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# Synthesis and Characterization of Some Novel 2-[(5-aryl)-4, 5-dihydro-1*H*-pyrazole-3-yl]-1*H*-benzimidazoles with Antimicrobial Activity

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**ABSTRACT**
A novel series of 4-(1*H*-benzo[*d*]imidazol-2-yl)-6-phenyl-2-pyrimidinamines **(6a-h)** have been synthesized in good to excellent yields by using commercially available *o*-phenylenediamine (*o*-PDA) **(1a-d)** and α-hydroxy propionic acid **2** and by involving 2-(α-hydroxy)ethyl benzimidazoles **(3a-d)**, 2-acetyl benzimidiazoles **(4a-d)** and 1-(1*H*-benzimidazol-2-yl)-3-(substituted phenyl) prop-2-en-1-ones **(5a-h)** as intermediates. The chemical structures of the all newly synthesized compounds were clarified by their IR, $^{1}H$ & $^{13}C$ NMR, mass spectral data and elemental analysis. Finally, the target compounds were used to find their antimicrobial activity against various microorganisms.

**Keywords:** Benzimidazoles, pyrimidines, antimicrobial activity.

## INTRODUCTION

Benzimidazole ring is an important heterocyclic pharmacophore in drug discovery. Benzimidazoles are regarded as a promising class of bioactive heterocyclic compounds that exhibit a range of biological activities such as antiviral, [1] antitumor, [2] anticancer [3] and antimicrobial activity. [4] Pyrimidines are associated with various therapeutic activities such as anti-HIV, [5] anti-tubercular, [6] antitumor, [7] anti-inflammatory, [8] diuretic [9] and antimalaria. [10]

## MATERIALS AND METHODS

All reagents and solvents were used as purchased without further purification. Melting points were determined on a Fisher–Johns melting point apparatus and are uncorrected. Crude products were purified by column chromatography on silica gel of 60-120 mesh. IR spectra were obtained on a Perkin Elmer BX serried FTIR 5000 spectrometer using KBr pellet. NMR spectra were recorded on a varian 300 MHz spectrometer for $^{1}H$ NMR. The chemical shifts were reported as ppm down field using TMS as an internal standard. Mass spectra were recorded on a VG-Micromass 7070H spectrometer operating at 70 eV.

**General procedure for the synthesis of 2-(α-hydroxy) ethyl benzimidazoles (3a-d)**

*o*-Phenylenediamine (1a-d) (0.01 mol) was treated with α-hydroxy propionic acid (2) (0.01 mol) in presence of 4N-hydrochloric acid (5 ml) and refluxed on water both for 24 h. After completion of the reaction, (monitored by TLC) the reaction mixture was cooled and neutralized with $NH_3$ solution. The solid was separated through filter and recrystallized from absolute ethanol to get compounds 3a-d.

