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Research Paper

A one-pot multi component synthesis of novel pyrimido[1,2-*a*]benzimidazoles

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Abstract: A one-pot multi-components synthesis of a series of novel pyrimido[1,2-*a*]benzimidazoles **(4a-j)** was achieved from acetoacetamide, aromatic aldehydes and 2-aminobenzimidazole with high yield and purity. The structures of the newly synthesized pyrimido[1,2-*a*]benzimidazoles **(4a-j)** were supported by FTIR, PMR and mass spectral data. All the newly synthesized compounds were tested for antimicrobial activity.

Introduction

Polysubstituted pyrimido[1,2-*a*]benzimidazoles possess a wide spectrum of biological activities and they are structurally related to natural purine bases. Literature survey revealed that pyrimido[1,2-*a*]benzimidazoles possess antimicrobial [1-3], aurora A kinase inhibitory [4], α-glucosidase inhibitory [5], antiproliferative [6], protein kinase inhibitory [7], T cell activation [8], angioprotein receptors and/or vascular endothelial growth factor receptor-2 (VEGFR-2) inhibitory [9], hypotensive; spasmolytic; and antiaggregant [10], anesthetic [11] and diuretic [12], antiInflammatory [13, 14], etc. activities.

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Pyrimido [1,2-a] benzimidazol-2-ones are generally synthesized by the reaction of propiolic esters [15, 16] and α,β-unsaturated esters [17, 18] with 2-aminobenzimidazole. Recently, many one pot synthetic approaches are reported for the synthesis of various substituted pyrimido[1,2-*a*]benzimidazoles [20-22]. Despite the variety of methods available for the synthesis of pyrimidobenzimidazoles, multi-component synthesis involving use of acetoacetamides is not reported in the literature.

Recognizing these facts, we have developed a new protocol for the synthesis of novel pyrimido[1,2-*a*]benzimidazoles **(4a-j)** from acetoacetamide **(1)**, different aromatic aldehydes **(2a-j)** and 2-aminobenzimidazole

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(3) with the advantages of short reaction time and high yield. **(Scheme-a)**.

Results and Discussion

The Plausible mechanism for the synthesis of 1,4-dihydropyrimido [1,2-*a*] benzimidazoles is based on the Biginelli like cyclocondensation of aromatic aldehydes and acetoacetic acid derivatives with 2-amino benzimidazole which contains a guanidine fragment.

A new series of 1,4-dihydropyrimido[1,2-*a*]benzimidazoles (**4a-j**) containing an acetoacetamide fragment was synthesized by condensation of *N*-(4-methylthiazol-2-yl)-3-oxobutanamide **(1)** with different aromatic aldehydes **(2a-j)** and 2-aminobenzimidazole **(3)**.The structures of all the newly synthesized compounds were elucidated by FT-IR, mass spectra, ^{1}H NMR and elemental analyses. Confirmatory bands for secondary amine and amidic carbonyl groups were observed at 3414-3210 cm^{-1} and 1690-1600 cm^{-1} respectively. Another characteristic C=N stretching band of imidazole ring was observed at 1626-1500 cm^{-1}. ^{1}H NMR spectra showed a singlet for the methine proton of pyrimidine ring at 6.00-6.90 δ ppm, and singlets for amino and amide group protons at 7.50-9.90 and 9.45-10.50 δ ppm, respectively. The newly synthesized compounds were subjected to antimicrobial activity.

Antimicrobial evaluation

All of the synthesized compounds **(4a-j**) were tested for their antibacterial and antifungal activity (MIC) *in vitro* by broth dilution method [23-25] with two Gram-positive bacteria Staphylococcus aureus MTCC-96, Streptococcus pyogenes MTCC 443, two Gram-negative bacteria Escherichia coli MTCC 442, Pseudomonas aeruginosa MTCC 441 and three fungal strains Candida albicans MTCC 227, Aspergillus Niger MTCC 282, Aspergillus clavatus MTCC 1323 taking gentamycin, ampicillin, chloramphenicol, ciprofloxacin, norfloxacin, nystatin and greseofulvin as standard drugs. The standard strains were procured from the Microbial Type Culture Collection (MTCC), Institute of Microbial Technology, Chandigarh, India.

