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An efficient method for the catalyst-free one-pot green synthesis of 2,4,5-trisubstituted imidazoles in water

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KEYWORDS
2,4,5-Trisubstituted imidazoles;
Diammonium hydrogen phosphate;
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Three-component.

Abstract. A mild, efficient and environmentally friendly method has been developed for the green synthesis of 2,4,5-trisubstituted imidazoles via a three-component one-pot condensation of 1,2-diketones, diammonium hydrogen phosphate, $(NH_4)_2HPO_4$ (DAHP) and aryl aldehydes in water under reflux conditions. The DAHP shows remarkable activities for the synthesis of title compounds. The key advantages of this method over conventional methods are experimental simplicity, good functional group tolerance, excellent yields, short routine, and selectivity, without the need for a transition metal or base catalyst.

1. Introduction

A multicomponent reaction (MCR) is generally defined as any process in which three or more reactants combine in one-pot to form a product that incorporates the structural features of each reagent [1-3].

Multisubstituted imidazoles are of considerable interest, as they possess a wide range of biological properties [4], such as antitumor [5], anti-inflammatory [6,7], anti-allergic [8], analgesic [9], and antibacterial [10] activities. Because of their great importance, many synthetic methods have been developed [11-15]. Recently, one-pot condensations of an aldehyde and ammonium acetate with an α-hydroxy ketone, an α-keto-oxime and a 1,2-diketone have been achieved using various catalysts, such as protic acids [16-20], Lewis acids [21-23], ionic liquids [24-27] and other catalysts [28-37]. Despite their potential utility, most of these methods are not environmentally friendly. They require a high temperature (180-200°C), organic solvents and toxic catalysts.

In recent years, organic synthesis in green solvents, such as water, has become a powerful tool for the generation of structurally diverse molecules. Compared with organic solvents, water has advantages, such as low cost, safety and environmental friendliness [38]. Diammonium hydrogen phosphate (DAHP) is an inexpensive, water-soluble, non-toxic and commercially available compound that can be used in the laboratory without special precautions [39]. This reagent has been used in important manufacturing processes, such as fire-proofing textiles, paper, wood and vegetable fibres [40,41]. There are a few reports regarding the application of DAHP in the preparation of organic compounds, for example, in the synthesis of dihydropyrimidinones [42], alkenes [43], 1,8-dioxo-octahydroxanthenes [44], tetrahydrobenzo[*b*]pyranes [45], 3,4-dihydropyrano[*c*]chromene [46], and 2-aminothiazole [47]. Due to the biological activities of multisubstituted imidazoles [48] and the significant number of compounds containing this moiety [49], we describe our very simple, green and efficient route to the synthesis of 2,4,5-trisubstituted imidazoles, using

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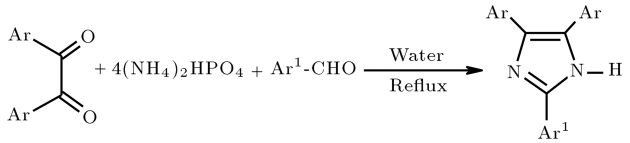


1a-c **2** **3a-m** **1-29**

Scheme 1. Green synthesis of 2,4,5-trisubstituted imidazoles by using DAHP in water.

DAHP as the source of ammonia in water, under reflux conditions, without using any catalyst (Scheme 1). To the best of our knowledge, there has been no example of the use of DAHP as a reagent for the synthesis of 2,4,5-trisubstituted imidazoles.

2. Experimental

Chemical reagents were purchased from the Merck Chemical Company in high purity. All materials were of commercial reagent grade. Melting points were determined in open capillaries using an Electrothermal Mk3 apparatus and are uncorrected. Infrared (IR) spectra were recorded using a Perkin-Elmer FT-IR 550 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker DRX-400 spectrometer at 400 and 100 MHz, respectively. NMR spectra were obtained in dimethylsulfoxide (DMSO-d_6) solutions and are reported as parts per million (ppm) downfield from a tetramethylsilane internal standard. The following abbreviations are used; singlet (s), doublet (d), triplet (t) and multiplet (m). The elemental analyses were performed with an Elementar Analysensysteme GmbH VarioEL CHNS mode.