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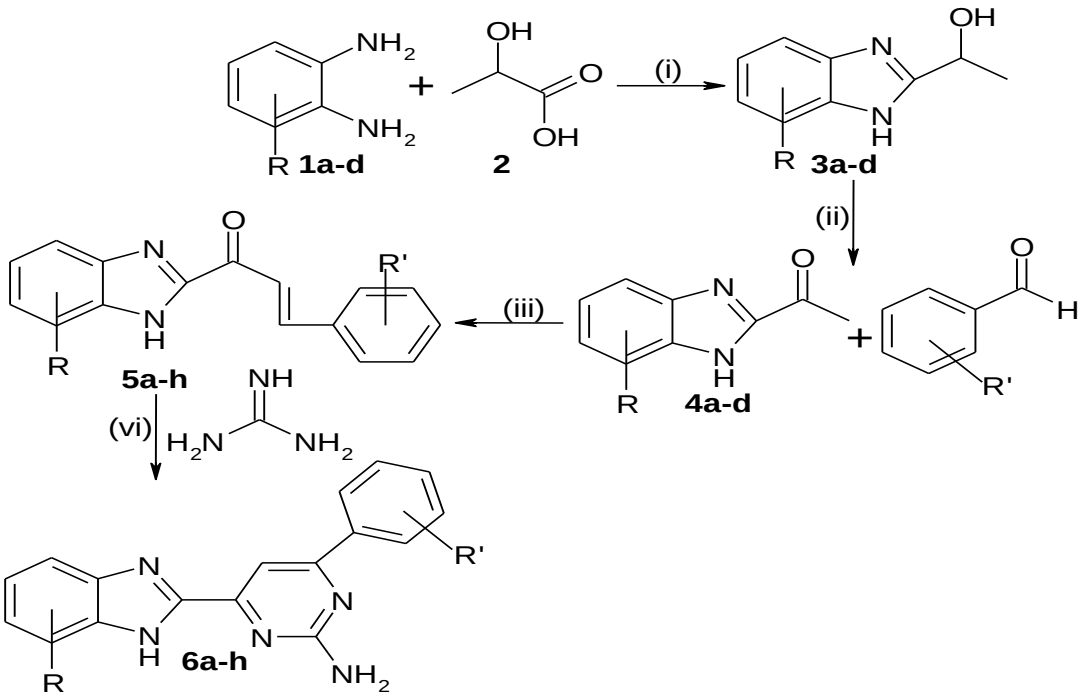


**Scheme 1** (i) HCl, reflux, 22-24 h, (ii) $K_2Cr_2O_7$, $H_2SO_4$, 2-3 h, (iii) EtOH, 60% KOH, 4-5 h, (iv) AcOH, reflux, 4-5h. **1/3/4a-d R** = a) H, b) 4-$CH_3$, c) 4-Cl; d) 4-$NO_2$. **5/6 a-h** R= a) H, b) H, c) H, d) 4-$CH_3$, e) 4-$CH_3$, f) 4-Cl, g) 4-Cl, h) 4-$NO_2$. **5/6 a-h** R'= a) H, b) 4-$OCH_3$, c) 3,4-$OCH_3$, d) H, e) 4-$C_2H_5$, f) 4-$C_2H_5$, g) 4-$NO_2$, h) 4-$C_2H_5$.

**Table 1: Antimicrobial activity of 4-(1*H*-benzo[*d*]imidazol-2-yl)-6-phenyl-2-pyrimidinamines (6a-h)**

| Compound | Antibacterial activity [a/b] | | | | Antifungal activity [a/b] | |
|---|---|---|---|---|---|---|
| | *B. subtilus* | *S. aureus* | *E. coli* | *K. pneumoniae* | *F. oxysporum* | *A. niger* |
| 6a | 05/04 | 05/04 | 05/04 | 05/04 | 02/02 | 02/01 |
| 6b | 13/11 | 13/12 | 09/07 | 10/08 | 05/03 | 05/03 |
| 6c | 15/12 | 15/10 | 13/11 | 12/11 | 04/03 | 03/02 |
| 6d | 13/12 | 15/13 | 13/11 | 13/12 | 05/03 | 04/03 |
| 6e | 10/07 | 09/08 | 10/08 | 08/07 | 03/02 | 03/02 |
| 6f | 13/12 | 13/11 | 08/07 | 07/06 | 04/03 | 03/02 |
| 6g | 13/12 | 15/13 | 09/08 | 11/10 | 05/03 | 05/03 |
| 6h | 09/08 | 09/07 | 10/08 | 05/04 | 03/03 | 03/02 |
| Streptomycin | 16/14 | 16/14 | 16/14 | 16/14 | - | - |
| Fluconazole | - | - | - | - | 06/04 | 06/04 |

[a]Zone of inhibition in mm at 500µg/ml concentration; [b]Zone of inhibition in mm at 250µg/ml concentration

