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LETTER

Microwave-assisted one-step rapid synthesis of dicyano imidazoles by HNO_3 as a high efficient promoter

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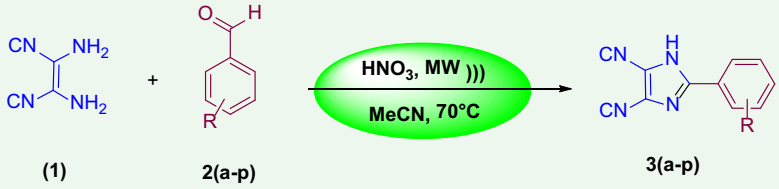
ABSTRACT

Microwave-activated synthesis is a special and remarkable technique in modern synthetic organic chemistry. In the current research, it is described the microwave-assisted synthesis of 2-aryl-4,5-dicarbonitrile imidazole derivatives *via* a one-step reaction between aromatic aldehydes and 2,3-diaminomaleonitrile (DAMN) using HNO_3 as a metal-free catalyst and a strong oxidizing agent. The present methodology has significant advantages as like as one-step synthesis, shorter reaction times, available starting materials, and higher yields of products with easy purification process, cleaner reaction than the previously reported processes. The valuable benefits of this method have provided a promising prospect for easier, greener, and faster synthesis of diciano imidazoles.



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KEYWORDS
Microwave-assisted synthesis; dicyano imidazole; nitric acid; metal-free oxidation catalyst; one-step reaction

Introduction

The synthesis of *N*-heterocycles with various functional groups is an important research domain in organic synthesis and medicinal chemistry, because the scope and applicability of such post-functionalized compounds may be increased (*1*). Imidazole, as one of the most important *N*-heterocycles, plays a significant role in pharmaceutical chemistry. The imidazole ring with diverse functional groups can have biological activities (*2–4*). Drugs based on functionalized imidazole skeleton are presented in Figure 1. Therefore, the development of efficient procedures for the synthesis of those privileged scaffolds is an active ongoing research area for chemists (*5–7*).

Cyano-containing imidazoles especially 2-aryl-4,5-dicarbonitrile imidazoles are considered an important class of organic heterocycles due to their pharmacological activities. These substituted imidazoles are used in the synthesis of new promising acceptor moieties (*8,9*). The first report for the synthesis of 4,5-dicyanoimidazole was presented in 1950 by Woodward (*10*). Although a great deal of chemistry on 4,5-dicyanoimidazoles has been described in the literature, there are few references about the synthesis of 2-aryl-4,5-dicarbonitriles. Among the reported methods (so far, four methods), the reaction between Schiff bases and oxidizing reagents such as 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) or diiminosuccinonitrile (DISY) (*11*), *N*-chlorosuccinimide (NCS) (*12*), iodine, and sodium acetate (*13*), and Pb $(OAc)_4$ (*14*) have been used for the preparation of these heterocyclic compounds. Recently, we have reported a better pathway for the synthesis of these compounds via a one-pot transformation of aldehydes and 2,3-diaminomaleonitrile using cerium(IV) ammonium nitrate (CAN) (*15*). But the usage of excess CAN reagent, long reaction time, the use of transition metal, and two-step reaction were the limitations of this approach. Also in another report, we were able to reduce a small amount of CAN as a catalyst and the reaction was performed under solvent or solvent-free conditions (*16,17*). All the reported methods have some disadvantages as like as hazardous reaction conditions, long reaction times, unsatisfactory yields, the use of stoichiometric amounts of toxic reagents and transition

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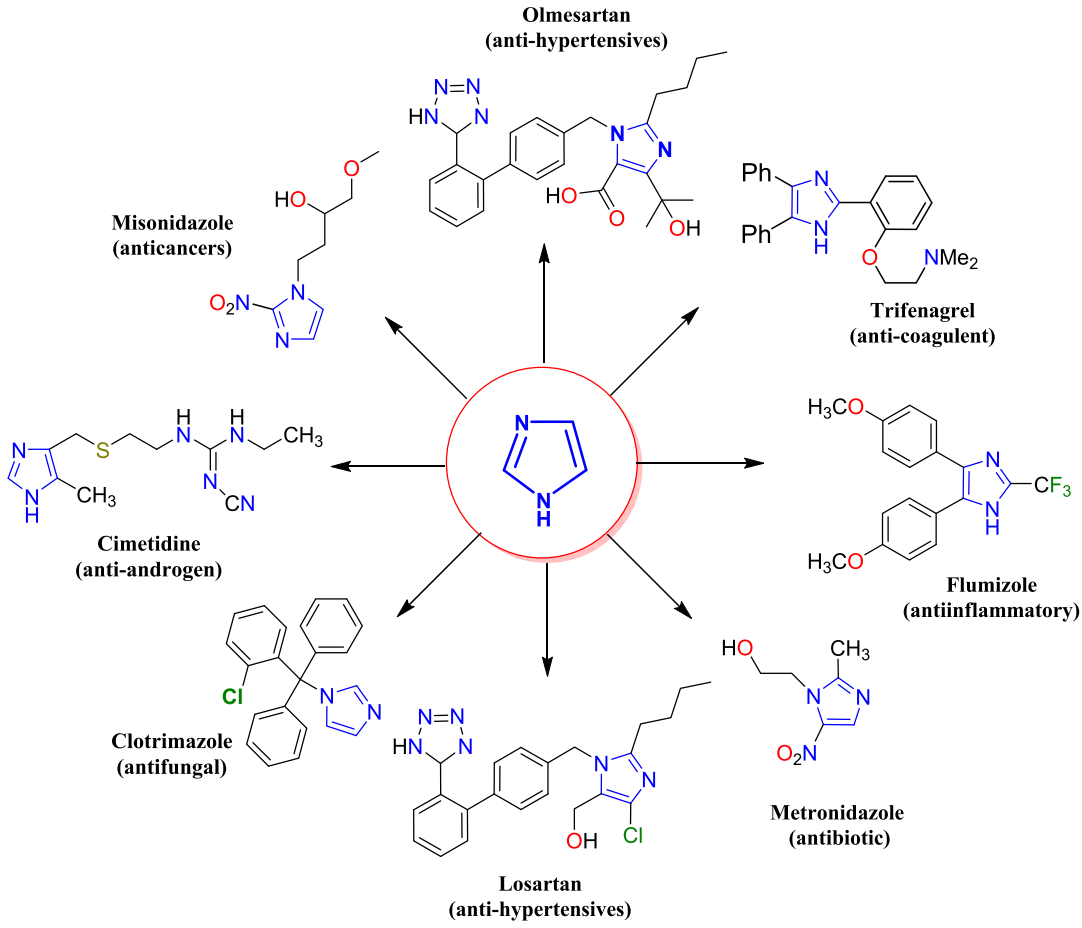


