SONICATED ASSISTED SYNTHESIS OF BENZIMIDAZOLES, BENZOXAZOLES AND BENZOTHIAZOLES IN AQUEOUS MEDIA

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ABSTRACT

Ammonium nickel sulphate [$(NH_4)_2SO_4.NiSO_4.6H_2O$] was found as a new catalyst to synthesis 2-aryl benzimidazole, 2-aryl benzothiazole and 2-aryl benzoxazole in aqueous media under sonication irradiation. The procedure is an eco-friendly, efficient and provides simple workup and good yield.

Keywords: - Benzimidazole, benzothiazole, benzoxazole, aqueous media, sonication, ammonium nickel sulphate.

INTRODUCTION

The benzimidazoles, benzoxazole and benzthaizoles are an important heterocyclic nucleus which has been widely used in medicinal chemistry [1,2]. These heterocycles are an important pharmacophore [3,4] in drug discovery and good intermediate [5] in synthesis of many important organic compounds. These heterocycles shows different pharmacological properties such as antibacterial [6], antiviral [7], antifugal [8], anticancer [9], anticonvulsant [10] and immunosuppressant [11].

These heterocycles can be prepared by condensing carboxylic acid [12], acid chloride [13, 14], orthoester [15-17], esters [18] and aldehydes [19-24] with o-phenylenediamine, o-aminophenols and o-aminothaiophenols, dehydration of o-acylaminophenols [25], reaction of o-quinones with amines [26] and Beckmann rearrangement of o-acylphenoloximes [27]. The most common method of synthesis of these heterocycles includes condensation of o-phenylenediamine, o-aminophenol or o-aminothiophenol with suitable aldehyde [28-32]. Most of these procedure have their own advantages and disadvantages, thus there is still a need to search better ecofriendly procedure.

The toxic and volatile natures of many organic solvents have posed serious environmental problems. Due to this organic reaction in aqueous media have attracted much attention in synthetic organic chemistry because water is one of the most abundant, cheap and environmental friendly solvent however there are very few reports for synthesis of 1,3 benzazoles in aqueous media.

Ultrasound irradiation has been established as an important technique in synthetic organic chemistry. It has been used as an efficient energy source for the organic reactions. Simple experimental procedure, very high yields, increased selectivity and clean reaction of many ultrasound induced organic transformations offers additional convenience in the field of synthetic organic chemistry [33-36].These finding promotes us to investigate the synthesis of benzimidazoles, benzoxazole and benzothiazoles in aqueous media.

EXPERIMENTAL

Bandelin Sonorex (35 kHz) ultrasonic bath was used for ultrasonic irradiation. ^{1}H NMR spectra were recorded on Mercury Plus Varian in DMSO at 400 MHz using TMS as an internal standard. Mass spectra were recorded on Micromass Quattro II using electrospray Ionization technique, showing (M+H) peak as a base peak. The progress of the reactions was monitored by TLC (silica, 80:20 hexane/ ethyl acetate).

General Procedure for the Preparation of **3a-3l**

o-phenylene diamine (1mmol), aromatic aldehyde (1.1mmol) and water (10mL) were mixed in 25mL single neck round bottom flask, and to this Ammonium Nickel Sulphate (10 mol %) was added. The reaction mixture was sonicated at room temperature (25^{0}C) for the appropriate time (Table 2, entries 1-12), and the progress of reaction was monitored by TLC. After completion of reaction, the mixture was extracted with ethyl acetate (2×10mL). The combined organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure; the crude material was purified by column chromatography over silica gel to afford products 3a-3l with high purity.

Selected spectral data

2-phenyl-1H-benzimidazole **3a**

^{1}H NMR(400MHz DMSO) δ12.7 (s, 1H, NH), 7.95(m, 2H, ArH), 7.25-7.35(m, 5H, ArH), 7.05(2H, ArH); *m/z* 195(M+H). Elemental analysis Calcd. for $C_{13}H_{10}N_2$. C, 80.39; H, 5.19; N, 14.42. Found: C, 80.42; H, 5.17; N, 14.41.