The minimal inhibitory concentration (MIC) values for all the newly synthesized compounds, defined as the lowest concentration of the compound preventing the visible growth, were determined by using micro dilution broth method according to NCCLS standards [23].

Materials and Methods

Melting points were determined in open capillary tubes and are uncorrected. Formation of the compounds was routinely checked by TLC on silica gel-G plates of 0.5 mm thickness and spots were located by iodine. IR spectra were recorded Shimadzu FT-IR-8400 instrument using potassium bromide (KBr) pellet method. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct injection probe technique. ^{1}H NMR was determined in DMSO-d_6 solution on a bruker Ac 400 MHz spectrometer. Elemental analysis of the all the synthesized compounds was carried out on elemental vario EL III carlo erba 1108 model and the results are in agreements with the structures assigned.

Preparation of 4-methyl-N-(4-methylthiazol-2-yl)-3-oxopentanamide (1)

Synthesis of 4-methyl-N-(4-methylthiazol-2-yl)-3-oxopentanamide was achieved using previously published method [26].

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General procedure for the synthesis of 4-(aryl)-2-isopropyl-N-(4-methyl-1,3-thiazol-2-yl)-1,4-dihydro pyrimido[1,2-a]benzimidazole-3-carboxamide (4a-j)

A mixture of the 2-aminobenzimidazole **(3)** (0.01 mol), 4-methyl-N-(4-methylthiazol-2-yl)-3-oxopentanamide **(1)** (0.01 mol) and appropriate aromatic aldehydes **(2a-j)** (0.01 mol) was refluxed in 4 ml of DMF for 30 min. After cooling, methanol (~12 ml) was added. The reaction mixture was allowed to stand overnight and then filtered to give the solid 1,4-dihydropyrimido[1,2-*a*]benzimidazoles products **(4a-j)**, which were recrystallized from ethanol.

4-(4-chlorophenyl)-2-isopropyl-N-(4-methyl-1,3-thiazol-2-yl)-1,4-dihydro pyrimido[1,2-a]benzimidazole-3-carboxamide (4a)

mp 221 ºC; ^{1}H NMR (DMSO-d_6) δ ppm: 1.24-1.27 (d, 3H, $H_{a,}$), 1.36-1.30 (d, 3H, $H_{b,}$), 2.24 (s, 3H, H_c), 3.39-3.44 (m, 1H, H_d), 5.95 (s, 1H, $H_{e,}$), 6.52 (s, 1H, H_f), 6.89-6.97 (m, 2H, $H_{gg'}$) 7.03-7.11 (m, 2H, $H_{hh'}$), 7.16-7.24 (m, 4H, H_{i-l}) 9.35 (s, 1H, H_m), 9.56 (s, 1H, H_n).

FT IR (cm^{-1}): 3227 (N-H stretching of secondary amine), 3049 (C-H stretching of aromatic ring), 2975 (C-H asymmetrical stretching of CH_3 group), 2883 (C-H asymmetrical stretching of CH_3 group), 1651 (C=O stretching of amide), 1631 (N-H deformation of pyrimidine ring), 1622, 1564 and 1519 (C=C stretching of aromatic ring), 1456 (C-H asymmetrical deformation of CH_3 group), 1392 (C-H symmetrical deformation of CH_3 group), 1298 and 1247 (C-N stretching), 1078 (C-H in plane deformation of aromatic ring), 825 (C-H out of plane bending of 1,4-disubstituion) 738 and 680 (C-Cl stretching). MS: *m/z* 463; Anal. Calcd. for $C_{24}H_{22}ClN_5OS$: C, 62.13; H, 4.78N, 15.09. Found: C, 61.95; H, 4.57; N,14.88%; Yield: 79%.