Figure 1. Drugs based on functionalized imidazole ring.

metals, high temperature, complex work-up procedures, and tedious purification steps. Therefore, the development of a simple, efficient, rapid, and high-yield and environmentally benign approach is required for the synthesis of this type of heterocyclic compounds.

In recent years, the development of new synthetic methods and straightforward protocol such as microwave-assisted synthesis using new and more efficient reagents for the synthesis of functionalized heterocycles is becoming more attractive. Microwave-assisted organic synthesis is a sustainable and economically acceptable synthetic tool for the preparation of functionalized *N*-heterocycles (*18–23*), Application of microwave technology in synthetic chemistry helps to the reduction in reaction time, increased in product yields, cleaner reaction, milder conditions, and suppression of unwanted byproducts formation (*19*).

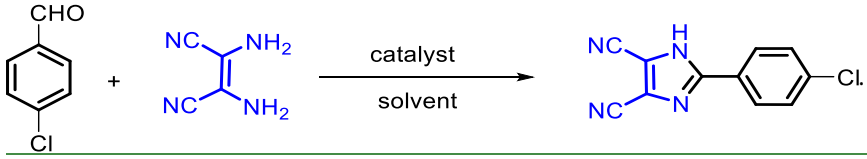
On the other hand, nitric acid is a key starting material in organic synthesis and analytical chemistry such as a precursor for nitration of organic compounds (*24*), a strong oxidizing agent (*25*), and an effective catalyst in catalytic processes (*26,27*). Also, it is an analytical reagent for determining metal trace in solutions (*28*), the production of fertilizers, helping to boost the arability and yield of farmland (*29*). Moreover, HNO_3 is used as a cleaning agent such as etching in printmaking, pickling stainless steel or cleaning silicon wafers in electronics (*30*). However, HNO_3 has not yet been used as a catalyst in the oxidative production of heterocycles under microwave irradiations.

By considering these facts and in our further research efforts for planning on easy synthesis of heterocyclic compounds (*31,32*), we now report HNO_3-catalyzed, efficient and time-saving one-pot protocol for the synthesis of 2-aryl-4,5-dicarbonitrile imidazoles from aromatic aldehydes and 2,3-diaminomaleonitrile using microwave heating technique.

Result and discussion

In the present work, we have reported a simple and rapid HNO_3-catalyzed and microwave-assisted synthesis of 2-aryl-4,5-dicarbonitriles. To optimize this procedure, *p*-chlorobenzaldehyde and 2,3-diaminomaleonitrile were selected as a model reaction. Different reaction conditions were evaluated and the results are

Table 1. Optimization of reaction conditions for **3c**.



Entry	Catalyst loading(equiv.) HNO_3	CAN	Solvent	Temperature (°C)	Power (W)	Time (min)	Yield (%)[a]
1	–	0.4	CH_3CN	70	600	20	–[b]
2	1	0.1	CH_3CN	70	600	7	90
3	1	0.05	CH_3CN	70	600	5	78
4	1	0.05	CH_3CN	70	600	7	90
5	1	0.03	CH_3CN	70	600	7	53
6	1	0.05	–	70	600	7	47
7	0.5	0.05	CH_3CN	70	600	7	73
8	APS (0.1)[c]	0.05	CH_3CN	70	600	20	–
9	H_2O_2 (1)	0.05	CH_3CN	70	600	20	–
10	H_2O_2 (1)	–	CH_3CN	90	600	20	–
11	1	–	CH_3CN	70	600	7	89
12	2	–	CH_3CN	70	600	7	57
13	1.5	–	CH_3CN	70	600	7	65
14	0.5	–	CH_3CN	70	600	7	70
15	1	–	CH_3CN	70	600	7	89
16	1	–	CH_3CN	70	600	7	75
17	**1**	–	**CH_3CN**	**70**	**500**	**5**	**89**
18	1	–	CH_3CN	70	400	5	78
19	1	–	CH_3CN	60	500	5	80
20	1	–	CH_3CN	80	500	5	89
21	1	–	EtOH	70	500	5	–
22	1	0.05	EtOH	70	500	20	–
23	1	–	CH_3CN	90	–	30	–[d]
24	1	–	CH_3CN	80	–	60	–

[a]Isolated yield.
[b]The product was Schiff base
[c]Ammonium per sulfate
[d]The reaction was performed under refluxing, but no pure product was obtained.

