



Original Research Article

Microwave-assisted synthesis of phenanthro[9, 10-d]imidazole derivatives under solvent-free and one pot conditions

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KEYWORDS

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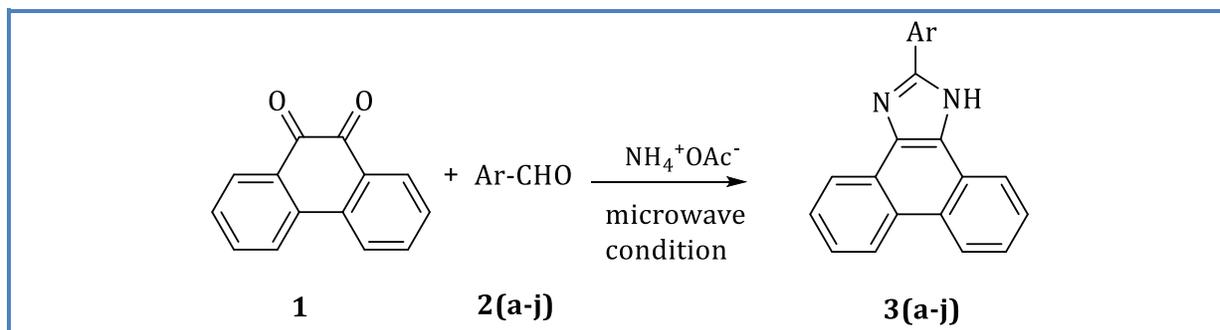
Imidazoles

Microwave

ABSTRACT

Phenanthro[9, 10-d]imidazole derivatives were synthesized with the combinations of phenanthroquinone and benzaldehyde derivatives in the presence of ammonium acetate. The microwave-assisted protocol was investigated under solvent-free condition for 2 min (400 w). The structure of all products was studied by IR and ¹HNMR Spectroscopy. Excellent yields, short reaction times, simplicity of operation and easy separation are the advantages of this technique.

Graphical Abstract



Introduction

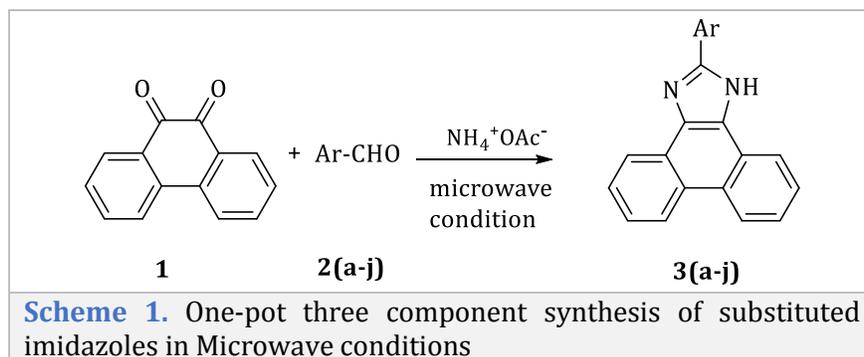
Imidazole derivatives are an important group of heterocyclic compounds that have excellent biological and chemical properties [1]. Nowadays these compounds are used in pharmacology, we well. They have different capacity including, anti-bacterial, anti-viral, anti-cancer, and anti-inflammatory [2-4]. Also, the imidazole ring system is one of the main substructures found in most of natural products and pharmacologically active compounds, such as the hypnotic agent [5]. Therefore, a great number of synthetic methods have been reported for the synthesis of multi substituted imidazoles [6].

Over the last decade, 2, 4, 5-trisubstituted imidazoles have been synthesized using one-pot three-component compression of an aldehyde and ammonium acetate with an α -hydroxy ketone, or an α -keto-oxime, or a 1, 2-dicarbonyl compound by using various catalyst such as ionic liquids [7, 8], Lewis acids [9, 10], protic acids [11-13], and other catalysts [14-17]. However, most of these methodologies are associated with low yields, high temperature requirement, longer reaction time, highly acidic conditions, use of expensive reagents and catalysts, requirement of large amount of catalysts, use of harmful solvents, formation of toxic wastes and tedious work-up [8].