2-(4-methoxy phenyl)-1H-benzimidazole **3b**

^{1}H NMR(400MHz DMSO) δ 3.8(s, 3H, OCH3), 7.09-7.11(d, 2H, *J* 9.2Hz, ArH), 7.16-7.18(m, 2H, ArH), 7.53-7.56(m, 2H, ArH), 8.08-8.11(d, 2H, *J* 8.8Hz, ArH); *m/z* 225 (M+H) . Elemental analysis Calcd. for $C_{14}H_{12}N_2O$. C, 74.98; H, 5.39; N, 12.49. Found: C, 75.03; H, 5.36; N, 12.45.

2-(4-chlorophenyl)-1H-benzimidazole **3c**

^{1}H NMR(400MHz DMSO) δ 12.5 (s, 1H, NH), 8.20 (d, 2H, ArH), 7.6 (d, 2H, ArH), 7.3 (m, 2H, ArH), 7.1 (m, 2H, ArH); *m/z* 229(M+H). Elemental analysis Calcd. for $C_{13}H_9N_2Cl$. C, 68.28; H, 3.97; N, 12.25. Found: C, 68.20; H, 4.01; N, 12.28.

5-Chloro-2-(4-methoxyphenyl)-1H-benzimidazole **3d**

^{1}H NMR(400MHz DMSO) δ 7.97 (d, *J* 9.2 Hz, 2H), 7.86 (s, 1H), 7.67 (d, *J* 8.1 Hz, 1H), 7.35 (d, *J* 8.1 Hz,1H), 6.92 (d, *J* 9.2 Hz, 2H), 3.75 (s, 3H) ; *m/z* 276 (M+H). Elemental analysis Calcd. for $C_{14}H_{11}ClN_2O$. C, 65.00; H, 4.29; N, 10.83. Found: C, 65.05; H, 4.25; N, 10.80.

5-Chloro-2-(4-nitrophenyl)-1H-benzimidazole **3e**

^{1}H NMR(400MHz DMSO-d_6) δ 8.52 (d, *J* 9.4 Hz, 2H), 7.96 (d, *J* 9.4 Hz, 2H), 7.85 (s, 1H), 7.71 (d, *J* 8.2 Hz, 1H),7.32 (d, *J* 8.2 Hz, 1H); *m/z* 274 (M+H). Elemental analysis Calcd. for $C_{13}H_8ClN_3O_2$. C, 57.05; H, 2.95; N, 15.35. Found: C, 56.98; H, 3.01; N, 15.30.

5-Chloro-2-(4-N,N-dimethylaminophenyl)-1H-benzimidazole: **3f**

^{1}H NMR(400MHz DMSO-d_6) δ 7.94 (d, *J* 8.9 Hz, 2H), 7.85 (s, 1H), 7.66 (d, *J* 8.3 Hz, 1H), 7.37 (d, *J* 8.3 Hz, 1H), 6.82 (d, *J* 8.9 Hz, 2H), 3.35 (s, 6H); *m/z* 272 (M+H). Elemental analysis Calcd. for $C_{15}H_{14}ClN_3$. C, 66.30; H, 5.19; N, 15.46. Found: C, 66.38; H, 5.12; N, 15.40.

2-(3-nitrophenyl)-1H- benzimidazole **3g**

^{1}H NMR(400MHz DMSO-d_6) δ 12.9 (s,1H NH), 8.90 (s,1H Ar H), 8.50 (d,1H Ar H), 8.10 (d,1H Ar H), 7.70 (t,1H Ar H), 7.50 (m, 2H ArH), 7.2 (m, 2H ArH); *m/z* 240(M+H). Elemental analysis Calcd. for $C_{13}H_9N_3O_2$. C, 65.27; H, 3.79; N, 17.56. Found: C, 65.32; H, 3.70; N, 17.62.

2-pyridin-3yl-1H-benzimidazole **3h**

^{1}H NMR(400MHz DMSO-d_6) δ 13.05 (s, 1H NH), 9.35(d,1H ArH), 8.75(m,1H ArH), 8.60(m,1H ArH), 7.70(m,3H ArH) 7.40 (m,2H ArH); *m/z* 196(M+H). Elemental analysis Calcd. for $C_{12}H_9N_3$. C, 73.83; H, 4.65; N, 21.52. Found: C, 73.90; H, 4.60; N, 21.50.