summarized in Table 1. For the first step, according to the results obtained in previous research (*15*), we examined the effect of CAN as a catalyst on the progress of the reaction at 70°C under microwave heating (600 W) and in MeCN solvent. But the isolated product was Schiff base in one-step reaction and imidazole was not produced (Table 1, entry 1). It was considered the necessity of using an oxidant in the presence of CAN for the synthesis of imidazole. Therefore, different amounts of HNO_3/CAN were investigated under similar condition and 1/0.05 eq. of catalyst led to the expected product **3c** in 90% yield in 7 min' (Table 1, entry 4). When the model reaction was carried out with H_2O_2 or $(NH_4)_2S_2O_8$, the catalytic process was not successful (Table 1, entries 8–10). Interestingly, the reaction showed admirable results in the presence of nitric acid without CAN under similar condition, because 89% yield of the product was obtained during 7 min (Table 1, entry 15). The removal of CAN (as a transition metal containing compound) compared to the previously reported method (*15*), was an effective step in the application of the principles of green chemistry for the preparation of dicyano imidazoles. Microwave technique could be another important goal of this research towards the goals of green chemistry. Because it was a key stage to reduce the reaction time and increase the yield. In order to show the effect of the power of microwave irradiation, the model reaction was conducted using different powers. According to the results, 500 W was chosen as the optimized power for the synthesis of substituted imidazole derivatives in 5 min (Table 1, entry 17). We continued our studies by examining the effect of temperature on the product yield in the model reaction using microwave irradiation. At 70°C the yield of the product increased while reaction time decreased (Table 1, entry 17). The reaction was not successful in ethanol solvent (Table 1, entries 21 and 22). To investigate the effect of using microwave irradiation as the source of energy on this chemical transformation, the model reaction was carried out in conventional heating under optimized reaction condition. But no pure product was obtained (Table 1, entry 23). The possibility of employing milder and less toxic reagents offers a further advantage of using this heating technology. Therefore, preparation of the **3c** imidazole with microwave heating was technically faster, simpler, and higher in yield than previous routes.

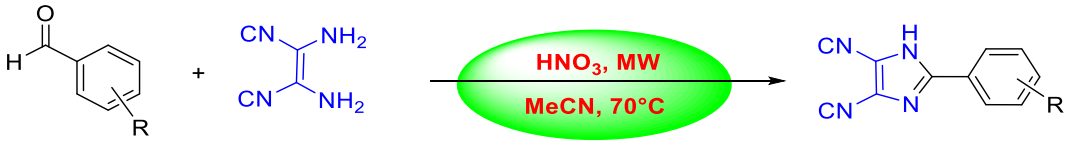


Figure 2. HNO_3 catalyzed synthesis of dicyano imidazoles under microwave irradiation.

To generalize the current method for the synthesis of dicyano midazoles, we evaluated the reaction of a series of aldehydes with diaminomaleonitrile in presence of microwave irradiation under optimal conditions (Figure 2).

The obtained results are summarized in Table 2. The reaction proceeded smoothly for a wide spectrum of aromatic aldehydes bearing substituent with varied electronic nature and the dicyano midazoles were obtained in moderate to excellent yields with high purity.

A plausible mechanism for the synthesis of dicyano imidazoles catalyzed by HNO_3 under microwave irradiation is suggested in Figure 3. HNO_3 is an oxidant as well as Brønsted acid catalyst in the synthesis of Schiff base. Furthermore, HNO_3 can act as a highly active oxidant in an oxidative process for closing the imidazole ring (*33*). The current method had been previously reported in a one-pot, two-step reaction with an excess CAN (0.45 equiv.) as the reagent (*15*). But microwave metal-free activated procedure has been carried out successfully using HNO_3 as an oxidant by one-step approach.

All synthesized compounds have been known and were identified using FT-IR, NMR, and Mass spectroscopy and by comparison with their authentic samples (*8,12,13,15,16*). In the ^{1}H NMR spectra of compounds **3a-p**, the absence of the $-NH_2$ resonance and the appearance of a broad singlet in the 12.44–14.62 ppm regions, related to the resonance of the imidazole ring –NH group, supports the formation of the product. However, the proton (NH) on the position of the imidazole ring was not observed in the spectrum of some synthesized imidazoles, probably due to the effect of exchange of this acidic proton with the deuterium of small amounts of D_2O, which is present in DMSO-d_6, used as a solvent (*34*). The other spectral data appeared in regions expected, which confirm the predicted structures of the products.

Table 3 summarizes a comparison of reaction conditions, substrates used, and percentage yields of all previous methods with the results in the present work. A glancing look at the table reveals that the present synthetic method, compared to previous methods, has outstanding advantages such as a very short reaction time and high yield with microwave technique. Therefore, it can be the best synthetic green approach for the synthesis of 2-aryl diciano imidazoles, which have been obtained so far under other difficult conditions.

Experimental

Materials and apparatus

All chemical reagents in high purity (commercial grade) were purchased from the Merck Chemical Company. Melting points were determined in open capillaries using an electro-thermal digital melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker spectrometer (400 or 500 MHz). NMR spectra were obtained in DMSO-d_6 solution and are reported as parts per million (ppm) downfield from Me_4Si as internal standard. FT-IR spectra were obtained with potassium bromide pellets in the range 400–4000 cm^{-1} with a JASCO 4200-A spectrometer. A mass spectrum was recorded by an Agilent model: 5975C VL MSD with a Triple-Axis detector spectrometer at 70 eV. The reaction was performed in a microwave oven (Flex-iWAVE, Milestone) equipped with a temperature controller.

