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Effective one pot synthesis of new biologically active pyrimido[1,2-*a*]benzimidazoles

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ABSTRACT

The synthesis of new pyrimido[1,2-*a*]benzimidazoles (4a-j) is based on the Biginelli like cyclo condensation of aromatic aldehydes and acetoacetamide derivatives with 2-amino benzimidazole containing a guanidine fragment. The cyclo condensations were achieved by heating of the starting materials in dimethylformamide (DMF) as solvent. Synthesized compounds were characterized by analytical and spectral (IR, ^{1}H NMR, mass spectral and elemental analyses) data and have been screened for their antimicrobial activity.

KEYWORDS

Biginelli like cyclo condensation;
Acetoacetamides;
Benzimidazole;
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. From the standpoint of biological activity, fused hetero aromatic systems are often of much greater interest than the constituent monocyclic compounds. Antimicrobial[1,2], antimalarial[3], antiproliferative[4], protein kinase inhibitor[5], T cell activation[6], angioprotein receptors and/or vascular endothelial growth factor receptor-2 (VEGFR-2) inhibitory activities[7], hypotensive, spasmolytic and antiaggregant activities[8], anesthetic activity[9], diuretic[10], anti-inflammatory[11,12] etc. activities have been reported for certain pyrimido[1,2-*a*]benzimidazole derivatives.

One of the synthetic pathways to 1,4-dihydropyrimido[1,2-*a*]benzimidazoles is based on the Biginelli like cyclo condensation of aromatic aldehydes and acetoacetic acid derivatives with 2-amino benzimidazole containing a guanidine fragment. There are literary data about the synthesis of 1,4-dihydropyrimido[1,2-*a*]benzimidazoles by treatment of 2-amino benzimidazole with aldehydes and ethyl acetoacetate or cyclic β-diketones. The cyclo condensations were achieved by heating of the starting materials in ethanol with catalytic amounts of hydrochloric acid under reflux conditions or using dimethylformamide (DMF) as solvent.

The use of acetoacetamides in these or similar reactions has not been described. In continuation to our work on bioactive heterocycles we report herein for the first time a rapid efficient, clean and environmentally benign exclusive synthesis of pyrimido[1,2-*a*]benzimidazoles (4a-j) (Scheme-a). An improved method for the synthesis of some new pyrimido[1,2-*a*]benzimidazoles from aromatic aldehydes, acetoacetamide and 2-amino benzimidazole with significant enhancement in reaction rates, short reaction time (30 min h.), good to excellent yields (59-80%) and ambient temperature. The biological evaluation re-

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vealed that the newly synthesized compounds (4a-j) and exhibited good antimicrobial activity and moderate antimicrobacterial activity.

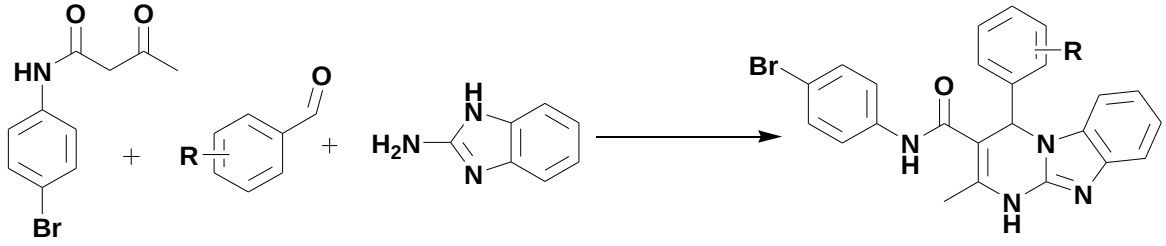
EXPERIMENTAL

Melting points are uncorrected and were taken in open glass capillaries using Gallenkamp melting point apparatus. 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. Elemental analysis of the all the synthesized compounds was carried out on elemental vario EL III carlo erba 1108 model. The IR spectra were recorded on a Shimadzu FT IR- 8400S spectrophotometer in KBr pellets and band positions are recorded in wave numbers (cm^{-1}). ^1H NMR spectra were recorded on Bruker advance II using DMSO-d_6 at 400 MHz and chemical shifts (δ) are given in ppm. TMS was used as internal reference. The mass spectra were recorded on GC-MS QP-2010 spectrometer. All used chemicals were of analytical reagent grade and were used without further purification.

