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RESEARCH ARTICLE

Diversity Oriented Synthesis and Bio-evaluation of [1,2,4]triazolo[1,5-*a*]pyrimidine

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ABSTRACT

A simple, efficient, and diversity oriented synthesis and structural characterization of [1,2,4]triazolo[1,5-*a*]pyrimidine derivatives was undertaken using 5-amino,1,2,4-triazole as a building block. The synthesized compounds were fully characterized by spectroscopic techniques like FT-IR, ^{1}H NMR, ^{13}C NMR, and mass spectroscopy. The biological evaluations of all synthesized compounds were also carried out.

KEYWORDS

[1,2,4] triazolo [1,5-*a*] pyrimidine, 5-amino,1,2,4-triazole, Diversity Oriented Synthesis, Spectroscopic Techniques

INTRODUCTION

From the standpoint of biological activity, fused heteroaromatic systems are often of much greater interest than the constituent monocyclic compounds. Recently, 1,2,4-triazolo[1,5-*a*]pyrimidines have aroused increasing attention from the chemical and biological view points, due to their diverse pharmacological activities, such as antitumor potency[1-2], inhibition of KDR kinase[3], antifungal effect[4] and macrophage activation[5]. They have proved to be promising anticancer agents with dual mechanisms of tubulin polymerization promotion[6-7] as well as cyclin dependent kinases 2 inhibition[8].

Furthermore, the chemistry of 1,2,4-triazolo[1,5-*a*]pyrimidines derivatives have received great attention due to their structural similarity with purines and hence several 1,2,4-triazolo[1,5-*a*]pyrimidines derivatives exhibited promising anticancer activity[9-14].

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Different mechanisms account for the cytotoxic effect of this class of compounds, where they had been reported to act as glycogen synthase kinase (GSK) inhibitors[15], cyclin dependent kinase (CDK) inhibitors[16], dual src/ Ab1kinase inhibitors[17] and epidermal growth factor receptor (EGFR) inhibitors[18]. Some examples of published derivatives of 1,2,4-triazolo[1,5-*a*]pyrimidine are depicted in figure 1.

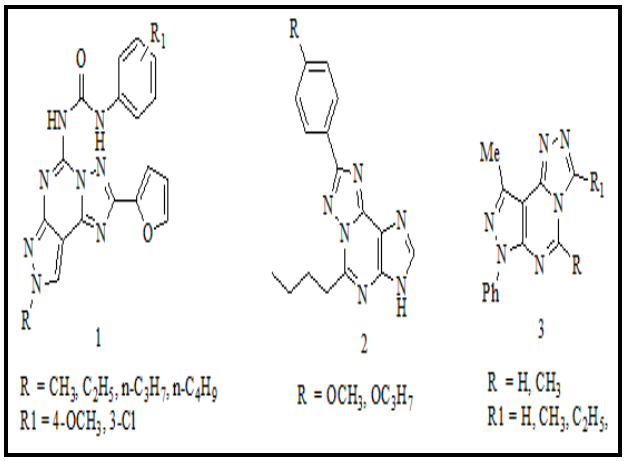


Figure 1: Reported ring systems of triazolopyrimidines

The application of fusion method in organic synthesis for conducting chemical reactions at highly accelerated rates is an emerging technique which is practiced widely due to their ability to curtail reaction time, the number of steps, energy consumption, waste production, and to maximize synthetic effectiveness and environmental benignity.[19] Thus in view of synthesizing novel [1,2,4]triazolo[1,5-*a*]pyrimidines diversely functionalized with various substituents, we set upon a synthetic program involving 5-amino,1,2,4-triazole and 1,3-dicarbonyl compound as the building blocks. Synthesis of twenty novel analogues of [1,2,4]triazolo[1,5-*a*]pyrimidine containing an appropriate 1-(thiophen-2-yl)butane-1,3-dione as 1,3-bifunctional synthon has been undertaken. The structures of all the newly synthesized compounds were elucidated by FT-IR, mass spectra, ^{1}H NMR, ^{13}C NMR and elemental analysis. The antimicrobial activities of the newly synthesized compounds against gram-positive and gram-negative bacteria were studied.