4-(4-fluorophenyl)-2-isopropyl-N-(4-methyl-1,3-thiazol-2-yl)-1,4-dihydro pyrimido[1,2-a]benzimidazole-3-carboxamide (4b)

mp 204 ºC; ^{1}H NMR (DMSO-d_6) δ ppm: 1.24-1.26 (d, 3H,), 1.40-1.39 (d, 3H, $H_{b,}$), 2.57 (s, 3H, H_c), 3.92 (m, 1H, H_d), 5.85 (s, 1H, $H_{e,}$), 6.59 (s, 1H, H_f), 6.90-6.98 (m, 2H, $H_{gg'}$) 7.20-7.22 (m, 2H, $H_{hh'}$), 7.27-7.30 (m, 2H, $H_{ii'}$), 7.52-7.54 (m, 2H, $H_{jj'}$) 9.68 (s, 1H, H_m), 9.84 (s, 1H, H_n).

FT IR (cm^{-1}): 3238 (N-H stretching of secondary amine), 3053 (C-H stretching of aromatic ring), 2974 (C-H asymmetrical stretching of CH_3 group), 2887 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1606 (N-H deformation of pyrimidine ring), 1573,1556 and 1508 (C=C stretching of aromatic ring), 1454 (C-H asymmetrical deformation of CH_3 group), 1394 (C-H symmetrical deformation of CH_3 group), 1294 and 1246 (C-N stretching), 1084 (C-H in plane deformation of aromatic ring), 1012 (C-F stretching), 827 (C-H out of plane bending of 1,4-disubstituion). MS: *m/z* 447; Anal. Calcd. for $C_{24}H_{22}FN_5OS$: C, 64.41; H, 4.95; N, 15.65. Found: C, 64.12; H, 4.68; N, 15.42. %; Yield: 69%.

4-(4-methylphenyl)-2-isopropyl-N-(4-methyl-1,3-thiazol-2-yl)-1,4-dihydro pyrimido[1,2-a]benzimidazole-3-carboxamide (4c)

mp 224 ºC; ^{1}H NMR (DMSO-d_6) δ ppm: 1.24-1.26 (d, 3H, $H_{a,}$), 1.34-1.36 (d, 3H, $H_{b,}$), 2.14 (s, 3H, H_c), 2.57 (s, 3H, H_d), 3.27 (s, 1H, $H_{e,}$), 5.29 (s, 1H, H_f), 6.58 (s, 1H, H_g) 6.92-6.93 (d, 2H, $H_{hh'}$), 7.05-7.09 (m, 1H, H_i), 7.18-7.24 (m, 2H, $H_{jj'}$), 7.39-7.41 (d, 1H, H_k), 7.52-7.54 (dd, 2H, $H_{ll'}$) 9.69 (s, 1H, H_m), 9.86 (s, 1H, H_n).

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FT IR (cm^{-1}): 3294 (N-H stretching of secondary amine), 3053 (C-H stretching of aromatic ring), 2958 (C-H asymmetrical stretching of CH_3 group), 2854 (C-H asymmetrical stretching of CH_3 group), 1649 (C=O stretching of amide), 1641 (N-H deformation of pyrimidine ring), 1560, 1521 and 1506 (C=C stretching of aromatic ring), 1456 (C-H asymmetrical deformation of CH_3 group), 1388 (C-H symmetrical deformation of CH_3 group), 1294 and 1236 (C-N stretching), 1078 (C-H in plane deformation of aromatic ring), 833 (C-H out of plane bending of 1,4-disubstituion). MS: *m/z* 443; Anal. Calcd. for $C_{25}H_{25}N_5OS$: C, 67.69; H, 5.68; N, 15.79; Found: C, 67.43; H, 5.41; N,15.29 %; Yield: 66%.