Microwave processing is a relatively new development in materials processing. Ability of microwaves to couple energy directly to the

material is the primary advantage of the microwave processing as compared to conventional techniques. The volumetric heating ability of microwaves allows for more rapid, uniform heating, decreased processing time, and often enhanced material properties. The application of microwave heating to the manufacturing of ceramic and polymeric materials has the potential to improve the quality and reduce the manufacturing costs. Understanding the electromagnetic fields, microwave/material interaction, material transformations, and heat transfer is essential for optimizing the process. There have been many studies reported the microwave effects related to both processing of ceramic and polymeric composites, and there continues to be debate as to the existence of these "effects". Clearly, the application of microwave and radio frequencies for processing of materials can have advantages over traditional heat transfer. In the past decade, there has been significant advancement in the understanding of microwaves for the processing of materials, but more research must be conducted to have a full understanding of the process [18-20].

The main advantages of microwave heating in mineral processes include non-contact heating, energy transfer, not heat transfer, rapid heating, material selective heating, volumetric heating, quick start-up and stopping, heating starts from interior of body, and higher level of safety and automation.



In this study we report the synthesis of phenanthroimidazole derivatives (**3a-j**) via a one-pot three-component condensation of [9, 10]-phenanthroquinone (**1**), aromatic aldehydes (**2a-j**), and ammonium acetate in microwave conditions.

Materials and Methods

All materials and reagents were purchased from Merck and Aldrich and utilized with no more purification. Melting point was measured using an Electro thermal type 9100 melting point apparatus. The IR spectra were recorded using a Thermo Nicolet AVATAR-370 FT-IR spectrophotometer. A Bruker DRX250 spectrometer was employed to obtain the ¹HNMR spectra. The reactions were investigated under Microwave Synthesis type MILESTONE conditions.

Typical procedure for synthesis of phenanthroimidazole derivatives in microwave condition

A mixture of aldehyde (1mmol), [9, 10]-phenanthroquinone (1 mmol), ammonium acetate (2.5 mmol) were stirred. The resulted mixture was put in the microwave for described conditions (at 80 °C and 400 watts, 2 min). At the end of the reaction (the reaction progress was monitored by TLC using *n*-hexan:ethyl acetat as an eluent solution) the sediment was separation with filtering, and the solid product was washed with cold water (3×20 cm³), and recrystallized in ethanol to provide pure product. After cooling, the filtration of mixture was filtered; then, it was dried in Oven for 1 hour at 100 °C. The weight of the dried product was taken with the balance and the melting point was taken from the sample.

Analytical data for selected compounds

2-(4-Nitrophenyl)-1H-phenanthro[9, 10-d]imidazole (**3b**)

Yellow crystal, m.p.=316°C. IR (KBr): $\bar{\nu}$ =3260 (N-H), 1591 (C=N), 1536 (NO₂), 1450(C=C), 1383(NO₂) cm⁻¹. ¹HNMR (250 MHz, DMSO-d₆): δ =7.63-8.83(m, 12 H, Ar-H), 13.80 (s, 1H, NH) ppm.

2-(2-Chlorophenyl)-1H-phenanthro[9, 10-d]imidazole (**3e**)

Yellow crystal, m.p.=232-234°C. IR (KBr): $\bar{\nu}$ =3435 (N-H), 1594 (C=N), 1450 (C=C) cm⁻¹. ¹HNMR (250 MHz, DMSO-d₆): δ = 7.37-8.88 (m, 12H, Ar-H), 13.57 (s, 1H, NH) ppm.

2-(4-Cyano)-1H-phenanthro[9, 10-d]imidazole (**3d**)

Yellow crystal, m.p.=228-230°C. IR (KBr): $\bar{\nu}$ =3432 (N-H), 1592 (C=N), 1673 (C=C) cm⁻¹. ¹HNMR (250 MHz, DMSO-d₆): δ =5.11 (s, 2H, CH₂), 7.16-8.83 (m, 17 H, Ar-H), 9.83 (s, 1H, NH) ppm.

2-(3-Nitrophenyl)-1H-phenanthro[9, 10-d]imidazole (**3c**)

Yellow crystal, m.p.=269-271°C. IR (KBr): $\bar{\nu}$ =3212 (N-H), 1591 (C=N), 1562 (C=C) cm⁻¹. ¹HNMR (250 MHz, DMSO-d₆): δ =2.08 (s, 3H, CH₃), 7.28-8.82 (m, 12H, Ar-H), 10.17 (s, 1H, NH), 13.40 (s, 1H, NH) ppm.