2-(2,3-Dimethoxyphenyl)-1H-benzimidazole **3i**

^{1}H NMR(400MHz DMSO-d_6) δ 12.19 (s, 1H, NH), 7.84 (dd, 1H, *J*

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7.3 Hz,1.1 Hz, ArH), 7.64 (m, 3H, ArH), 7.20 (m, 3H, ArH), 3.90 (s, 3H, OCH3), 3.85 (s, 3H, OCH3); *m/z* 255 (M+H). Elemental analysis Calcd. for $C_{15}H_{14}N_2O_2$. C, 70.85; H, 5.55; N, 11.02. Found: C, 70.89; H, 5.49; N, 11.07.

2-(3-Fluorophenyl)-1H-benzimidazole **3j**

^{1}H NMR(400MHz DMSO-d_6) δ 13.00 (s, 1H, NH), 8.02 (d, 1H, *J* 7.7 Hz, ArH), 7.96 (m, 1H, ArH), 7.69 (m, 1H, ArH), 7.59 (m, 2H, ArH), 7.34 (m, 1H, ArH), 7.23 (m, 2H, ArH); *m/z* 213 (M+H). Elemental analysis Calcd. for $C_{13}H_9FN_2$. C, 73.57; H, 4.27; N, 13.20. Found: C, 73.51; H, 4.32; N, 13.28.

2-(3-chloro phenyl)-1H-benzimidazole **3k**

^{1}H NMR(400MHz DMSO-d_6) δ 8.41(t, 1H, *J* 1.2Hz, 2.0Hz, ArH), 8.20-8.29(dd, 1H, *J* 1.2 ,7.6Hz, ArH), 7.80-7.84(m, 2H, ArH), 7.69-7.77(m, 2H, ArH), 7.50-7.54(m, 2H,ArH); *m/z* 229 (M+H). Elemental analysis Calcd. for $C_{13}H_9ClN_2$. C, 68.28; H, 3.97; N, 12.25. Found: C, 68.35; H, 3.92; N, 12.20.

2-(4-nitrophenyl)-1H- benzimidazole **3l**

^{1}H NMR(400MHz DMSO-d_6) δ 8.37-8.39(d,2H,*J* 8.4Hz, ArH), 8.14-8.17(d, 2H, *J* 8.8Hz, ArH), 7.70-7.72(d,1H,*J* 7.6 Hz, ArH), 7.65-7.67(d, 1H, *J* 8.4Hz, ArH) 7.32-7.35(m, 1H,ArH), 7.25-7.29(m,1H, ArH); *m/z* 240(M+H). Elemental analysis Calcd. for $C_{13}H_9N_3O_2$. C, 65.27; H, 3.79; N, 17.56. Found: C, 65.20; H, 3.87; N, 17.50.

General Procedure for the Preparation of **4a-4m**

o-amino thiophenol (1mmol), aromatic aldehyde (1.1mmol) and water (10mL) were mixed in 25mL single neck round bottom flask, and to this Ammonium Nickel Sulphate (10 mol %) was added. The reaction mixture was sonicated at room temperature (25^{0}C) for the appropriate time (Table 2, entries 13-25), and the progress of reaction was monitored by TLC. After completion of reaction, the mixture was extracted with ethyl acetate (2×10mL). The combined organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure; the crude material was purified by column chromatography over silica gel to afford products 4a-4m with high purity.

Selected spectral data

2-Phenyl-1,3-benzothiazole **4a**

^{1}H NMR(400MHz DMSO) δ 8.12(d, *J* 7.38Hz, 1H, ArH), 8.02(t, *J* 7.42 Hz, 1H, ArH), 7.65(t, *J* 7.42Hz, 1H, ArH), 7.33-7.39(m, 3H, ArH), 7.19-7.25(m, 3H, ArH).;*m/z* 212(M+H). Elemental analysis Calcd. for $C_{13}H_9NS$. C, 73.90; H, 4.29; N, 6.63. Found: C, 73.82; H, 4.35; N, 6.58.

