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Water extract of onion: chemoselective synthesis of 2-substituted benzimidazole derivatives

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Abstract: A facile, efficient, green synthetic route was developed for the selective synthesis of 2-substituted benzimidazole derivatives via the reaction of 1,2-diamines with aromatic, aliphatic and hetero aromatic nitroalkenes in the presence of an onion extract as a green catalyst. In this reaction, fifteen 2-substituted benzimidazole derivatives were obtained in good to excellent yields (80-95%). The method presented here offers several benefits, including minimal energy usage, cheap, nontoxic catalyst, simple workup procedure and without column purification. The usage of onion extract creates this approach is environmentally friendly and makes a significant addition to the currently available techniques for the creation of 2-substituted benzimidazoles. Further, the scope and constraints were also investigated, and a conceivable reaction mechanism was put forth.

Keywords: Chemoselectivity; water extract of onion; green catalyst; 2-substituted benzimidazoles; 1,2-Diamines.

1. Introduction

Benzimidazoles are important classes of heterocyclic compounds and have been widely used as a key intermediate to build a variety of pharmaceutical agents[1-8] and functional materials.[9-13] Its analogs have demonstrated outstanding biological properties, including antioxidant,[14] antiviral,[15,16] anti-inflammatory,[17,18] antimicrobial[19-21] and anticancer[22-24] activities. In addition, several of its derivatives act as therapeutic agents, including PPI (proton pump inhibitors),[25] antidiabetics[26,27] and level modulators[28] (Figure 1). Because of their extensive utility and growing importance, several useful methods have been developed to assemble these heterocycles. A traditional method for creating benzimidazole is the condensation of carboxylic acid with aryl-1,2-diamine **1** under very acidic conditions.[29-31] Another well-known method to synthesize benzimidazole includes the condensation of 1,2-phenylenediamine **1** and aldehyde or alcohol with different oxidizing agents.[32-36] Also, many other diverse catalytic methodologies have been reported to prepare benzimidazoles.[37-44] Unfortunately, many of these methods suffer limitations such as expensive catalysts, toxic solvents and some metal based Lewis acids that are hazardous to the environment. In addition, these approaches provide a mixture of 2-substituted and 1,2-disubstituted benzimidazoles due to non-regioselective amino groups of 1,2-phenylenediamine.

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Among these, 2-substituted products are found to be valuable building blocks for numerous pharmaceutical applications. Hence, developing a highly discerning, mild and environmentally benign synthetic procedure is still required to synthesize these important classes of heterocyclic compounds. Therefore, we describe a selective synthesis of 2-substituted benzimidazoles **3a-o** employing aqueous onion extract as a green catalyst with mild conditions.

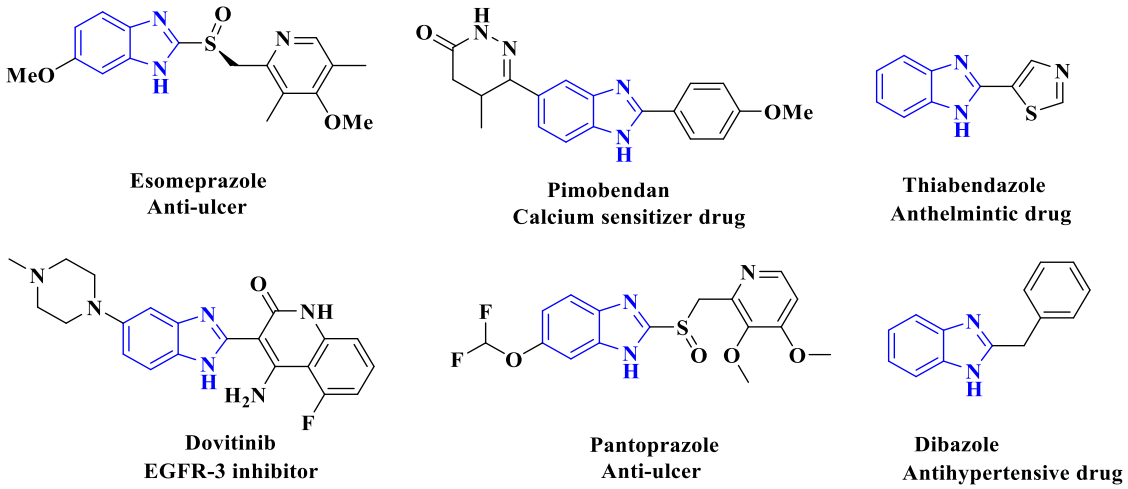
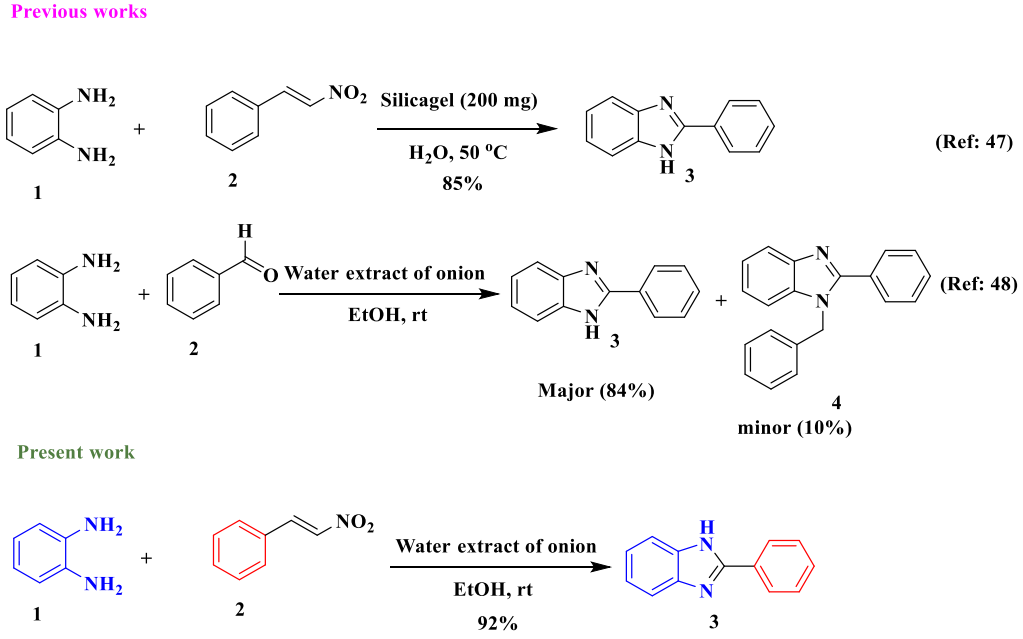


