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Design, Synthesis and Biological Evaluation of Benzimidazolyl and Benzothiazolyl Picolinamide Derivatives as Antimicrobial Agents

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A series of benzothiazolyl amides and benzimidazolyl amides (**6a-f**) has been synthesized from the coupling reaction of substituted picolinic acid with benzothiazole and benzimidazoles, respectively. The newly synthesized compounds were evaluated for their efficacy as antimicrobial agents against various Gram-positive and Gram-negative strains of bacteria and fungal strains. Amongst these compounds **6f** was found to be the most potent against *Bacillus subtilis* and *Candida albicans*. Moreover, other compounds also found to be potential antibacterial agents in comparison to the standard drugs.

Keywords: Benzothiazoles, Benzimidazoles, Antimicrobial activities.

INTRODUCTION

The demand for developing novel and potent antibacterial agents remains an attractive field in the medicinal chemistry. For last few decades, continuous efforts have been carried out on the structural modifications on the existing scaffolds for the identification of novels antibacterial agents. However, the rapid emergence of resistance to the organisms limited the clinical use of current antibacterial drugs and development of antibacterials is increasingly becoming global health problem. For this reason, there is a strong need to develop more effective antibacterial agents to treat infections caused by antibiotic resistant bacterial pathogens.

Benzothiazoles belong to an important class of heterocyclic compounds which display a variety of biological properties including antibacterial and antifungal[1-3], anti-HIV[4,5], hypertension[6], anti-inflammatory[7], anticancer[8], anticonvulsant[9], antiinflammation[10] and antidepressant activities[11,12]. In the past few years, benzothiazole ring system has attracted much interest for the development of potent antibacterial agents either by the structural modification of this scaffold or by developing hybrid compounds. On the other hand, benzimidazoles are found to exhibit diverse biological activities such as antibacterial, antifungal and anticancer *etc*. During past few years there have been considerable interesting developments in the biological activities of benzimidzoles with remarkable pharmacological potentialities. In last few years it was reported that benzothiazole, its bioisosters and derivatives had antimicrobial activities against Gram-negative and Gram-positive bacteria (*e.g.*, *Enterobacter*, *Pseudomonas aeruginosa*, *E. coli* and *Staphylococcus epidermidis etc*.) and the yeast (*e.g.*, *Candida albicans*)[12,13]. Furthermore, sulfur and nitrogen atoms constitute the core structure of thiazole and many pharmacologically and biologically active compounds. Therefore, various benzothiazole compounds are of considerable interest for their diverse pharmaceutical uses and play a vital role in the synthesis of fused heterocyclic systems.

The goal of outset of this research is to find and develop new effective antimicrobial agents possessing benzothiazole and benzimidazole nuclei in their structures. In continuation of our research, herein we have prescribed the synthesis and antibacterial studies of two series, benzothiazole and benzimidazole derivatives coupled with other heteroaryl ring system. Almost all compounds showed promising antibacterial activity against Gram-positive and Gram-negative bacterial strains.

EXPERIMENTAL

All reagents and solvents were used as purchased without further purification. Crude products were purified by column chromatography on silica gel of 60-120 mesh. NMR spectra

were recorded on a Varian 400 MHz spectrometer for ^{1}H NMR. Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. The chemical shifts were reported as ppm down field using TMS as an internal standard. A mass spectrum was recorded on a VG-Micro mass 7070H spectrometer operating at 70 eV.

Synthesis of 2-amino benzothiazole (2a-d): To a mixture of aniline (**1**) (2.0 g, 0.021 mol) and ammonium thiocyanate (6.5 g, 0.086 mol), bromine (2.2 mL, 0.043 mol) in dichloromethane (20 mL) and stirred for 16 h at ambient temperature. Later than water was added to the reaction mixture and the product was extracted in dichloromethane (3 × 30 mL). The solvent was evaporated under vacuum to afford the as crude, which was further purified by column chromatography using EtOAc:Hexane (4:6) to give compounds **2a-d**.

