N), 72.1 (CH), 109.5, 115.8, 116.4, 119, 121.1 (C-Br), 122.8, 128, 128, 128.9, 129.4, 129.7, 129.8, 130.6, 130.9, 139.3, 155.9 (C–OH).

3.1.1.2. 1-(Phenyl(piperidin-1-yl)methyl)naphthalen-2,7-diol (Table 1, Entry 8). White powder, yield: 94% m.p. = 209–210 °C, IR: (KBr, cm^{-1}) 3453 (OH), 2856 (CH), 1623, 1558 (C═C), 1157 (C–N). ^{1}H NMR (400 MHz, $CDCl_3$, ppm, δ): 1.48–2.32 (m, 10H, pipiridine-10H), 4.99 (s, 1H, CH), 6.77–7.57 (m, 10 H, ArH), 9.5 (brs, 1H, OH), 13.67 (brs, 1H, OH). ^{13}C NMR (100 MHz, δ, ppm, $CDCl_3$): 23.5 (CH_2), 25.6 (CH_2), 45.5 (CH_2–N), 70.7 (CH), 103.4, 114.3, 114.5, 115.9, 116.1, 122.6, 127.6, 128.6, 129, 130.1, 133.6, 139.9, 155.3 (C–OH), 155.7 (C–OH).

3.1.1.3. 1-((3,5-Dichlorophenyl)(piperidin-1-yl)methyl)naphthalene-2,7-diol (Table 1, entry 9). White powder, yield: 96% m.p. = 231–232 °C, IR: (KBr, cm^{-1}) 3396 (OH), 2945 (CH), 1627, 1558 (C═C), 1155 (C–N). ^{1}H NMR (400 MHz, $CDCl_3$, ppm, δ): 1.45–2.34 (m, 10H, pipiridine-10H), 5.14 (s, 1H, CH), 6.81–7.61 (m, 9H, ArH), 9.02 (brs, 1H, OH), 13.67 (brs, 1H, OH). ^{13}C NMR (100 MHz, δ, ppm, $CDCl_3$): 23.5 (CH_2), 25.5 (CH_2), 52.1 (CH_2–N), 68.8 (CH), 103.4, 114.6, 116, 122.6, 127.1, 127.1, 127.3, 127.5, 129.4, 130.2, 133.5, 134.1, 155.3 (C–OH), 156.1 (C–OH).

3.1.1.4. 1-((4-Hydroxyphenyl)(piperidin-1-yl)methyl)naphthalene-2,7-diol (Table 1, entry 10). White powder, yield: 94% m.p. = 210–211 °C, IR: (KBr, cm^{-1}) 3365 (OH), 2933 (CH), 1558, 1508 (C═C), 1157 (C–N). ^{1}H NMR (400 MHz, $CDCl_3$, ppm, δ): 1.48–2.33 (m, 10H, pipiridine-10H), 4.86 (s, 1H, CH), 6.68–7.57 (m, 9H, ArH), 9.02 (brs, 1H, OH), 13.76 (brs, 1H, OH). ^{13}C NMR (100 MHz, δ, ppm, $CDCl_3$): 23.5 (CH_2), 24.6 (CH_2), 25.6 (CH_2), 45.2 (CH_2–N), 70.2 (CH), 103.5, 114.9, 115.1, 116.1, 122.6, 128.4, 129, 129.8, 130.0, 133.6, 155.2 (C–OH), 155.7 (C–OH), 156.8 (C–OH).

3.2. Synthesis of N-((2-hydroxynaphthalene-1-yl)(aryl)methyl)acetamide derivatives: general procedure

A mixture of 2–naphthol (1 mmol), aromatic aldehyde (1 mmol), acetamide (1.1 mmol) and Fe_3O_4 MNPs (0.1 g) in acetic acid (2 mL) was sonicated at 80 °C in an US bath having a frequency of 40 kHz and an input power of 600 W. The flask was suspended at the center of the bath for the appropriate time, as shown in Table 1, entries 11–16. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to ambient temperature, and the nanoparticles were separated with an external magnet. The mixture was washed with 15 mL H_2O/EtOH (v/v = 1/1), and the collected solid was recrystallized from ethanol to afford pure crystals of the proper *N*-((2-hydroxynaphthalene-1-yl)(aryl)methyl)acetamide derivatives in 95–98% yields. The products were characterized by comparison of their mp, IR and ^{1}H NMR with those reported for the authentic samples.

4. Conclusion

We have developed a simple, clean, no need for anhydrous condition, an efficient and one-pot procedure for the synthesis of functionalized 2-naphthols by the three-component coupling of aldehyde, 2-naphthol, piperidine or acetamide using Fe_3O_4 MNPs as a magnetically recoverable catalyst under ultrasound irradiation.

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