2.1. General procedure for synthesis of 2,4,5-trisubstituted imidazoles

In a 50 mL round-bottom flask, a mixture of 1,2-diketone (1 mmol), DAHP (4 mmol) and aldehyde (1 mmol) was refluxed in water (20 mL), with stirring for the stipulated time (Table 1). The progress of the reaction was monitored by Thin-Layer Chromatography (TLC). After completion of the reaction, the mixture was cooled to room temperature, filtered and washed with cold water. For further purification, this product was recrystallized from a 9:1 acetone-water solution. Pure products were obtained in good to excellent yields, as summarized in Table 1. Most of the products are known and were identified by comparison of their physical and spectral data with those of authentic samples.

2.2. Spectral data for new derivatives of 2,4,5-trisubstituted imidazoles

3-[4,5-bis(4-methoxyphenyl)-1H-imidazol-2-yl]phenol (16). Cream powder; mp: 230-232°C; IR (cm^{-1}, KBr): 3415 (N-H), 3338 (O-H), 1613 (C=C), 1500 (C=N), 1247 (C-O); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.42 (s, 1H, NH), 9.52 (s, 1H, OH), 7.38-7.49 (m, 6H, Ar-H), 7.23 (t, 1H, J = 8.0 Hz, Ar-H), 7.00 (d, 2H, J = 8.4 Hz, Ar-H), 6.86 (d, 2H, J = 8.4 Hz, Ar-H), 6.74 (dd, 1H, J = 8.0, 2.8 Hz, Ar-H), 3.78 (s, 3H, OMe), 3.73 (s, 3H, OMe) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 159.2, 158.4, 158.0, 145.4, 136.7, 132.2, 130.2, 130.1, 128.6, 128.4, 127.5, 124.0, 116.4, 115.6, 114.5, 114.1, 112.5, 55.6, 55.5 ppm; Anal. Calcd. for $C_{23}H_{20}N_2O_3$ (372.448): C, 74.18; H, 5.41; N, 7.52. Found: C, 74.17; H, 5.40; N, 7.51.

2-(3-methoxyphenyl) -4, 5-bis (4-methoxyphenyl) -1H-imidazole (17). White powder; mp: 234-236°C; IR (cm^{-1}, KBr): 3430 (N-H), 1608 (C=C), 1519 (C=N), 1246 (C-O); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.50 (s, 1H, NH), 7.64 (d, 1H, J = 8.0 Hz, Ar-H), 7.62 (s, 1H, Ar-H), 7.36-7.46 (m, 5H, Ar-H), 7.00 (d, 2H, J = 8.4 Hz, Ar-H), 6.91 (dd, 1H, J = 8.4, 2.2 Hz, Ar-H), 6.87 (d, 2H, J = 8.4 Hz, Ar-H), 3.82 (s, 3H, OMe), 3.79 (s, 3H, OMe), 3.74 (s, 3H, OMe) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 160.0, 159.3, 158.4, 145.2, 136.9, 132.3, 130.3, 130.0, 128.7, 128.3, 127.7, 124.1, 118.0, 115.5, 114.4, 114.3, 110.5, 55.7, 55.6, 55.5 ppm; Anal. Calcd. for $C_{24}H_{22}N_2O_3$ (386.448): C, 74.59; H, 5.74; N, 7.25. Found: C, 74.58; H, 5.73; N, 7.24.