**General procedure for the synthesis of synthesis of 2-acetyl benzimidazoles (4a-d)**

To a solution of 2-(α-hydroxy)ethyl benzimidazoles **(3a-d)** (0.01 mol) in dilute $H_2SO_4$ (5%, 40 ml) was drop wise added the solution of $K_2Cr_2O_7$ (0.15 mol) and aqueous $H_2SO_4$ (25%, 80ml) with constant stirring at room temperature over a period of 20 min. Further the reaction mixture was stirred at room temperature for 2 h. After completion of the reaction, (monitored by TLC), the reaction mixture neutralized with $NH_3$ solution (1:1) and formed orange solid was filtered, washed with water, dried and recrystallized from ethyl acetate to give compounds **4a-d** in pure form.

**General procedure for the synthesis of 1-(1*H*-benzimidazol-2-yl)-3-(substituted phenyl) prop-2-en-1-ones (5a-h)**

2-Acetyl benzimidazoles **(4a-d)** (0.01 mol) and aromatic benzaldehyde (0.01 mol) were mixed in ethanol (20 ml) and added 60% aq. KOH (5 ml) and the reaction was carried out with constant stirring at room temperature for 4 h. After completion of reaction (monitored by TLC) the reaction mixture was poured into ice cold water and neutralized with dilute HCl solution. The solid formed was filtered and dried, recrystallized from absolute ethanol to achieve compounds **5a-h**.

**General procedure for the synthesis of 2-[(5-aryl)-4,5-dihydro-1*H*-pyrazole-3-yl]-1*H*-benzimidazoles (6a-h)**

1-(1*H*-Benzimidazol-2-yl)-3-(substituted phenyl) prop-2-en-1-ones **(5a-h)** (0.01 mol) and guanidine (0.02 mol) was dissolved in glacial acetic acid (10 ml) and refluxed the reaction mixture on water both for 4-6 h. After completion of reaction (monitored by TLC) the reaction mixture was poured into ice cold water and neutralized with ammonia solution. The formed solid was filtered, dried and recrystallized from ethyl acetate to obtain compounds **6a-h** in pure form.

**1-(1*H*-benzo[*d*]imidazol-2-yl)-1-ethanol (3a)**
Yellow solid, yield 90%, mp 180-182°C. IR (KBr) $cm^{-1}$: 2971, 1623, 1458, 1215, 1103. $^1H$ NMR ($CDCl_3$) δ: 10.30 (1H, bs), 7.52 (2H, m, *J*=7.8 Hz), 7.12 (2H, m, *J*=7.6), 4.8 (1H, s), 3.05 (1H, q, *J*=7.4 Hz), 1.62 (3H, d, *J*=7.2 Hz). MS *m/z*: 163 ($M^+$+1).

**1-(5-methyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanol (3b)** Dark yellow solid, yield 90%, mp 160-162°C. IR (KBr) $cm^{-1}$: 3038, 2701, 1629, 1449, 1316, 1101. $^1H$ NMR ($CDCl_3$) δ: 9.61 (1H, bs), 7.32 (3H, m, *J*=8.0 Hz), 4.85 (1H, s), 3.05 (1H, q, *J*=7.8 Hz), 1.62 (3H, d, *J*=7.4 Hz). MS *m/z*: 177 ($M^+$+1).

**1-(5-chloro-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanol (3c)** Brown solid, yield 65%, mp 171-173°C. IR (KBr) $cm^{-1}$: 2981, 1623, 1444, 1210, 1082. $^1H$ NMR ($CDCl_3$) δ: 12.50 (1H, s), 7.55 (2H, d, *J*=7.2 Hz), 7.20 (1H, d, *J*=7.4 Hz), 4.91 (1H, m, *J*=6.8 Hz), 1.52 (3H, d, *J*=7.0 Hz). MS *m/z*: 197 ($M^+$+1).