4-(4-methoxyphenyl)-2-isopropyl-N-(4-methyl-1,3-thiazol-2-yl)-1,4-dihydro pyrimido[1,2-a]benzimidazole-3-carboxamide (4d)

mp 212 ºC; ^{1}H NMR (DMSO-d_6) δ ppm: 1.24-1.26 (d, 3H, $H_{a,}$), 1.34-1.36 (d, 3H, $H_{b,}$), 3.14 (s, 3H, H_c), 2.57 (s, 3H, H_d), 3.27 (s, 1H, $H_{e,}$), 5.29 (s, 1H, H_f), 6.58 (s, 1H, H_g) 6.92-6.93 (d, 2H, $H_{hh'}$), 7.05-7.09 (m, 1H, H_i), 7.18-7.24 (m, 2H, $H_{jj'}$), 7.39-7.41 (d, 1H, H_k), 7.52-7.54 (dd, 2H, $H_{ll'}$) 9.69 (s, 1H, H_m), 9.86 (s, 1H, H_n).

FT IR (cm^{-1}): 3294 (N-H stretching of secondary amine), 3053 (C-H stretching of aromatic ring), 2958 (C-H asymmetrical stretching of CH_3 group), 2854 (C-H asymmetrical stretching of CH_3 group), 1649 (C=O stretching of amide), 1641 (N-H deformation of pyrimidine ring), 1560, 1521 and 1506 (C=C stretching of aromatic ring), 1456 (C-H asymmetrical deformation of CH_3 group), 1388 (C-H symmetrical deformation of CH_3 group), 1294 and 1236 (C-N stretching), 1241 (C-O-C stretching).1078 (C-H in plane deformation of aromatic ring), 833 (C-H out of plane bending of 1,4-disubstituion). MS: *m/z* 459. Anal. Calcd. for $C_{25}H_{25}N_5O_2S$: C, 65.34; H, 5.48; N, 15.24; Found: C, 65.11; H, 5.19; N, 15.05%: Yield: 68%.

4-(3-bromophenyl)-2-isopropyl-N-(4-methyl-1,3-thiazol-2-yl)-1,4-dihydro pyrimido[1,2-a]benzimidazole-3-carboxamide (4e)

mp 211 ºC; ^{1}H NMR (DMSO-d_6) δ ppm: 1.24-1.26 (d, 3H, $H_{a,}$), 1.40-1.39 (d, 3H, $H_{b,}$), 2.57 (s, 3H, H_c), 3.92 (m, 1H, H_d), 5.85 (s, 1H, $H_{e,}$), 6.59 (s, 1H, H_f), 6.90-6.98 (m, 2H, $H_{gg'}$) 7.20-7.22 (m, 2H, $H_{hh'}$), 7.27-7.30 (m, 2H, $H_{ii'}$), 7.52-7.54 (m, 2H, $H_{jj'}$) 9.68 (s, 1H, H_m), 9.84 (s, 1H, H_n).

FT IR (cm^{-1}): 3238 (N-H stretching of secondary amine), 3053 (C-H stretching of aromatic ring), 2974 (C-H asymmetrical stretching of CH_3 group), 2887 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1606 (N-H deformation of pyrimidine ring), 1573,1556 and 1508 (C=C stretching of aromatic ring), 1454 (C-H asymmetrical deformation of CH_3 group), 1394 (C-H symmetrical deformation of CH_3 group), 1294 and 1246 (C-N stretching), 1084 (C-H in plane deformation of aromatic ring), 1012 (C-Br stretching), 720 (C-H out of plane bending of 1,3-disubstituion). MS: *m/z* 508. Anal. Calcd. for $C_{24}H_{22}BrN_5OS$: C, 56.70; H, 4.36; N, 13.77; Found: C, 56.53; H, 4.17; N, 13.51%; Yield: 64%.