2-(4-Boromophenyl)-1H-phenanthro[9,10-d]imidazole(**3i**)

Yellow crystal, m.p.=228-230°C. IR (KBr): $\bar{\nu}$ =3260 (N-H), 1595 (C=N), 1670 (C=C) cm⁻¹. ¹HNMR (250 MHz, DMSO-d₆): δ =7.61-8.85(m, 12 H, Ar-H), 13.80 (s, 1H, NH) ppm.

2-(4-methylphenyl)-1H-phenanthro[9, 10-d]imidazole(**3h**)

Yellow crystal, m.p.=290-292°C. IR (KBr): $\bar{\nu}$ =3350 (N-H), 1590 (C=N), 1665 (C=C) cm⁻¹.

^1H NMR (250 MHz, DMSO- d_6): δ =7.60-8.79(m, 12 H, Ar-H), 13.80 (s, 1H, NH), 3.12 (s, 1H, NH) ppm.

Results and Discussion

Substituents with pi bonds to electronegative atoms (-C=O, -NO₂) adjacent to the pi system are electron withdrawing groups (EWG)-they deactivate the aromatic ring by decreasing the electron density on the ring through a resonance withdrawing effect. Alkyl substituents (-CH₃, -CH₂CH₃) are also electron donating groups – they activate the aromatic ring by increasing the electron density on the ring through an inductive donating effect.

In benzaldehyde, the carbonyl group is an electron withdrawing group, so the carbonyl group pulls the electron from the electron-rich benzene ring. The electron-withdrawing groups such as Cyano (CN), Nitro (NO₂), and halogens activated the carbonyl group of aromatic ring. As a result, aromatic ring became an affective attack of groups congaing nitrogen. For instance,

in this study, aldehydes that had the electron-withdrawing substituent reacted effectively with ammonium acetate and electrophile (NH₄OAc) attack on the carbonyl group of benzaldehyde simply. Other groups like electron donating such as methyl (-CH₃) and methoxy (-OCH₃) weakens the activity of the carbonyl group of aromatic ring of benzaldehyde, therefore, the aromatic ring with Electron-Donating Substituents that does not affect the attack of ammonium acetate well. In all cases, that was confirmed. In all reactions that benzaldehyde was carried electron withdrawing group, products were produced with high-yield (80-95%) but reactions that had Electron-Donating Substituents Products were produced at a lower yield (70-80%).

After optimizing the reaction conditions, we prepared a range of imidazole derivatives (Table 4). In all cases, aldehydes reacted effectively with either electron-donating (entries 7-10) or electron-withdrawing (entry 2-4) groups and provided the estimated products in good to yields.

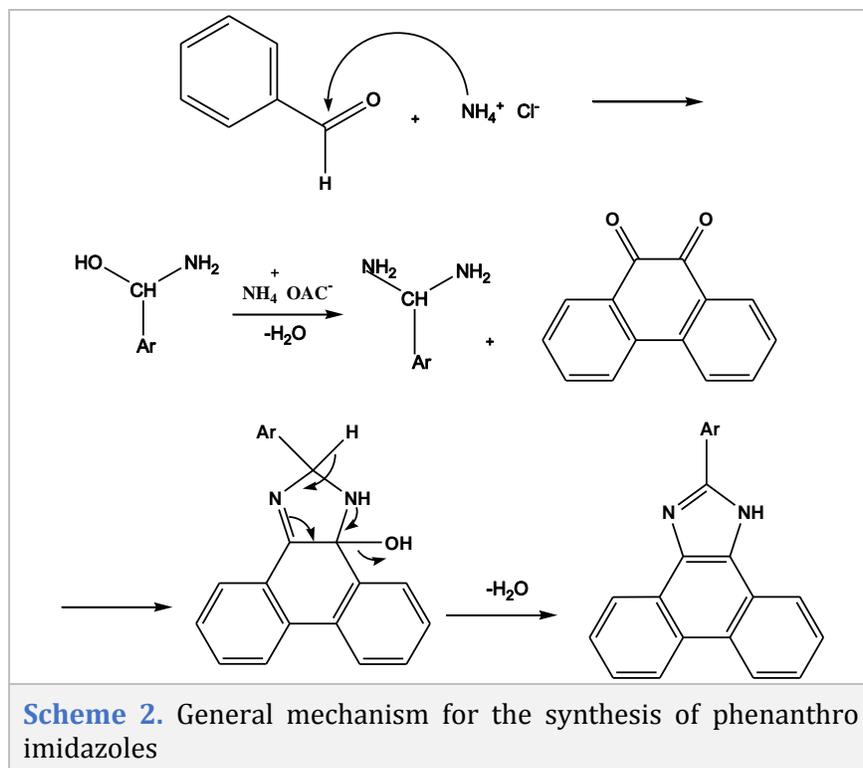
Table 1. One-pot three component synthesis of substituted imidazoles.