REACTION SCHEME

General procedure for the synthesis of N-(bromophenyl)-2-methyl-4-(4-substitutedphenyl)-1,4-dihydropyrimido[1,2-*a*]benzimidazole-3-carboxamide (4a-j). Synthesis of N-(4-bromophenyl)-3-oxobutanamide (1) was achieved using previously published method[13].

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



1 2a-j 3 (Scheme-a) 4a-j

R = 4-OCH_3 (a), 4-F (b), 4-CH_3 (c), 4-Cl (d), 4-Br (e), 3-Cl (f), 4-NO_2 (g), 3-NO_2 (h), 2-NO_2 (i), 4-OH (j)

Reaction scheme

N-(4-bromophenyl)-2-methyl-4-(4-methoxyphenyl) -1,4-dihydro-pyrimido[1,2-*a*] benzimidazo-le-3-carboxamide (4a)

Yield: 70%; m.p. 202 ºC; Anal. Calcd. for $C_{25}H_{21}BrN_4O_2$: C, 61.36; H, 4.33; N, 11.45. Found: C, 61.09; H, 4.08; N, 11.21; FT IR (KBr,cm^{-1}): 3157 (N-H stretching of secondary amine), 3051 (C-H stretching of aromatic ring), 2958 (C-H asymmetrical stretching of CH_3 group), 2899 (C-H asymmetrical stretching of CH_3 group), 1683 (C=O stretching of amide), 1627 (N-H deformation of pyrimidine ring), 1575 and 1510 (C=C stretching of aromatic ring), 1454 (C-H asymmetrical deformation of CH_3 group), 1365 (C-H symmetrical deformation of CH_3 group), 1261 (C-O-C asymmetrical stretching of OCH_3), 1174 (C-N stretching), 1095 (C-H in plane deformation of aromatic ring), 1030 (C-Br stretching), 825 (C-H out of plane bending of 1,4-disubstituion); ^1H-NMR (400 MHz, DMSO-d_6, δ / ppm): 1.75 (3H, *s*, -CH_3), 3.73 (3H, *s*, -OCH_3), 5.96 (1H, *s*, -CH), 6.75-6.80 (3H, *m*, aromatic), 6.82-6.86 (3H, *m*, aromatic) 6.95-6.99 (2H, *s*, aromatic), 7.21-7.23 (3H, *m*, aromatic), 7.27-7.29 (1H, *d*, aromatic, *J* = 7.92 Hz), 7.93 (1H, *s*, -NH), 9.27 (1H, *s*, -NH-CO); MS: *m/z* 488(M^+).

N-(4-bromophenyl)-2-methyl-4-(4-flurophenyl)-1,4-dihydro-pyrimido[1,2-a]benzimidazole-3-carboxamide (4b)

Yield: 68%; m.p. 221 ºC; Anal. Calcd. for $C_{24}H_{18}BrFN_4O$: C, 60.39; H, 3.80; N, 11.74. Found: C, 60.09; H, 3.64; N, 11.58%; FT IR (KBr,cm^{-1}): 3273

(N-H stretching of secondary amine), 3057 (C-H stretching of aromatic ring), 2970 (C-H asymmetrical stretching of CH_3 group), 2895 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1688 (N-H deformation of pyrimidine ring), 1508 and 1467 (C=C stretching of aromatic ring), 1410 (C-H asymmetrical deformation of CH_3 group), 1357 (C-H symmetrical deformation of CH_3 group), 1294 and 1228 (C-N stretching), 1087 (C-H in plane deformation of aromatic ring), 1012 (C-F stretching), 819 (C-H out of plane bending of 1,4-disubstituion); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 1.26 (3H, *s*, -CH_3), 6.59 (1H, *s*, -CH), 6.90-6.99 (6H, *m*, aromatic), 7.03-7.07 (1H, *m*, aromatic), 7.28-7.31 (2H, *m*, aromatic), 7.37-7.39 (1H, *d*, aromatic, *J* = 8.02 *Hz*), 7.48-7.52 (2H, *m*, aromatic), 9.59 (1H, *s*, -NH), 9.72 (1H, *s*, -NH-CO); MS: *m/z* 476 (M^+).