2-(3,5-dimethoxyphenyl) -4, 5-bis (4-methoxyphenyl)-1H-imidazole (18). White powder; mp: 195-197°C; IR (cm^{-1}, KBr): 3420 (N-H), 1604 (C=C), 1519 (C=N), 1248 (C-O); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.50 (s, 1H, NH), 7.45 (d, 2H, J = 7.6 Hz, Ar-H), 7.40 (d, 2H, J = 8.0 Hz, Ar-H), 7.26 (s, 2H, Ar-H), 7.0 (d, 2H, J = 8.0 Hz, Ar-H), 6.87 (d, 2H, J = 8.0 Hz, Ar-H), 6.48 (s, 1H, Ar-H), 3.80 (s, 3H, OMe), 3.79 (s, 3H, OMe), 3.73 (s, 6H, OMe), ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 161.2, 158.9, 158.1, 145.1, 137.0, 134.3, 132.8, 130.1, 128.8, 128.6, 124.0, 114.3, 114.1, 103.4, 100.8, 55.8, 55.7, 55.5 ppm; Anal. Calcd. for $C_{25}H_{24}N_2O_4$ (416.474): C, 72.10; H, 5.81; N, 6.73. Found: C, 72.09; H, 5.80; N, 6.72.

2-(3-nitrophenyl) -4,5-bis (4-methoxy-phenyl)-1H-imidazole (20). Yellow powder; mp: 240-242°C; IR (cm^{-1}, KBr): 3428 (N-H), 1615 (C=C), 1523 (C=N), 1460 (N=O), 1348 (N-O), 1249 (C-O); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.92 (s, 1H, NH), 8.92 (s, 1H, Ar-H), 8.50 (d, 1H, J = 8.2 Hz, Ar-H), 8.20 (d, 1H, J = 8.2 Hz, Ar-H), 7.75 (t, 1H, J = 8.2 Hz, Ar-H), 7.47 (d, 2H, J = 8.4 Hz, Ar-H), 7.43 (d, 2H, J = 8.4 Hz, Ar-H), 7.00 (d, 2H, J = 8.4 Hz, Ar-H), 6.90 (d, 2H, J = 8.4 Hz, Ar-H), 3.80 (s, 3H, OMe), 3.75 (s, 3H, OMe) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 159.4, 158.6, 148.8, 143.1, 137.5, 132.5,

Table 1. One-pot and green synthesis of 2,4,5-trisubstituted imidazoles via condensation of various aromatic aldehydes, 1,2-diketones and DAHP in water.

Entry	Benzil	Ar	Aldehyde	Ar^1	Product	Yield (%)[a]	Time (h)	m.p. (°C)	
								Found	Reported
1	**1a**	C_6H_5	**3a**	C_6H_5	**1**	92	2.0	272-274	272-273[b]
2	**1a**	C_6H_5	**3b**	4-MeO C_6H_4	**2**	97	2.2	228-231	230-232[c]
3	**1a**	C_6H_5	**3c**	3-HO C_6H_4	**3**	95	2.1	258-260	259[d]
4	**1a**	C_6H_5	**3d**	3-MeO C_6H_4	**4**	93	2.1	260-262	259-262[e]
5	**1a**	C_6H_5	**3e**	3,5-$(MeO)_2$ C_6H_3	**5**	93	2.0	256-257	254-256[e]
6	**1a**	C_6H_5	**3f**	4-F C_6H_5	**6**	94	2.0	250-252	251-253[c]
7	**1a**	C_6H_5	**3g**	4-Cl C_6H_4	**7**	94	2.0	260-261	262-264[c]
8	**1a**	C_6H_5	**3h**	3-Br C_6H_4	**8**	92	2.0	300-302	303-304[c]
9	**1a**	C_6H_5	**3i**	3-O_2N C_6H_4	**9**	90	1.8	264-266	265-267[b]
10	**1a**	C_6H_5	**3j**	2-Naphthyl	**10**	94	2.0	272-274	273-276[e]
11	**1a**	C_6H_5	**3k**	2-Furyl	**11**	90	1.6	241-243	242[d]
12	**1a**	C_6H_5	**3l**	3-Pyridyl	**12**	92	1.9	230-232	230-234[c]
13	**1a**	C_6H_5	**3m**	2-Thienyl	**13**	94	1.8	261-263	262-266[c]
14	**1b**	4-MeO C_6H_5	**3a**	C_6H_5	**14**	90	3.0	200-202	201-203[c]
15	**1b**	4-MeO C_6H_5	**3b**	4-MeO C_6H_4	**15**	90	3.3	185-186	183-185[c]
16	**1b**	4-MeO C_6H_5	**3c**	3-HO C_6H_4	**16**	86	3.2	230-232	-
17	**1b**	4-MeO C_6H_5	**3d**	3-MeO C_6H_4	**17**	88	3.2	234-236	-
18	**1b**	4-MeO C_6H_5	**3e**	3,5-$(MeO)_2$ C_6H_3	**18**	89	3.0	195-197	-
19	**1b**	4-MeO C_6H_5	**3h**	3-Br C_6H_4	**19**	87	3.0	250-253	248-251[c]
20	**1b**	4-MeO C_6H_5	**3i**	3-O_2N C_6H_4	**20**	85	2.9	240-242	-
21	**1b**	4-MeO C_6H_5	**3k**	2-Furyl	**21**	83	2.7	164-166	160 dec.[c]
22	**1b**	4-MeO C_6H_5	**3m**	2-Thienyl	**22**	84	2.8	192-194	192-195[c]
23	**1c**	4-F C_6H_5	**3c**	3-HO C_6H_4	**23**	93	1.3	271-273	-
24	**1c**	4-F C_6H_5	**3e**	3,5-$(MeO)_2$ C_6H_3	**24**	95	1.2	224-227	-
25	**1c**	4-F C_6H_5	**3f**	4-F C_6H_5	**25**	97	1.0	246-248	-
26	**1c**	4-F C_6H_5	**3h**	3-Br C_6H_4	**26**	94	1.2	288-290	287-290[e]
27	**1c**	4-F C_6H_5	**3i**	3-O_2N C_6H_4	**27**	92	1.0	303-305	-
28	**1c**	4-F C_6H_5	**3k**	2-Furyl	**28**	90	0.8	268-270	-
29	**1c**	4-F C_6H_5	**3m**	2-Thienyl	**29**	92	1.0	280-282	-

