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A Facile Catalytic One-Pot Synthesis of Benzimidazole and Benzothiazole Compounds using Amberlite IRA 400-Cl Resin as Green Catalyst

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A series of pharmaceutically valuable functionalized fused heteroaromatic compounds such as benzimidazoles and benzothiazoles have been synthesized *via* catalytic cyclocondensation between 1,2-phenylenediamine or 2-aminothiophenol and aryl aldehydes at ambient conditions. The Amberlite IRA400-Cl resin have been proved to be an efficient green catalyst in this protocol. The salient features of this method are the mild condition, easy work-up, an excellent yield of product, green catalyst and reusability of the catalyst.

Keywords: Cyclocondensation, Amberlite IRA-400 Cl resin, Green catalyst, Benzimidazoles, Benzothiazoles.

INTRODUCTION

Solid base heterogeneous catalysts such as quaternary ammonium halide type of anion exchange resin, [Amberlite IRA400 (Cl^-)], has been achieved great interest from both environmental and economic points of view [1]. The main benefits such as low cost, reusability, ease of handling and no side reactions making the process economically viable. Furthermore, this heterogeneous catalyst Amberlite IRA400 (Cl^-) has been used for a wide range of organic transformations [2-5]. Benzofused heteroaromatic compounds display an array of applications in pharmaceutical and medicinal chemistry. This class of heterocycles also show a wide range of biological activities including antihypertensive, antiulcer, antifungal, anticancer, antihistamine, antihelminthic, antiparasitic, antiviral, anticoagulant, antiallergic, analgesic, anti-inflammatory, antimicrobial and immunosuppressant [6-13].

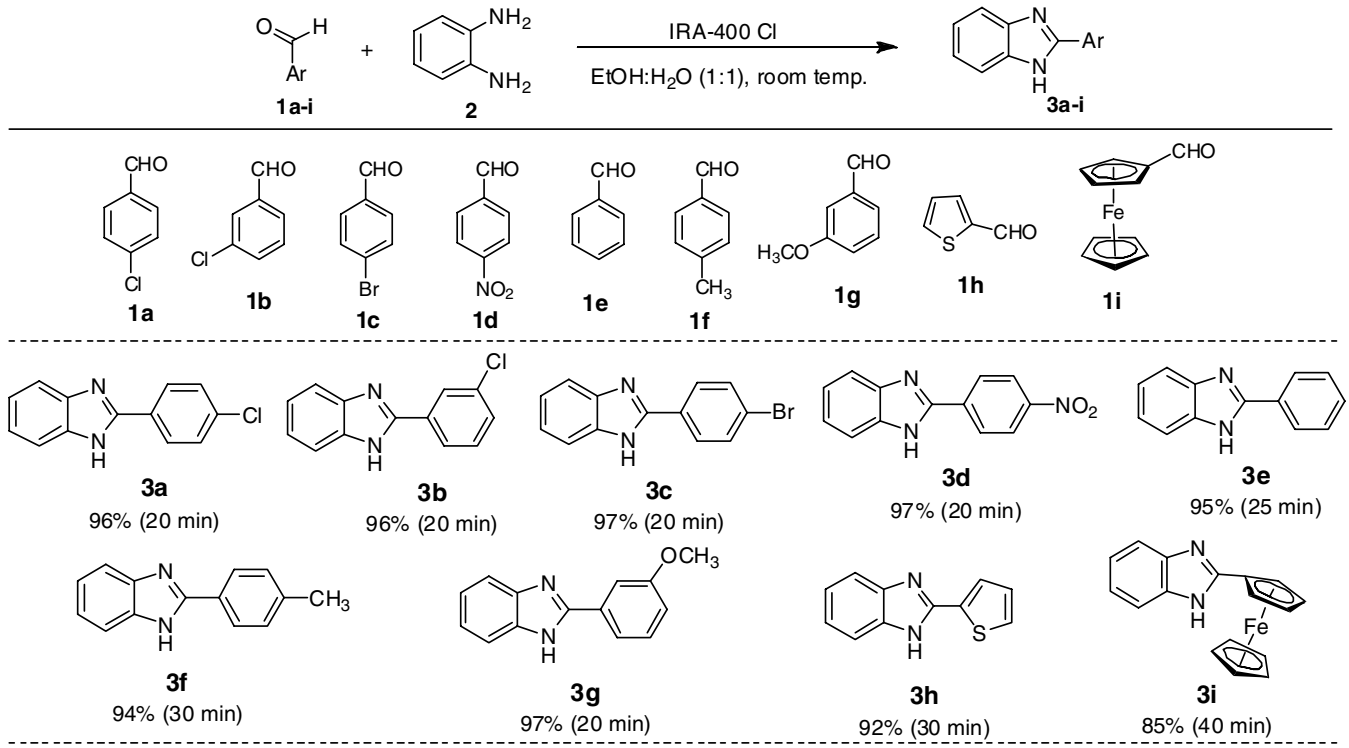
Benzimidazole derivatives are an integral part of various clinical medicines against several viruses such as herpes (HSV-1) [14], HIV [15], RNA [16] and influenza [17]. Benzothiazoles and its derivatives have been used as radiolabeling for positron emission tomography (PET) imaging in the diagnosis of Alzheimer's disease and to enhance the donor-acceptor effects in the chromophores [18]. Further, benzothiazoles are also known to be powerful antitumour agents [19-24], calmodulin antagonists [25], neurotransmission blocker [26-28] and neuroprotective agent [29,30]. Several catalytic methods have been reported for the construction of benzofused heterocyclic compounds, using Mont-K10, Air/DMSO and H_2O_2/CAN catalytic systems [31-38]. The disadvantages of this catalysts are expensive, excess catalysts loading, long reaction times and tedious work-up procedures. In this context, developing an efficient and eco-friendly greener method for the synthesis of benzimidazole and benzothiazole is still in demand. To our knowledge, there is no report available for the synthesis of benzimidazole and benzothiazole derivatives using Amberlite IRA 400-Cl resin as a green catalyst. Therefore, our approach to utilize the Amberlite IRA-400 Cl ion exchange resin as solid base catalyst for cyclocondensation between 1,2-phenylenediamine or 2-aminothiophenol and aryl aldehydes. The optimization, synthetic utility and characterization of benzimidazole and benzothiazole compounds have been discussed.

