



Original Research article

Microwave Assisted Solvent-free Synthesis of 1-Phenyl-1, 2-dihydro-3H-naphtho[1, 2-e][1, 3]oxazin-3-one Catalyzed by FeCl₃



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KEYWORDS

Iron (III) chloride

Catalyst

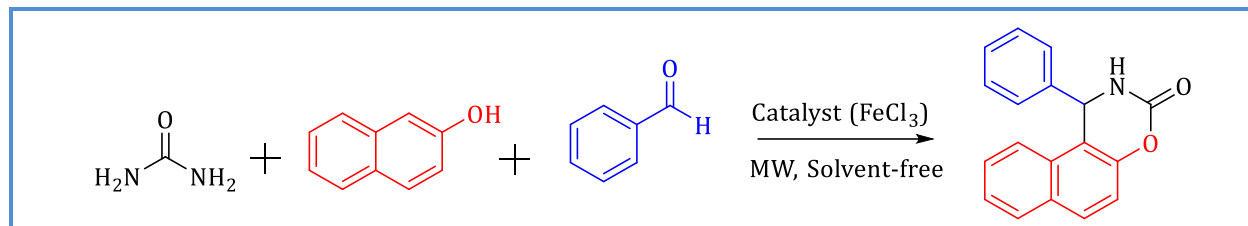
Solvent free

ABSTRACT

Three-component coupling of 2-naphthol, aldehydes, and urea has been accomplished in the presence of FeCl₃ under microwave irradiation and solvent-free conditions to afford the corresponding synthesis of 1-phenyl-1, 2-dihydro-3H-naphtho[1,2-e][1,3]oxazin-3-one derivatives in excellent yields. It is a promising catalyst for the microwave-assisted reaction providing high product yield in a short period.

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Graphical Abstract

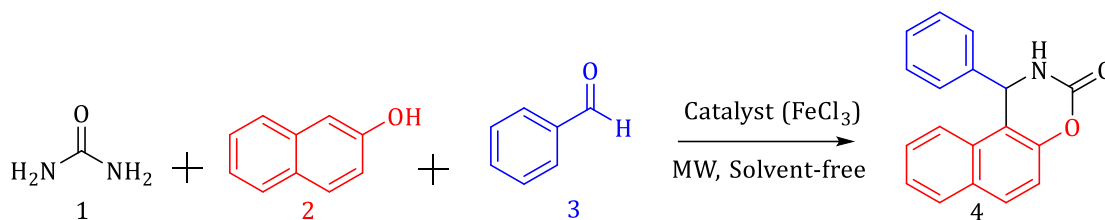


Introduction

Microwave (MW) irradiation as a novel, efficient and harmless method for reagent activation in the synthesis of organic compounds, and in special heterocyclic compounds, has been applied to achieve milder reaction conditions [1-4].

Multicomponent reactions (MCRs) constitute a particularly attractive synthetic strategy due to the fact that the products are made in a single step while diversity can be promoted only by varying the reacting components [5-11]. Furthermore, multicomponent reactions (MCRs) by the virtue of their convergence, productivity, ease of implementation and generally higher yields of products have attracted considerable attention in the area of combinatorial chemistry [12-16]. The first MCR was described by Strecker in 1850 for the synthesis of amino acids [17]. Yet, in the past decade, there have occurred tremendous developments in the three and four component reactions and, yet, great attempts are continually being appeared to develop new MCRs [18-22].

Over the past few decades, chemistry has become a major field of study for chemists [23-26]. Hence, chemical reactions have greatly caused the environmental problems [27-31]. To overcome these problems and facilitate chemical reactions, alternative energy sources such as UV or microwave are used. Iron is one of the most abundant metals on Earth and FeCl_3 (Iron (III) chloride) is an efficient catalyst in modern organic synthesis, environmentally friendly and atom-economical organic transformations that can increase the yield and speed of the reaction [32-35]. FeCl_3 has been explored as a powerful catalyst for various organic transformations such as synthesis of tetrasubstituted imidazoles [36], α -amino phosphonates [37], quinoline derivatives [17, 38], 3,4-dihydropyrimidinone derivatives [19] and synthesis of dihydropyrimidinones [18]. The reported route is an efficient, convenient and novel method for the condensation of the aldehyde with β -naphthol and urea in the presence of FeCl_3 to afford condensed naphthoxazine-3-one derivatives in good yields (Scheme 1).