[a]: Isolated yield based on aldehyde; [b]: Ref. [21]; [c]: Ref. [6]; [d]: Ref. [24]; [e]: Ref. [35].

131.4, 130.8, 130.2, 128.8, 128.7, 127.9, 123.5, 122.7, 119.7, 114.6, 114.1, 55.7, 55.5 ppm; Anal. Calcd. for $C_{23}H_{19}N_3O_4$ (401.419): C, 68.82; H, 4.77; N, 10.47. Found: C, 68.81; H, 4.76; N, 10.47.

3-[4,5-bis (4-fluorophenyl) -1H-imidazol-2-yl] phenol (23). Golden crystalline powder; mp: 271-273°C; IR (cm^{-1}, KBr): 3437 (N-H), 3300 (O-H), 1605 (C=C), 1517 (C=N);^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.62 (s, 1H, NH), 9.54 (s, 1H, OH), 7.45-7.58 (m, 6H, Ar-H), 7.30 (t, 2H, J = 7.6 Hz, Ar-H), 7.24 (d, 1H, J = 8.0 Hz, Ar-H), 7.15 (t, 2H, J = 8.3 Hz, Ar-H), 6.78 (d, 1H, J = 8.0 Hz, Ar-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.2 (C-F, d, J = 246.0 Hz), 161.6 (C-F, d, J = 243.0 Hz), 158.1, 146.1, 136.7, 132.2, 131.9, 131.1 (d, J = 7.0 Hz), 130.3, 129.4 (d, J = 7.0 Hz), 127.8, 127.6, 118.1, 116.1 (d, J = 21.0 Hz), 115.6 (d, J = 22.0 Hz), 114.7, 112.7 ppm; Anal. Calcd. for $C_{21}H_{14}F_2N_2O$ (348.352): C, 72.41; H, 4.05; N, 8.04. Found: C, 72.40; H, 4.04; N, 8.03.