**1-(5-nitro-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanol (3d)** Brown solid, yield 75%, mp 148-150°C. IR (KBr) $cm^{-1}$: 3342, 3215, 3024, 2865, 2240, 1420, 1248. $^1H$ NMR ($CDCl_3$) δ: 8.63 (1H, s), 7.91 (1H, d, *J*=7.0 Hz), 7.76 (1H, d, *J*=7.2 Hz), 6.64 (1H, s), 6.59 (1H, d, *J*=7.4 Hz), 5.16 (1H, m, *J*=7.6 Hz), 1.77 (1H, d, *J*=7.8 Hz). MS *m/z*: 208 ($M^+$+1).

**1-(1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (4a)** Yellow solid, yield 78%, mp 189-191°C. IR (KBr) $cm^{-1}$: 3289, 3059, 3015, 1674, 1580, 1445, 1235, 1147. $^1H$ NMR ($CDCl_3$) δ: 13.02 (1H, s), 7.85 (1H, d, *J*=7.8 Hz), 7.52 (1H, d, *J*=7.6 Hz), 7.32 (2H, t, *J*=7.4 Hz), 2.74 (3H, s). MS *m/z*: 161 ($M^+$+1).

**1-(5-methyl-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (4b)** Yellow solid, yield 80%, mp 170-172°C. IR (KBr) $cm^{-1}$: 3365, 2919, 2852, 1693. $^1H$ NMR ($CDCl_3$) δ: 11.23 (1H, s), 7.65 (1H, d, *J*=8.0 Hz), 7.48 (1H, d, *J*=7.8 Hz), 7.24 (1H, s), 3.42 (3H, s), 2.45 (3H, s). MS *m/z*: 174 ($M^+$+1).

**1-(5-chloro-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (4c)** Yellow solid, yield 65%, mp 185-187°C. IR (KBr) $cm^{-1}$: 3294, 3066, 3021, 1677, 1574, 1335, 1219, 1060. $^1H$ NMR ($CDCl_3$) δ: 10.70 (1H, s), 7.82 (1H, t, *J*=7.6 Hz), 7.51 (1H, m, *J*=7.4 Hz), 7.30 (1H, m, *J*=7.2 Hz), 2.81 (3H, s). MS *m/z*: 195 ($M^+$+1).

**1-(5-nitro-1*H*-benzo[*d*]imidazol-2-yl)-1-ethanone (4d)** Pale yellow solid, yield 70%, mp 155-157°C. IR (KBr) $cm^{-1}$: 3360, 3040, 2865, 2160, 1720, 1356, 1240. $^1H$ NMR ($CDCl_3$) δ: 8.91 (1H, s), 8.77 (1H, s), 8.13 (1H, d, *J*=7.2 Hz), 8.09 (1H, d, *J*=7.4 Hz), 2.79 (3H, s). MS *m/z*: 206 ($M^+$+1).

**(*E*)-1-(1*H*-benzo[*d*]imidazol-2-yl)-3-phenyl-2-propen-1-one (5a)** Pale yellow solid, yield 69%, mp 162-164°C. IR (KBr) $cm^{-1}$: 3276, 2856, 1589, 1487, 1238. $^1H$ NMR ($CDCl_3$) δ: 8.77 (1H, s), 8.11 (2H, d, *J*=8.0 Hz), 7.76 (2H, dd, *J*=8.2 Hz), 7.43 (2H, d, *J*=7.8 Hz), 7.23 (2H, dd, *J*=7.6 Hz), 6.90 (1H, d, *J*=7.4 Hz). MS *m/z*: 249 ($M^+$+1).

**(*E*)-1-(1*H*-benzo[*d*]imidazol-2-yl)-3-(4-methoxyphenyl)-2-propen-1-one (5b)** Dark yellow solid, yield 78%, mp 175-177°C. IR (KBr) $cm^{-1}$: 3282, 2848, 1601, 1508, 1245. $^1H$ NMR ($CDCl_3$) δ: 12.28 (1H, s), 7.51-7.02 (8H, m, *J*=8.0 Hz), 6.12-5.64 (1H, dd, *J*=7.8 Hz), 3.82 (3H, s), 3.44-3.38 (1H, dd, *J*=7.6 Hz). MS *m/z*: 279 ($M^+$+1).