Figure 1. Therapeutic agents having 2-substituted benzimidazole moieties

Aqueous extract of onion, a mild acidic, inexpensive, nontoxic and readily available, can function as a catalyst in the condensation processes.[45,46] The use of onion extract catalyst instead of metal-based catalysts has several benefits, including the simplicity of product separation and the use of an ecologically benign alternative. To the best of our knowledge, very few reports are accessible for the selective production of 2-substituted benzimidazole derivatives **3** with 1,2-diamine and β-nitrostyrene (Scheme 1). For example, Qi and coworkers[47] reported the synthesis of 2-substituted benzimidazoles from 1,2-diamine **1** and β-nitrostyrene with 200 mg of silicagel in water at 50 °C.



Scheme 1. Synthesis of 2-substituted benzimidazole derivatives

Recently, we established an affordable, environmentally friendly method for the selective synthesis of 2-substituted and 1,2-disubstituted benzimidazoles[48] using o-phenylenediamine and an aldehyde with onion extract as a catalyst. During this experiment, we discovered that the reaction produced selectively 2-substituted benzimidazoles **3** when β-nitrostyrene was used instead of aldehyde. Therefore, we describe a green procedure for the selective production of 2-substituted benzimidazole derivatives **3a-o** by employing onion extract as a green catalyst under mild conditions in our present work.

2. Experimental

2. 1. General

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) data were collected using BRUKER (400 MHz)-FT-NMR spectrometer using DMSO-d_6 and $CDCl_3$ as a solvent where TMS was used as an internal standard (chemical shift in δ ppm). The chemical shifts are stated in the downfield from the signal of internal TMS. The FT-IR spectral data were collected on JASCO FT-IR spectrophotometer model 400 plus using KBr pellets. Uncorrected melting points were found using a capillary melting point apparatus obtained from Guna Enterprises, India. TLC experiments were performed on glass plates (2.5×7.5 cm) coated with 250 mμ Merck GF_{254} silica gel. The spots were envisaged on exposure to iodine vapor or UV light. Column chromatography was performed using CDH silica gel (60-120 mesh). Anisaldehyde, *o*-nitrobenzaldehyde, benzaldehyde, *p*-methylbenzaldehyde and cyclohexanecarboxaldehyde were purchased from SRL, India. *p*-hydroxybenzaldehyde, *p*-cyanobenzaldehyde, thiophene-2-carboxaldehyde, furfural and methyl-4-formylbenzoate were supplied by Sigma Aldrich. *p*-bromobenzaldehyde and *N,N*-dimethylaminobenzaldehyde were obtained from CDH. The solvent ethanol was purified using by dry distillation method and obtained from Changshu Yangquan Chemicals, China.

2.2. Preparation of Water Extract of Onion

The required onion extract was prepared as follows: Two gram of cut pieces of onion were taken into a 100 mL clean beaker. To this 10 mL of Milli-Q water was added and stirred for half an hour. The stirred suspension was allowed to stand for 10 min. followed by filtration. The filtrate was used as a catalyst and stored in the refrigerator. The strength of the onion extract is 0.0034 N, which is determined by using acid-base titrations and the pH of the catalyst is 3.6. The strength and pH of the catalyst were examined periodically over the month and found to be consistent.