4-(3-chlorophenyl)-2-isopropyl-N-(4-methyl-1,3-thiazol-2-yl)-1,4-dihydro pyrimido[1,2-a]benzimidazole-3-carboxamide (4f)

mp 221 ºC; %; ^{1}H NMR (DMSO-d_6) δ ppm: 1.24-1.26 (d, 3H, $H_{a,}$), 1.40-1.39 (d, 3H, $H_{b,}$), 2.57 (s, 3H, H_c), 3.92 (m, 1H, H_d), 5.85 (s, 1H, $H_{e,}$), 6.59 (s, 1H, H_f), 6.90-6.98 (m, 2H, $H_{gg'}$) 7.20-7.22 (m, 2H, $H_{hh'}$), 7.27-7.30 (m, 2H, $H_{ii'}$), 7.52-7.54 (m, 2H, $H_{jj'}$) 9.68 (s, 1H, H_m), 9.84 (s, 1H, H_n).

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FT IR (cm^{-1}): 3238 (N-H stretching of secondary amine), 3053 (C-H stretching of aromatic ring), 2974 (C-H asymmetrical stretching of CH_3 group), 2887 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1606 (N-H deformation of pyrimidine ring), 1573,1556 and 1508 (C=C stretching of aromatic ring), 1454 (C-H asymmetrical deformation of CH_3 group), 1394 (C-H symmetrical deformation of CH_3 group), 1294 and 1246 (C-N stretching), 1084 (C-H in plane deformation of aromatic ring), 1012 (C-Br stretching), 720 (C-H out of plane bending of 1,3-disubstituion). MS: *m/z* 463 Anal. Calcd. for $C_{24}H_{22}ClN_5OS$: C, 62.01; H, 4.51; N, 15.09; Found: , 62.13; H, 4.78,; N, 14.92%: Yield: 59%.

4-(4-nitrophenyl)-2-isopropyl-N-(4-methyl-1,3-thiazol-2-yl)-1,4-dihydro pyrimido[1,2-a]benzimidazole-3-carboxamide (4g)

mp 201 ºC; ^{1}H NMR (DMSO-d_6) δ ppm: 1.24-1.26 (d, 3H, H_a,), 1.40-1.39 (d, 3H, H_b,), 2.57 (s, 3H, H_c), 3.92 (m, 1H, H_d), 5.85 (s, 1H, H_e,), 6.59 (s, 1H, H_f), 6.90-6.98 (m, 2H, $H_{gg'}$) 7.20-7.22 (m, 2H, $H_{hh'}$), 7.27-7.30 (m, 2H, $H_{ii'}$), 7.52-7.54 (m, 2H, $H_{jj'}$) 9.68 (s, 1H, H_m), 9.84 (s, 1H, H_n).

FT IR (cm^{-1}): 3238 (N-H stretching of secondary amine), 3053 (C-H stretching of aromatic ring), 2974 (C-H asymmetrical stretching of CH_3 group), 2887 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1606 (N-H deformation of pyrimidine ring), 1573,1556 and 1508 (C=C stretching of aromatic ring), 1454 (C-H asymmetrical deformation of CH_3 group), 1394 (C-H symmetrical deformation of CH_3 group), 1316 (Nitro N-O),1294 and 1246 (C-N stretching), 1084 (C-H in plane deformation of aromatic ring, 827 (C-H out of plane bending of 1,4-disubstituion). MS: *m/z* 475. Anal. Calcd. for $C_{24}H_{22}N_6O_3S$: C, 60.75; H, 4.67; N, 17.71; Found: C, 60.51; H, 4.39; N, 17.48%: Yield: 64%.

4-(3-nitrophenyl)-2-isopropyl-N-(4-methyl-1,3-thiazol-2-yl)-1,4-dihydro pyrimido[1,2-a]benzimidazole-3-carboxamide (4h)

mp 199 ºC; ^{1}H NMR (DMSO-d_6) δ ppm: 1.24-1.26 (d, 3H, H_a,), 1.40-1.39 (d, 3H, H_b,), 2.57 (s, 3H, H_c), 3.92 (m, 1H, H_d), 5.85 (s, 1H, H_e,), 6.59 (s, 1H, H_f), 6.90-6.98 (m, 2H, $H_{gg'}$) 7.20-7.22 (m, 2H, $H_{hh'}$), 7.27-7.30 (m, 2H, $H_{ii'}$), 7.52-7.54 (m, 2H, $H_{jj'}$) 9.68 (s, 1H, H_m), 9.84 (s, 1H, H_n).