2-Amino-benzothiazole (2a): Off-white solid; yield: 70 %, m.p.: 126-128 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 6.98-7.00 (m, 1H, Ar-H), 7.18-7.20 (m, 1H, Ar-H), 7.32-7.34 (m, 1H, Ar-H), 7.40-7.42 (s, 2H, NH_2), 8.02-8.21 (m, 1H, Ar-H); MS: *m/z* (%) 150.8 [M^+], UPLC purity (99.89 %).

2-Amino-4-fluoro-benzothiazole (2b): Yellow solid; yield: 76 %, m.p.: 140-142 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.00-7.04 (m, 1H, Ar-H), 7.22-7.24 (m, 1H, Ar-H), 7.40-7.42 (s, 2H, NH_2), 7.50-7.52 (m, 1H, Ar-H); MS: *m/z* (%) 168.8 [M^+], UPLC purity (99.03 %).

2-Amino-6-fluoro-benzothiazole (2c): Yellow solid; yield: 78 %, m.p.: 145-147 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 6.98-7.02 (m, 1H, Ar-H), 7.25-7.28 (m, 1H, Ar-H), 7.38-7.42 (s, 2H, NH_2), 7.53-7.56 (m, 1H, Ar-H); MS: *m/z* (%) 168.8 [M^+], UPLC purity (99.23 %).

2-Amino-6-methoxy-benzothiazole (2d): White solid; yield: 72 %, m.p.: 160-162 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.82 (s, 3H, OCH_3), 6.85-6.98 (m, 1H, Ar-H), 7.22-7.35 (m, 1H, Ar-H), 7.46-7.57 (s, 2H, NH_2), 8.11-8.24 (m, 1H, Ar-H); MS: *m/z* (%) 179.8 [M^+], UPLC purity (99.89 %).

Synthesis of 2-amino benzimidazole (2e, f): To a stirred solution of 2-amino aniline **1** (2.85 g, 0.026 mol) in acetonitrile (20 mL) and water (4 mL) at 0 °C, was added cyanogen bromide 5 M in ACN (6.45 mL, 0.032 mol), the reaction mixture was stirred for 16 h at ambient temperature. Later than reaction was quenched with saturated aqueous sodium hydrogen carbonate (100 mL) and shaken the resulting solid was filtered off, was washed with water and dried under reduced pressure to afford compounds **2e, f**.

2-Amino-benzimidazole (2e): Off-white solid; yield: 70 %, m.p.: 229- 231°C; ^{1}H NMR (400 MHz, DMSO- d_6) δ: 6.06-6.08 (s, 2H, NH_2), 6.82-6.86 (m, 2H, Ar-H), 7.08-7.10 (m, 2H, Ar-H), 10.60-10.65 (broad s, 1H, NH); MS: *m/z* (%) 133.85 (M^+], HPLC purity (99.83 %).

2-Amino-5-fluoro-benzimidazole (2f): Yellow solid; yield: 78 %, m.p.: 232-234 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 6.10-6.12 (s, 2H, NH_2), 6.94-6.98 (m, 2H, Ar-H), 7.08-7.10 (s, 1H, Ar-H), 10.64-10.68 (broad s, 1H, NH);MS: *m/z* (%) 151.84 [M^+], UPLC purity (99.05 %).

Synthesis of N-(benzo[d]thiazol-2-yl)-5-bromo-6-methoxypicolinamide and N-(1H-benzo[d]imidazol-2-yl)-5-bromo-6-methoxypicolinamide (4): To a solution of compound **2** (150 mg, 0.001 mol) in dichloromethane (4 mL), cooled to 0 °C, was added compound **3** (255 mg, 0.0011 mol), O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU) (570 mg, 0.0015 mol), N,N-diisopropylethylamine (DIPEA) (0.358 mL, 0.0020 mol) and the mixture was stirred for 16 h at ambient temperature. Water was added and extracted with ethyl acetate, dried and purified by column chromatography using a gradient of hexane-EtOAc (8:2-5:5) to give compound **4**.