2. 3. General procedure for the synthesis of 2-substituted benzimidazole

A stirred mixture of 1,2-phenylenediamine **1** (1 mmol, 0.108 g) in ethanol (5 mL) and water extract of onion (1 mL) at room temperature was added nitro alkene **2** (1 mmol), dissolved in 5 mL of ethanol The mixture was stirred at room temperature for 24 h. Once all of the initial ingredients have been converted completely, as determined by TLC, the solvent was evaporated under vacuum. Water (5 mL) was added to this residue and organic phase was extracted with ethyl acetate (2x10 mL). The combined organic phase was washed with water and brine (5 mL each), dried over Na_2SO_4, filtered, and evaporated to give 2-substituted benzimidazole **3**.

2. 3. Spectral Data for Synthesized Compounds

*4-(1H-benzo[d]imidazole-2yl) phenol (**3a**)*: Yield: 0.200 g; 95%; Pale yellow solid; Mp: 246-248 °C (lit.[47] Mp: 249- 252 °C); IR (KBr): 3253, 3053, 1609, 1501, 1470, 1273, 836, 735 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.64 (s, 1H, -NH), 9.97 (s, 1H, -OH), 8.01 (d, 2H, *J* = 8.4 Hz, Ar-H), 7.58-7.51 (m, 2H, -Ar-H), 7.18-7.13 (m, 2H, -Ar-H), 6.92 (d, 2H, *J* = 8.4 Hz, -Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6):[49] δ 159.59, 152.25, 128.62, 122.08, 121.59, 116.16.

*2-(4-methoxyphenyl)1H-benzo[d]imidazole (**3b**)*: Yield: 0.192 g; 85%; Pale brown solid; Mp: 220-223 °C (lit.[37] 222- 225 °C); IR (KBr): 3053, 3005, 2835, 1610, 1498, 1433, 1251, 1177, 1032, 963, 844,

744 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.73 (s, 1H, -NH), 8.12 (d, 2H, *J* = 8.80 Hz, -Ar-H), 7.59-7.53 (m, 2H, -Ar-H), 7.20-7.12 (m, 2H, -Ar-H), 7.11 (d, 2H, *J* = 8.8 Hz, -Ar-H), 3.84 (s, 3H, OMe); ^{13}C NMR (100 MHz, DMSO-d_6):[50] δ 161.07, 151.81, 128.47, 123.15, 122.24, 121.55, 114.84, 55.80; MS (*m/z*): 225.1024 $[M+1]^+$.

*2-(p-tolyl)-1H-benzo[d]imidazole (**3c**)*: Yield: 0.175 g; 84%; White solid; Mp: 277-279 °C (lit.[38] Mp: 275-277 °C); IR (KBr): 3762, 3053, 2882, 1607, 1498, 1429, 1273, 1110, 819, 738 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.82 (s, 1H, -NH), 8.06 (d, 2H, *J* = 7.6 Hz, Ar-H), 7.64 (d, 1H, *J* = 6.4 Hz, -Ar-H), 7.51 (d, 1H, *J* = 6.4 Hz, -Ar-H), 7.36 (d, 2H, *J* = 8.0 Hz, -Ar-H), 7.20-7.19 (m, 2H, -Ar-H), 2.38 (s, 3H, Me); ^{13}C NMR (100 MHz, DMSO-d_6):[51] δ 151.84, 140.05, 129.99, 127.89, 126.85, 122.42, 21.44; MS (*m/z*): 209.1077 $[M+1]^+$.

*2-phenyl-1H-benzo[d]imidazole (**3d**)*: Yield: 0.179 g; 92%; Brown solid; Mp: 283-284 °C (lit.[47] Mp: 283- 285 °C); IR (KBr): 3046, 2623, 1677, 1546, 1405, 1310, 1271, 1113, 965, 738 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.00 (s, 1H, -NH), 8.21 (d, 2H, *J* = 8.0 Hz -Ar-H), 7.76-7.46 (m, 5H, -Ar-H), 7.21 (d, 2H, *J* = 8.0 Hz -Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6):[52] δ 151.75, 143.99, 135.42, 130.47, 130.40, 129.46, 126.92, 122.93, 119.28, 111.88; MS (*m/z*): 195.0913 $[M+1]^+$.

*2-(4-nitrophenyl)-1H-benzo[d]imidazole (**3e**)*: Yield: 0.213 g; 89%; Yellow solid; Mp: 308-310 °C (lit.[37] Mp: 311-312 °C); IR (KBr): 3430, 3034, 2912, 1603, 1514, 1433, 1340, 1278, 1101, 855, 747 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.28 (s, 1H, -NH), 8.40 (m, 4H, -Ar-H), 7.80-7.66 (m, 1H, -Ar-H), 7.65-7.40 (m, 1H, -Ar-H), 7.30-7.08 (m, 2H, -Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6):[53] δ 149.48, 148.30, 144.30, 136.51, 135.70, 127.88, 124.80, 124.08, 122.81, 119.93, 112.29; MS (*m/z*): 240.0772 $[M+1]^+$.