EXPERIMENTAL

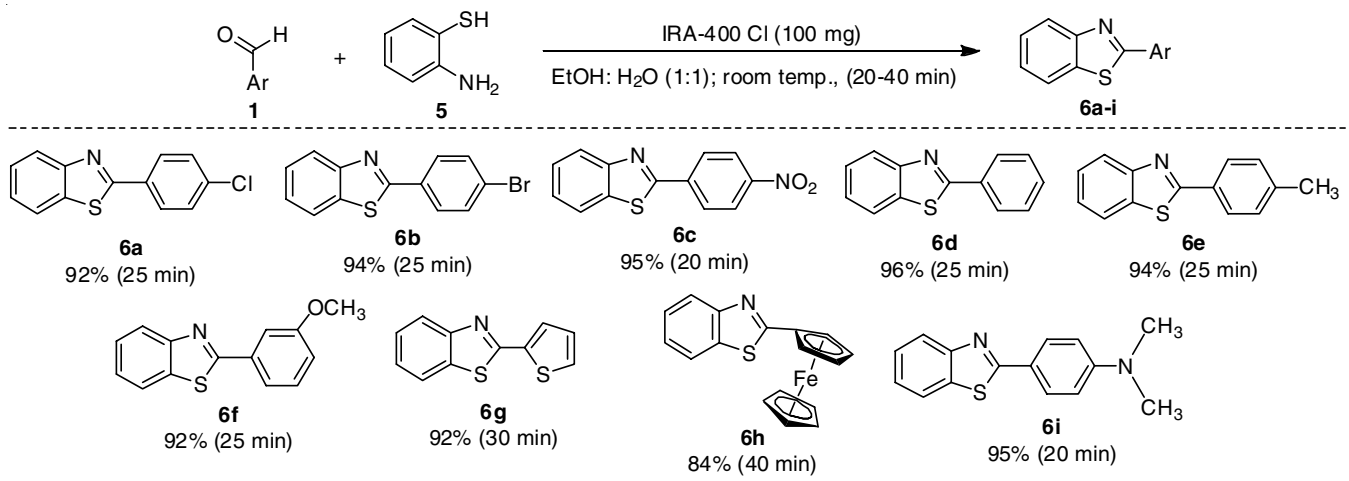
All chemicals and solvents were commercially available and were used after distillation or treatment with drying agents. All the reactions were carried out in over-dried glasswares.

Progress of reactions was monitored by thin layer chromatography (TLC) while purification of crude compounds was done by column chromatography using silica gel (100-200 mesh). FT-IR spectra were recorded on a Thermo Mattson Satellite Fourier Transform-IR 3000 spectrophotometer using KBr. NMR spectra were recorded at Bruker NMR spectrometer (300.13 and 75.47 MHz/400.13 and 100.61). Chemical shifts were reported in δ (ppm) relative to TMS (^{1}H) o r $CDCl_3$/DMSO-d_6 (^{13}C) as internal standards. All ^{13}C NMR spectra were recorded with complete proton decoupling. Yields refer to quantities obtained after chromatography.