N-(Benzo[d]thiazol-2-yl)-5-bromo-6-methoxypicolinamide (4a): Off-white solid; yield: 66 %, m.p.: 190-192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.20 (s, 3H, OCH_3), 7.37-7.39 (m, 1H, Ar-H), 7.42-7.44 (m, 1H, Ar-H), 7.80-7.84 (m, 3H, Ar-H), 8.06-8.08 (m, 1H, Ar-H), 10.76-10.78 (s, 1H, NH); MS: *m/z* (%) 365.65 [M^{+2}], UPLC purity (98.61 %).

5-Bromo-N-(4-fluorobenzo[d]thiazol-2-yl)-6-methoxypicolinamide (4b): Pale yellow solid; yield: 61 %, m.p.: 190-192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.02 (s, 3H, OCH_3), 7.20-7.22 (m, 1H, Ar-H), 7.58-7.60 (m, 1H, Ar-H), 7.76-7.78(m, 2H, Ar-H), 8.07-8.09 (m, 1H, Ar-H), 10.70-10.72 (s, 1H, NH); MS: *m/z* (%) 383.8 [M^{+2}], UPLC purity (98.01 %).

5-Bromo-N-(6-fluorobenzo[d]thiazol-2-yl)-6-methoxypicolinamide (4c): Pale yellow solid; yield: 63 %, m.p.: 186-188 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.18 (s, 3H, OCH_3), 7.18-7.20 (m, 1H, Ar-H), 7.56-7.58 (m, 1H, Ar-H), 7.78-7.82 (m, 2H, Ar-H), 8.06-8.08 (m, 1H, Ar-H), 10.70(s, 1H, NH); MS: *m/z* (%) 383.8 [M^{+2}], UPLC purity (95.10 %).

5-Bromo-N-(6-methoxybenzo[d]thiazol-2-yl)-6-methoxypicolinamide (4d): White solid; Yield: 65 %, m.p.: 182-184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.12 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 7.20-7.22 (m, 1H, Ar-H), 7.43-7.55 (m, 1H, Ar-H), 7.51-7.62 (m, 2H, Ar-H), 7.90-8.00 (m, 1H, Ar-H), 10.62 (s, 1H, NH); MS: *m/z* (%) 395.9 (M^{+2}), UPLC purity (97.10 %).

N-(1H-Benzo[d]imidazol-2-yl)-5-bromo-6-methoxypicolinamide (4e): Off-white solid; yield: 66 %, m.p.: 210-212°C ^{1}H NMR (400 MHz, DMSO-d_6) δ: 4.15 (s, 3H, OCH_3), 7.25 (m, 2H, Ar-H), 7.45 (m, 1H, Ar-H), 7.62 (m, 1H, Ar-H), 7.80 (d, 1H, Ar-H), 8.05 (d, 1H, Ar-H) 10.42 (broad s, 1H, NH), 11.02 (broad s, 1H, NH); MS: *m/z* (%) 348.7 [M^{+2}], UPLC purity (98.9 %).

5-Bromo-N-(5-fluoro-1H-benzo[d]imidazol-2-yl)-6-methoxypicolinamide (4f): Pale yellow solid; yield: 63 %, m.p.: 218-220 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 4.16 (s, 3H, OCH_3), 7.26-7.18 (m, 1H, Ar-H), 7.46-7.52 (m, 1H, Ar-H), 7.64-7.71 (m, 1H, Ar-H), 7.84 (d, 1H, Ar-H, J = 7.98 Hz), 8.08 (d, 1H, Ar-H), 10.44 (broad s, 1H, NH), 11.05 (broad s, 1H, NH); MS: *m/z* (%) 366.7 [M^{+2}], UPLC purity (98.2 %).