Microwave-assisted synthesis of dicyano imidazoles

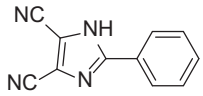
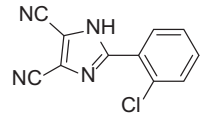
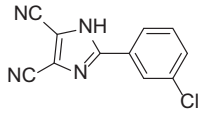
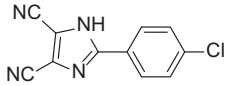
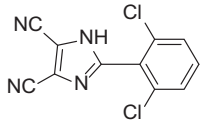
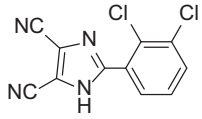
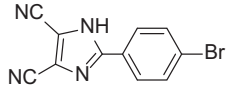
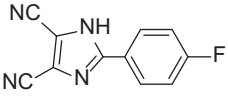
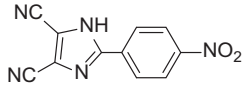
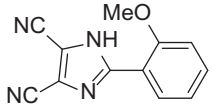
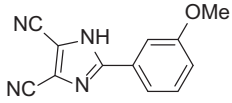
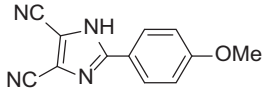
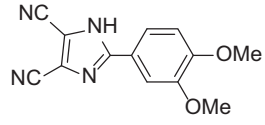
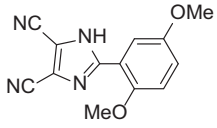
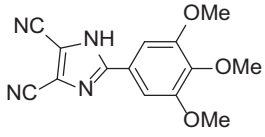
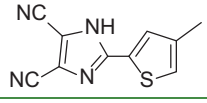
Aromatic aldehyde (0.5 mmol), 2,3-diaminomaleonitrile (0.5 mmol), and HNO_3 (1 equiv.) and acetonitrile (2 mL) were combined into a 50 mL round-bottomed flask and contents were irradiated under microwave for 5–8 min at 70°C and 500 W (Table 2). After completion of the reaction (monitored by TLC; ethyl acetate/*n*-hexane, 2:1), the organic solvent was removed and the crude product was purified by adding the minimum amounts of ethanol and water. Most of the dicyano imidazole products were known and characterized by comparison of their physical (Mp) and spectral data (IR, ^{1}H NMR, and ^{13}C NMR) with those of authentic samples.

Spectral data for the derivatives of dicyano imidazoles

2-Phenyl-1*H*-imidazole-4,5-dicarbonitrile (3a).

FT-IR (KBr) (ν_{max}): 3430 (N–H), 2237 (C≡N), 1637 (C=N), 1458, 1291 (C=C), 1113, 1029, 715 cm^{-1}; ^{1}H NMR

Table 2. Synthesis of dicyano imidazoles catalyzed with HNO_3 under microwave irradiation.

No.	Product	Mp (°C) [b]	Time (min)	Yield (%)[a]
3a		240–242 (220–222)	8	80
3b		203–206 (202–204)	5	85
3c		218–220 (227–228)	8	89
3d		290–292 (288-290)	5	92
3e		232–235 (233–235)	5	88
3f		242–245 (242–245)	5	87
3g		319–321 (316–321)	5	90
3h		213–216 (211–212)	5	85
3i		254 (252–254)	5	92
3j		220–222 (223–225)	5	88
3k		180–182 (173–177)	5	80
3l		230–232 (230–232)	5	90
3m		240 (238–241)	5	80
3n		245–247 (245–248)	5	88
3o		243–245 (243–246)	5	90
3p		228–231 (229–231)	8	80

[a]Isolated yields
[b]Melting points in parentheses are reported in the literature [8, 12, 13,15, 16]

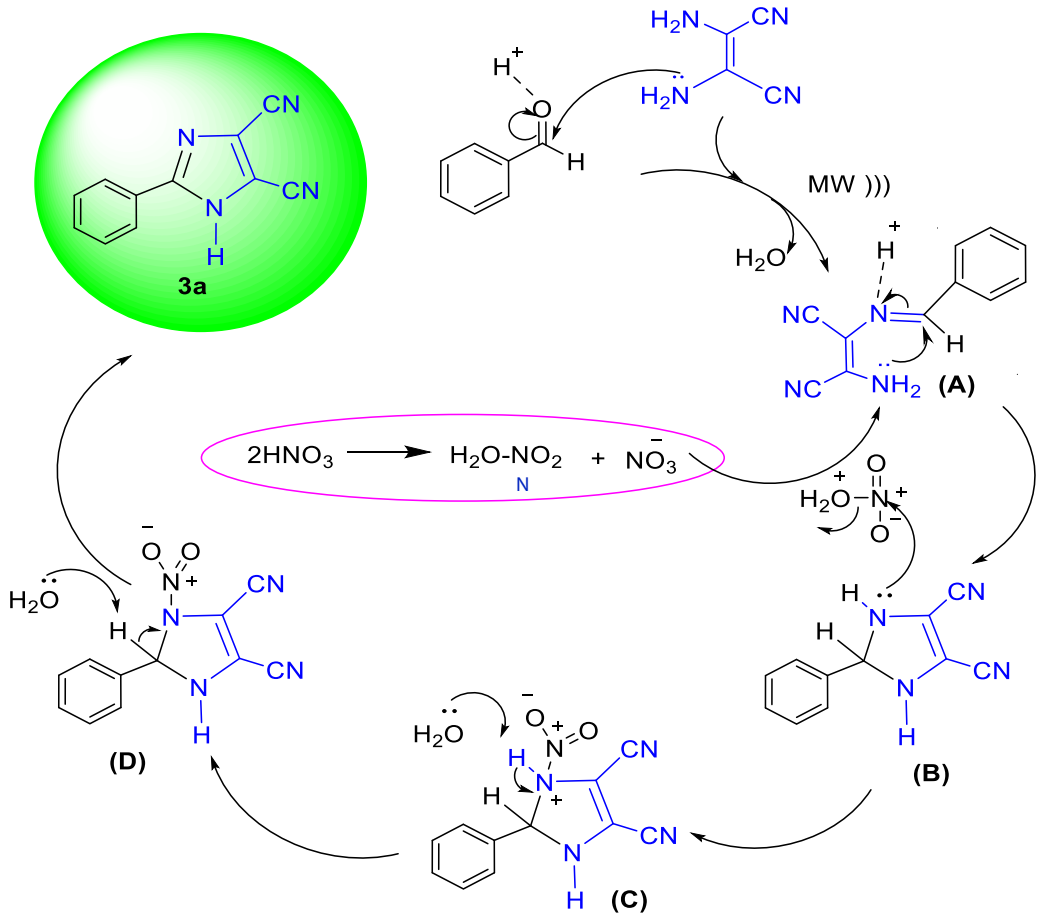


Figure 3. Suggested mechanism for the synthesis of dicyano imidazole by HNO_3.