Synthesis of benzimidazoles (3) and benzothiazoles (6): In 50 mL round bottom flask, *o*-phenlylenediamine (**2**) or *o*-aminothiophenol 5 (1 mmol) and aldehyde **1** (1 mmol) were thoroughly mixed with 5 mL of water/ethanol (1:1). To this 100 mg Amberlite IRA-400 Cl was added and stirred for the appropriate period of time (20-40 min). After the completion of the reaction (TLC monitoring), the catalyst was separated by filtration and washed with 15 mL ethyl acetate. The filtrate was evaporated under reduced pressure, the resulting solid product was recrystallized from ethanol to afford pure products **3** (**Scheme-I**) and 6 (**Scheme-II**). The compounds which are



Scheme-I: Catalytic cyclocondensation between *o*-phenylenediamine (**2**) and aldehydes (**1a-i**) (Reaction conditions: Aldehydes (**1**), *o*-phenylenediamine (**2**), were taken in a 1:1 ratio in the presence of IRA-400 Cl in 5 mL of H_2O:EtOH (1:1) under room temp.; Isolated yield



Scheme-II: Synthesis of benzothiazoles catalyzed by Amberlite IRA-400 Cl resin (Reaction conditions: Aldehyde (**1**), 2-ATP (2-aminothiophenol) (**5**), were taken in a 1:1 ratio in the presence of 0.1 g of IRA -400 Cl in 5 mL of EtOH:H_2O (1:1) under room temp.; Isolated yield)

not crystalizes well were purified using column chromatography.

2-(4-Chlorophenyl)-1*H*-benzimidazole (3a): White crystalline solid. Yield: 96%; m.p.: 290 ºC (lit. [39] m.p.: 290-292 ºC). R_f (40% EtOAc-petroleum ether): 0.54. IR (KBr, ν_{max}, cm^{-1}): 3429 (-NH), 1573 (C=N), 1422 (C=C). ^{1}H NMR (400.13 MHz, DMSO-d_6): δ 13.05 (s, 1H, NH), 8.23 (s, 1H), 8.13-8.16 (m, 1H), 7.69 (d, *J* = 7.2 Hz, 1H), 7.55-7.62 (m, 3H), 7.23 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (100.61 MHz, DMSO-d_6): δ 149.6, 133.7, 132.1, 130.9, 129.5, 125.9, 124.9, 122.9, 121.9, 119.0, 111.4

2-(3-Chlorophenyl)-1*H*-benzimidazole (3b): White crystalline solid. Yield: 96%; m.p.: 228–230 ºC (lit. [41] m.p.: 230-232 ºC). R_f (40% EtOAc-petroleum ether): 0.53. IR (KBr, ν_{max}, cm^{-1}): 3445 (-NH), 1623 (C=N), 1456 (C=C). ^{1}H NMR (400.13 MHz, DMSO-d_6): δ 12.99 (s, 1H, NH), 8.18 (d, *J* = 8.4 Hz, 2H), 7.56-7.64 (m, 4H), 7.21 (d, *J* = 4.4 Hz, 2H). ^{13}C NMR (100.61 MHz, DMSO-d_6): δ 150.1, 134.4, 129.0, 128.1, 124.9, 122.9, 122.0, 119.0, 111.5.

2-(4-Bromophenyl)-1*H*-benzimidazole (3c): White crystalline solid, Yield: 97%; m.p.: 270-272 ºC (lit. [39] m.p.: 268-270 ºC). R_f (40% EtOAc-petroleum ether): 0.55. IR (KBr, ν_{max}, cm^{-1}): 3438 (-NH), 1635 (C=N), 1434 (C=C). ^{1}H NMR (400.13 MHz, DMSO-d_6): δ 12.99 (s, 1H, NH), 8.12 (d, *J* = 8.4 Hz, 2H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.18-7.26 (m, 2H). ^{13}C NMR (100.61 MHz, DMSO-d_6): δ 150.1, 143.7, 134.9, 131.9, 129.3, 128.3, 123.2, 122.7, 121.8, 118.9, 111.3.

2-(4-Nitrophenyl)-1*H*-benzimidazole (3d): Yellow crystalline solid. Yield: 97%; m.p.: 320 ºC (lit. [39] m.p.: 318-320 ºC). R_f (40% EtOAc-petroleum ether): 0.53. IR (KBr, ν_{max}, cm^{-1}): 3448 (-NH), 1626 (C=N), 1529 (C=C), 1356 (NO_2). ^{1}H NMR (400.13 MHz, DMSO-d_6): δ 8.62 (s, 1H, NH), 8.31 (d, *J* = 8.0 Hz, 2H), 8.06 (d, *J* = 8.0 Hz, 2H), 7.11-7.15 (m, 2H), 6.75-6.81 (m, 2H). ^{13}C NMR (100.61 MHz, DMSO-d_6): δ 153.7, 143.1, 141.9, 129.2, 129.1, 124.0, 118.4, 116.9, 115.8.

