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A Facile One-Pot Solvent-Free Synthesis of 1,2-Dihydro-1-arylnaphtho [1,2-e] [1,3] oxazine-3-ones Catalyzed by Nano-Fe_2O_3

Farhad Hatamjafari

Assistant Professor, Department of Chemistry, Faculty of Science, Islamic Azad University-Tonekabon Branch, Tonekabon, Iran

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ABSTRACT

One of the most important goals in medicinal chemistry is the development of new techniques and new heterocyclic compounds with pharmaceutical activity. The present study aimed to use a method for the synthesis of some 1,2-Dihydro-1-arylnaphtho [1,2-e] [1,3] oxazine-3-ones. The question this study tried to answer was this reaction can be performed in present of nano-Fe_2O_3 as an acid catalyst and solvent-free conditions or not. Therefore, to find answer to the question, some of the1,2-Dihydro-1-arylnaphtho [1,2-e] [1,3] oxazine-3-one derivatives with medicinal properties were synthesized with rapid, high yield, novel, facile, and one-pot condensation of β-naphthol, aromatic aldehydes and urea using by nano-Fe_2O_3 under solvent-free conditions. The one-pot synthesis on solid inorganic support provides the products in good yields. The synthesized some of oxazine-3-one derivatives has been reported.Nano-Fe_2O_3 was reused for four runs without significant loss of activity and the effect of the solvents on the model reaction was carried out in various solvents.

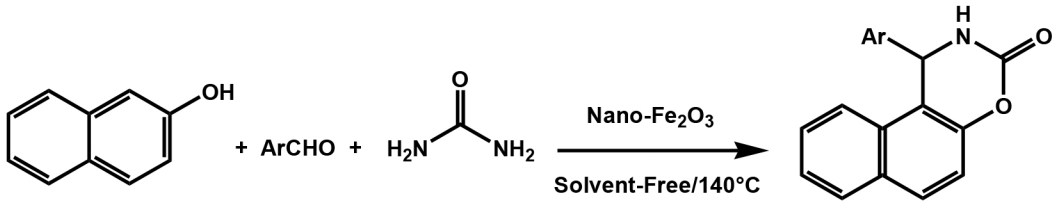
Keyword: Naphthoxazinones; Naphthols; Three-component Reactions; Solvent-Free; Nano-Fe_2O_3.

1. INTRODUCTION

New studies have been recently focused on the development of catalytic systems owing to their importance in synthetic organic chemistry. One of the most attractive synthetic strategies favored by organic chemists is the use of heterogeneous catalyst in increasing the efficiency of a wide range of organic synthesis. Heterogeneous catalysis is being used in the fine chemicals industry because of the need for more environmentally friendly production technology [1-3].

Heterocycles are of special interest because they constitute an important class of natural products, many of which exhibite useful pharmacological activities. 1,3-oxazine compounds has shown that they possess varied biological properties such as anticonvulsant, antitubercular, antibacterial, analgesic and anticancer activity [4-7]. Recently, several improved methodolo-

(*) Corresponding Author - e-mail: f_hatamjafari@tonekaboniau.ac.ir



Scheme 1: *Synthesis of oxazine-3-one derivatives the presence of nano-Fe_2O_3 as a catalyst.*

gies have been developed that are used for synthesis of [1,3] oxazine-3-one derivatives [8-21].

Recently nano-Fe_2O_3 have used as a nano-particles heterogeneous catalysis employing in synthesis reactions. Nano-Fe_2O_3 is as an available, environmentallyfriendly, non-volatile, reusable, non-expensive, inexpensive catalyst [22, 23].

Some of these methods are expensive, environmentally unfriendly, non-reusable produce low yields, are incompatible with other functional groups, and involve labor-intensive product isolation procedures. Therefore, a simple, efficient, and reusable procedure for one-pot synthesis arylnaphthoxazine-3-one derivatives under mild and solvent-free conditions is required.

We aimed to demonstrate the use of nano-Fe_2O_3 as a catalyst in a one-pot, three component reaction between aromatic aldehydes, β-naphtholand urea to produce 1,2-Dihydro-1-arylnaphtho[1,2-e][1,3] oxazine-3-ones under solvent-free conditions.