Entry	Ar	Product	Yield (%)	m.p. (°C)
				Found/reported[Ref.]
1	C ₆ H ₅	3a	89	286-288/>300[17]
2	4-NO ₂ C ₆ H ₄	3b	92	>300 [17]
3	3-NO ₂ C ₆ H ₄	3c	89	269-271/278-280[13]
4	4-CNC ₆ H ₄	3d	86	>300 [17]
5	2-ClC ₆ H ₄	3e	87	232-234/236-237[17]
6	4-ClC ₆ H ₄	3f	94	268-270/263-265[13]
7	4-MeOC ₆ H ₄	3g	83	258-260/265-267[13]
8	4-MeC ₆ H ₄	3h	84	290-292/292-294[13]
9	4-BrC ₆ H ₄	3i	68	228-230/ new
10	2-NO ₂ C ₆ H ₄	3j	74	246-248/ new

a. Reaction conditions: aldehyde (1mmol), [9, 10]phenanthraquinone (1mmol), ammonium acetate (2.5 mmol) at microwave condition

The mechanism of the reaction was proposed in Scheme 2. Ammonia molecules obtained from ammonium acetate.





Examination of the effects of temperature, power, time on the synthesis of the three -substituted phenanthro derivatives of imidazole in microwave conditions

For optimization, we selected 3-nitro phenanthro imidazole derivative as a sample. To investigate the effects of temperature, time, and power in microwave conditions on chemical reactions, we changed one of the

variables in each reaction, and examined the results separately.

Three separate reactions with constant power of 400 W and 2 min were defined by the temperature variable for the microwave system. The first reaction synthesized at 70 °C, the second reaction was investigated at 80 °C and the third reaction at 90 °C. The results are presented in [Table 2](#).

Table 2. Optimization results in temperature variable

m.p.(°C)	Sediment weight (g)	Time (min)	Power (w)	Temperature (°C)
271	0.12	2	400	70
268	0.12	2	400	80
273	0.12	2	400	90

In the next step, power has been studied as the main variable. The reaction mixture was investigated at a constant temperature and time, and three different powers (400, 450, and 500 W). In all three cases, the product structure was

confirmed by the IR spectra and the measurements of the melting point. The results are shown in [Table 3](#).

Table 3. Optimization results in power variable

m.p (°C)	Sediment weight (g)	Time(min)	Power(w)	Temp (°C)
269	0.11	2	400	80
272	0.10	2	450	80
275	0.11	2	500	80

The first reaction was investigated in the four-minute round, the second in the four-minute round and the third reaction in the four-minute round with the constant power of 400 W and the constant temperature of 80 °C in

microwave conditions. In all cases, the product was formed and the product structure was confirmed by the IR spectra and melting point. The results obtained are observed in the following table.

Table 4. Optimization results in time variable

m.p.(°C)	Sediment weight(g)	Time (min)	Power (w)	Temp(°C)
273	0.13	2	400	80
270	0.14	3	400	80
268	0.13	5	400	80

In the changes applied in all reactions that were done separately, the obtained IR spectra and sediment weight were identical. These results shown that products are formed by the same yield. Therefore, it can be concluded that the optimal conditions for formation of the three - substituted imidazole derivatives of imidazole are the temperature of 70 °C, the power of 400 W, and the time of 2 min.

Conclusion

The results showed that we could benefit from one pot synthesis for the preparation of substituted imidazoles through three-component condensation of aldehydes, [9, 10]-phenanthroquinone and ammonium acetate in Microwave conditions. Excellent yields, short reaction times, simplicity of operation, and easy separation are the several advantages of this technique. The results showed that the optimal conditions for formation of phenanthro

derivative of imidazole are the temperature of 70 °C, the power of 400 W, and the time of 2 min.

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