Scheme 1. Synthesis of 1-phenyl-1, 2-dihydro-3H-naphtho [1, 2-e] [1, 3] oxazin-3-one

Material and Methods

General

Starting materials were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. Melting points were measured on an electrothermal 9100 apparatus and are uncorrected. The microwave-assisted procedures were carried out in a milestone microwave oven operating at 1600 W. All the obtained products are known compounds and were identified by comparing their melting points with those reported in the literature. The progress of reactions was monitored by thin layer chromatography (TLC). ¹H (DMSO-d₆) and ¹³C NMR (DMSO-d₆) spectra were recorded on a Bruker DRX-250 avance spectrometer at 250.13 and 62.90 MHz, respectively.

General procedure for the synthesis of naphthoxazine-3-one derivatives

A mixture of urea **1** (1 mmol), 2-naphthol **2** (1 mmol), benzaldehyde **3** (1 mmol), and 12 mol% of FeCl₃ anhydrous (0.02 g) under solvent-free condition was placed for 15 min with the power of 500 W in the microwave. The progress of the reaction was checked by TLC (petroleum ether: EtOAc, 10:2). After completion of the reaction followed by TLC, hot ethanol was added and the catalyst was filtrated off. Then, the residue was poured into crushed ice and stirred for several minutes. The solid product was filtered and the pure product was obtained by recrystallization from hot ethanol.

The selected spectral data

1,2-dihydro-1-phenylnaphtho[1,2-e][1,3]oxazin-3-one (Table 3, Entry 1): white solid, yield, 90%, ¹H NMR (250 MHz, DMSO-d₆): δ 8.85 (s, 1H, NH), 7.29-7.99 (m, 10H, Ar-H), 6.16 (s, 1H). ¹³C NMR (62.90 MHz, DMSO, d₆): δ 149.7, 147.8, 143.8, 130.8, 130.6, 129.4, 129, 128.4, 127.8, 127.4, 125.5, 123.5, 117.3, 114.4, 54.2.

Results and Discussion

Today, the use of catalysts in multi-component reactions is significant. Although the use of FeCl₃ having a catalytic role has been proven, the catalytic role of FeCl₃ in multi-particulate reactions in free-solvent

reactions was investigated in this study and was confirmed according to the NMR and melting point. We optimized the reaction conditions such as catalyst dosage, microwave power, and reaction times. First, the efficiency and amount of the FeCl₃ catalyst were investigated in a model reaction of urea **1** (1 mmol), β -naphthol **2** (1 mmol) and benzaldehyde **3a** (1 mmol) for the synthesis of compound **4a** (Table 3, entry 1). As shown in Table 1, the optimum yield of the product was obtained when 12 mol% of FeCl₃ was used (Table 1, entry 2).

Table 1. Effect of the catalyst dosage on the synthesis of naphthoxazine-3-one derivatives

Entry	Catalyst (mol%)	Microwave power (W)	Time (min)	Yield (%) ^a
1	9	500	15	83
2	12	500	15	90
3	15.5	500	15	90

Reaction conditions: urea **1** (1 mmol), β -naphthol **2** (1 mmol) and benzaldehyde **3a** (1 mmol) under microwave irradiation (500 W)
an Isolated yields

The effect of microwave power inputs from 300 to 600 W on the synthesis of compound **4a** (Table 3, entry 1) as a model reaction was evaluated (Table 2). The reaction yield increased with the microwave power at 400 W in comparison to 500 W.

Table 2. Effect of microwave power on the synthesis of naphthoxazine-3-one derivatives

Entry	Catalyst (mol%)	Microwave power (W)	Time (min)	Yield (%) ^a
1	12	300	15	71
2	12	400	15	82
3	12	500	15	90
4	12	600	15	90