2-(4-Methoxyphenyl)- 1,3-benzothiazole **4b**

^{1}H NMR(400MHz DMSO) δ 8.19(d, *J* 8.22Hz, 1H,ArH), 8.05(d, *J* 8.22Hz, 1H, ArH), 7.07(d, *J* 7.75Hz, 2H, ArH), 7.12-7.41(m, 4H, ArH), 3.92(s 3H, OCH3); *m/z* 242(M+H). Elemental analysis Calcd. for $C_{14}H_{11}NOS$. C, 69.68; H, 4.59; N, 5.80. Found: C, 69.59; H, 4.65; N, 5.85.

2-(4-Nitrophenyl) benzothiazole **4c**

^{1}H NMR(400MHz DMSO-d_6) δ 8.9 (d, *J* 8.0 Hz, 2H, Ar-H); 8.32 (d, *J* 8.0 Hz, 2H, Ar- H); 8.23 (d, *J* 8.0 Hz, 1H, Ar-H); 8.02 (d, *J* 8.0 Hz, 1H, Ar-H); 7.44-7.53 (m, 2H, Ar-H); *m/z* 256 (M+H). Elemental analysis Calcd. for $C_{13}H_8N_2O_2S$. C, 60.93; H, 3.15; N, 10.93. Found: C, 61.03; H, 3.20; N, 10.85.

2-Thienyl-1,3-benzothiazole **4d**

^{1}H NMR(400MHz DMSO) δ 8.22 (d, *J* 8.0 Hz, 1H, ArH); 8.13 (d, *J* 8.0 Hz, 1H, ArH); 7.74 (d, *J* 4.0 Hz, 1H, thiophene CH); 7.69 (d, *J* 4.0 Hz, 1H, thiophene CH); 7.54-7.63 (m, 2H, Ar-H);7.33 (t, *J* 4.0 Hz, 1H, thiophene CH); *m/z* 217(M+H). Elemental analysis Calcd. for $C_{11}H_7NS_2$. C, 60.80; H, 3.25; N, 6.45. Found: C, 60.84; H, 3.20; N, 6.52.

2-(4-Fluoro phenyl) benzothiazole **4e**

^{1}H NMR(400MHz DMSO-d_6) δ 8.7 (s, 1H, pyrazolyl-H), 8.03 (d, *J* 6 Hz, 2H), 7.74 7.85 (m, 5H, Ar-H), 7.45-7.60 (m, 5H, Ar-H), 7.31-7.38 (dd, *J* 8Hz , 6 Hz, 2H); *m/z* 230 (M+H). Elemental analysis Calcd. for $C_{13}H_8FNS$. C, 68.16; H, 3.52; N, 6.11. Found: C, 68.16; H, 3.45; N, 6.18.

2-(4 methyl phenyl) benzothiazole **4f**

^{1}H NMR(400MHz DMSO-d_6) δ 7.92-8.10(m 3H Ar H), 7.41(t *J* 7.38Hz, 1H Ar H), 7.30 (t *J* 7.38Hz, 1H Ar H), 7.26(d *J* 8.12Hz 2H Ar H),2.45(s 3H CH_3) ;*m/z* 226(M+H). Elemental analysis Calcd. for $C_{14}H_{11}NS$. C, 74.63; H, 4.92; N, 6.22. Found: C, 74.69; H, 4.88; N, 6.28.

2-(4-cyanophenyl) benzothiazole **4g**

^{1}H NMR(400MHz DMSO-d_6) δ 8.09(d, *J* 8.15Hz, 2H, ArH), 8.05(dd, *J* 2.42Hz, 7.55 Hz, 2H, ArH), 7.85(d,*J* 8.15Hz,2H,ArH),7.61(dd, *J* 7.55Hz, 7.75Hz, 2H, ArH) ;*m/z* 237(M+H). Elemental analysis Calcd. for $C_{14}H_8N_2S$. C, 71.16; H, 3.41; N, 11.86. Found: C, 71.21; H, 3.44; N, 11.80.