(400 MHz, DMSO-d_6): δ_H 7.54 (s br, 3H, H-ph), 7.97 (s br, 2H, H-ph) (NH of the imidazole ring was not observed that probably due to the effect of the exchange of this acidic proton with deuterium in small amounts of D_2O, which is present in DMSO-d_6) ppm.

Table 3. Comparison of conditions used for the synthesis of dicyano imidazole **3c**.

Entry	Starting materials	Conditions	Yield (%)[a] (*Ref.*)
1	Schiff base[a]	DDQ[b], MeCN, Reflux for 4 days	33 (*10*)
2	Schiff base	NCS[c], nicotinamide DMF, 40°C, 3h	64[d] (*11*)
3	Schiff base	I_2, AcONa and 1-methyl pyrrolidin-2-one, 100 °C, 24h	59 (*12*)
4	Schiff base	$Pb(OAc)_4$, Benzene, 5–10 °C, overnight	55 (*13*)
5	DAMN, aldehyde	CAN (0.40 eq.), MeCN, 50 °C, 40 min, two-step	84 (*14*)
6	DAMN, aldehyde	CAN/ HNO_3, solvent-free, 120 °C, 15 min, one-step	88 (*16*)
7	DAMN, aldehyde	CAN/HNO_3 (0.05/0.4), MeCN, 70°C, 25 min, one-step	82 (*17*)
8	**DAMN, aldehyde**	**HNO_3 (1 eq.), MWI, MeCN, 70°C, 5 min, one-step**	**89 (This work)**

[a]Schiff bases from condensation of DAMN with aldehydes
[b]2,3-dichloro-5,6-dicyano-1,4-benzoquinone
[c]*N*-chloro-succinimide
[d]The yield of **3b**

2-(2-Chlorophenyl)-1*H*-imidazole-4,5-dicarbonitrile (3b).

FT-IR (KBr) (ν_{max}): 3288 (N–H), 2240 (C≡N), 1655 (C=N), 1223 (C=C), 1121, 786 (C–Cl), 686 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ_H 7.52 (t, J = 7.55 Hz, 1H, H-Ar), 7.58 (t, J = 7.95 Hz, 1H, H-Ar), 7.66 (d, J = 8.05 Hz, 1H, H-Ar), 7.76 (d, J = 7.70 Hz, 1H, H-Ar), (NH of the imidazole ring was not observed that probably due to the effect of exchange of this acidic proton with deuterium in small amounts of D_2O, which is present in DMSO-d_6) ppm; EIMS (*m/z*, %): 228 (M^+, 100), 201 (7), 193 (12), 149 (15), 123 (18), 114 (25), 102 (20), 75 (21), 53 (24).

2-(3-Chlorophenyl)-1*H*-imidazole-4,5-dicarbonitrile (3c).

FT-IR (KBr) (ν_{max}): 3436, 3179 (N-H), 3090 (C–H), 2261, 2234 (C≡N), 1644 (C=N), 1466 (C=C), 1120, 799 (C-Cl), 725 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ_H 7.57 (d, J = 7.55 Hz, 2H, H-Ar), 7.91 (d, J = 6.85 Hz, 1H, H-Ar), 7.98 (s, ^1H, H-Ar), (NH of the imidazole ring was not observed that probably due to the effect of the exchange of this acidic proton with deuterium in small amounts of D_2O, which is present in DMSO-d_6) ppm.

2-(4-Chlorophenyl)-1*H*-imidazole-4,5-dicarbonitrile (3d).

FT-IR (KBr) (ν_{max}): 3447, 3176 (N-H), 3098 (C–H), 2260, 2232 (C≡N),1606 (C=N), 1481, 1092, 843 (C–Cl) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 7.61 (d, $J = 8.00$ Hz, 2H, H-Ar), 7.95 (d, $J = 8.00$ Hz, 2H, H-Ar) ppm.

2-(2,6-Dichlorophenyl)-1*H*-imidazole-4,5-dicarbonitrile (3e).

FT-IR (KBr) (ν_{max}): 3220 (N-H), 3097 (C–H), 2252, 2236 (C≡N), 1585 (C=N), 1434, 1383, 1196 (C=C), 701 (C-Cl) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 7.61 (m, 3H, H-Ar) ppm.

2-(2,3-Dichlorophenyl)-1*H*-imidazole-4,5-dicarbonitrile (3f).

FT-IR (KBr) (ν_{max}): 3289 (N-H), 2240 (C≡N), 1651 (C=N), 1541, 1506, 1446, 1417, 1308, 1237 (C=C), 1193, 1156, 1135, 1083, 1055, 975, 804 (C–Cl), 710, 500 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ_H 7.54 (t, $J = 7.92$ Hz, 1H, H-Ar), 7.72 (d, $J = 7.65$ Hz, 1H, H-Ar), 7.86 (d, $J = 8.00$ Hz, 1H, H-Ar) ppm, (NH of the imidazole ring was exchanged with D_2O); ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 111.1, 115.8, 128.6, 129.4, 130.1, 130.7, 132.7, 133.0, 148.1 ppm; EIMS (m/z, %): 263 (M^+, 80), 262 (100), 227 (22), 192 (12), 183, 157 (15), 148 (20), 87 (18), 53 (28).

2-(4-Bromophenyl)-1*H*-imidazole-4,5-dicarbonitrile (3 g).

FT-IR (KBr) (ν_{max}): 3442, 3171 (N-H), 3093 (C–H), 2258, 2234 (C≡N), 1600 (C=N), 1557, 1540, 1473, 1424 (C=C), 1010, 832 (C–Br), 728, 577 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ_H 7.77 (d, $J = 8.40$ Hz, 2H, H-Ar), 7.92 (d, $J = 8.40$ Hz, 2H, H-Ar) ppm, (NH of the imidazole ring was exchanged with D_2O).

2-(4-Fluorophenyl)-1*H*-imidazole-4,5-dicarbonitrile (3 h).