Synthesis of N-(R-benzo[d]thiazol-2-yl)-6-methoxy-5-(4-methyl-1H-imidazol-1-yl)picolinamide and N-(R-benzo-[d]imidazol-2-yl)-6-methoxy5-(4-methyl-1H-imidazol-1-yl)picolinamide (6): Compound **4** (50 mg, 0.00013 mol), compound **5** (16.9 mg, 0.0002 mol), CuI (13 mg, 0.000068 mol), K_3PO_4 (58.2 mg, 0.00027mol), *trans*-1,2-diaminocyclohexane (7.82 mg, 0.000068 mol) in dioxane (1.0 mL), were heated at 120 °C for 16 h. The solvent was evaporated *in vacuo* and the residue on purification by column chromatography using CH_2Cl_2-MeOH (9.8:0.2-9.5:0.5) gave the title compound **6**.

N-(Benzo[d]thiazol-2-yl)-6-methoxy 5-(4-methyl-1H-imidazol-1-yl)picolinamide (6a): Off-white solid; yield: 68 %, m.p.: 166-170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.32

(s, 3H), 4.22 (s, 3H, OCH_3), 7.05 (s, 1H, Ar-H), 7.35-7.40 (m, 1H, Ar-H), 7.49-7.51(m, 1H, Ar-H), 7.80 (d, 1H, Ar-H, *J* = 7.87 Hz), 7.85-7.88 (m, 2H, Ar-H), 7.91 (s, 1H, Ar-H), 8.09 (d, 1H, Ar-H, *J* = 8.22 Hz), 10.75 (s, 1H, NH); ^{1}H NMR (400 MHz, D_2O exchange) δ: 2.32 (s, 3H), 4.22 (s, 3H, OCH_3), 7.05 (s, 1H, Ar-H), 7.35-7.40 (m, 1H, Ar-H), 7.49-7.51 (m, 1H, Ar-H), 7.80 (d, 1H, Ar-H, *J* = 7.78 Hz), 7.85-7.88 (m, 2H, Ar-H), 7.91 (s, 1H, Ar-H), 8.08 (d, 1H, Ar-H, *J* = 8.31 Hz), MS: *m/z* (%) 365.9 [M^+], UPLC purity (96.02 %). Anal. calcd. for $C_{18}H_{15}N_5O_2S$: C, 59.16; H, 4.14; N, 19.17. Found C, 59.20; H, 4.12; N, 19.22.

N-(4-Fluoro-benzo[d]thiazol-2-yl)-6-methoxy-5-(4-methyl-1H-imidazol-1-yl)picolinamide (6b): Pale yellow solid; yield: 65 %, m.p.: >220 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.33 (s, 3H), 4.24 (s, 3H, OCH_3), 7.06 (s, 1H, Ar-H), 7.20-7.22 (m, 1H, Ar-H), 7.56 (d, 1H, Ar-H, *J* = 7.98 Hz), 7.80-7.82 (m, 2H, Ar-H), 7.95 (s, 1H, Ar-H), 8.11 (d, 1H, Ar-H, *J* = 6.85 Hz), 10.74 (s, 1H, NH); ^{1}H NMR (400 MHz, D_2O exchange) δ: 2.33(s, 3H), 4.24 (s, 3H, OMe), 7.06 (s, 1H, Ar-H), 7.20-7.22 (m, 1H, Ar-H), 7.56 (d, 1H, Ar-H, *J* = 7.95 Hz), 7.80-7.82 (m, 2H, Ar-H), 7.95 (s, 1H, Ar-H), 8.12 (d, 1H, Ar-H, *J* = 6.88 Hz), MS: *m/z* (%) 383.9 [M^+], UPLC purity (98.01 %). Anal. calcd. for $C_{18}H_{14}FN_5O_2S$: C, 56.39; H, 3.68; N, 18.27. Found C, 56.44; H, 3.66; N, 18.21.