FT IR (cm^{-1}): 3238 (N-H stretching of secondary amine), 3053 (C-H stretching of aromatic ring), 2974 (C-H asymmetrical stretching of CH_3 group), 2887 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1606 (N-H deformation of pyrimidine ring), 1573,1556 and 1508 (C=C stretching of aromatic ring), 1454 (C-H asymmetrical deformation of CH_3 group), 1394 (C-H symmetrical deformation of CH_3 group), 1316 (Nitro N-O), 1294 and 1246 (C-N stretching), 1084 (C-H in plane deformation of aromatic ring, 720 (C-H out of plane bending of 1,3-disubstituion). MS: *m/z* 475. Anal. Calcd. for $C_{24}H_{22}N_6O_3S$: C, 60.75; H, 4.67; N, 17.71; Found: , 60.55; H, 4.48; N, 17.52%: Yield: 66%.

4-(2-nitrophenyl)-2-isopropyl-N-(4-methyl-1,3-thiazol-2-yl)-1,4-dihydro pyri mido[1,2-a]benzimidazole-3-carboxamide (4i)

mp 200 ºC; ^{1}H NMR (DMSO-d_6) δ ppm: 1.24-1.26 (d, 3H, H_a,), 1.40-1.39 (d, 3H, H_b,), 2.57 (s, 3H, H_c), 3.92 (m, 1H, H_d), 5.85 (s, 1H, H_e,), 6.59 (s, 1H, H_f), 6.90-6.98 (m, 2H, $H_{gg'}$) 7.20-7.22 (m, 2H, $H_{hh'}$), 7.27-7.30 (m, 2H, $H_{ii'}$), 7.52-7.54 (m, 2H, $H_{jj'}$) 9.68 (s, 1H, H_m), 9.84 (s, 1H, H_n).

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FT IR (cm^{-1}): 3238 (N-H stretching of secondary amine), 3053 (C-H stretching of aromatic ring), 2974 (C-H asymmetrical stretching of CH_3 group), 2887 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1606 (N-H deformation of pyrimidine ring), 1573,1556 and 1508 (C=C stretching of aromatic ring), 1454 (C-H asymmetrical deformation of CH_3 group), 1394 (C-H symmetrical deformation of CH_3 group), 1316 (Nitro N-O),1294 and 1246 (C-N stretching), 1084 (C-H in plane deformation of aromatic ring, 720 (C-H out of plane bending of 1,3-disubstituion). MS: *m/z* 471. Anal. Calcd. for $C_{26}H_{22}FN_5O_3$: C, 66.23; H, 4.70; N, 14.85; Found: C, 66.03; H, 4.53; N, 14.61%: Yield: 80%;

4-(4-hydroxyphenyl)-2-isopropyl-N-(4-methyl-1,3-thiazol-2-yl)-1,4-dihydro pyri mido[1,2-a]benzimidazole-3-carboxamide (4j)

mp 209 ºC; ^{1}H NMR (DMSO-d_6) δ ppm: 1.24-1.26 (d, 3H, H_a,), 1.34-1.36 (d, 3H, H_b,), 10.14 (s, 1H, H_c), 2.57 (s, 3H, H_d), 3.27 (s, 1H, H_e,), 5.29 (s, 1H, H_f), 6.58 (s, 1H, H_g) 6.92-6.93 (d, 2H, $H_{hh'}$), 7.05-7.09 (m, 1H, H_i), 7.18-7.24 (m, 2H, $H_{jj'}$), 7.39-7.41 (d, 1H, H_k), 7.52-7.54 (dd, 2H, $H_{ll'}$) 9.69 (s, 1H, H_m), 9.86 (s, 1H, H_n).