**(*E*)-1-(1*H*-benzo[*d*]imidazol-2-yl)-3-(3,4-dimethoxyphenyl)-2-propen-1-one (5c)** Yellow solid, yield 72%, mp 210-212°C. IR (KBr) $cm^{-1}$: 3232, 1655, 1612, 1545, 1253, 1177, 833. $^1H$ NMR ($CDCl_3$) δ: 8.77 (1H, s), 8.11 (2H, d, *J*=6.8 Hz), 7.76 (2H, dd, *J*=7.0 Hz), 7.59 (1H, d, *J*=7.2 Hz), 7.13 (1H, s), 6.90 (1H, d, *J*=7.4 Hz), 6.82 (1H, d, *J*=7.6 Hz), 6.79 (1H, d, *J*=7.8 Hz), 3.80 (6H, s). MS *m/z*: 309 ($M^+$+1).

**(*E*)-1-(5-methyl-1*H*-benzo[*d*]imidazol-2-yl)-3-phenyl-2-propen-1-one (5d)** Yellow solid, yield 72%, mp 178-180°C. IR (KBr) $cm^{-1}$: 3245, 2925, 1662, 1624, 1564, 1243, 1210, 846. $^1H$ NMR ($CDCl_3$) δ: 8.76 (1H, s), 7.71 (1H, d, *J*=8.0 Hz), 7.66 (1H, d, *J*=7.8 Hz), 7.56 (1H, d, *J*=7.6 Hz), 7.43 (2H, d, *J*=7.2 Hz), 7.39 (1H, dd, *J*=7.4 Hz), 7.36 (1H, d, *J*=7.0 Hz), 7.23 (1H, dd, *J*=6.8 Hz), 6.94 (1H, d, *J*=7.2 Hz), 2.43 (3H, s). MS *m/z*: 263 ($M^+$+1).

**(*E*)-3-(4-ethylphenyl)-1-(5-methyl-1*H*-enzo[*d*]imidazol-2-yl)-2-propen-1-one (5e)** Yellow solid, yield 65%, mp 168-170°C. IR (KBr) $cm^{-1}$: 3230, 2932, 1654, 1612, 1572, 1234, 1222, 864. $^1H$ NMR ($CDCl_3$) δ: 8.77 (1H, s), 7.73 (1H, d, *J*=7.8 Hz), 7.68 (1H, d, *J*=6.8 Hz), 7.61 (1H, d, *J*=7.6 Hz), 7.39 (1H, d, *J*=7.0 Hz), 7.26 (2H, d, *J*=7.4 Hz), 7.20 (2H, d, *J*=6.6 Hz), 6.94 (1H, d, *J*=7.2 Hz), 2.47 (2H, q, *J*=6.8 Hz), 2.43 (3H, s), 1.37 (3H, t, *J*=7.0 Hz). MS *m/z*: 291 ($M^+$+1).

**(*E*)-1-(5-chloro-1*H*-benzo[*d*]imidazol-2-yl)-3-(4-ethylphenyl)-2-propen-1-one (5f)** Brown solid, yield 55%, mp 173-175°C. IR (KBr) $cm^{-1}$: 3255, 2956, 1674, 1635, 1594, 1256, 1243, 884. $^1H$ NMR ($CDCl_3$) δ: 8.75 (1H, s), 7.88 (1H, d, *J*=7.2 Hz), 7.79 (1H, d, *J*=7.8 Hz), 7.60 (1H, d, *J*=7.4 Hz), 7.58 (1H, d, *J*=8.0 Hz), 7.26 (2H, d, *J*=7.2 Hz), 7.21 (2H, d, *J*=7.4 Hz), 6.94 (1H, d, *J*=7.8 Hz), 2.47 (3H, q, *J*=7.6 Hz), 1.37 (3H, t, *J*=8.2 Hz). MS *m/z*: 311 ($M^+$+1).