2-Phenyl-1*H*-benzimidazole (3e): White crystalline solid. Yield: 95%; m.p.: 288-290 ºC (lit. [39] m.p.: 292-294 ºC). R_f (40% EtOAc-petroleum ether): 0.53; IR (KBr, ν_{max}, cm^{-1}): 3452 (-NH), 1618 (C=N), 1460 (C=C). ^{1}H NMR (400.13 MHz, DMSO-d_6): δ 12.94 (s, 1H, NH), 8.20 (d, *J* = 7.6 Hz, 2H), 7.44–7.61 (m, 5 H), 7.14–7.25 (m, 2 H). ^{13}C NMR (100.61 MHz, DMSO-d_6): δ 151.2, 130.1, 129.8, 128.9, 128.4, 126.4, 122.4.

2-(4-Methylphenyl)-1*H*-benzimidazole (3f): White crystalline solid. Yield: 94%; m.p.: 262-264 ºC (lit. [39] m.p.: 260-262 ºC). R_f (40% EtOAc-petroleum ether): 0.52. IR (KBr, ν_{max}, cm^{-1}): 3429 (-NH), 1573 (C=N), 1442 (C=C). ^{1}H NMR (400.13 MHz, DMSO-d_6): δ 12.82 (s, 1H, NH), 8.07 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.51 (d, *J* = 7.2 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.16-7.22 (m, 2H), 2.51 (s, 3H). ^{13}C NMR (100.61 MHz, DMSO-d_6): δ 151.3, 143.7, 139.5, 134.9, 129.4, 127.4, 126.3, 122.2, 121.5, 118.6, 111.1, 20.9.

2-(3-Methoxyphenyl)-1*H*-benzimidazole (3g): White crystalline solid, Yield: 97%; m.p.: 210-212 ºC (lit. [42] m.p.: 212-213 ºC). R_f (40% EtOAc-petroleum ether): 0.51. IR (KBr, ν_{max}, cm^{-1}): 3354 (-NH), 1621 (C=N), 1552 (C=C). ^{1}H NMR (400.13 MHz, DMSO-d_6): δ 12.90 (s, 1H, NH), 7.75-7.77 (m, 2H), 7.66 (br, s, 1H), 7.545 (br, s, 1H), 7.46 (t, J = 8.0 Hz, 1H), 7.21 (d, *J* = 3.6 Hz, 2H), 7.05-7.08 (m, 1H), 3.87 (s, 3H). ^{13}C NMR (100.61 MHz, DMSO-d_6): δ 159.6, 151.0, 131.4, 130.0, 122.5, 121.6, 118.7, 115.8, 111.3, 55.2.

2-(2-Thienyl)-1*H*-benzimidazole (3h): Yellow crystalline solid. Yield: 92%; m.p.: 330 ºC (lit. [40] m.p.: 329-331 ºC). R_f (40% EtOAc-petroleum ether): 0.51; IR (KBr, ν_{max}, cm^{-1}): 3447 (-NH), 1620 (C=N), 1452 (C=C). ^{1}H NMR (400.13 MHz, DMSO-d_6): δ 12.91 (s, 1H, NH), 7.80 (d, *J* = 3.6 Hz, 1H), 7.72 (d, *J* = 4.8 Hz, 1H), 7.60 (d, *J* = 7.2 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.15-7.27 (m, 3H). ^{13}C NMR (100.61 MHz, DMSO-d_6): δ 146.9, 143.5, 134.6, 133.6, 128.7, 128.2, 127.0, 126.6, 122.5, 121.7, 118.5, 111.0.

2-(2-Ferrocenyl)-1*H*-benzimidazole (3i): Yellow crystalline solid. Yield: 85%; m.p.: 230 ºC (lit. [41] m.p.: 228-230 ºC). R_f (40% EtOAc-petroleum ether): 0.51. IR (KBr, ν_{max}, cm^{-1}): 3423 (-NH), 1602 (C=N), 1444 (C=C). ^{1}H NMR (400.13 MHz, DMSO-d_6): δ 12.36 (s, 1H, NH), 7.54 (d, *J* = 7.2 Hz, 1H), 7.43-7.45 (m, 1H), 7.09-7.17 (m, 2H), 5.03-5.04 (m, 2H), 4.47-4.48 (m, 2H), 4.10 (s, 5H). ^{13}C NMR (100.61 MHz, DMSO-d_6): δ 152.9, 143.8, 121.4, 121.0, 117.9, 110.5, 74.3, 69.6, 69.3, 67.2.