N-(6-Fluoro-benzo[d]thiazol-2-yl)-6-methoxy5-(4-methyl-1H-imidazol-1-yl)picolinamide (6c): Pale yellow solid; yield: 64 %, m.p.: >220 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.32 (s, 3H), 4.21 (s, 3H, OCH_3), 7.05 (s, 1H, Ar-H), 7.19-7.21 (m, 1H, Ar-H), 7.55 (d, 1H, Ar-H, *J* = 7.22 Hz), 7.78-7.80 (m, 2H, Ar-H), 7.92 (s, 1H, Ar-H), 8.08 (d, 1H, Ar-H, *J* = 8.20 Hz), 10.71(s, 1H, NH); ^{1}H NMR (400 MHz, D_2O exchange) δ: 2.32 (s, 3H), 4.21 (s, 3H, OCH_3), 7.05 (s, 1H, Ar-H), 7.19-7.21 (m, 1H, Ar-H), 7.55 (d, 1H, Ar-H, *J* = 7.22 Hz), 7.78-7.80 (m, 2H, Ar-H), 7.92 (s, 1H, Ar-H), 8.08 (d, 1H, Ar-H, *J* = 8.21 Hz), MS: *m/z* (%) 383.9 [M^+], UPLC purity (98.01 %). Anal. calcd. For $C_{18}H_{14}FN_5O_2S$: C, 56.39; H, 3.68; N, 18.27. Found C, 56.42; H, 3.66; N, 18.22.

N-(6-Methoxy-benzo[d]thiazol-2-yl)-6-methoxy5-(4-methyl-1H-imidazol-1-yl)picolinamide (6d): Pale yellow solid; yield: 76 %, m.p.: 172-174 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.29 (s, 3H), 4.23 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 7.14 (s, 1H, Ar-H), 7.22-7.29 (m, 1H, Ar-H), 7.51 (d, 1H, Ar-H, *J* = 6.87 Hz), 7.61-7.74 (m, 2H, Ar-H), 7.85 (s, 1H, Ar-H), 8.28 (d, 1H, Ar-H, *J* = 8.12 Hz), 10.81(s, 1H, NH); ^{1}H NMR (400 MHz, D_2O exchange) δ: 2.29 (s, 3H), 4.23 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 7.14 (s, 1H, Ar-H), 7.22-7.29 (m, 1H, Ar-H), 7.51 (d, 1H, Ar-H, *J* = 6.87 Hz), 7.61-7.74 (m, 2H, Ar-H), 7.85 (s, 1H, Ar-H), 8.28 (d, 1H, Ar-H, *J* = 8.12 Hz), MS: *m/z* (%) 395.9 [M^+], UPLC purity (98.01 %). Anal. calcd. for $C_{19}H_{17}N_5O_3S$: C, 57.71; H, 4.33; N, 17.71. Found C, 57.77; H, 4.30; N, 17.73.

N-(1H-Benzo[d]imidazol-2-yl)-6-methoxy-5-(4-methyl-1H-imidazol-1-yl)picolinamide (6e): Off-white solid; yield: 68 %, m.p.: 212-214 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.32 (s, 3H), 4.20 (s, 3H, OCH_3), 7.04 (s, 1H, Ar-H), 7.25 (s, 1H, Ar-H), 7.44 (m, 2H, Ar-H), 7.62 (m, 1H, Ar-H), 7.78 (m, 1H, Ar-H), 7.92 (s, 1H, Ar-H), 8.04 (m, 1H, Ar-H), 10.42 (m, 1H, NH), 11.02 (m, 1H, NH); ^{1}H NMR (400 MHz, D_2O exchange) δ: 2.32 (s, 3H), 4.20 (s, 3H, OCH_3), 7.04 (s, 1H, Ar-H), 7.25 (s, 1H, Ar-H), 7.44 (m, 2H, Ar-H), 7.62 (m, 1H, Ar-H), 7.78 (m, 1H, Ar-H), 7.92 (s, 1H, Ar-H), 8.04 (m, 1H, Ar-H), MS: *m/z* (%) 348.9 [M^+], UPLC purity (95.02 %). Anal. calcd. For $C_{18}H_{16}N_6O_2$: C, 62.06; H, 4.63; N, 24.12. Found C, 61.99; H, 4.65; N, 24.10.