**(*E*)-1-(5-chloro-1*H*-benzo[*d*]imidazol-2-yl)-3-(4-nitrophenyl)-2-propen-1-one (5g)** Red solid, yield 45%, mp 212-214°C. IR (KBr) $cm^{-1}$: 3243, 2946, 1663, 1644, 1584, 1236, 1254, 906. $^1H$ NMR ($CDCl_3$) δ: 8.77 (1H, s), 8.07 (2H, d, *J*=7.8 Hz), 7.89 (1H, d, *J*=7.4 Hz), 7.78 (1H, d, *J*=7.6 Hz), 7.73 (2H, d, *J*=6.8 Hz), 7.62 (2H, s), 7.58 (1H, d, *J*=7.4 Hz), 6.94 (1H, d, *J*=7.6 Hz). MS *m/z*: 328 ($M^+$+1).

**(*E*)-3-(4-ethylphenyl)-1-(5-nitro-1*H*-benzo[*d*]imidazol-2-yl)-2-propen-1-one (5h)** Brown solid, yield 53%, mp 168-170°C. IR (KBr) $cm^{-1}$: 3234, 2941, 1668, 1654, 1576, 1246, 1263, 879. $^1H$ NMR ($CDCl_3$) δ: 9.09 (1H, s), 8.75 (1H, s), 8.30 (1H, d, *J*=8.0 Hz), 8.29 (1H, d, *J*=7.8 Hz), 7.61 (1H, d, *J*=7.6 Hz), 7.26 (2H, d, *J*=7.4 Hz), 7.20 (2H, d, *J*=7.4 Hz), 6.90 (1H, d, *J*=8.0 Hz), 2.47 (3H, q, *J*=8.2 Hz), 1.37 (3H, t, *J*=7.0 Hz). MS *m/z*: 322 ($M^+$+1).

**4-(1*H*-benzo[*d*]imidazol-2-yl)-6-phenyl-2-pyrimidinamine (6a)** Yellow solid, yield 65%, mp 192-194°C.IR (KBr) $cm^{-1}$: 3342, 3025, 2165, 1514, 1482. $^1H$ NMR ($CDCl_3$) δ: 11.61 (1H, s), 7.75 (2H, d, *J*=7.4 Hz), 7.66 (3H, dd, *J*=7.8Hz), 7.44 (2H, d, *J*=6.8 Hz), 7.40 (2H, dd, *J*=7.0 Hz), 6.56 (3H, s). MS *m/z*: 288 ($M^+$+1).

**4-(1*H*-benzo[*d*]imidazol-2-yl)-6-(4-methoxyphenyl)-2-pyrimidinamine (6b)** Red solid, yield 68%, mp 187-189°C. IR (KBr) $cm^{-1}$: 3385, 3024, 2915, 2115, 1554, 1085. $^1H$ NMR ($CDCl_3$) δ: 11.53 (1H, s), 7.92 (2H, d, *J*=8.0 Hz), 7.44 (2H, d, *J*=7.2 Hz), 7.40 (2H, dd, *J*=7.8 Hz), 7.07 (2H, d, *J*=7.8 Hz), 6.56 (3H, s), 3.70 (3H, s). MS *m/z*: 318 ($M^+$+1).

**4-(1*H*-benzo[*d*]imidazol-2-yl)-6-(3,4-dimethoxyphenyl)-2-pyrimidinamine (6c)** Brown solid, yield 73%, mp 177-179°C. IR (KBr) $cm^{-1}$: 3410, 3015, 2885, 2115, 1478, 1115. $^1H$ NMR ($CDCl_3$) δ: 11.59 (1H, s), 7.91 (1H, d, *J*=7.8 Hz), 7.44 (2H, d, *J*=7.2 Hz), dd, *J*=7.6 Hz), 6.80 (1H, d, *J*=7.4 Hz), 6.76 (1H, s), 6.56 (3H, s), 3.84 (6H, s). MS *m/z*: 348 ($M^+$+1).