N-(4-bromophenyl) -2-methyl-4-(4-methylphenyl)-1,4-dihydro-pyrimido[1,2-*a*]benzimidazo- le-3-carboxamide (4c)

Yield: 61%; m.p. 212 ºC; ; Anal. Calcd. for $C_{25}H_{21}BrN_4O$: C, 63.43; H, 4.47; N, 11.84. Found: C, 63.25; H, 4.29; N, 11.61; FT IR (KBr,cm^{-1}): 3288 (N-H stretching of secondary amine), 3055 (C-H stretching of aromatic ring), 2978 (C-H asymmetrical stretching of CH_3 group), 2824 (C-H asymmetrical stretching of CH_3 group), 1651 (C=O stretching of amide), 1624 (N-H deformation of pyrimidine ring), 1562 and 1510 (C=C stretching of aromatic ring), 1458 (C-H asymmetrical deformation of CH_3 group), 1280 (C-H symmetrical deformation of CH_3 group), 1228 (C-N stretching), 1076 (C-H in plane deformation of aromatic ring), 833 (C-H out of plane bending of 1,4-disubstituion), 682 (C-Br stretching); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 1.35 (3H, *s*, -CH_3), 2.58 (3H, *s*, Ar-CH_3) 6.57 (1H, *s*, -CH), 6.90-6.99 (4H, *m*, aromatic) 7.06-7.10 (1H, *m*, aromatic), 7.17-7.23 (4H, *m*, aromatic), 7.41-7.43 (1H, *d*, aromatic, *J* = 8.00 *Hz*), 7.48-7.51 (2H, *m*, aromatic), 9.53 (1H, *s*, -NH), 9.69 (1H, *s*, -NHCO);MS: *m/z* 473(M^+).

N-(4-bromophenyl)-2-methyl-4-(4-chlorophenyl)-1,4-dihydropyrimido[1,2-*a*]benzimidazole-3-carboxamide (4d)

Yield: 72%; m.p. 251 ºC; Anal. Calcd. for $C_{24}H_{18}BrClN_4O$: C, 58.38; H, 3.67; N, 11.35. Found: C, 58.12; H, 3.51; N, 11.14; FT IR (KBr,cm^{-1}): 3273 (N-H stretching of secondary amine), 3057 (C-H stretching of aromatic ring), 2970 (C-H asymmetrical stretching of CH_3 group), 2895 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1688 (N-H deformation of pyrimidine ring), 1508 and 1467 (C=C stretching of aromatic ring), 1410 (C-H asymmetrical deformation of CH_3 group), 1357 (C-H symmetrical deformation of CH_3 group), 1294 and 1228 (C-N stretching), 1087 (C-H in plane deformation of aromatic ring), 1012 (C-Cl stretching), 819 (C-H out of plane bending of 1,4-disubstituion); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 1.26 (3H, *s*,-CH_3), 6.59 (1H, *s*, -CH), 6.90-6.99 (6H, *m*, aromatic), 7.03-7.07 (1H, *m*, aromatic), 7.28-7.31 (2H, *m*, aromatic), 7.37-7.39 (1H, *d*, aromatic, *J* = 8.00 *Hz*), 7.48-7.52 (2H, *m*, aromatic), 9.59 (1H, *s*, -NH), 9.72 (1H, *s*, -NHCO); MS: *m/z* 493(M^+).