N-(5-Fluoro-1H-benzo[d]imidazol-2-yl)-6-methoxy-5-(4-methyl-1H-imidazol-1-yl)picolinamide (6f): Pale yellow solid; yield: 64 %, m.p.: 224-226 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ:2.34 (s, 3H), 4.20 (s, 3H, OCH_3), 7.02 (s, 1H, Ar-H), 7.32 (m, 1H, Ar-H), 7.40 (m, 1H, Ar-H), 7.58 (m, 1H, Ar-H), 7.78 (m, 1H, Ar-H), 7.88 (s, 1H, Ar-H), 8.04 (m, 1H, Ar-H), 10.36 (bs, 1H, NH), 10.98 (bs, 1H, NH); ^{1}H NMR (400 MHz, D_2O exchange). 2.34 (s, 3H), 4.20 (s, 3H, OCH_3), 7.02 (s, 1H, Ar-H), 7.32 (m, 1H, Ar-H), 7.40 (m, 1H, Ar-H), 7.58 (m, 1H, Ar-H), 7.78 (m, 1H, Ar-H), 7.88 (s, 1H, Ar-H), 8.04 (m, 1H, Ar-H): MS: *m/z* (%) 366.9 [M^+], UPLC purity (96.4 %). Anal. calcd. For $C_{18}H_{15}FN_6O_2$: C, 59.01; H, 4.13; F, 5.19; N, 22.94. Found: C, 59.15; H, 4.12; N, 22.89.

Antibacterial assay: The minimum inhibitory concentration (MIC) of the test compound was obtained against a panel of bacteria using a conventional method. The Muller Hinton agar medium was used as test media. Tests were performed in 96-well round bottom sterile culture plates. All the compounds previously solubilized in DMSO were serially diluted to two folds in the liquid medium and gave a range of concentrations from 10 to 500 µg/mL. The final bacterial inoculum contained approximately 5-10^5 CFU/mL was run on microtiter plates. The volume in each well was 100 µL and the plates were inoculated at 35 °C for 18 h. The standard antibiotic ampicillin was used as positive control, whereas, the equivalent amount of solvent (DMSO) did not exhibit any activity in the assay[14].

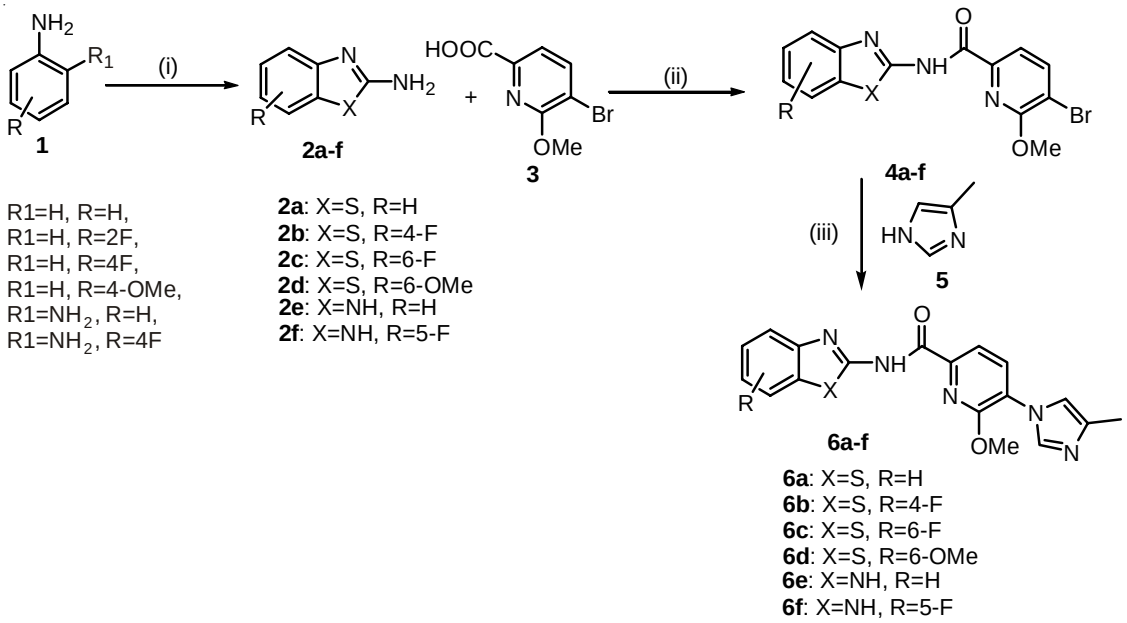
Antifungal assay: The method followed for antifungal bioassay is similar to that followed for antibacterial assay, where the medium is PDA 39 g/L. All the test compounds were studied for their antifungal activity at concentration 100-150 mg/mL using DMSO as a solvent. The solvent did not exhibit any activity at the concentrations used. The treated and the controls were kept in an incubator at 28 °C for 48 h and inhibition zones were measured to the nearest millimeter. Three replicates were maintained for each treatment. Amphotericin-B (50 mg/mL) was used as positive control.