2-(3,4,5 trimethoxy phenyl) benzothiazole **4h**

^{1}H NMR(400MHz DMSO-d_6) δ 8.31(t, 1H, ArH), 8.22(t, 1H, ArH), 7.45(dd *J* 2.42Hz,7.55Hz, 2H, ArH), 6.57(d, *J* 2.42Hz, 2H, ArH), 3.61(s, 9H, OCH3).;*m/z* 302(M+H). Elemental analysis Calcd. for $C_{16}H_{15}NO_3S$. C, 63.77; H, 5.02; N, 4.65. Found: C, 63.69; H, 4.99; N, 4.71.

2-(4-chlorophenyl) benzothiazole **4i**

^{1}H NMR(400MHz DMSO-d_6) δ 8.15(d, *J* 7.3Hz, 1H, ArH), 8.05(d, *J* 8.4 Hz, 2H, ArH), 7.80 (d, *J* 7.3 Hz, 1H, ArH), 7.41(t, *J* 7.6 Hz, 1H, ArH), 7.30(t, *J* 7.6 Hz, 1H, ArH),7.16(d, *J* 8.22Hz, 2H, ArH); *m/z* 246(M+H). Elemental analysis Calcd. for $C_{13}H_8ClNS$. C, 63.54; H, 3.28; N, 5.70. Found: C, 63.61; H, 3.30; N, 5.65.

6-Chloro-2-phenyl benzothiazole **4j**

^{1}H NMR(400MHz DMSO-d_6) δ 8.19(d, *J* 8.3Hz, 1H, ArH), 8.13(d, *J* 2.12Hz, 1H, ArH), 7.56(dd, *J* 7.61Hz, 2.17, 2H, ArH), 7.36(t, *J* 7.61Hz, 2H,ArH),7.16(m, 1H, ArH); *m/z* 246(M+H). Elemental analysis Calcd. for $C_{13}H_8ClNS$. C, 63.54; H, 3.28; N, 5.70. Found: C, 63.49; H, 3.32; N, 5.78.

6-chloro-2(3-methoxy phenyl) benzothaizole **4k**

^{1}H NMR(400MHz DMSO-d_6) δ 7.99(d, *J* 2.5Hz, 1H,ArH), 7.77(d, *J* 7.7Hz, 1H, ArH), 7.60-7.70(m, 2H,ArH), 7.32-7.50(m, 2H,ArH), 7.16(dd *J* 2.5Hz, 7.8 Hz, 1H, ArH), 3.91(s 3H, OCH3); *m/z* 276(M+H). Elemental analysis Calcd. for $C_{14}H_{10}ClNOS$. C, 60.98; H, 3.66; N, 5.08. Found: C, 61.05; H, 3.58; N, 5.13.

6-chloro-2-(4-chlorophenyl) benzothiazole **4l**

^{1}H NMR(400MHz DMSO-d_6) δ 8.17(d, *J* 7.9Hz, 1H, ArH), 8.13(d, *J* 2.2Hz, 1H, ArH), 7.56(dt, *J* 7.9Hz, 2.2Hz, 1H, ArH), 7.41(d, *J* 8.1Hz, 2H, ArH), 7.32(d, *J* 8.1Hz, 2H, ArH); *m/z* 280(M+H). Elemental analysis Calcd. for $C_{13}H_7Cl_2NS$. C, 55.73; H, 2.52; N, 5.00. Found: C, 55.70; H, 2.48; N, 5.06.

2-(4-(piperidin-1-yl)phenyl)benzothiazole **4m**

^{1}H NMR(400MHz DMSO-d_6) δ 7.92-8.00(m, 2H, ArH), 7.84-7.90(d, *J* 7.6Hz, 2H,ArH), 7.25(m,2H, ArH), 6.94-6.97(d, *J* 7.6Hz, 2H,ArH), 3.31-3.34(m, 4H,piperidine N-CH_2,), 1.53-1.71(m, 6H, piperidine CH_2); *m/z* 295(M+H). Elemental analysis Calcd. for $C_{18}H_{18}N_2S$. C, 73.43; H, 6.16; N, 9.51. Found: C, 73.50; H, 6.20; N, 9.45.