2-((*Z*)-(2-Aminophenylimino)methyl)-4-chlorobenzene (4a): Yellow crystalline solid, Yield: 2%; m.p.: 167 ºC (lit. [43] m.p.: 166-168 ºC). R_f (40% EtOAc-petroleum ether): 0.68. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 8.42 (s, 1H, ArH), 7.61 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.17-7.13 (m, 2H), 6.82-6.74 (m, 2H), 5.02 (br, 2H, NH_2); ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 160.1, 143.2, 141.6, 135.6, 129.7, 129.2, 124.3, 119.46 116.9, 115.9.

2-(4-Chlorophenyl)benzothiazole (6a): White crystalline solid. Yield: 92%; m.p.: 108-110 ºC (lit. [44] m.p.: 113-114 ºC). R_f (20% EtOAc-petroleum ether): 0.75. IR (KBr, ν_{max}, cm^{-1}): 3060 (=C-H), 1588 (C=N), 1476 (C=C). ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 8.07 (d, *J* = 8.0 Hz, 1H,), 8.01 (d, *J* = 8.4 Hz, 2H,), 7.89 (d, *J* = 8.0, 1H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 8.0, 1H). ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 166.5, 153.9, 136.6, 129.5, 126.9, 125.3, 122.7, 122.5, 116.5, 116.3.

2-(4-Bromophenyl)benzothiazole (6b): White crystalline solid. Yield: 94%; m.p.: 130 ºC (lit. [44] m.p.: 131-132 ºC). R_f (20% EtOAc-petroleum ether): 0.73. IR (KBr, ν_{max}, cm^{-1}): 3060 (=C-H), 1583 (C=N), 1472 (C=C). ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 8.11 (d, *J* = 8.0 Hz, 1H), 8.0 (d, *J* = 8.5 Hz, 2H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 2H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 1H). ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 167.1, 154.5, 135.3, 133.0, 132.6, 129.4, 126.8, 125.4, 125.5, 123.6, 122.0.

2-(4-Nitrophenyl)benzothiazole (6c): Yellow crystalline solid. Yield: 95%; m.p.: 230 ºC (lit. [44] m.p.: 231-232 ºC). R_f (20% EtOAc-petroleum ether): 0.72. IR (KBr, ν_{max}, cm^{-1}): 3085 (=C-H), 1574 (C=N), 1458 (C=C). ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 8.16 (d, *J* = 12.0 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 2H), 6.97-7.05 (m, 2H), 6.73-6.82 (m, 2H), 6.41 (s, 1H). ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 149.3, 147.7, 145.8, 127.2, 127.1, 127.0, 125.9, 125.8, 124.0, 121.8, 121.4.

2-Phenyl benzothaizole (6d): Yellow crystalline solid. Yield: 96%; m.p.: 110-112 ºC (lit. [44] m.p.: 111-112 ºC). R_f (20% EtOAc-petroleum ether): 0.74; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 8.14-8.10 (m, 3H), 7.84 (d, *J* = 6.4 Hz, 1H), 7.50-7.45 (m, 4H), 7.35 (t, *J* = 5.6 Hz, 1H). ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 167.9, 154.0, 135.0, 133.5, 130.8, 128.9, 127.4, 126.2, 125.1, 123.1, 121.5.

2-(4-Methylphenyl)benzothiazole (6e): White crystalline solid. Yield: 94%; m.p.: 82-84 ºC (lit. [44] m.p.: 85-86 ºC). R_f (20% EtOAc-petroleum ether): 0.72. FT-IR (KBr, ν_{max}, cm^{-1}): 3056 (=C-H), 1604 (C=N), 1479 (C=C). ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 8.17 (d, *J* = 7.6 Hz, 1H), 8.06 (d, *J* = 7.6 Hz, 2H), 7.91 (d, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 2H), 2.46 (s, 3H). ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 168.7, 154.1, 138.9, 135.1, 133.5, 132.9, 126.4, 125.5, 125.2, 123.2, 121.7, 21.3.

2-(3-Methoxylphenyl) benzothiazole (6f): Yellow crystalline solid. Yield: 92%; m.p.: 86-88 ºC (lit. [45] m.p.: 83-85 ºC). R_f (20% EtOAc-petroleum ether): 0.73. FT-IR (KBr, ν_{max}, cm^{-1}): 3056 (=C-H), 1604 (C=N), 1459 (C=C). ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 8.07-8.09 (m, 1H), 7.88 (s, 1H), 7.63-7.67 (m, 2H), 7.47-7.51 (m, 1H), 7.37-7.38 (m, 2H), 7.02-7.04 (m, 1H), 3.91 (s, 3H). ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 166.9, 158.9, 152.9, 134.0, 133.8, 128.9, 124.1, 122.1, 120.5, 119.1, 116.2, 110.9, 54.4.