FT IR (cm^{-1}): 3599 (Free -OH), 3294 (N-H stretching of secondary amine), 3053 (C-H stretching of aromatic ring), 2958 (C-H asymmetrical stretching of CH_3 group), 2854 (C-H asymmetrical stretching of CH_3 group), 1649 (C=O stretching of amide), 1641 (N-H deformation of pyrimidine ring), 1560, 1521 and 1506 (C=C stretching of aromatic ring), 1456 (C-H asymmetrical deformation of CH_3 group), 1388 (C-H symmetrical deformation of CH_3 group), 1294 and 1236 (C-N stretching), 1078 (C-H in plane deformation of aromatic ring), 833 (C-H out of plane bending of 1,4-disubstituion). MS: *m/z* 445.Anal. Calcd. for $C_{24}H_{23}N_5O_2S$: C, 64.70; H, 5.20; N, 15.72; Found: C, 64.49; H, 5.02; N, 15.56%: Yield: 73%.

Conclusion

A simple, convenient and rapid one-pot three-component preparation of pyrimido[1,2-*a*]benzimidazoles **(4a-j)** derivatives is developed. The present methodology offers very attractive features such as short reaction time, mild reaction condition, good to excellent product yields. The newly synthesized compounds **(4a-j)** exhibited moderate to good antimicrobial activity.

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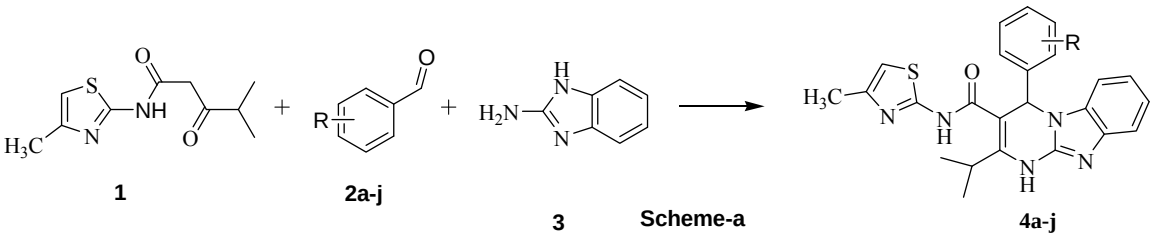
Reaction Scheme



R = 4-Cl (a), 4-F (b), 4-CH3 (c), 4-OCH3 (d), 4-Br (e), 3-Cl (f), 4-NO2 (g), 3-NO2 (h), 2-NO2 (i), 4-OH (j)

Table-1:- ***In vitro*** **Antimicrobial Screening Results for 4a-j**

Code	**Minimal inhibition concentration (µg mL^{-1})**						
	Gram-positive		**Gram-negative**		**Fungal species**		
	S.a.	***S. p.***	***E.c.***	***P.a.***	***C. a.***	***A. n.***	***A.c.***
4a	500	500	250	250	500	500	500
4b	500	500	250	250	500	500	500
4c	1000	1000	500	500	500	500	500
4d	250	500	250	500	500	500	500
4e	500	500	500	500	1000	250	250
4f	150	500	1000	1000	250	1000	1000
4g	1000	250	250	500	250	1000	1000
4h	1000	150	1000	500	250	1000	1000
4i	250	250	150	150	1000	500	1000
4j	1000	500	500	250	500	>1000	1000
Gentamycin	0.25	0.5	0.05	1	-	-	-
Ampicillin	250	100	100	100	-	-	-
Chloramphenicol	50	50	50	50	-	-	-
Iprofloxacin	50	50	25	25	-	-	-
Norfloxacin	10	10	10	10	-	-	-
Nystatin	-	-	-	-	100	100	100
Greseofulvin	-	-	-	-	500	100	100

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