2- (3,5-dimethoxyphenyl) -4,5-bis (4-fluorophenyl)-1H-imidazole (24). Off-white powder; mp: 224-227°C; IR (cm^{-1}, KBr): 3440 (N-H), 1603 (C=C), 1515 (C=N), 1227 (C-O). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.68 (s, 1H, NH), 7.47-7.58 (m, 4H, Ar-H),

7.30 (t, 2H, J = 8.4 Hz, Ar-H), 7.25 (d, 2H, J = 1.6 Hz, Ar-H), 7.14 (t, 2H, J = 8.4 Hz, Ar-H), 6.50 (t, 1H, J = 1.6 Hz, Ar-H), 3.80 (s, 6H, OMe) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.2 (C-F, d, J = 243.0 Hz), 161.5 (C-F, d, J = 242.0 Hz), 161.2, 145.7, 136.6, 132.5, 131.9 (d, J = 2.0 Hz), 131.2 (d, J = 8.0 Hz), 129.4 (d, J = 8.0 Hz), 127.8 (d, J = 2.0 Hz), 127.6, 116.2 (d, J = 21.0 Hz), 115.6 (d, J = 21.0 Hz), 103.6, 101.1, 55.8, 55.6 ppm; Anal. Calcd. for $C_{23}H_{18}F_2N_2O_2$ (392.403): C, 70.40; H, 4.62; N, 7.14. Found: C, 70.39; H, 4.61; N, 7.14.

2,4,5-tris(4-fluorophenyl)-1H-imidazole (25). Cream crystalline powder; mp: 246-248°C; IR (cm^{-1}, KBr): 3440 (N-H), 1606 (C=C), 1505 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.70 (s, 1H, NH), 8.10 (t, 2H, J = 8.0 Hz, Ar-H), 7.48-7.58 (m, 4H, Ar-H), 7.24-7.35 (m, 4H, Ar-H), 7.15 (t, 2H, J = 8.0 Hz, Ar-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.6 (C-F, d, J = 244.0 Hz), 162.2 (C-F, d, J = 243.0 Hz), 161.5 (C-F, d, J = 242.0 Hz), 145.2, 136.7, 131.9 (d, J = 3.0 Hz), 131.1 (d, J = 8.0 Hz), 129.3 (d, J = 8.0 Hz), 127.8, 127.5, 127.3 (d, J = 3.0 Hz), 116.3 (d, J = 21.0 Hz), 116.0 (d, J = 21.0 Hz), 115.7, 115.5 ppm; Anal. Calcd. for $C_{21}H_{13}N_2F_3$ (350.342): C, 72.00; H, 3.74; N, 8.00. Found: C, 71.98; H, 3.73; N, 8.00.

2-(3-nitrophenyl)-4,5-bis (4-fluorophenyl) -1H-imidazole (27). Yellow powder; mp: 303-305°C; IR (cm^{-1}, KBr): 3433 (N-H), 1601 (C=C), 1490 (N=O), 1350 (N-O), 1522 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 13.10 (s, 1H, NH), 8.93 (s, 1H, Ar-H), 8.50 (d, 1H, J = 7.2 Hz, Ar-H), 8.22 (d, 1H, J = 7.2 Hz, Ar-H), 7.78 (t, 1H, J = 7.9 Hz, Ar-H), 7.52-7.60 (m, 4H, Ar-H), 7.33 (t, 2H, J = 8.2 Hz, Ar-H), 7.17 (t, 2H, J = 8.3 Hz, Ar-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 163.7 (C-F, d, J = 244.0 Hz), 161.6 (C-F, d, J = 242.0 Hz), 148.8, 143.8, 137.2, 132.1, 131.5 (d, J = 8.0 Hz), 131.0, 130.8, 129.5 (d, J = 8.0 Hz), 128.5, 127.9, 127.5, 123.1, 119.8, 116.2 (d, J = 22.0 Hz), 115.6 (d, J = 21.0 Hz) ppm; Anal. Calcd. for $C_{21}H_{13}F_2N_3O_2$ (377.349): C, 66.84; H, 3.47; N, 11.14. Found: C, 66.83; H, 3.47; N, 11.14.