RESULTS AND DISCUSSION

The synthesis of 2-amino benzothiazoles was carried out by the action of ammonium thiocyanate and bromine on substituted anilines (**1**) to afford substituted 2-aminobenzothiazoles (**2a-d**) as reported in the literature[15] (**Scheme-I**). Similarly, 2-amino benzimidazoles (**2e-f**) were synthesized by the reaction of substituted anilines (**1**) with cyanogens bromide. Compounds **2a-f** were coupled with **3** using HATU and DIPEA to afford **4a-f** Finally, compounds **4a-f** were reacted with methylimidazole (**5**) in the presence of CuI, *trans*-1,2-diamino cyclohexane and K_3PO_4 furnished the final targets **6a-f**.

Conclusion

In summary, the synthesis and screening of antibacterial and antifungal activities for a novel series of benzothiazole and benzimidazole conjugates have been investigated. All the



Reaction and condition: (i) Ammonium thiocyanate, Br_2, DCM, RT, 16 h (for **2a-d**) and cyanogen bromide, acetonitrile/water, 0 °C-RT (for **2e-f**); (ii) HATU, DIPEA, RT, 16 h, (iii) K_3PO_4, CuI, *trans*-1,2-diamino cyclohexane, dioxane, 16 h, 120 °C

Scheme-I

TABLE-1
ANTIBACTERIAL ACTIVITY (MIC IN µg/mL) AND ANTIFUNGAL ACTIVITY (ZONE OF INHIBITION IN mm AT 100 µg/mL) OF **6a-f**

Compd.	Antibacterial strains				Antifungal strains	
	B. subtilis[a]	*S. aureus*[a]	*M. luteus*[a]	*E. coli*[b]	*C. albicans*[c]	*A. fumigatus*[c]
6a	180	–[d]	–[d]	10	–[d]	–[d]
6b	125	180	240	–[d]	–[d]	–[d]
6c	210	270	–[d]	120	15	–[d]
6d	120	150	180	240	-	5
6e	150	180	–[d]	180	–[d]	–[d]
6f	90	150	150	–[d]	10	5
Ampicillin	60	120	150	120	–	–
Amphotericin-B	–	–	–	–	–	–

[a]Gram-positive bacteria: *Bacillus subtilis* MTCC 2415, *Staphylococcus aureu*s MTCC 9886 and *Micrococcus luteus* MTCC 1538; [b]Gram-negative bacteria: *Escherichia coli* MTCC 448. [c]Yeasts: *Candida albicans* ATCC 1369 and *Aspergillus fumigates* MTCC 9657.

compounds have shown mild to potent inhibitory activity against *B. subtilis* and exhibited mild to moderate antibacterial activities against the other tested organisms (Table-1). Compounds **6b**, **6c** and **6f** were found to be the most active against most of the tested organisms. Some of the compounds have shown significant antibacterial activity in comparison to the controls. This novel class of new benzothiazole/benzimidazole pyridine imidazole derivatives reported to have a great probability to emerge as a valuable lead series to be used as antibacterial agent and as promising candidates for further evaluation. Further studies on the structural modification of bioactive scaffold to get more efficient antibacterial agents are underway in our program.

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