General Procedure for the Preparation of **5a-5f**

o-amino phenol (1mmol), aromatic aldehyde (1.1mmol) and water (10mL) were mixed in 25mL single neck round bottom flask, and to this Ammonium Nickel Sulphate (10 mol %) was added. The reaction mixture was sonicated at room temperature (25^{0}c) for the appropriate time (Table 2, entries 26-31), and the progress of reaction was monitored by TLC. After completion of reaction, the mixture was extracted with ethyl acetate (2×10mL). The combined organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure; the crude material was purified by column chromatography over silica gel to afford products 5a-5f with high purity.

Selected spectral data

2- phenyl benzoxazole **5a**

^{1}H NMR(400MHz DMSO-d_6) δ 8.32(dd, *J* 5.6Hz, 2.1Hz, 2H, ArH), 7.79-7.86(m, 1H, ArH), 7.53-7.67(m, 4H, ArH), 7.36-7.44(m, 2H, ArH).; *m/z* 196(M+H). Elemental analysis Calcd. for $C_{13}H_9NO$. C, 79.98; H, 4.65; N, 7.17. Found: C, 79.91; H, 4.70; N, 7.20.

2-(4-methoxyphenyl)benzoxazole **5b**

^{1}H NMR(400MHz DMSO) δ 8.22(d, *J* 8.2Hz, 2H, ArH), 7.85 (m, 1H, ArH), 7.61(m, 1H, ArH), 7.37-7.42(m, 2H, ArH), 7.16(d, *J* 8.2Hz, 2H, ArH), 3.89(s, 3H, OCH3); *m/z* 226(M+H). Elemental analysis Calcd. for $C_{14}H_{11}NO_2$. C, 74.65; H, 4.92; N, 6.22. Found: C, 74.70; H, 4.88; N, 6.17.

2-(4-cyanophenyl)benzoxazole **5c**

^{1}H NMR(400MHz DMSO-d_6) δ 8.32(d, *J*8.5Hz, 2H, ArH), 7.81-7.97(m,3H, ArH), 7.51(m, 1H, ArH), 7.31-7.49(m, 2H,ArH); *m/z* 221(M+H). Elemental analysis Calcd. for $C_{14}H_8N_2O$. C, 76.35; H, 3.66; N, 12.72. Found: C, 76.28; H, 3.70; N, 12.68.

2-(3,4- dichlorophenyl)benzoxazole **5d**

^{1}H NMR(400MHz DMSO) δ 8.37(d *J* 8.1Hz, 1H, ArH), 8.19(dd, *J* 8.2Hz, 1.8Hz, 1H, ArH), 7.72-7.83(m, 1H, ArH), 7.62-7.71(m, 2H, ArH), 7.40-7.45(m, 2H, ArH); *m/z* 264(M+H). Elemental analysis Calcd. for $C_{13}H_7Cl_2NO$. C, 59.12; H, 2.67; N, 5.30. Found: C, 59.20; H, 2.62; N, 5.24.

6-methyl-2phenyl benzoxazole **5e**

^{1}H NMR(400MHz DMSO-d_6) δ 8.26-8.39(m, 2H, ArH), 7.70(d, *J* 8.2Hz, 1H,ArH), 7.55-7.62(m, 3H, ArH), 7.35(m, 1H, ArH), 7.09(m, 1H, ArH), 2.51(s, 3H, CH_3); *m/z* 210(M+H). Elemental analysis Calcd. for $C_{14}H_{11}NO$. C, 80.36; H, 5.30; N, 6.69. Found: C, 80.43; H, 5.26; N, 6.60.

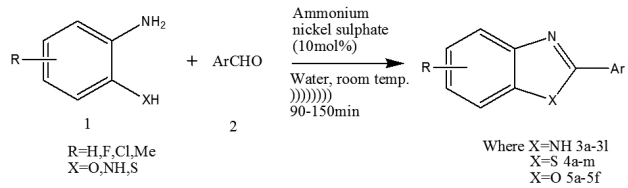
6-fluoro -2-phenyl benzoxzole **5f**

^{1}H NMR(400MHz DMSO) δ 8.20-8.28(m, 2H, ArH), 7.79(dd, *J* 8.8Hz, 4.9Hz, 1H,ArH), 7.52-7.61(m, 3H,ArH), 7.29(dd, *J* 8.0, 2.3Hz, 1H, ArH), 7.11(m, 1H, ArH); *m/z* 214(M+H). Elemental analysis Calcd. for $C_{13}H_8FNO$. C, 73.23; H, 3.78; N, 6.57. Found: C, 73.20; H, 3.83; N, 6.50.