2-Thiophen-2-yl-benzothiazole (6g): Pale white crystalline solid. Yield: 92%; m.p.: 102-104 ºC (lit. [44] m.p.: 99-100 ºC). R_f (20% EtOAc-petroleum ether): 0.68. FT-IR (KBr, ν_{max}, cm^{-1}): 3095 (=C-H), 1581 (C=N), 1464 (C=C). ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 8.04 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 2.8 Hz, 1H), 7.49-7.45 (m, 2H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.11 (t, *J* = 3.6 Hz, 1H). ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 161.2, 153.5, 137.2, 134.5, 129.2, 128.5, 127.9, 126.3, 125.1, 122.8, 121.3.

2-Ferrocen-2-yl-benzothiazole (6h): Yellow crystalline solid. Yield: 84%; m.p.: 210 ºC (lit. [46] m.p.: 210 ºC). R_f (20% EtOAc-petroleum ether): 0.67. IR (KBr, ν_{max}, cm^{-1}): 3075 (=C-H), 1527 (C=N), 1423 (C=C). ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.42-7.46 (m, 1H), 7.32-7.35 (m, 1H), 5.00 (s, 2H), 4.49 (s, 2H), 4.15 (s, 5H). ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 168.7, 152.8, 133.6, 125.0, 123.3, 121.1, 120.3, 69.7, 69.3, 68.6, 67.6.

2-(4-*N*,*N*-Dimethylphenyl)benzothiazole (6i): Yellow crystalline solid. Yield: 95%; m.p.: 176-178 ºC (lit. [44] m.p.: 173-175 ºC). R_f (20% EtOAc-petroleum ether): 0.74. IR (KBr, ν_{max}, cm^{-1}): 2918 (C-H), 1606 (C=N), 1475 (C=C). ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.94-7.99 (m, 3H), 7.83-7.85 (m, 1H), 7.41-7.45 (m, 1H), 7.25-7.32 (m, 1H), 6.74 (d, *J* = 8.0 Hz, 2H), 3.05 (s, 6H). ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 168.8, 154.3, 152.1, 134.5, 128.8, 126.0, 124.2, 122.2, 121.3, 112.2, 111.6, 40.2.

6*H*-Indolo[2,3-*b*]quinoxaline (8a): Yellow crystalline solid. Yield: 95%; m.p.: 246 ºC (lit. [54] m.p.: 244 ºC). R_f (40% EtOAc-petroleum ether): 0.50. IR (KBr, ν_{max}, cm^{-1}): 3442 (-NH), 1606 (C=N), 1455 (C=C). ^{1}H NMR (400.13 MHz, $CDCl_3$/DMSO-d_6): δ 11.89 (s, 1H, NH), 8.35 (d, *J* = 8.0 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.76 (t, *J* = 8.0 Hz, 1H), 7.64-7.70 (m, 2H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.34 (t, *J* = 8.0 Hz, 1H). ^{13}C NMR (100.61 MHz, $CDCl_3$/DMSO-d_6): δ 145.5, 143.5, 139.8, 139.4, 138.2, 130.4, 128.5, 127.8, 127.0, 125.1, 121.6, 119.9, 118.7, 111.4.

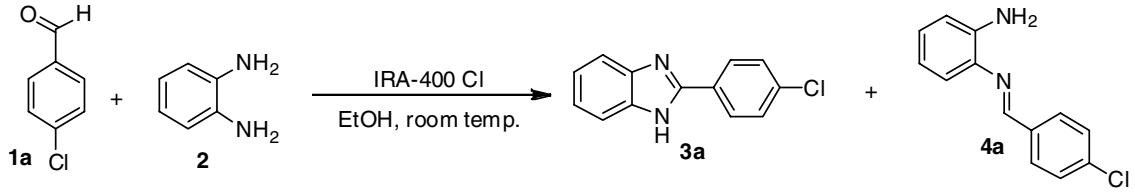
RESULTS AND DISCUSSION

Initially, for the synthesis of benzimidazole **3a**, a 1:1 mixture of *o*-phenylenediamine **2** (1 mmol) and 4-chlorobenzaldehyde **1a** (1 mmol) was treated with Amberlite IRA-400 Cl resin (0.1 g) in EtOH at ambient temperature (60 min). The reaction afforded -(4-chlorophenyl)-1*H*-benzimidazole **3a** and imine **4a**, in 75% and 15% yields (**Scheme-III**, Table-1, entry 1), respectively. To suppress the side product **4a** and improving the yield of expected product **3a**, the reaction condition has been exten-sively optimized. To study the influence of solvent, the reaction was carried out with various solvents. The reaction in MeOH afforded **3a** in 65% yield (Table-1, entry 2) and imine derivative in 25% yield. Similar trend was noticed with CH_3CN (Table-1, entry 3). In water, the formation of side product **4a** is the predominant (Table-1, entry 4). To increase the yield of 2-(4-chlorophenyl)-1*H*-benzimidazole (**3a**), the reaction was carried out with Amberlite IRA-400 Cl resin (0.1 g), in H_2O:EtOH (1:1). The yield of the product **3a** was substantially improved to 96% within a shorter time (Table-1, entry 6). We then compared the influences of different ratio of the aqueous ethanol and found that 1:1 ratio of water and ethanol seemed