N-(4-bromophenyl)-2-methyl-4-(4-bromophenyl)-1,4-dihydropyrimido [1,2-*a*] benzimidazole -3-carboxamide (4e)

Yield: 64%; m.p. 218 ºC; Anal. Calcd. for $C_{24}H_{18}Br_2N_4O$: C, 53.56; H, 3.37; N, 10.41. Found: C, 53.21; H, 3.12; N, 10.11; FT IR (KBr,cm^{-1}): 3273 (N-H stretching of secondary amine), 3057 (C-H stretching of aromatic ring), 2970 (C-H asymmetrical stretching of CH_3 group), 2895 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1688 (N-H deformation of pyrimidine ring), 1508 and 1467 (C=C stretching of aromatic ring), 1410 (C-H asymmetrical deformation of CH_3 group), 1357 (C-H symmetrical deformation of CH_3 group), 1294 and 1228 (C-N stretching), 1087 (C-H in plane deformation of aromatic ring), 1012 (C-Br stretching), 825 (C-H out of plane bending of 1,4-disubstituion); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 1.26 (3H, *s*, -CH_3), 6.59 (1H, *s*, -CH), 6.90-6.99 (6H, *m*, aromatic) 7.03-7.07 (1H, *m*, aromatic), 7.28-7.31 (2H, *m*, aromatic), 7.37-7.39 (1H, *d*, aromatic, *J* = 7.92 *Hz*), 7.48-7.52 (2H, *m*, aromatic), 9.59 (1H, s, -NH), 9.72 (1H, s, -NHCO); MS: *m/z* 538(M^+).

N-(4-bromophenyl)-2-methyl-4-(3-chlorophenyl)-1,4-dihydropyrimido[1,2-*a*]benzimidazole-3-carboxamide (4f)

Yield: 72%; m.p. 211 ºC; Anal. Calcd. for

$C_{24}H_{18}BrClN_4O$: C, 58.38; H, 3.67; N, 11.35. Found: C, 58.23; H, 3.60; N, 11.12; FT IR (KBr,cm^{-1}): 3273 (N-H stretching of secondary amine), 3057 (C-H stretching of aromatic ring), 2970 (C-H asymmetrical stretching of CH_3 group), 2895 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1688 (N-H deformation of pyrimidine ring), 1508 and 1467 (C=C stretching of aromatic ring), 1410 (C-H asymmetrical deformation of CH_3 group), 1357 (C-H symmetrical deformation of CH_3 group), 1294 and 1228 (C-N stretching), 1087 (C-H in plane deformation of aromatic ring), 1048 (C-Cl stretching), 712 (C-H out of plane bending of 1,4-disubstituion); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 1.26 (3H, *s*, -CH_3), 6.59 (1H, *s*, -CH), 6.90-6.99 (6H, *m*, aromatic), 7.03-7.07 (1H, *m*, aromatic), 7.28-7.31 (2H, *m*, aromatic), 7.37-7.39 (1H, *d*, aromatic, *J* = 7.90 *Hz*), 7.48-7.52 (2H, *m*, aromatic), 9.59 (1H, *s*, -NH), 9.72 (1H, *s*, -NHCO); MS: *m/z* 493(M^+).

N-(4-bromophenyl)-2-methyl-4-(4-nitrophenyl)-1,4-dihydropyrimido[1,2-*a*]benzimidazole-3-carboxamide (4g)

Yield: 71%; m.p. 242 ºC; Anal. Calcd. for $C_{24}H_{18}BrN_5O_3$: C, 57.16; H, 3.60; N, 13.89. Found: C, 57.01; H, 3.39; N, 13.63; FT IR (KBr,cm^{-1}): 3273 (N-H stretching of secondary amine), 3057 (C-H stretching of aromatic ring), 2970 (C-H asymmetrical stretching of CH_3 group), 2895 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1688 (N-H deformation of pyrimidine ring), 1508 and 1467 (C=C stretching of aromatic ring), 1410 (C-H asymmetrical deformation of CH_3 group), 1357 (C-H symmetrical deformation of CH_3 group), 1294 and 1228 (C-N stretching), 1087 (C-H in plane deformation of aromatic ring), 1012 (C-F stretching), 819 (C-H out of plane bending of 1,4-disubstituion); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 1.26 (3H, *s*, -CH_3), 6.59 (1H, *s*, -CH), 6.90-6.99 (6H, *m*, aromatic), 7.03-7.07 (1H, *m*, aromatic), 7.28-7.31 (2H, *m*, aromatic), 7.37-7.39 (1H, *d*, aromatic, *J* = 8.00 *Hz*), 7.48-7.52 (2H, *m*, aromatic), 9.59 (1H, *s*, -NH), 9.72 (1H, *s*, -NHCO); MS: *m/z* 504(M^+).