RESULT AND DISCUSSION

We developed an ecofriendly, one pot Ammonium Nickel Sulfate catalyzed synthesis of 2-aryl substituted benzimidazole, benzoxazole and benzothiazole in water.

2-(4-methoxy phenyl)benzimidazole (**3b**)(scheme 1) was selected as a proto type compound to optimize the reaction condition (Table 1) from o-phenylene diamine (**1**) and anisaldehyde (2). We first conducted the reaction of **1** (1 equivalent) and **2** (1.1 equivalent) in the presence of Ammonium Nickel Sulfate in water at different temperature (Table 1 entries 10 to12). The yield increases from 30% to 50% up to 80ºC in 8hours. With the aim to reduce reaction time and temperature, we move to non-conventional energy source i.e. ultrasound energy, so we carried the reaction under ultrasound, to afford the corresponding 2-(4-methoxy phenyl)benzimidazole (**3b**) in 85% yield (Table 1 entry 13)in much shorter time at room temperature. To know the effect of solvent, We kept the catalyst constant and used different solvent CH_2Cl_2 , CH_3CN, THF, $CHCl_3$, DMF, EtOH ,DMSO and Dioxane but all afford a very low yield (Table 1 entries 1-8). These indicate that water is the best solvent for the synthesis of **3b**; it may be due to solubility of catalyst, varying the amount of catalyst did not improve the yield (Table 1 entries14, 15)



Scheme 1

With optimal condition in hand, we reacted various substituted o-phenylene diamine **1** and aromatic aldehyde **2** to give the corresponding substituted 2-aryl benzimidazole product **3a** to **3l** (Table 2 entries1-12). A wide variety of aldehydes were used, which have both electron donating and electron withdrawing substituents along with substituted o-phenylene diamine. The method is also suitable for heteroaromatic aldehyde.

Table 1. Solvent effect on the reaction of anisaldehyde and o-phenylene diamine in presence of ammonium nickel sulphate.

Entry	solvent	catalyst	Temp./^{0}C	Time/min	Product[a]	Yield (%)[b]
1	CH_2Cl_2	10	RT*	120	3b	Traces
2	$CHCl_3$	10	RT*	120	3b	Traces
3	DMSO	10	RT*	120	3b	45
4	DMF	10	RT*	120	3b	45
5	EtOH	10	RT*	120	3b	30
6	CH_3CN	10	RT*	120	3b	40
7	Dioxane	10	RT*	120	3b	38
8	THF	10	RT*	120	3b	36
9	H_2O	10	RT	8Hours	3b	Traces
10	H_2O	10	40	8 Hours	3b	25
11	H_2O	10	60	8 Hours	3b	40
12	H_2O	10	80	8 Hours	3b	50
13	H_2O	10	RT*	120	3b	85
14	H_2O	05	RT*	120	3b	65
15	H_2O	15	RT*	120	3b	85

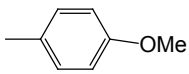
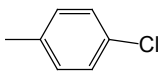
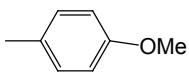
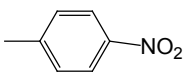
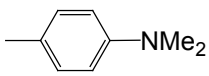
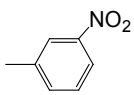
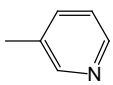
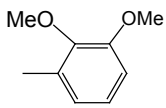
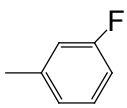
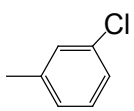
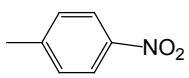
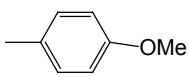
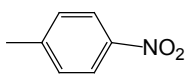
***** Under ultra-sonication.