TABLE-1
OPTIMIZATION OF REACTION FOR THE SYNTHESIS OF COMPOUND BENZIMIDAZOLE **3a**

Entry	Solvent	Amb-400 Cl (mg)	Time (min)	Yield[a] (%)	
				3a	**4a**
1	EtOH	100	60	75	15
2	MeOH	100	90	65	25
3	CH_3CN	100	90	70	20
4	H_2O	100	120	15	78
5	EtOH/H_2O (3:1)	100	20	90	8
6	EtOH/H_2O (1:1)	100	20	96	2
7	EtOH/H_2O (1:3)	100	20	88	10
8	EtOH/H_2O (1:1)	50	20	78	8

[a]Isolated yield.



Scheme-III

to be the best solvent combination for this reaction. It was also noted that the best catalytic activity of Amberlite IRA-400 Cl resin was optimized to be 0.1 g (Table-1, entry 6) and any beyond this proportion (0.05 g), did not show any increase in the conversion and the product yield (Table-1, entry 8).

Having optimized conditions in hand, the scope of the reaction was extended with various aryl aldehydes (**1a–i**). This catalytic cyclocondensation between *o*-phenylenediamine (**2**) and aldehydes underwent smoothly to afford benzimidazoles (**3a–i**) in excellent yields (**Scheme-I**).

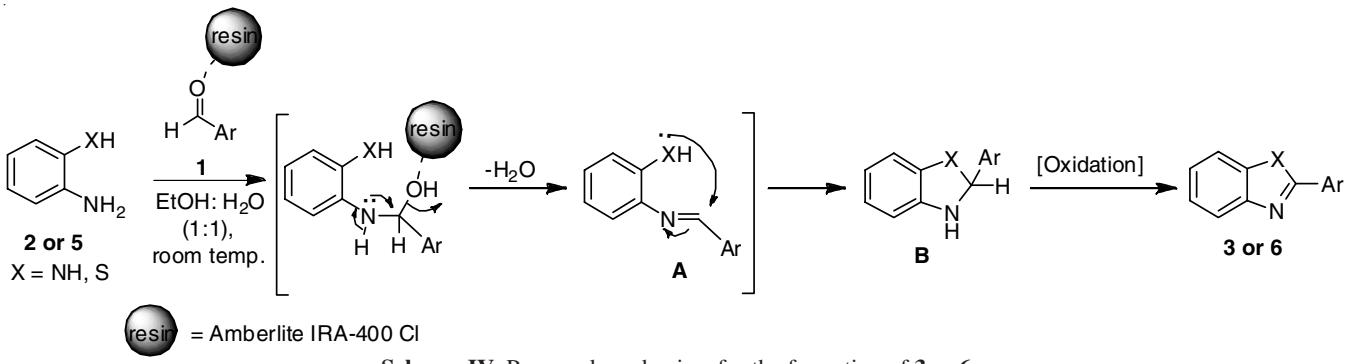
Reaction with both electron withdrawing (4-Cl, 3-Cl, 4-Br and 4-NO_2; **1a-d**) and electron donating substituents (4-Me **1f** and 3-OMe **1g**) on the aryl aldehyde are well tolerated under optimal conditions and provided good to excellent yields (94-97%). It is noteworthy that heteroaryl and organometallic aldehydes such as 2-thiophenealdehyde (**1h**) and ferrocene-aldehyde (**1j**) also took part in the reaction to provide the corresponding products **3h** and **3i** in good yields (92% and 85%). The isolated compounds were characterized using spectroscopic techniques and it was compared with the reported data [39-43].

The successful syntheses of benzimidazoles (**3a–i**) prompted us to explore the further syntheses of sulphur analogue, benzothiazoles (**6a–i**). Thus, reactions of 2-aminothiophenol (**5**, 1 mmol) with aromatic aldehydes **1** (1 mmol) were carried out under H_2O:EtOH (1:1) condition at room temperature to obtain benzothiazoles (**6a–i**) are shown in **Scheme-II**. The reaction smoothly gave the product in good to excellent yield (ranging from 84 to 96%) within a short period of time (*ca.* 20–40 min). From the experimental results, with aldehydes containing both electron-donating and withdrawing group did not alter the yields of the products significantly. Further, 2-thiophene-aldehyde (**1h**) and ferrocenealdehyde (**1i**) also took part in the reaction to provide corresponding benzothiazoles **6g** and **6h** (92 and 84% yield).