FT-IR (KBr) (ν_{max}): 3433, 3196 (N–H), 3117 (C–H), 2256, 2225 (C≡N), 1610 (C=N), 1487, 1433, 1398, 1237 (C=C), 1161 (C–N), 1108 (C-F), 960, 844, 735, 529 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 7.38 (t, $J = 8.78$ Hz, 2H, H-Ar), 8.00 (dd, $J_1 = 5.39$ Hz, $J_2 = 3.19$ Hz, 2H, H-Ar) ppm, (NH of the imidazole ring was exchanged with D_2O).

2-(4-Nitrophenyl)-1*H*-imidazole-4,5-dicarbonitrile (3i).

FT-IR (KBr) (ν_{max}): 3447 (N-H), 2232 (C≡N), 1605 (C=N), 1518, 1348 (NO_2), 1475 (C=C), 1112, 860, 716 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 8.20 (d, $J = 8.40$ Hz, 2H, H-Ar), 8.33 (d, $J = 8.40$ Hz, 2H, H-Ar) ppm; EIMS (*m/z*, %): 239 (M^+, 100), 209 (44), 181 (54), 139, 102 (19), 75 (15), 50 (25).

2-(2-Methoxyphenyl)-1*H*-imidazole-4,5-dicarbonitrile (3j).

FT-IR (KBr) (ν_{max}): 3276 (N-H), 2238 (C≡N), 1603 (C=N), 1475 (C=C) 1247 (C–O), 1209 (C–O), 1091,1021, 749 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 3.25 (s, 3H, OMe), 7.08 (t, $J = 4.40$ Hz, 1H, H-Ar), 7.22 (d, $J = 5.20$ Hz, 1H, H-Ar), 7.50 (d, $J = 5.60$ Hz, 1H, H-Ar), 8.04 (d, $J = 6.00$ Hz, 1H, H-Ar), 13.72 (br, 1H, NH), ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 55.7 (OMe), 111.1, 112.1, 115.3, 119.1, 121.0, 129.4, 132.6, 147.9 (C=N), 156.5 (C–O) ppm.

2-(3-Methoxyphenyl)-1*H*-imidazole-4,5-dicarbonitrile (3k).

FT-IR (KBr) (ν_{max}): 3546 (N-H), 2243 (C≡N), 1585 (C=N) 1237, 1046 (C–O), 739 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 3.38 (s, 3H, OMe), 7.07 (s, 1H, H-Ar), 7.26-7.95 (m, 3H, H-Ar) ppm.

2-(4-Methoxyphenyl)-1*H*-imidazole-4,5-dicarbonitrile (3 l).

FT-IR (KBr) (ν_{max}): 3186 (N-H), 3114, 2938 (C–H), 2260, 2226 (C≡N), 1613 (C=N), 1490, 1440, 1398, 1303 (C=C), 1257, 1180 (C–O), 1028, 840, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 3.88 (s, 3H, OMe), 6.99 (d, $J = 8.40$ Hz, 2H, H-Ar), 7.88 (d, $J = 8.40$ Hz, 2H, H-Ar), 12.44 (s, 1H, NH) ppm; ^1H NMR (400 MHz, DMSO-d_6): δ_H 3.81 (s, 3H, OMe), 7.08 (d, $J = 8.40$ Hz, 2H, H-Ar), 7.90 (d, $J = 8.40$ Hz, 2H, H-Ar) ppm.

2-(3,4-Dimethoxyphenyl)-1*H*-imidazole-4,5-dicarbonitrile **(3 m).**

FT-IR (KBr) (ν_{max}): 3546, 3199 (N-H), 2240 (C≡N), 1607 (C=N), 1498, 1447, 1406 (C=C), 1261, 1132, 1017 (C–O), 844, 733 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 3.75 (s, 3H, OMe), 3.81 (s, 3H, OMe), 7.10 (m, 1H, H-Ar), 7.52 (d br, 2H, H-Ar), 14.62 (br, 1H, NH) ppm; EIMS (m/z, %): 254.3 (M^+, 100), 238.2 (26), 211.2 (42), 168.2 (23), 103.1 (6), 63.1 (12).

2-(2,5-Dimethoxyphenyl)-1*H*-imidazole-4,5-dicarbonitrile (3n).

FT-IR (KBr) (ν_{max}): 3277 (N–H), 2234 (C≡N), 1591 (C=N), 1543, 1490, 1438, 1307 (C=C), 1281, 1196 (C–O), 1171, 1146 (O-Me), 1084, 1042, 1018, 811, 743 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ_H 3.78 (s, 3H, OMe), 3.92 (s, 3H, OMe), 7.10 (dd, $J_1 = 2.90$ Hz, $J_2 = 6.15$ Hz, 1H, H–Ar), 7.17 (d, $J = 9.05$ Hz, 1H, H–Ar), 7.56 (d, $J = 2.80$ Hz, 1H, H–Ar), 13.72 (br, 1H, NH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ_C 55.6, 56.0 (OMe), 111.3 (2C), 113.3, 115.6, 118.5 (2C), 147.9, 150.9, 153.1 ppm; EIMS (m/z, %): 254 (M^+, 100), 239 (45), 236 (90), 221 (35), 211 (25), 202 (18), 181 (21), 168 (27), 142 (14), 53 (10).

2-(3,4,5-Tri methoxyphenyl)-1*H*-imidazole-4,5-dicarbonitrile **(3o).**

FT-IR (KBr) (ν_{max}): 3462, 3297 (N–H), 2940 (C–H), 2230, 2208 (C≡N), 1614 (C=N), 1585, 1508, 1382, 1330 (C=C), 1242, 1128 (C–O), 989 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 3.71 (s, 3H, OMe), 3.83 (s, 6H, OMe), 7.25 (d, $J = 1.58$ Hz, 2H, H-Ar), ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ_C 56.0, 60.2 (OMe), 103.6, 111.2, 122.5, 139.6, 145.4, 150.6, 153.3 (C–O) ppm.