*2-(2-nitrophenyl)-1H-benzo[d]imidazole (**3f**)*: Yield: 0.201 g; 84%; Brown solid; Mp: 261-264°C (lit.[54] Mp: 264- 265 °C); IR (KBr): 3079, 2920, 1616,1525,1413, 1345, 1127, 858, 744, 683 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.06 (s, 1H, -NH), 8.04 (d, 1H, *J* = 7.6 Hz, -Ar-H), 7.98 (d, 1H, *J* = 7.6 Hz, -Ar-H), 7.87 (t, 1H, *J* = 7.6 Hz, -Ar-H), 7.76 (t, 1H, *J* = 7.6 Hz, -Ar-H), 7.67 (d, 1H, *J* = 7.6 Hz, -Ar-H), 7.57 (d, 1H, *J* = 7.6 Hz, -Ar-H), 7.33-7.18 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6):[55] δ 149.40, 147.83, 144.04, 135.08, 133.17, 131.42,131.37, 124.78, 124.74, 123.56, 122.44, 119.68, 112.18; MS (*m/z*): 240.0763 $[M+1]^+$.

*2-(3-nitrophenyl)-1H-benzo[d]imidazole (**3g**)*: Yield: 0.208 g; 87%; Brown solid; Mp: 288-290 °C; IR (KBr): 3459, 1684, 1623, 1589, 1519, 1476, 1455, 1348, 1274, 975, 810, 742 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.29 (s, 1H, -NH), 9.01 (s, 1H, -Ar-H), 8.61 (d, 1H, *J* = 7.2 Hz, -Ar-H), 8.33 (d, 1H, *J* = 7.6 Hz, -Ar-H), 7.85 (t, 1H, *J* = 8.0 Hz, -Ar-H), 7.68-7.52 (m, 2H, -Ar-H), 7.26 (s, 2H, -Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6):[56] δ 149.50, 148.78, 132.91, 132.14, 131.09, 124.63, 123.18, 121.27.

*2-(4-bromophenyl)-1H-benzo[d]imidazole (**3h**)*: Yield: 0.224 g; 82%; Dark brown solid; Mp: 291-294 °C (lit.[57] Mp: 294- 296 °C); IR (KBr): 3052, 2992, 1591, 1424, 1316, 1269, 1111, 1008, 822, 751 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.0 (s, 1H, -NH), 8.12 (d, 2H, *J* = 7.2 Hz, -Ar-H), 7.77 (d, 2H, *J* = 7.2 Hz, -Ar-H), 7.74-7.62 (m, 1H, -Ar-H), 7.60-7.40 (m, 1H, -Ar-H), 7.28-7.12 (m, 2H, -Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6):[48] δ 150.6, 144.2, 135.5, 132.4, 129.8, 128.8, 123.7, 123.2, 119.4, 111.8.

*4-(1H-benzo[d]imidazole-2-yl)benzonitrile (**3i**)*: Yield: 0.198 g; 90%; Pale yellow solid; Mp: 234-235 °C; IR (KBr): 3426, 2918, 1696, 1618, 1429, 1270, 963, 820, 751 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.21 (s, 1H, -NH), 8.34 (d, 2H, *J* = 8.0 Hz, -Ar-H), 8.04 (d, 2H, *J* = 8.4 Hz, -Ar-H), 7.80-7.64 (m, 1H, -Ar-H), 7.60-7.48 (m, 1H, -Ar-H), 7.32-7.16 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6):[58] δ 149.84, 144.20, 135.58, 134.73, 133.47, 127.46, 123.91, 122.70,119.83, 119.10, 112.36, 112.20; MS (*m/z*): 220.0872 $[M+1]^+$.

*methyl-4-(1H-benzo[d]imidazol-2-yl)benzoate (**3j**)*: Yield: 0.225 g; 89%; Pale yellow solid; Mp: 192-194 °C (lit[47] Mp: 191-192 °C); IR (KBr): 3377, 3054, 2949, 1692, 1432, 1279, 1116, 961, 742 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.15 (s, 1H, -NH), 8.32 (d, 2H, *J* = 7.6 Hz, -Ar-H), 8.13 (d, 2H, *J* = 7.2 Hz, -Ar-H), 7.71 (d, 1H, *J* = 6.8 Hz, Ar-H), 7.57 (d, 1H, *J* = 6.4 Hz, -Ar-H), 7.25 (t, 2H, *J* = 8.4

Hz, -Ar-H), 3.90 (s, 3H, -OMe); ^{13}C NMR (100 MHz, DMSO-d_6):[59] δ 166.28, 150.45, 144.26, 135.58, 134.80, 130.75, 130.27, 127.06, 123.62, 122.51, 119.68, 112.08, 52.75; MS (*m/z*): 253.0 $[M+1]^+$.