We report herein the nano-Fe_2O_3 as a new catalyst for the one-pot solvent-free synthesis of arylnaphtho [1,2-e] [1,3] oxazine-3-one derivatives high yields by condensation of aromatic aldehydes, β-naphthol and urea (Scheme 1).

2. EXPERIMENTAL

All chemicals were obtained from Merck or Fluka. Melting points were measured on an Electrothermal 9100. Silica gel SILG/UV 254 plates were used for TLC. IR spectra were measured using a Shimadzu IR-470 Spectrophotometer. ^{1}H NMR spectra were determined on Bruker 400 DRX AVANCE instrument at 400 MHz, respectively.

2.1. General procedure for the preparation of oxazine-3-ones (4a-e)

A mixture of aromatic aldehyde (1 mmol), β-naphthol

Table 1: *Effect of nano-Fe_2O_3 catalyst amount on the model reaction[a].*

Entry	Catalyst (mol%)	t (ºC)	Time (min)	Yield (%)[b]
1	None	120	100	trace
2	(30 mol%) Fe_2O_3	120	100	65
3	20	130	90	55
4	25	130	90	73
5	25	140	90	80
6	30	130	90	86
7	30	140	90	94
8	30	150	90	91
9	40	130	90	85
10	40	140	90	86

[(a)] Reaction condition: Benzaldehyde (1 mmol), β-naphthol (1 mmol), urea (1.2 mmol) and nano-Fe_2O_3 (different amount) under solvent-free conditions at different temperature; [(b)] Isolated yields.

(1 mmol), urea (1.2 mmol) and nano-Fe_2O_3 (0.3 mmol) was heated in oil bath at 140°C. The progress of reaction was monitored by TLC. After complete conversion as indicated by TLC, the reaction after 90 min, the mixture was filtered and opportunity was cooled, again water was added. The precipitate was filtered and recrystallized from ethanol to give compound 4a-e in high yields (Table 1).

3. RESULTS AND DISCUSSION

In this research, we report a novel and effective procedure for the one-pot synthesis, three component reaction of aromatic aldehyde, and urea, β-naphthol and nano-Fe_2O_3 as a reusable catalyst. The catalyst is cheap, available, reusable and environmentally friendly. The reaction was carried out between aryl aldehydes, 2-naphthol and urea in the presence of mentioned catalyst (Scheme 1). To determine the optimum quantity of nano-Fe_2O_3 in reaction of benzaldehayde, 2-naphthol andurea under solvent-free conditions, we used different amounts including 0, 20, 25, 30 and 40 mol% of nano-Fe_2O_3. The best amount of corresponding catalyst was obtained 30 mol% in 90 min (Table 1, entry 7). Table 1 clearly illustrates that nano-Fe_2O_3 is an effective catalyst in terms of reaction times and yields of product. we compared results of nano-Fe_2O_3 with Fe_2O_3 non-nano in the synthesis of 1,2-dihydro-1-arylnaphtho [1,2-e] [1, 3] oxazine-3-one. As shown in Table 1, nano-Fe_2O_3 can act as effective catalyst with respect to reaction times, yields and the obtained products. The result of the synthesis of arylnaphthoxazine-3-one derivatives are summarized in Table 2.

The catalyst was easily recovered by simple filtration after dilution of the reaction mixture with ethyl acetate and was reused after being vacuum dried. nano-Fe_2O_3 was reused for four runs without significant loss of activity (Run 1: 94%; Run 2: 89%; Run 3: 87%; Run 4: 85%).

In order to survey the effect of the solvents on the

Table 2: *Synthesis of naphthoxazinone-3-one derivatives 4a-fa[a].*

Entry	Aromatic aldehyde	Product	Yield (%)[b]	mp ºC Found [c]	Reported
4a	C_6H_5CHO	4a	94	216-218	219-222 [24]
4b	2-ClC_6H_4CHO	4b	91	247-250	249-251 [24]
4c	4-BrC_6H_4CHO	4c	90	222-225	221-223 [24]
4d	2,4-$DiClC_6H_4CHO$	4d	85	212-215	214-217 [25]
4e	3-$NO_2C_6H_4CHO$	4e	87	228-230	226-227 [24]

[a] Reaction condition: Aromatic aldehyde (1 mmol), β-naphthol (1 mmol), urea (1.2 mmol) and nano-Fe_2O_3 (0.3 mmol)under solvent-free conditions at 140ºC; [b] Isolated yields; [c] Uncorrected.