2-(4-Methylthiophen-2-yl)-1*H*-imidazole-4,5-dicarbonitrile (3p).

FT-IR (KBr) (ν_{max}): 3462, 3187, 3156 (NH), 3118, 2925 (C–H), 2260, 2226 (C≡N), 1601 (C=N), 1513, 1446, 1309

(C=C), 1088 (C–S), 925, 807, 716 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ_H 2.49 (s, 3H, Me), 6.92 (s, 1H, H-Ar), 7.52 (d, J = 3.20 Hz, 1H, H-Ar) ppm; EIMS (m/z, %): 214.1 (M^+, 100), 169.1 (24), 122.1 (12), 69.1 (16).

Conclusion

In summary, we developed a general and green microwave-assisted synthesis of dicyano imidazoles promoted by HNO_3 as a high efficient promoter and a robust metal-free catalyst under mild conditions. The higher environmental sustainability and compatibility factors such as very short reaction time, the use of microwave irradiation, the economy of steps, transition metal-free conditions, available starting materials, and easy isolation and purification of the product along with satisfactory yields make the present methodology a greener process for the synthesis of dicyano imidazoles compared to previously reported methods. The use of this green method opens the window to unique opportunities for the synthesis of heterocyclic compounds with diverse applications, which is not easily achievable *via* other synthesis techniques.

Supporting information

Supporting Information is available on the publisher's website along with the article.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

References

[1] (a) Xie, L.Y.; Qu, J.; Peng, S.; Liu, K.J.; Wang, Z.; Ding, M.H.; Wang, Y.; Cao, Z.; He, W.M. Selectfluor-mediated Regioselective Nucleophilic Functionalization of N-Heterocycles Under Metal- and Base-free Conditions. *Green Chem*. **2018**, *20* (3), 760–764. (b) Charris-Molina, A.; Castillo, J.C.; Macías, M.; Portilla, J. One-step synthesis of fully functionalized pyrazolo[3,4-b]pyridines via isobenzofuranone ring opening, *J. Org. Chem*. **2017**, *82* (23), 12674−12681.

[2] Ali, I.; Lone, M.N.; Aboul-Enein, H.Y. Imidazoles as Potential Anticancer Agents. *Med. Chem. Commun* **2017**, *8* (9), 1742–1773.

[3] Khalid, M.H.; Tokunaga, Y.; Caputy, A.J.; Walters, E. Inhibition of Tumor Growth and Prolonged Survival of Rats with Intracranial Gliomas Following Administration of Clotrimazole. *J. Neurosurg* **2005**, *103* (1), 79–86.

[4] Shargel, L.; Mutnick, A.H.; Souney, P.F.; Swanson, L.N. Comprehensive Pharmacy Review (7th ed.), Lippincott Williams & Wilkins, 2009.

[5] Allahvirdinesbat, M.; Fozi, M.; Safa, K.D.; Alyari, M.; Nakhostin Panahi, P.; Niaei, A. Synthesis of Silyl-Protected Terminal Thioalkyne-substituted Tetraaryl Imidazoles: Utilization of Ag–Fe/ZSM-5 Bimetallic Nanooxides for Cyclocondensation of Polysubstituted Imidazoles. *Res. Chem. Intermed*. **2017**, *43* (4), 2653–2668.

[6] Zarnegar, Z.; Safari, J. Fe_3O_4@Chitosan Nanoparticles: A Valuable Heterogeneous Nanocatalyst for the Synthesis of 2,4,5-Trisubstituted Imidazoles. *RSC Adv*. **2014,** *4* (40), 20932–20939.

[7] Amirfirouzkouhi, H.; Nemati Kharat, A. Application of Ionic Liquids as Recyclable Green Catalysts for Selective Alkylation of Phenol. *Sep. Purif. Technol* **2018,** *196*, 132–139.

[8] Wittine Karlo, Stipković Babić Maja, Makuc Damjan, Plavec Janez, Kraljević Pavelić Sandra, Sedić Mirela, Pavelić Krešimir, Leyssen Pieter, Neyts Johan, Balzarini Jan, Mintas Mladen Novel 1,2,4-Triazole and Imidazole Derivatives of l-Ascorbic and Imino-ascorbic Acid: Synthesis, Anti-HCV and Antitumor Activity Evaluations. *Bioorg. Med. Chem*. **2012,** *20* (11), 3675–3685.

[9] Nepras, M.; Almonasy, N.; Bures, F.; Kulhánek, J.; Dvořák, M.; Michl, M. Fluorescence and Photophysical Properties of D-π-A Push-Pull Systems Featuring a 4,5-Dicyanoimidazole Unit. *Dyes Pigments* **2011**, *91* (3), 466–473.

[10] Woodward, D.W.; US. Patent 2534331, 1950.

[11] Begland, R.W.; Hartter, D.R.; Jones, F.N.; Sam, D.J.; Sheppard, W.A.; Webster, O.W.; Weigert, F.J. Hydrogen Cyanide Chemistry. VIII. New Chemistry of Diaminomaleonitrile: Heterocyclic Synthesis. *J. Org. Chem* **1974,** *39* (16), 2341–2350.

[12] Moriya, O.; Minamide, H.; Urata, Y. A Convenient Synthesis of 2-Aryl-4,5-Dicyanoimidazoles and -Imidazolines from Diaminomaleonitrile. *Synthesis. (Mass)* **1984,** *12*, 1057–1058.

[13] Feldwick, G.A.; Hatton, L.R.; Hewett, R.H.; Pedgrift, B.L. EP0269238, 1988.

[14] Patel, N.R.; Kans, S.M. US4220466, 1980.

[15] Kalhor, M.; Seyedzade, Z. Rapid Synthesis of 2-Amino Maleonitrile Schiff Bases in Aqueous Media Catalyzed by Cerium(IV) Ammonium Nitrate (Can) and a New Method for the One-pot Preparation of Their Dicyano Imidazoles (DCI). *Res. Chem. Intermed* **2017**, *43* (5), 3349–3360.