2-(2-furyl)-4,5-bis (4-fluorophenyl) -1H-imidazole (28). Cream powder; mp: 268-270°C; IR (cm^{-1}, KBr): 3434 (N-H), 1600 (C=C), 1509 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.87 (s, 1H, NH), 7.90 (d, 1H, J = 4.6 Hz, Ar-H), 7.70 (d, 1H, J = 4.6 Hz, Ar-H), 7.48-7.58 (m, 4H, Ar-H), 7.31 (t, 2H, J = 8.2 Hz, Ar-H), 7.22 (t, 1H, J = 4.6 Hz, Ar-H), 7.15 (t, 2H, J = 8.2 Hz, Ar-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.9 (C-F, d, J = 244.0 Hz), 162.0 (C-F, d, J = 242.0 Hz), 154.2, 151.1, 146.3, 137.5, 134.4, 131.8, 131.0 (d, J = 9.0 Hz), 129.4 (d, J = 8.0 Hz), 128.3, 127.6, 124.0, 116.2 (d, J = 21.0 Hz), 115.6 (d, J = 21.0 Hz) ppm; Anal. Calcd. for $C_{19}H_{12}F_2N_2O$ (322.313): C, 70.80; H, 3.75; N, 8.69. Found: C, 70.78; H, 3.74; N, 8.67.

2-(2-thienyl)-4,5-bis (4-fluorophenyl) -1H-imidazole (29). Cream crystalline powder; mp: 280-282°C; IR (cm^{-1}, KBr): 3432 (N-H), 1601 (C=C), 1504 (C=N); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.80 (s, 1H, NH), 7.66 (d, 1H, J = 4.4 Hz, Ar-H), 7.45-7.58 (m, 5H, Ar-H), 7.30 (t, 2H, J = 8.0 Hz, Ar-H), 7.10-7.20 (m, 3H, Ar-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.9 (C-F, d, J = 244.0 Hz), 162.0 (C-F, d, J = 243.0 Hz), 142.1, 134.3, 131.6, 131.0 (d, J = 8.0 Hz), 130.1, 129.5, 129.0 (d, J = 8.0 Hz), 128.3, 127.6, 126.7, 124.8, 116.2 (d, J = 22.0 Hz), 115.9 (d, J = 21.0 Hz) ppm; Anal. Calcd. for $C_{19}H_{12}F_2N_2S$ (338.374): C, 67.44; H, 3.57; N, 8.28. Found: C, 67.43; H, 3.56; N, 8.27.

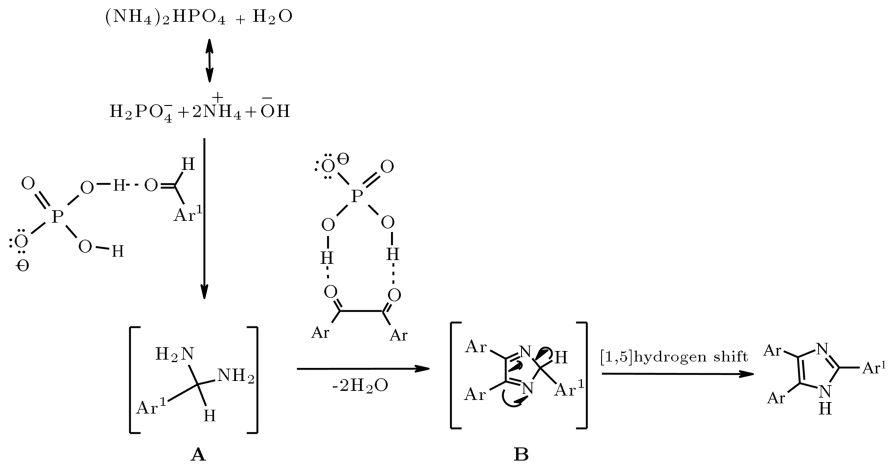
3. Results and discussion

In order to determine the most appropriate reaction conditions and evaluate the solvent efficiency, a series of experiments was implemented (Table 2). For this purpose, initially, we started the condensation of benzil (1 mmol), benzaldehyde (1 mmol), and DAHP (4 mmol) at 90°C for 8 h under solvent-free conditions, which led to a very poor yield (< 10%) of 2,4,5-triphenyl imidazole (Table 2, entry 1). To enhance the yield of the desired product, the temperature of the reaction was increased to 120°C, but no appreciable increment in the product yield was observed. Then, it was thought worthwhile to carry out the reaction in the presence of different solvents. Among the tested

Table 2. Solvent effect on synthesis of 2,4,5-trisubstituted imidazoles[a].