EXPERIMENTAL

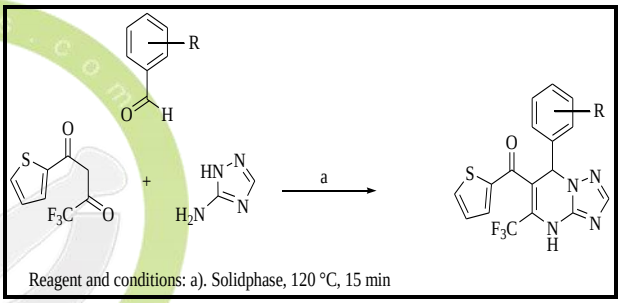
All research chemicals were purchased from Sigma–Aldrich and used as such for the reactions. Reactions were monitored by thin-layer chromatography (TLC) on pre-coated silica gel GF254 plates from E-Merck Co and compounds visualized either by exposure to UV. Melting points were determined in open capillaries and are uncorrected. The IR spectra were recorded on SHIMADZU- FTIR-8400 spectrophotometer using KBr pellet method. ^{1}H spectra were recorded on Bruker 400-MHz NMR spectrometer in $CDCl_3$ with TMS as internal standard. Mass spectrum was recorded on JOEL SX 102/DA-600-Mass spectrometer and elemental analysis was carried out using Heraus C,H,N rapid analyzer.

Synthesis of 1-(thiophen-2-yl) butane-1,3-dione [1]

1-(thiophen-2-yl) butane-1,3-dione was prepared by known literature method.[20]

General Procedure for the Synthesis of (5-(trifluoromethyl)-4,7-dihydro-7-aryl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone LK-21 to LK-40

A mixture of the aminoazole 1 (0.01 mol), 1-(thiophen-2-yl)butane-1,3-dione (0.01 mol) and an appropriate aromatic aldehyde 3 (0.01 mol) was fused at 120 °C for 15 min. Solid was converted in liquids and again after completion of reaction gives solid. The reaction mixture was allowed to stand cool at room temperature and acetone was added and put it for overnight. The solid was filtered it to affords the solid triazolopyrimidine products **LK-21 to 40**, which were washed with methanol and dried in air. Triazolopyrimidines were obtained in high purity and did not require further purification by recrystallization or column chromatography.



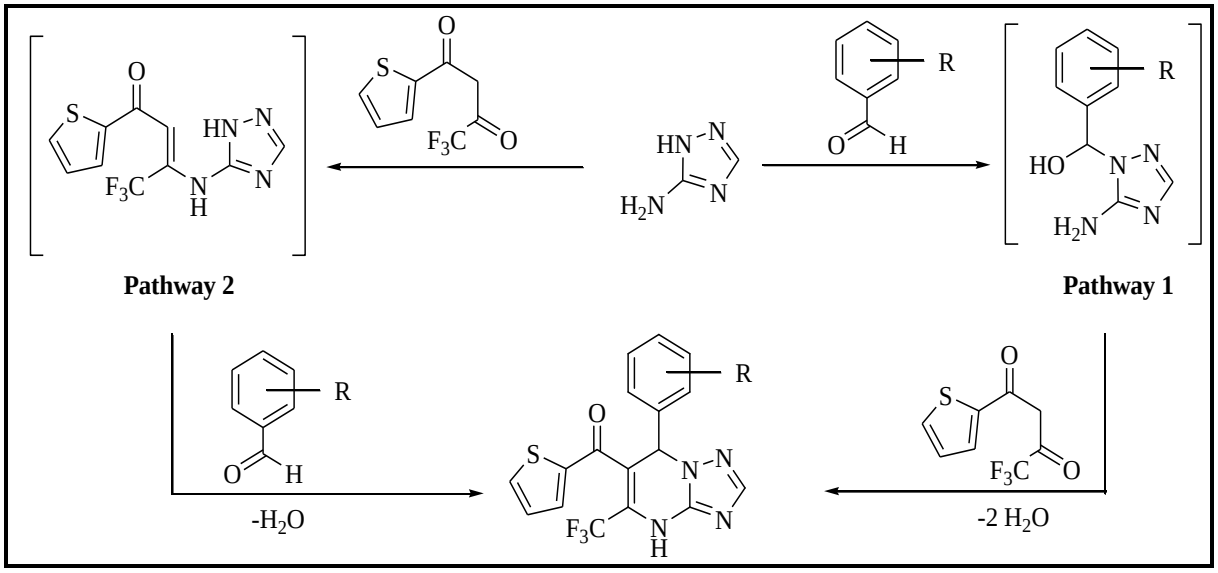
Scheme 1 Synthesis of (5-(trifluoromethyl)-4,7-dihydro-7-aryl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone