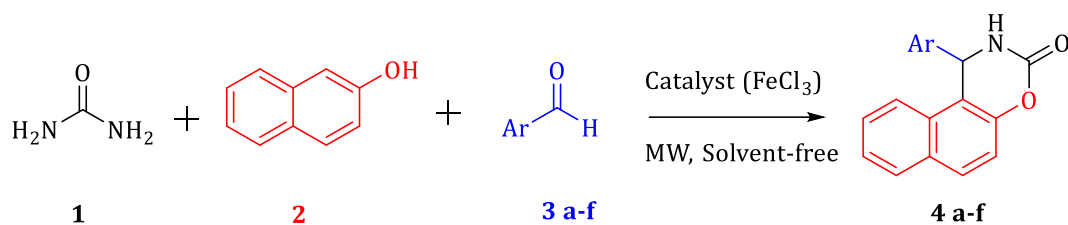
Reaction conditions: urea **1** (1 mmol), β -naphthol **2** (1mmol) and benzaldehyde **3a** (1 mmol) and 12 mol% (20 mg) of catalyst.
an Isolated yields

Using this optimized condition, a wide range of aldehydes, urea, and β -naphthol (Scheme 2) were subjected to undergo three-component condensation in the presence of FeCl₃ under solvent-free conditions (Table 3). Then, various aromatic aldehydes carrying electron-donating and electron-withdrawing groups on the aromatic ring in the ortho, meta, and para positions and heterocyclic aldehydes were evaluated. Yields of all reactions were good to excellent.

Table 3. FeCl₃ catalyzed the synthesis of naphthoxazine-3-one derivatives

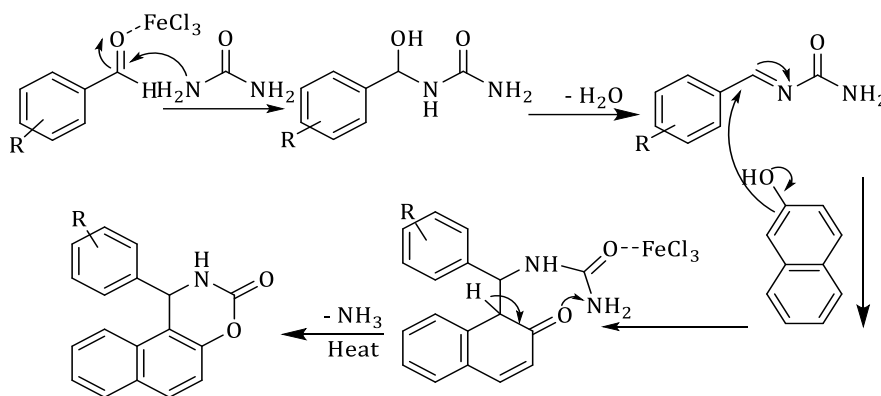
Entry	Ar	Product	Time (min)	Yield (%) ^a	M.P. (°C)	M.P. (°C) [Ref.]
1	Ph	4a	15	90	223-225	220-222 [39]
2	3-Cl-C ₆ H ₄	4b	15	88	193-195	194-196 [40]
3	4-Cl-C ₆ H ₄	4c	15	90	208-210	210-212 [40]
4	2-NO ₂ -C ₆ H ₄	4d	15	84	197-199	195-197 [39]
5	4-NO ₂ -C ₆ H ₄	4e	15	89	189-192	188-190 [39]

Reaction conditions: urea **1** (1 mmol), β -naphthol **2** (1 mmol) and benzaldehyde **3a-f** (1 mmol) and 12 mol% of the catalyst under microwave irradiation (500 W) in solvent-free conditions
Isolated yields



Scheme 2. FeCl₃ catalyzed the synthesis of naphthoxazine-3-one derivatives

Mechanistically, the initial condensation of an aromatic aldehyde with urea in the presence of FeCl₃ following by dehydration leads to the formation of benzylidene urea. The nucleophilic addition of the 2-naphthol to benzylidene urea followed by intramolecular cyclization of the resulting species produce the 1,2-dihydro-1-arylnaphtho[1,2-e][1,3]oxazine-3-one (Scheme 3).



Scheme 3. The proposed mechanism for the synthesis of naphthoxazine-3-one derivatives

Conclusions

In summary, we have described a highly efficient solvent-free synthesis for the preparation of naphthoxazine-3-one derivatives in the three-component cyclo-condensation reaction of 2-naphthol, aromatic aldehydes, and urea under microwave irradiation. According to the results of FeCl₃, the catalyst can be used for other multicomponent reactions. It can also be said that the method used in this synthesis is optimal, inexpensive and in line with green chemistry.

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