*2-(furan-2-yl)-1H-benzo[d]imidazole (**3k**)*: Yield: 0.159 g; 86%; Pale brown solid; Mp: 284-286 °C (lit.[57] Mp: 286-287 °C); IR (KBr): 3457, 3059, 2858, 1627, 1413, 1363, 1228, 973, 736 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.91 (s, 1H, -NH), 7.94 (s, 1H, -Ar-H), 7.62 (d, 1H, *J* = 7.2 Hz, -Ar-H), 7.49 (d, 1H, *J* = 6.8 Hz, -Ar-H), 7.28-7.12 (m, 3H, -Ar-H), 6.73 (s, 1H, -Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6):[60] δ 146.03, 145.09, 144.10, 134.70, 123.08, 122.29, 119.23, 112.79, 111.80, 110.94; MS (*m/z*): 185.0709 $[M+1]^+$.

*2-(thiophen-2-yl)-1H-benzo[d]imidazole (**3l**)*: Yield: 0.174 g; 87%; Pale brown solid; Mp: 253-255 °C (lit[38] Mp: 254 °C); IR (KBr): 3425, 3047, 3008, 2925, 2856, 1567, 1422, 1271, 943, 849, 750 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.95 (s, 1H, -NH), 7.83 (s, 1H), 7.73 (d, 1H, *J* = 4.4 Hz, -Ar-H), 7.66-7.48 (m, 2H, -Ar-H), 7.28-7.12 (m, 3H, -Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6):[61] δ 147.49, 144.03, 134.14, 129.23, 128.76, 127.16, 123.09, 122.28, 119.02, 111.57; MS (*m/z*): 201.0483 $[M+1]^+$.

*2-cyclohexyl-1H-benzo[d]imidazole (**3m**)*: Yield: 0.161 g; 80%; White crystalline solid; Mp: 255-258 °C; IR (KBr): 3055, 2923, 2852, 1616, 1531, 1420, 1267, 1043, 981, 738 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.09 (s, 1H, -NH), 7.60-7.52 (m, 1H, -Ar-H), 7.52-7.36 (m, 1H), 7.20-7.18 (m, 2H), 2.90-2.78 (m, 1H, -CH), 2.10-2.86 (m, 2H, -CH_2), 1.78-1.70 (m, 2H, -CH_2), 1.68-1.45 (m, 3H, -aliphatic), (1.40-1.16 (m, 3H, -aliphatic); ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.36, 121.52, 118.68, 111.22, 38.15, 31.70, 26.03, 25.98; MS (*m/z*): 201.1382 $[M+1]^+$.

*4-(1H-benzo[d]imidazole-2-yl)-N, N-dimethylaniline (**3n**)*: Yield: 0.206 g; 88%; Half-white solid; Mp: 249-252 °C; IR (KBr): 3413, 3051, 2804, 1607, 1501, 1437, 1364, 1196, 944, 817, 736 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.53 (s, 1H, -NH), 7.99 (d, 2H, *J* = 8.8 Hz, -Ar-H), 7.57-7.55 (m, 1H, -Ar-H), 7.44-7.43 (m, 1H, -Ar-H), 7.18-7.10 (m, 2H, -Ar-H), 6.84 (d, 2H, *J* =7.6 Hz, -Ar-H), 3.00 (s, 6H, $N(Me)_2$); ^{13}C NMR (100 MHz, DMSO-d_6):[62] δ 152.73, 151.71, 144.54, 135.41, 128.00, 121.97, 121.62, 118.48, 117.85, 112.31, 111.12, 40.29.

*4-(6-chloro-1H-benzo[d]imidazole-2-yl)phenol (**3o**)*: Yield: 0.198 g; 81%; Pale yellow solid; Mp: 215-217 °C; IR (KBr): 3006, 2988, 1599, 1344, 1275, 1172, 1106, 836, 751 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.83 (s, 1H, -NH), 10.03 (s, 1H, -OH), 8.00 (d, 2H, *J* = 8.8 Hz, -Ar-H), 7.66-7.48 (m, 2H, Ar-H), 7.18 (s, 1H, -Ar-H), 6.92 (d, 2H, *J* = 8.8 Hz, -Ar-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.91, 153.67, 128.80, 126.37, 122.26, 121.06, 116.22.