The reaction mechanism of this three-component condensation is probably similar to the described[21] mechanism for the "classical" Biginelli reaction (Pathway 1). The first step is a nucleophilic addition of N_2 of the aminoazole to a carbonyl carbon of aldehyde, followed by subsequent cyclization with respective 1,3-carbonyl compound to form the dihydropyrimidine ring. An alternate sequence is also possible and cannot be excluded[22] (Pathway 2), which is the initial formation of an enamine by reaction of aminoazole with respective 1,3-carbonyl followed by cyclocondensation. The third alternative involving the formation of arylidene derivatives as intermediates requires the presence of a strong base[23] and is most likely not possible for the case described herein.

Table 1: Physical parameters of substituted - [1,2,4]triazolo[1,5-a]pyrimidin derivatives

Code	R	M.F.	M.W.	M.P. °C	Yield %	R_f
LK-21	H	$C_{17}H_{11}F_3N_4OS$	376	208-210	63	0.55
LK-22	4-CH_3	$C_{18}H_{13}F_3N_4OS$	390	243-245	69	0.51
LK-23	4-OCH_3	$C_{18}H_{13}F_3N_4O_2S$	406	253-255	72	0.61
LK-24	2,5-OCH_3	$C_{19}H_{15}F_3N_4O_3S$	436	237-239	78	0.57
LK-25	3,4-OCH_3	$C_{19}H_{15}F_3N_4O_3S$	436	261-263	88	0.48
LK-26	3,4,5-OCH_3	$C_{20}H_{17}F_3N_4O_4S$	466	265-267	79	0.60
LK-27	4-Cl	$C_{17}H_{10}ClF_3N_4OS$	410	223-225	85	0.52
LK-28	3-Cl	$C_{17}H_{10}ClF_3N_4OS$	410	270-272	81	0.62
LK-29	2-Cl	$C_{17}H_{10}ClF_3N_4OS$	410	261-263	80	0.50
LK-30	2,4-Cl	$C_{19}H_9Cl_2F_3N_4OS$	445	256-258	76	0.56
LK-31	2,6-Cl	$C_{19}H_9Cl_2F_3N_4OS$	445	192-194	71	0.49
LK-32	4-Br	$C_{17}H_{10}BrF_3N_4OS$	455	198-200	79	0.47
LK-33	3-Br	$C_{17}H_{10}BrF_3N_4OS$	455	188-190	70	0.52
LK-34	2-Br	$C_{17}H_{10}BrF_3N_4OS$	455	118-120	74	0.50
LK-35	4-F	$C_{17}H_{10}F_4N_4OS$	394	194-196	73	0.58
LK-36	4-OH	$C_{17}H_{11}F_3N_4O_2S$	392	108-110	84	0.61
LK-37	2-OH	$C_{17}H_{11}F_3N_4O_2S$	392	261-263	80	0.56
LK-38	4-NO_2	$C_{17}H_{10}F_3N_5O_3S$	421	242-244	79	0.49
LK-39	3-NO_2	$C_{17}H_{10}F_3N_5O_3S$	421	250-252	82	0.53
LK-40	2-NO_2	$C_{17}H_{10}F_3N_5O_3S$	421	131-133	80	0.59

TLC Solvent system R_{f1}: Chloroform: Methanol - 9:1.