**4-(4-methoxyphenyl)-6-(5-methyl-1*H*-benzo[*d*]imidazol-2-yl)-2-pyrimidinamine (6d)** Yellow solid, yield 80%, mp 155-157°C. IR (KBr) $cm^{-1}$: 3418, 3025, 2925, 2184, 1524, 1245, 974. $^1H$ NMR ($CDCl_3$) δ: 11.53 (1H, s), 7.92 (2H, d, *J*=8.2 Hz), 7 Hz), 7.22 (1H, s), 7.11 (1H, d, *J*=7.8 Hz), 7.07 (2H, d, *J*=7.8 Hz), 6.56 (3H, s), 3.70 (3H, s), 2.43 (3H, s). MS *m/z*: 332 ($M^+$+1).

**4-(4-ethylphenyl)-6-(5-methyl-1*H*-benzo[*d*]imidazol-2-yl)-2-pyrimidinamine (6e)** Pale yellow solid, yield 65 %, mp 144-146°C. IR (KBr) $cm^{-1}$: 3368, 3045, 2865, 2164, 1552, 1045, 1214, 965. $^1H$ NMR ($CDCl_3$) δ: 11.44 (1H, s), 7.71 (2H, d, *J*=7.8 Hz), 7.24 (1H, d, *J*=7.2 Hz), 7.23 (2H, d, *J*=6.8 Hz), 7.21 (1H, s), 7.11 (1H, d, *J*=8.2 Hz), 6.56 (3H, s), 2.54 (2H, q, *J*= 7.8 Hz), 2.43 (3H, s), 1.20 (3H, t, *J*=8.0 Hz). MS *m/z*: 330 ($M^+$+1).

**4-(5-chloro-1*H*-benzo[*d*]imidazol-2-yl)-6-(4-ethylphenyl)-2- pyrimidinamine (6f)** Yellow solid, yield 68 %, mp 158-160°C. IR (KBr) $cm^{-1}$: 3416, 3021, 2892, 2118, 1547, 1210, 714. $^1H$ NMR ($CDCl_3$) δ: 11.44 (1H, s), 7.71 (2H, d, *J*=7.6 Hz), 7.49 (1H, d, *J*=7.2 Hz), 7.44 (1H, s), 7.23 (2H, d, *J*=8.2 Hz), 7.21 (1H, d, *J*=8.4 Hz), 6.56 (3H, s), 2.54 (2H, q, *J*=7.6 Hz), 1.20 (3H, t, *J*=7.6 Hz). MS *m/z*: 351 ($M^+$+1).

**4-(5-chloro-1*H*-benzo[*d*]imidazol-2-yl)-6-(4-nitrophenyl)-2-pyrimidinamine (6g)** Pale yellow **s**olid, yield 72 %, mp 170-172°C. IR (KBr) $cm^{-1}$: 3415, 3024, 2114, 1542, 1416, 1245, 712. $^1H$ NMR ($CDCl_3$) δ: 11.44 (1H, s), 8.16 (2H, d, *J*=7.4 Hz), 8.13 (2H, d, *J*=7.8 Hz), 7.49 (1H, d, *J*=6.8 Hz), 7.44 (1H, s), 7.26 (1H, d, *J*=8.2 Hz), 6.56 (3H, s). MS *m/z*: 367 ($M^+$+1).