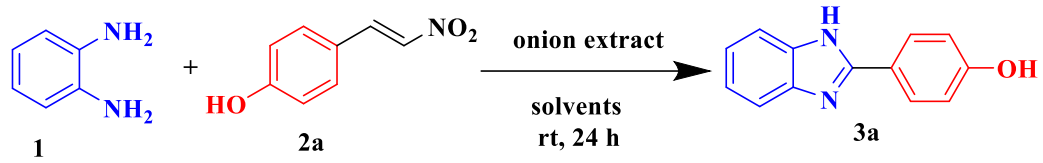
3. Results and Discussion

3.1. Chemistry

In connection with our earlier report for the development of eco-friendly benign protocol[45,46,48,63,64] the use of an onion extract, we are desperately involved in creating the green synthetic route for the selective production of 2-substituted benzimidazoles **3**. To continue our importance for the particular production of 2-substituted benzimidazoles **3**, we have studied the reaction between 1,2-phenylenediamine **1** and β-nitrostyrene **2a** with water extract of onion at room temperature in ethanol. The reactions progressed efficiently with water extract of onion (1 mL) to give 2-substituted benzimidazole **3** in good to excellent yields (95%). The procedure for making the needed water extract of onion[45] and the main ingredient[65-68] present in it were reported previously. Initially, the β-nitrostyrene **2a** which was prepared from the reaction of nitromethane and an aldehyde, was subjected to the reaction with 1,2-phenylenediamine **1** with water extract of onion at room temperature in different solvents, such as MeOH, EtOH, ^{i}PrOH, H_2O, CH_3CN, DMSO, DMF, DCM, toluene and hexane. The results are shown in Table 1. When polar protic solvents such as MeOH, EtOH and ^{i}PrOH were used as reaction media, the reaction gave only 2-substituted benzimidazole **3a** with excellent yields (90-95%) (Table 1, entries 1–3). At the same time, polar aprotic solvents (CH_3CN, DMSO, DMF, DCM) gave 86%, 82%, 88%, and 85% yields, respectively (Table 1, entries 5–8). When we used non-polar solvents, toluene and hexane gave 2-substituted benzimidazole **3a** with 77% and 72%

yields, respectively (Table 1, entries 9–10), whereas the reaction in water gave benzimidazole **3a** in 78% yield (Table 1, entry 4). Even though it was discovered that the process was more efficient in all solvents, the hazardous qualities of most organic solvents prompted us to pick ethanol as the environmentally benign solvent for all subsequent reactions.

Table 1. Optimization of the reaction conditions by using different solvents



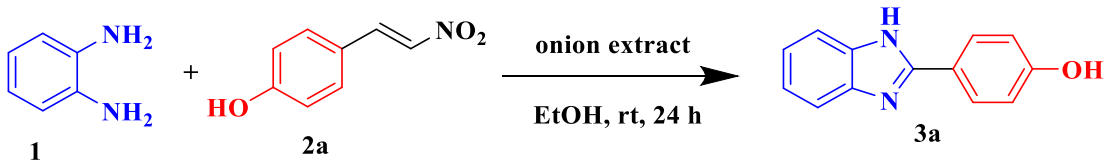
1 2a 3a

Entry[a]	Solvents	Yield (%)[b]
1	MeOH	94
2	**EtOH**	**95**
3	^{i}PrOH	90
4	H_2O	78
5	CH_3CN	86
6	DMSO	82
7	DMF	88
8	DCM	85
9	Toluene	77
10	Hexane	72

[a] The reactions were performed using o-phenylenediamine **1** (1 eq) and nitroalkene **2a** (1 eq) and solvent (5 mL) with water extract of onion (1 mL) at room temperature for 24 h. [b] The yields all are calculated via isolated products.

Additionally, efforts were undertaken to modify the amount of water extract of onion needed to perform the reaction. We have investigated the interaction between 1,2-phenylenediamine **1** and β-nitrostyrene **2a** in ethanol. The starting materials **1** and **2a** were agitated at room temperature for 24 h with 0.1 mL, 0.5 mL, 0.8 mL, 1 mL and 1.5 mL of catalyst and individually calculated the yield. The obtained results are shown in Table 2. It was observed that when we used 1.0 mL and 1.5 mL of the catalyst, it gave the desired product **3a** (Table 2, entries 4-5) with 95% and 96% yield respectively. The reaction of 1,2-phenylenediamine **1** and a β-nitrostyrene **2** with water extract of onion (1 mL) at room temperature for 24 h gave a 95% yield (Table 2, Entry 4). Hence, the ethanolic medium of the reaction for 24 h with onion extract (1 mL) was discovered to be the ideal reaction condition to produce the target product **3a** with a greater yield.

Table 2. Optimization of the reaction conditions by loading the amount of catalyst



1 2a 3a

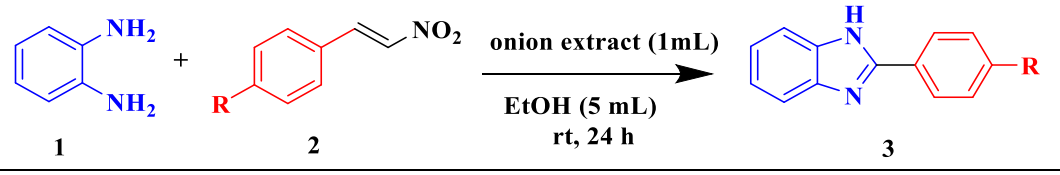
Entry[a]	Catalyst	Time (h)	Yield (%)[b]
1	0.1	24	73
2	0.5	24	89
3	0.8	24	91
4	**1**	**24**	**95**
5	1.5	24	96
6	0	24	-