N-(4-bromophenyl)-2-methyl-4-(3-nitrophenyl)-1,4-dihydropyrimido[1,2-*a*]benzimidazole-3-carboxamide (4h)

Yield: 72%; m.p. 207 ºC; Anal. Calcd. for $C_{24}H_{18}BrN_5O_3$: C, 57.16; H, 3.60; N, 13.89. Found: C, 57.06; H, 3.43; N, 13.67; FT IR (KBr,cm^{-1}): 3273 (N-H stretching of secondary amine), 3057 (C-H stretching of aromatic ring), 2970 (C-H asymmetrical stretching of CH_3 group), 2895 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1688 (N-H deformation of pyrimidine ring), 1508 and 1467 (C=C stretching of aromatic ring), 1410 (C-H asymmetrical deformation of CH_3 group), 1357 (C-H symmetrical deformation of CH_3 group), 1294 and 1228 (C-N stretching), 1087 (C-H in plane deformation of aromatic ring), 1012 (C-F stretching), 819 (C-H out of plane bending of 1,4-disubstituion); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 1.26 (3H, *s*, -CH_3), 6.59 (1H, *s*, -CH), 6.90-6.99 (6H, *m*, aromatic), 7.03-7.07 (1H, *m*, aromatic), 7.28-7.31 (2H, *m*, aromatic), 7.37-7.39 (1H, *d*, aromatic, *J* = 8.00 *Hz*), 7.48-7.52 (2H, *m*, aromatic), 9.59 (1H, *s*, -NH), 9.72 (1H, *s*, -NHCO); MS: *m/z* 504(M^+).

N-(4-bromophenyl)-2-methyl-4-(2-nitrophenyl)-1,4-dihydropyrimido[1,2-*a*]benzimidazole-3-carboxamide (4i)

Yield: 72%; m.p. 227 ºC; Anal. Calcd. for $C_{24}H_{18}BrN_5O_3$: C, 57.16; H, 3.60; N, 13.89. Found: C, 57.02; H, 3.41; N, 13.70; FT IR (KBr,cm^{-1}): 3273 (N-H stretching of secondary amine), 3057 (C-H stretching of aromatic ring), 2970 (C-H asymmetrical stretching of CH_3 group), 2895 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1688 (N-H deformation of pyrimidine ring), 1508 and 1467 (C=C stretching of aromatic ring), 1410 (C-H asymmetrical deformation of CH_3 group), 1357 (C-H symmetrical deformation of CH_3 group), 1294 and 1228 (C-N stretching), 1087 (C-H in plane deformation of aromatic ring), 1012 (C-F stretching), 819 (C-H out of plane bending of 1,4-disubstituion); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 1.26 (3H, *s*, -CH_3), 6.59 (1H, *s*, -CH), 6.90-6.99 (6H, *m*, aromatic), 7.03-7.07 (1H, *m*, aromatic), 7.28-7.31 (2H, *m*, aromatic), 7.37-7.39 (1H, *d*, aromatic, *J* = 7.92 *Hz*), 7.48-7.52 (2H, *m*, aromatic), 9.59 (1H, *s*, -NH), 9.72 (1H, *s*, -NHCO); MS: *m/z* 504(M^+).

N-(4-bromophenyl)-2-methyl-4-(4-hydroxyphenyl) -1,4-dihydropyrimido[1,2-*a*]benzimidazo- le-3-

carboxamide (4j)