**4-(4-ethylphenyl)-6-(5-nitro-1*H*-benzo[*d*]imidazol-2-yl)-2-pyrimidinamine (6h)** Brown **s**olid, yield 74 %, mp 178-180°C. IR (KBr) $cm^{-1}$: 3415, 3044, 2865, 2134, 1514, 1453, 1245, 954. $^1H$ NMR ($CDCl_3$) δ: 11.44 (1H, s), 8.42 (1H, s), 8.01 (1H, d, *J*=8.4 Hz), 7.71 (2H, d, *J*=8.0 Hz), 7.67 (1H, d, *J*=7.8 Hz), 7.25 (2H, d, *J*=7.6 Hz), 6.56 (3H, s), 2.54 (2H, q, *J*=7.4 Hz), 1.20 (3H, t, *J*=8.2 Hz). MS *m/z*: 361 ($M^+$+1).

## RESULTS AND DISCUSSION

The therapeutic importance of benzimidazoles and pyrimidines prompted us to develop selective molecules to display higher pharmacological activities. In this article, we have reported a novel series of 4-(1*H*-benzo[*d*]imidazol-2-yl)-6-phenyl-2-pyrimidinamine and their derivatives **(6a-h)** in good to excellent yields by involving 2-(α-hydroxy)ethyl benzimidazoles **(3a-d)**, 2-acetyl benzimidiazoles **(4a-d)** and 1-(1*H*-benzimidazol-2-yl)-3-(substituted phenyl) prop-2-en-1-ones **(5a-h)** as intermediates and commercially available *o*-phenylenediamine (*o*-PDA) **(1)** with α-hydroxy propionic acid **(2)** as raw materials (Scheme 1). Thus the initial intermediate **3** has been prepared on cyclization between the compounds **1a-d** and **2** in acidic medium (HCl) under reflux for 22-24 h. Then the intermediate **3a-d** is turned into the next intermediate **4a-d** on oxidation with potassium dichromate in presence of $H_2SO_4$ at room temperature for 2-3 h. Further, the intermediate **4a-d** was treated with the various aryl aldehydes in ethanol solvent in alkaline medium (60% KOH) at ambient temperature for 4-5 h to obtain the final intermediate **5a-h** in good yields. Subsequently condensation followed by cyclization of compound **5a-h** with guanidine in acetic acid under reflux for 4-5 h gave the title compounds **6a-h** in good to excellent yields. The chemical structures of the newly prepared compounds were confirmed by their IR, $^1H$ NMR and Mass spectral data. Further the compounds have been used to evaluate their anti microbial activity.

### Antibacterial Activity

The *in vitro* antibacterial activity of the newly synthesized compounds was evaluated against two representative gram-positive bacteria viz., *B. subtilus* and *S. aureus*, two gram-negative bacteria viz., *E. coli* and *K. pneumoniae* through 'Cup-plate method' [11] using Streptomycin as standard drugs and DMSO as solvent. Each sample is tested at two different concentrations (500µg/ml and 250µg/ml) and the results are expressed in zone of inhibition in mm (Table 1). According to the results, it has been observed that the compounds exhibited interesting biological activity however, with a degree of variation. Among all the compounds, compound **6b** displayed high activity against *B. subtilus* and good activity against *E. coli* and *K. pneumoniae*. Compound **6c** shows good activity against all organisms except *E. coli*. Compound **6d** exhibits good activity against both gram-negative bacteria. It is interesting to note that compound **6f** has excellent activity against all bacterial organisms. The remaining compounds showed good to moderate activity against all the organisms employed.

### Antifungal Activity

The newly prepared compounds were also screened for their antifungal activity against two fungal organisms namely *F. oxysporum* and *A. niger* through 'Cup-plate method' [11] using Fluconazole as standard drug by using DMSO as solvent and the results are summarized in Table 1. It has been observed that the compounds exhibited good to excellent antifungal activity, with a degree of variation. Among all the synthesized compounds, compounds **6b, 6c, 6g** and **6h** were high active against *F. oxysporum* and compounds **6g** and **6h**

have excellent activity against *A. niger*. The remaining compounds showed low to moderate activity against two organisms employed.

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