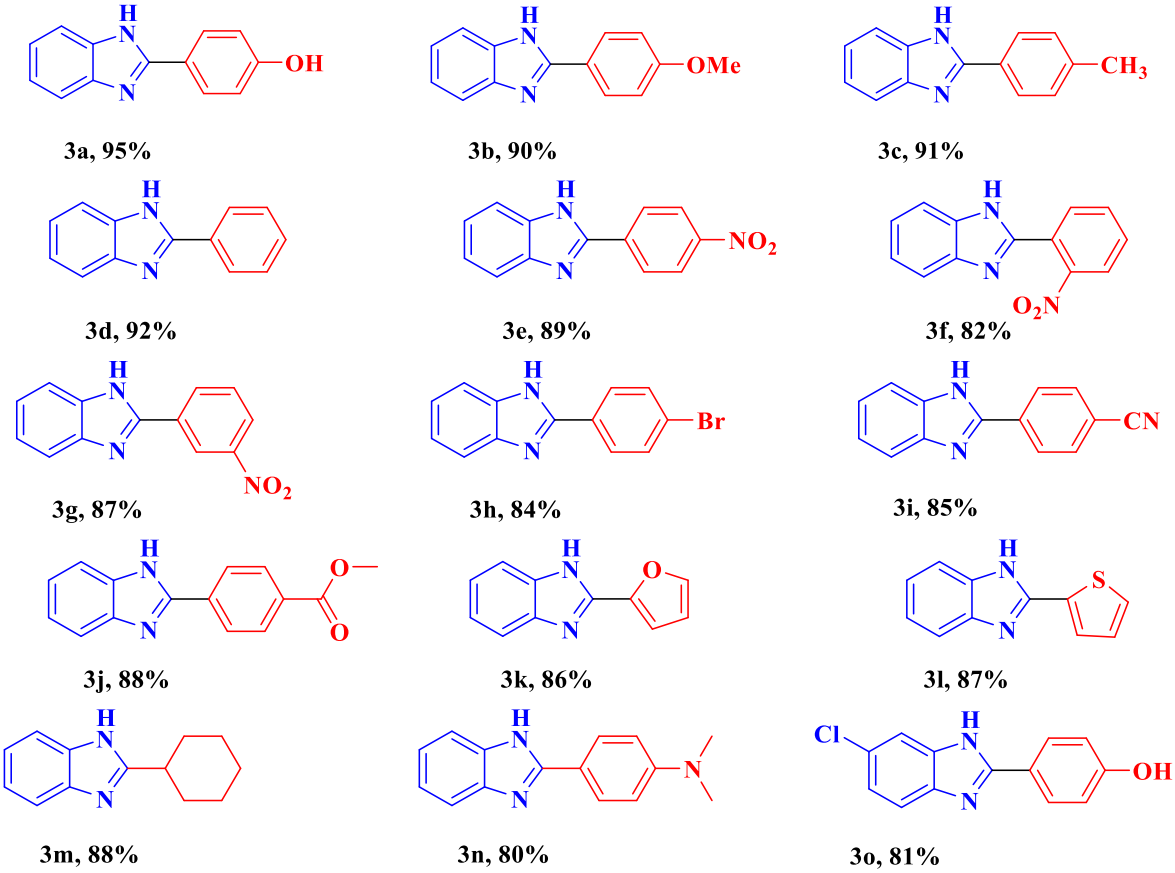
[a] The reactions performed by o-phenylenediamine **1** (1 eq), nitroalkene **2a** (1 eq) and ethanol (5 mL) with various amount of onion extract at RT for 24 h. [b] The yields all are calculated via isolated products.

We then investigated the scope of the reaction for the synthesis of different 2-substituted benzimidazole derivatives **3a-o** under the aforementioned optimised reaction conditions by alternating the substituted 1,2-phenylenediamine **1** and β-nitrostyrene **2** (Table 3). Table 3 displays that a variety of substituted groups of β-nitrostyrene **2** produced the required products in good to exceptional yields, which include –OH, -OCH_3, -CH_3, -NO_2, -Br_2, -CN, -COOR, *N,N'*-dimethyl and cyclohexyl groups. It is observed that the strong electron-releasing substituent present in the benzene part of the β-nitrostyrene **2** gave excellent yields (90-95%, Table 3, **3a-d**). It is also noted that strong electron-withdrawing substituent present in the benzene part of the β-nitrostyrene **2** gave slightly lesser yields (82-89%, Table 3, **3e-j**). Additionally, it should be observed that good results were also obtained by using other heteroaromatic systems, such as 2-[2-Nitrovinyl]thiophene, 2-[2-Nitrovinyl]furan and an aliphatic system like 2-[2-Nitrovinyl]cyclohexane (Table 3, **3k-m**).