Yield: 66%; m.p. 210 ºC; Anal. Calcd. for $C_{24}H_{19}BrN_4O_2$: C, 60.64; H, 4.03; N, 11.79. Found: C, 60.44; H, 3.93; N, 11.59; FT IR (KBr,cm^{-1}): 3599 (Free -OH), 3273 (N-H stretching of secondary amine), 3057 (C-H stretching of aromatic ring), 2970 (C-H asymmetrical stretching of CH_3 group), 2895 (C-H asymmetrical stretching of CH_3 group), 1637 (C=O stretching of amide), 1688 (N-H deformation of pyrimidine ring), 1508 and 1467 (C=C stretching of aromatic ring), 1410 (C-H asymmetrical deformation of CH_3 group), 1357 (C-H symmetrical deformation of CH_3 group), 1294 and 1228 (C-N stretching), 1087 (C-H in plane deformation of aromatic ring), 1012 (C-F stretching), 819 (C-H out of plane bending of 1,4-disubstituion); ^{1}H-NMR (400 MHz, DMSO-d_6, δ / ppm): 1.26 (3H, *s*, -CH_3), 5.40 (1H, *s*, -OH) 6.59 (1H, *s*, -CH), 6.90-6.99 (6H, *m*, aromatic), 7.03-7.07 (1H, *m*, aromatic), 7.28-7.31 (2H, *m*, aromatic), 7.37-7.39 (1H, *d*, aromatic, *J* = 7.92 *Hz*), 7.48-7.52 (2H, *m*, aromatic), 9.59 (1H, *s*, -NH), 9.72 (1H, *s*, -NHCO); MS: *m/z* 475(M^+).

Pharmacological screening

The isolated compound (1) was tested for its antibacterial and antifungal activity (MIC) *in vitro* by broth dilution method[14-16] 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 ampicillin, chloramphenicol, ciprofloxacin, norfloxacin, nystatin, and griseofulvin as standard drugs. In primary screening 1000 µg/mL, 500 µg/mL and 250 µg/mL concentrations of the synthesized drugs were taken. The active synthesized drugs found in this primary screening were further tested in a second set of dilution against all microorganisms. The drugs found active in primary screening were similarly diluted to obtain 200 µg/mL, 100 µg/mL, 50 µg/mL, 25 µg/mL, 12.5 µg/mL, and 6.250 µg/mL concentrations. The highest dilution showing at least 99 % inhibition zone is taken as MIC. The result of this is much affected by the size of the inoculums. The test mixture should contain $10^{[8]}$ organism/mL.

TABLE 1 : In vitro antimicrobial screening results for 4a-j.

Code	Minimal inhibition concentration (µg mL^{-1})						
	Gram-positive		Gram-negative		Fungal species		
	S. aureus	S. pyogenes	E.coli	P. aerugi-nosa	C. albicans	A. niger	A. clavatus
4a	200	500	150	200	1000	250	500
4b	250	500	100	200	1000	500	500
4c	500	1000	250	500	1000	1000	>1000
4d	500	500	250	200	1000	>1000	>1000
4e	200	250	200	200	1000	>1000	>1000
4f	1000	250	500	150	1000	500	500
4g	150	500	100	150	500	>1000	>1000
4h	1000	250	100	500	>1000	>1000	>1000
4i	200	62.5	62.5	500	>1000	>1000	>1000
4j	500	500	1000	1000	500	500	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

RESULTS AND DISCUSSION

Pyrimido[1,2-*a*]benzimidazoles (4a-j) was synthesized by the Biginelli like cyclo condensation of aromatic aldehydes (2a-j) and acetoacetic acid derivatives (1) with 2-amino benzimidazole (3) containing a guanidine fragment. For 1,4-dihydropyrimido[1,2-*a*]benzimidazoles (4a-j), confirmatory bands for secondary amine and amidic carbonyl groups were observed at 3414-3282 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 aromatic ring protons and *J* value were found to be in accordance with substitution pattern on phenyl ring. Further, mass spectrum shows M^+ according to the structures, which suggested

formation of desired products (4a-j). The newly synthesized compounds were subjected to antimicrobial activity. The results obtained are depicted in TABLE 1.

CONCLUSION

In connection with our ongoing work on multi-component domino synthesis and in view of our interest in the convenient and rapid one-pot three-component preparation of pyrimido[1,2-*a*]benzimidazoles (4a-j) derivatives. We have demonstrated a simple route for the synthesis of the present methodology offers very attractive features such as short reaction time, mild reaction condition, good to excellent product yields, minimum environmental effects. This protocol is general and provides pyrimido[1,2-*a*]benzimidazoles in good to excellent yields depending on the reactivity of arylaldehydes. The newly synthesized compounds 4a-j exhibited good antimicrobacterial and antibacterial activities.

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