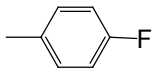
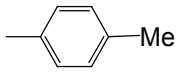
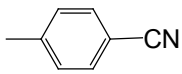
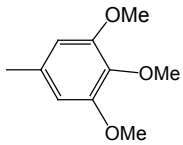
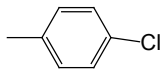
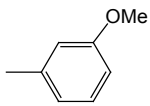
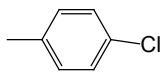
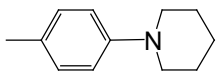
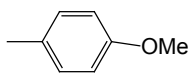
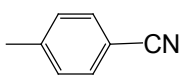
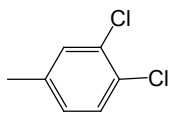
[a]1mmole of o-phenylene diamine , 1.1mmol anisaldehyde, 10mol% catalyst, solvent, room temperature. [b]Isolated yield based on starting o-phenylene diamine.

The scope of above procedure was expanded to the synthesis of2-aryl benzoxazole from o-amino phenol and 2-aryl benzothiazole from o-aminothiophenol, the results are summarized in Table 2. Aromatic aldehyde with electron donating as well as electron withdrawing groups participated in the reaction, the nature and position of substituent on the aryl ring does not make much difference in reactivity. The structures of the products were confirmed by ^{1}H NMR, mass spectra.

Table 2. Ammonium nickel sulphate [$(NH_4)_2SO_4.NiSO_4.6H_2O$] catalyzed of 2-arylbenzimidazole, 2-arylbenzothiazole and 2-arylbenzoxazole under ultrasonication in water

Standard condition: 1mmole of o-phenylene diamine or o-aminothiophenol or o-aminophenol, 1.1mmol ArCHO, 10mol% catalyst(ammonium nickel sulphate) , water , room temperature. Isolated yield based on starting o-phenylene diamine or o-aminothiophenol or o-aminophenol

entry	R	Ar	X	product	Time(min)	yield	M.Pt ^{0}C	
							observed	reported
1	H		N	3a	135	80	287-288	292 [37]
2	H		N	3b	120	85	228-230	226 [37]
3	H		N	3c	110	89	288-291	294 [37]
4	5-Cl		N	3d	140	86	276-279	278-279 [40]
5	5-Cl		N	3e	105	87	258-259	260-261 [40]
6	5-Cl		N	3f	150	85	311-313	310-312 [43]
7	H		N	3g	95	85	200-202	204-206 [38]
8	H		N	3h	110	88	243-246	245-248 [42]
9	H		N	3i	145	83	175-177	178-179 [39]
10	H		N	3j	120	87	219-221	220-222 [39]
11	H		N	3k	125	88	230-231	234 [37]
12	H		N	3l	110	90	308-310	316 [37]
13	H		S	4a	90	91	110-112	113 – 114 [40]
14	H		S	4b	95	90	121-124	120 – 122 [40]
15	H		S	4c	85	86	224-227	226 – 228 [40]

16	H		S	4d	110	83	101-104	100 – 102 [40]
17	H		S	4e	95	86	98-100	101 – 102 [41]
18	H		S	4f	105	85	83-84	85-87 [41]
19	H		S	4g	90	86	98-99	100-102 [31]
20	H		S	4h	115	83	----------	Color less oil
21	H		S	4i	90	91	115-118	116 – 118 [40]
22	6-Cl		S	4j	95	85	102-103	104-105 [31]
23	6-Cl		S	4k	110	85	71-74	72-74 [31]
24	6-Cl		S	4l	90	86	141-142	140-142 [31]
25	H		S	4m	100	85	72-74	--------
26	H		O	5a	130	83	100-101	101-102 [31]
27	H		O	5b	135	85	96-97	98 [31]
28	H		O	5c	120	83	200-202	201-204 [31]
29	H		O	5d	120	83	140-143	142-144 [31]
30	6-Me		O	5e	130	85	93-96	95 [31]
31	6-F		O	5f	120	86	110-112	108-111 [31]

CONCLUSIONS

Ammonium Nickel Sulphate as a catalyst provides cheap, safe and environment friendly procedure for the synthesis of 2-aryl substituted benzimidazole, benzoxazole and benzothiazole derivatives from various aromatic aldehydes with o-phenylene diamine, o-amino phenol and o-amino thiophenol. The advantages offered by this method are operational simplicity, good yield of product.

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