Scheme 2: Plausible mechanism for the formation of substituted pyranopyrazoles using base as a catalyst

(5-(trifluoromethyl)-4,7-dihydro-7-phenyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-21)

Yield: 63%; mp: 208-210 ºC; IR (cm^{-1}): 3350 (N-H stretching of secondary amine), 3090 (C-H stretching of aromatic ring), 1692 (C=N stretching), 1601 (N-H deformation of pyrimidine ring), 1507, 1478 and 1409 (C=C stretching of aromatic ring), 1351 (C-N stretching), 1218 (C-F stretching), 890 (C-S stretching), 752 (C-H out of plane bending of monosubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 6.24 (s, 1H, CH (Chiral)), 6.64-6.62 (m, 3H, Ar-H), 7.16-7.21 (t, 1H, Ar-H (Thiophene)), 7.38-7.42 (d, 2H, Ar-H), 7.71-7.73 (dd, 1H, Ar-H (Thiophene)), 7.78-7.81 (dd, 1H, Ar-H (Thiophene)), 8.31 (s, 1H, Ar-H (Triazole)), 10.20 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 54.38, 102.28, 111.57, 123.38, 127.11, 135.15, 149.57, 153.17, 156.68, 172.37; MS: m/z 376; Anal. Calcd. for $C_{17}H_{11}F_3N_4OS$: C, 54.25; H, 2.95; F, 15.14; N, 14.89. Found: C, 54.27; H, 2.94; F, 15.11; N, 14.92%.

(5-(trifluoromethyl)-4,7-dihydro-7-p-tolyl-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-22)

Yield: 69%; mp: 243-245 ºC; IR (cm^{-1}): 3213 (N-H stretching of secondary amine), 3080 (C-H stretching of aromatic ring), 2949 (C-H asymmetrical stretching of CH_3 group), 1689 (C=N stretching), 1602 (N-H deformation of pyrimidine ring), 1560, 1491 and 1448 (C=C stretching of aromatic ring), 1384 (C-H asymmetrical deformation of CH_3 group), 1238 (C-N stretching), 1210 (C-F stretching), 885 (C-S stretching), 819 (C-H out of plane bending of p-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 1.44 (s, 3H, CH_3), 6.20 (s, 1H, CH (Chiral)), 7.12-7.16 (t, 1H, Ar-H (Thiophene)), 7.24-7.26 (d, 2H, Ar-H), 7.32-7.36 (d, 2H, Ar-H), 7.58-7.61 (dd, 1H, Ar-H (Thiophene)), 7.70-7.75 (dd, 1H, Ar-H (Thiophene)), 8.30 (s, 1H, Ar-H (Triazole)), 10.21 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 22.47, 54.10, 103.78, 111.45, 121.45, 126.98, 127.24, 128.42, 134.76, 150.10, 155.05, 157.02, 179.11; MS: m/z 384; Anal. Calcd. for $C_{18}H_{13}F_3N_4OS$: C, 55.38; H, 3.36; N, 14.35. Found: C, 55.40; H, 3.35; N, 14.35%.

(5-(trifluoromethyl)-4,7-dihydro-7-(4-methoxyphenyl)-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-23)

Yield: 72%; mp: 253-255 ºC; IR (cm^{-1}): 3176 (N-H stretching of secondary amine), 3095 (C-H stretching of aromatic ring), 2974 (C-H asymmetrical stretching of CH_3 group), 2922 (C-H asymmetrical stretching of CH_3 group), 1693 (C=N stretching), 1606 (N-H deformation of pyrimidine ring), 1506, 1471 and 1400 (C=C stretching of aromatic ring), 1352 (C-H asymmetrical deformation of CH_3 group), 1307 (C-H symmetrical deformation of CH_3 group), 1255 (C-N stretching), 1221 (C-F stretching), 897 (C-S stretching), 810 (C-H out of plane bending of p-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 3.12 (s, 3H, CH_3), 6.15 (s, 1H, CH (Chiral)), 7.10-7.14 (t, 1H, Ar-H (Thiophene)), 7.20-7.23 (d, 2H, Ar-H), 7.30-7.33 (d, 2H, Ar-H), 7.71-7.74 (dd, 1H, Ar-H (Thiophene)), 7.67-7.71 (dd, 1H, Ar-H (Thiophene)), 8.32 (s, 1H, Ar-H (Triazole)), 10.19 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 32.74, 54.10, 103.45, 112.14, 121.62, 126.78, 128.42, 129.17, 134.87, 150.18, 155.11, 158.06, 170.72; MS: m/z 406; Anal. Calcd. for $C_{18}H_{13}F_3N_4O_2S$: C, 53.20; H, 3.22; N, 13.79. Found: C, 53.21; H, 3.22; N, 13.77%.