[16] Kalhor, M.; Seyedzade, Z.; Zarnegar, Z. $(NH_4)_2Ce(NO_3)_6$/HNO_3 as a High-performance Oxidation Catalyst for the one-Step, Solvent-free Synthesis of Dicyano Imidazoles. *Polycycl. Aromat. Compd* **2019**, 1–9. DOI:10.1080/10406638.2019.1686402.

[17] Kalhor, M.; Seyedzade, Z. One-step Synthesis of Dicyano Imidazoles by $(NH_4)_2Ce(NO_3)_6$/HNO_3 Promoted Oxidative Cyclocondensation of an Aldehyde and 2,3-Diaminomaleonitrile. *Iran. J. Chem. Chem. Eng* **2020**, *39* (6), 1–8.

[18] Wolkenberg, S.E.; Wisnoski, D.D.; Leister, W.H.; Wang, Y.; Zhao, Z.; Lindsley, C.W. Efficient Synthesis of Imidazoles from Aldehydes and 1,2-Diketones Using Microwave Irradiation. *Org. Lett* **2004**, *6* (9), 1453–1456.

[19] Gawande, M.B.; Shelke, S.N.; Zboril, R.; Varma, R.S. Microwave-assisted Chemistry: Synthetic Applications

for Rapid Assembly of Nanomaterials and Organics. *Acc. Chem. Res* **2014**, *47* (4), 1338–1348.
[20] Shi, F.; Li, C.M.; Xia, M.; Miao, K.J.; Zhao, Y.X.; Tu, S.J.; Zheng, W.F.; Zhang, G.; Ma, N. Green Chemoselective Synthesis of Thiazolo[3,2-a]Pyridine Derivatives and Evaluation of Their Antioxidant and Cytotoxic Activities. *Bioorg. Med. Chem. Lett* **2009**, *19* (19), 5565–5568.
[21] Padmaja, R.D.; Meena, D.R.; Maiti, B.; Chanda, K. [Cu(Phen)$(PPh_3)_2$]NO_3-Catalyzed Microwave-assisted Green Synthesis of 5-Substituted 1*H*-Tetrazoles. *Res. Chem. Intermed* **2017**, *43* (12), 7365–7374.
[22] Vaddula, B.R.; Varma, R.S.; Leazer, J. Mixing with Microwaves: Solvent-free and Catalyst-free Synthesis of Pyrazoles and Diazepines. *Tetrahedron Lett.* **2013**, *54* (12), 1538–1541.
[23] Safari, J.; Zarnegar, Z. Magnetic Nanoparticles Supported Imidazolium-based Ionic Liquids as Nanocatalyst in Microwave-Mediated Solvent-free Biginelli Reaction. *J. Nanopart. Res* **2014**, *16* (8), 2509–2514.
[24] Sheremetev, A.B.; Aleksandrova, N.S.; Suponitsky, K.Y.; Antipin, M.Y.; Tartakovsky, V.A. One-pot Synthesis of 4,6,8-Trinitro-4,5,7,8-Tetrahydro-6H-Furazano[3,4-f]-1,3,5-Triazepine in Ionic Liquids. *Mendeleev Commun.* **2010,** *20* (5), 249–252.
[25] Wang, J.Z.; Wang, L.Q.; Chen, M.M.; Wang, C.Y.; Zhang, C.; He, F. Nanoporous Carbons from Oxidized Green Needle Coke for use in High Performance Supercapacitors. *New Carbon Mater.* **2015**, *30* (2), 141–149.
[26] Muralidharan, P.; Venkateswarlu, M.; Satyanarayana, N. AC Conductivity Studies of Lithium Borosilicate Glasses: Synthesized by Sol–gel Process with Various Concentrations of Nitric Acid as a Catalyst. *Mater. Chem. Physic* **2004**, *88* (1), 138–144.
[27] Joo, H.W.; Kim, Y.J.; Park, J.; Chang, Y.K. Hydrolysis of Golenkinia sp. Biomass Using Amberlyst 36 and Nitric Acid as Catalysts. *Algal. Res.* **2017,** *25*, 32–38.
[28] Clesceri, L.S.; Greenberg, A.E.; Eaton, A.D. *Standard Methods for the Examination of Water and Wastewater* (20th ed.); American Public Health Association, American Water Works Association, Water Environment Federation: Washington, DC, 1998.
[29] Thiemann, M.; Scheibler, E.; Wiegand, K.W. *Nitric Acid, Nitrous Acid, and Nitrogen Oxides. Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH: Weinheim, 2000.
[30] O'Neal, C.L.; Crouch, D.J.; Fatah, A.A. Validation of Twelve Chemical Spot Tests for the Detection of Drugs of Abuse. *Forensic Sci. Int* **2000,** *109* (3), 189–201.
[31] Kalhor, M.; Banibairami, S.; Mirshokraie, S.A. Ni@Zeolite-Y Nanoporous; a Valuable and Efficient Nanocatalyst for the Synthesis of *N*-Benzimidazole-1,3-Thiazolidinones. *Green Chem. Lett. Rev* **2018**, *11* (3), 334–344.
[32] Kalhor, M.; Zarnegar, Z.N. Fe_3O_4/SO_3H@Zeolite-Y as a Novel Multi-functional and Magnetic Nanocatalyst for Clean and Soft Synthesis of Imidazole and Perimidine Derivatives. *RSC Adv.* **2019**, *9*, 19333–19346.
[33] Dingas, S.; Suriboot, J. *Multistep Reaction Sequence Benzaldehyde to Benzilic Acid*; General Chemistry Labs. https://www.odinity.com/multistep-reaction-sequence-benzaldehyde-benzilic-acid.
[34] Vaughan, J.D.; Mughrabi, Z.; Wu, E.C. Kinetics of Deuteration of Imidazole. *J. Org. Chem* **1970**, *35* (4), 1141–1145.