Entry	Solvent	Time (h)	Temperature (°C)	Yield (%)
1	None	8	90	8
2	None	8	120	10
3	CH_2Cl_2	6	Reflux	13
4	$CHCl_3$	6	Reflux	16
5	CH_3CN	6	Reflux	11
6	Dioxane	6	Reflux	18
7	EtOH	6	Reflux	45
8	MeOH	6	Reflux	39
9	Water	2	Reflux	92

[a]: Benzil (1 mmol), DAHP (4 mmol), benzaldehyde (1 mmol).



Scheme 2. Reasonable mechanism.

solvents, such as CH_2Cl_2, $CHCl_3$, CH_3CN, dioxane, EtOH, MeOH, and water, the formation of product **1** was more facile and proceeded to give not only high yield, but also a high reaction rate in water (92 yield in 120 min) (Table 2, entry 9). Owing to the bad solubility of DAHP in other solvents, negligible product yields were obtained in longer reaction times (Table 2, entries 3-8). According to the data presented in Table 2, water has been chosen as the best solvent for this reaction. A possible explanation for the better yield in water is that the DAHP is hydrolyzed to ammonia and dihydrogen phosphate ion. Dihydrogen phosphate ion activates benzil and aldehyde through hydrogen bonding (see Scheme 2).

To show the generality of this method, optimized conditions were used for the synthesis of other imidazole derivatives. The condensation of benzil with various aromatic aldehydes bearing electron-withdrawing groups (such as nitro and halide) or electron-releasing groups (such as hydroxyl, mono and di, methoxy groups) and DAHP was carried out in water under reflux conditions. The obtained results for the current method are illustrated in Table 1. As shown, the process tolerates both electron withdrawing and donating substitutes on the aldehydes.

The aryl group substituted, with different positions of the aromatic ring, has not shown much effect on formation of the final product (Table 1, entries 1-10). However, aromatic aldehydes having electron withdrawing groups reacted at a faster rate compared with aromatic aldehydes substituted with electron donating groups. Beside this, our methodology has been used successfully for heteroaromatic aldehydes, and corresponding imidazoles were obtained in excellent yields (Table 1, entries 11-13). To evaluate the generality of this method, we also concentrated our study on benzil with an electron donating group (Table 1, entries 14-22) and electron withdrawing group (Table 1, entries 23-29). The results illustrate the high ability of this method for the synthesis of 2,4,5-triarylimidazoles with different benzils. As shown in Table 1, 4,4′-dimethoxybenzil was compared with benzil reacted at a slower rate. Also, 4,4′-difluorobenzil reacted at the fastest rate. All the products obtained were fully characterized by spectroscopic methods, such as Infrared (IR), ^{1}H NMR and ^{13}C NMR and also by making a comparison with the reported spectral data. Also, their melting points were compared with literature reports. All products exhibited a singlet in ^{1}H NMR spectra at about $\delta = 12.42 - 13.10$ ppm and also a distinguishing peak at 3400-3440 cm^{-1} in IR spectra for N-H.

We have not established an exact mechanism for the formation of 2,4,5-trisubstituted imidazoles, however, a reasonable possibility is shown in Scheme 2. Formation of diamine intermediate **A**, condenses with benzil to form intermediate **B**, which, in turn, rearranges to the trisubstituted imidazole by a [1,5] hydrogen shift (Scheme 2).

In summary, we have successfully developed an easy and efficient three-component method to prepare a variety of trisubstituted imidazoles in the presence of DAHP in water. We have demonstrated for the first time that diammonium hydrogen phosphate is a potential alternative to the use of ammonia sources for green synthesis of a wide range of trisubstituted imidazoles. The use of low cost, commercially available and water soluble DAHP as a reagent for the synthesis of imidazoles in excellent yields is also significant regarding environmentally benign processes. The mild reaction conditions, easy workup, clean reaction profiles, and being catalyst-free render this approach an interesting alternative to existing methods.

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