Table 3: *Effect of solvents on the model reaction.*

Entry	Solvent	Time (h)	Yield (%)[a]
1	EtOH	3	56
2	CH_3CN	3	61
3	$CHCl_3$	3	15
4	H_2O	3	22
5	DMF	3	10
6	Solvent free	1.5	94

[a] Isolated yield.

model reaction synthesis of arylnaphthoxazine-3-one derivative, the reaction of benzaldehayde, 2-naphthol and urea was carried out in various solvents (Table 3). It is observed that the excellent results were obtained in solvent-free conditions at 140°C using nano-Fe_2O_3 as catalyst.

Spectral data

1-Phenyl-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one (4a): Yield 94% as a white solid; mp. 216-218°C. IR (KBr, cm^{-1}): 3256 (N-H Str.); 3047 (C-H_{arom} Str.); 1725 (C=O Str.). ^{1}HNMR (400 MHz, $CDCl_3$, δ, ppm): 6.10 (1H, d,CH); 6.29(1H, s, 1NH); 7.28-7.90 (11H_{arom}, m, 11CH_{arom}).

1-(2-Chlorophenyl)-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one (4b): Yield 91% as a white solid; mp. 247-250°C. IR (KBr, cm^{-1}): 3209 (N-H Str.); 3015 (C-H_{arom} Str.); 1723 (C=O Str.). ^{1}HNMR (400 MHz, $CDCl_3$, δ, ppm): 6.15(1H, s, 1NH); 6.61(1H, d, 1CH); 6.75 (1H_{arom}, d, 1CH); 7.08(1H_{arom}, t, 1CH); 7.24-7.95 (8H_{arom}, m, 8CH).

1-(4-Bromophenyl)-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one (4c): Yield 90% as a white solid; mp. 222-225°C; (KBr, cm^{-1}): 3214(N-H Str.); 3024(C-H_{arom} Str.); 1730(C=O Str.). ^{1}HNMR (400 MHz, $CDCl_3$, δ, ppm): 6.09(1H, d, 1CH); 6.91(1H, s, 1NH); 7.20-7.30(4H_{arom}, m, 4CH); 7.35(1H_{arom}, d, 3J=8.6 Hz, 1CH); 7.43-7.86 (4H_{arom}, m, 4CH); 7.90(1H_{arom}, d, 3J=8.6 Hz, 1CH).

1-(2,4-Dichlorophenyl)-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one (4d): Yield 85% as a white solid; mp. 212-215°C. IR (KBr, cm^{-1}): 3208(N-H Str.); 3066(C-H_{arom} Str.); 1743(C=O Str.). ^{1}HNMR (400 MHz, $CDCl_3$, δ, ppm): 6.79(1H, s, 1NH); 6.92(1H, dd, 1CH); 7.27-7.66(6H_{arom}, m, 6CH); 7.84(2H_{arom}, t, 2CH); 8.68(1H_{arom}, d, 1CH).

1-(3-Nitrophenyl)-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one (4e): Yield 87% as a White-yellow solid; mp. 228-230°C. IR (KBr, cm^{-1}): 3217(N-H Str.); 3159(C-H_{arom} Str.); 1739(C=O Str.); 1532, 1368(NO_2 Str.). ^{1}HNMR (400 MHz, $CDCl_3$, δ, ppm): 6.24(1H, d, 1CH); 6.46(1H, s, 1NH); 7.39-8.21(10H_{arom}, m, 10 CH).

4. CONCLUSIONS

In conclusion, we have demonstrated that nano-Fe_2O_3 is a novel, an efficient and environmentally friendly for the synthesis of arylnaphthoxazine-3-one derivatives. The one-pot three-component condensation of aryl aldehydes, 2-naphthol and urea in the presence of nano-Fe_2O_3 afforded arylnaphthoxazine-3-ones under solvent-free conditions. The advantages of this method are shorter reaction times, simple work-up, environmentally benign, high yield, and reusability of catalyst in comparison with the other reported methods.

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