We then investigated the scope of the reaction for the synthesis of different 2-substituted benzimidazole derivatives **3a-o** under the aforementioned optimised reaction conditions by alternating the substituted 1,2-phenylenediamine **1** and β-nitrostyrene **2** (Table 3). Table 3 displays that various substituted groups of β-nitrostyrene **2** produced the required products in good to exceptional yields.

Table 3. Synthesis of 2-substituted benzimidazole derivatives[a]





[a] All the reactions were performed by o-phenylenediamine **1** (1 eq) and nitroalkene **2** (1 eq), water extract of onion (1 mL) and ethanol (5 mL) at RT for 24 h.

All the structures **3a-o** were characterised by physical and spectroscopic techniques such as IR, Mass, ^{1}H NMR and ^{13}C NMR. Compound **3a,** ^{1}H NMR spectrum, as an example, shows the presence of two singlet signals δ 12.64 and 9.97 due to the –NH group of benzimidazole and phenolic –OH at the fourth position of the phenyl group. The two doublets at δ 8.01 (d, 2H, *J* = 8.4 Hz) and 6.92 (d, 2H, *J* = 8.4 Hz) are correspond to aromatic phenol protons. Also, two multiplets at δ 7.58-7.51 (m, 2H), 7.18-7.13 (m, 2H) are correspond to the aromatic protons of benzimidazole.

We performed the reaction of equimolar quantities (5 mmol) of diamine **1** with β-nitrostyrene **2a** to assess the viability of using this technology on a large scale. Similar yields to the small-scale process (2 mmol) were used to produce the 2-substituted benzimidazole **3a**.

Based on our previous observations on the onion extract catalyzed reactions[45,46,48] and the analogous mechanisms confirmed in the literature,[47] a feasible mechanism for this reaction was hypothesized and is depicted in Figure 2. The Michael addition occurred between 1,2-phenylenediamine **1** and β-nitrostyrene **2** to give intermediate **4**. Which on rearranged to eliminate nitromethane (via Retro-aza-Henry-Type Process) and form the imine **5.**[69] The resulting imine activated by the catalyst and another $–NH_2$ group of o-phenylenediamine **1** attacked electrophilic imine carbon via intramolecular fashion to form the intermediate **6** which underwent aerial oxidation to produce the corresponding 2- substituted benzimidazole **3** (Figure **2**).

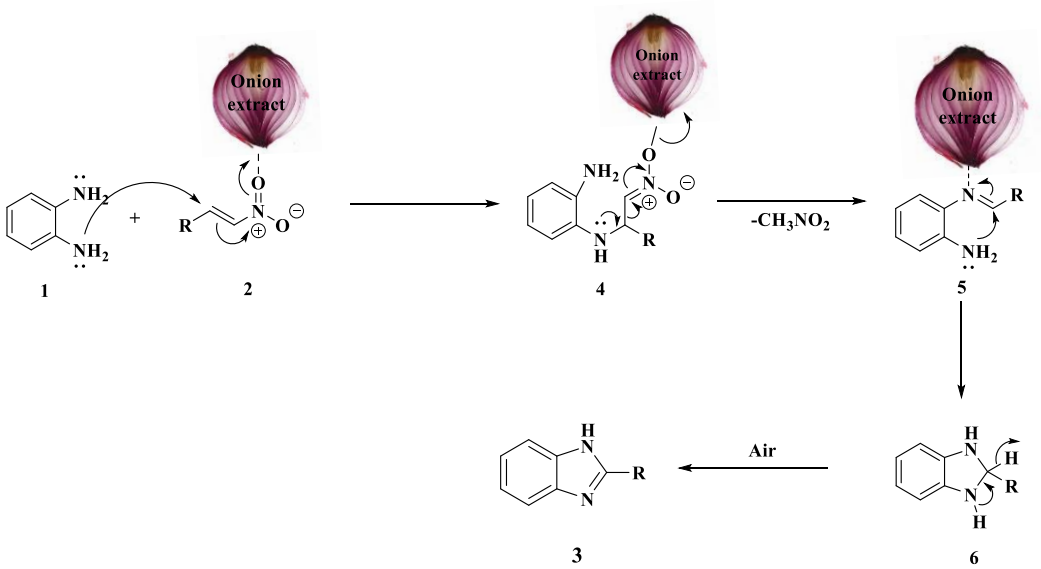


Figure 2. Plausible mechanism for the formation of benzimidazole

4. Conclusion

In summary, we have demonstrated a facile, efficient, green procedure for selective synthesis of 2-substituted benzimidazole derivatives **3a-o** from 1,2-diamines **1** and β-nitrostyrene **2** using environmentally friendly water extract of onion catalyst. This process has several advantages over the other methods such as inexpensive, operational easiness, nontoxic, mild reaction conditions without column purification and simple workup procedure. This technique for producing the 2-substituted benzimidazole derivatives **3a–o** is distinctly helpful in organic and medicinal chemistry.

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Supporting Information

Supporting information accompanies this paper on http://www.acgpubs.org/journal/organic-communications

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