A plausible mechanism for the formation of benzimidazoles (**3**) and benzothiazoles (**6**) derivatives is shown in **Scheme-IV**. Initially the formation of intermediate **A** (Schiff base) from aldehyde **1** and aromatic amine **2** or **5** was promoted by the catalyst IRA-400 Cl resin. The intramolecular cyclization by *o*-amino group in intermediate **A** leads to the adduct **B** (dihydrobenzimidazole or hydrobenzothiazole). Subsequent aerial oxidation of adduct **B** yields the corresponding product **3** or **6**.

A comparative study between present results and other previously reported catalysts [47-53] for the synthesis of benzimidazoles (**3a**) and benzothiazoles (**6a**) revealed that the IRA-400 Cl is found to be most efficient. This environmentally benign and recyclable nature of the ion exchange catalyst (Amberlite IRA-400 Cl) shows high activity under non-toxic solvent medium at a shorter reaction time. Further, Ease of workup under ambient temperature for this catalytic process leads to excellent yield of the product (≈ 94%). These are noteworthy advantages of the present protocol over previous reports and are been presented in Table-2.

The recyclability of the Amberlite IRA-400 Cl catalyst has been studied for the reaction of 4-chlorobenzldehye and *o*-Phenylenediamine under optimized conditions (Table-3).



Scheme-IV: Proposed mechanism for the formation of **3** or **6**

TABLE-2
COMPARISON OF AMBERLITE IRA 400-Cl RESIN WITH SOME OTHER CATALYSTS FOR SYNTHESIS OF **3a** AND **6a**

Product	Catalyst	Solvent/Temp. (°C)	Time (min)	Yield (%)	Ref.
3a	$Cu(OH)_2$	CH_3OH, room temp.	240	99	[47]
	$VOSO_4$	EtOH, room temp.	45	89	[48]
	TBN	THF, room temp.	120	90	[49]
	CuO-np/SiO_2	CH_3OH, room temp.	300	92	[50]
	$NiEuFe_2O_4$	H_2O, 100 °C	45	87	[51]
	Fe_3O_4@SiO_2/collagen	EtOH, room temp.	20	60	[52]
	UiO-66-NH_2-TC-Cu	EtOAc, 50 °C	20	91	[53]
	IRA-400 Cl	EtOH: H_2O (1:1), room temp.	20	96	This work
6a	$VOSO_4$	EtOH, room temp.	40	87	[48]
	$NiEuFe_2O_4$	H_2O, 100 °C	40	89	[51]
	Fe_3O_4@SiO_2/collagen	EtOH, room temp.	60	73	[52]
	UiO-66-NH_2-TC-Cu	Neat, room temp.	15	92	[53]
	IRA-400 Cl	EtOH: H_2O (1:1), room temp.	25	92	This work

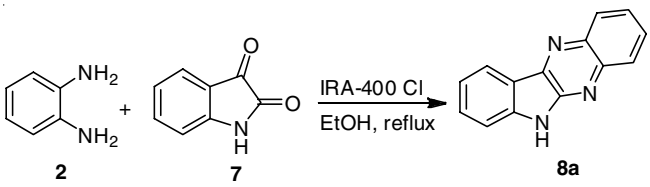
TABLE-3
RECYCLIZATION OF THE CATALYST
FOR THE SYNTHESIS OF **3a**

Entry	Run	Time (min)	Yield (%)
1	0	20	96
2	1	20	95
3	2	20	94
4	3	20	92

Reaction condition: 4-Chlorobenzaldehyde **1a** (1 mmol): *o*-phenylenediamine **2** (1 mmol) in 5 mL of EtOH: H_2O (1:1), room temp.

The regenerated catalyst was used three times without loss of activity [55], however the small retarded in the activity over the fourth cycle might be due to the loss of small amounts of catalyst while washing and drying process.

The versatility of the reaction was explored for the synthesis of another biologically valuable scaffold, quinoxaline. The reaction between 1,2 diketone (**7**, 1 mmol) and *o*-phenylenediamine (**2**, 1 mmol) was carried out under Amberlite resin catalyst at ethanol reflux condition. Interestingly within 10 min, the reaction successfully afforded 6*H*-indolo-[2,3-*b*]-quinoxaline (**8a**) in 95% yield (**Scheme-V**).



Scheme-V: Synthesis of quinoxaline **8a**

Conclusion

The ion exchange resins are good solid base catalyst for the dehydration and condensation reactions. Interestingly, Amberlite IRA-400 Cl resin has been found as an efficient catalytic system for the reaction of diketones and amines with various aldehydes, affording benzimidazoles and benzothiazoles in good yields under ambient temperature. This method is of great value because of its environmentally benign, efficient, easy handling, low cost and ready availability of reagents.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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