(5-(trifluoromethyl)-4,7-dihydro-7-(2,5-dimethoxyphenyl)-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-24)

Yield: 78%; mp: 237-239 ºC; 3215 (N-H stretching of secondary amine), 3085 (C-H stretching of aromatic ring), 2942 (C-H asymmetrical stretching of CH_3 group), 2912 (C-H asymmetrical stretching of CH_3 group), 1678 (C=N stretching), 1615 (N-H deformation of pyrimidine ring), 1512, 1454 and 1410 (C=C stretching of aromatic ring), 1378 (C-H asymmetrical deformation of CH_3 group), 1314 (C-H symmetrical deformation of CH_3 group), 1242 (C-N stretching), 1230 (C-F stretching), 887 (C-S stretching); ^{1}H NMR (DMSO-d_6) δ

ppm: 3.32 (s, 3H, OCH_3), 3.39 (s, 3H, OCH_3), 6.21 (s, 1H, CH (Chiral)), 6.86-6.90 (m, 2H, Ar-H), 7.13-7.16 (t, 1H, Ar-H (Thiophene)), 7.34-7.36 (s, 1H, Ar-H), 7.62-7.65 (dd, 1H, Ar-H (Thiophene)), 7.81-7.84 (dd, 1H, Ar-H (Thiophene)), 8.15 (s, 1H, Ar-H (Triazole)), 10.01 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 28.55, 31.70, 53.15, 104.30, 111.69, 120.52, 126.72, 126.97, 128.78, 134.91, 150.17, 154.86, 157.10, 170.78; MS: m/z 436; Anal. Calcd. for $C_{19}H_{15}F_3N_4O_3S$: C, 52.29; H, 3.46; N, 12.84. Found: C, 52.32; H, 3.44; N, 12.85%.

(5-(trifluoromethyl)-4,7-dihydro-7-(3,4-dimethoxyphenyl)-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-25)

Yield: 88%; mp: 261-263 ºC; IR (cm^{-1}): 3180 (N-H stretching of secondary amine), 3105 (C-H stretching of aromatic ring), 2978 (C-H asymmetrical stretching of CH_3 group), 2910 (C-H asymmetrical stretching of CH_3 group), 1684 (C=N stretching), 1612 (N-H deformation of pyrimidine ring), 1521, 1445 and 1417 (C=C stretching of aromatic ring), 1345 (C-H asymmetrical deformation of CH_3 group), 1324 (C-H symmetrical deformation of CH_3 group), 1258 (C-N stretching), 1232 (C-F stretching), 891 (C-S stretching); ^{1}H NMR (DMSO-d_6) δ ppm: 3.27 (s, 3H, OCH_3), 3.31 (s, 3H, OCH_3), 6.17 (s, 1H, CH (Chiral)), 6.77-6.81 (d, 1H, Ar-H), 7.13-7.16 (t, 1H, Ar-H (Thiophene)), 7.30-7.34 (dd, 1H, Ar-H), 7.56 (s, 1H, Ar-H), 7.67-7.71 (dd, 1H, Ar-H (Thiophene)), 7.81-7.84 (dd, 1H, Ar-H (Thiophene)), 8.29 (s, 1H, Ar-H (Triazole)), 10.13 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 30.64, 31.77, 54.37, 103.77, 111.41, 120.76, 126.97, 127.45, 129.11, 134.73, 149.54, 154.75, 157.10, 171.11; MS: m/z 436; Anal. Calcd. for $C_{19}H_{15}F_3N_4O_3S$: C, 52.29; H, 3.46; N, 12.84. Found: C, 52.30; H, 3.45; N, 12.84%.

(5-(trifluoromethyl)-4,7-dihydro-7-(3,4,5-trimethoxyphenyl)-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-26)

Yield: 79%; mp: 265-267 ºC; IR (cm^{-1}): 3145 (N-H stretching of secondary amine), 3078 (C-H stretching of aromatic ring), 2965 (C-H asymmetrical stretching of CH_3 group), 2931 (C-H asymmetrical stretching of CH_3 group), 1687 (C=N stretching), 1619 (N-H deformation of pyrimidine ring), 1515, 1473 and 1423 (C=C stretching of aromatic ring), 1342 (C-H asymmetrical deformation of CH_3 group), 1323 (C-H symmetrical deformation of CH_3 group), 1265 (C-N stretching), 1209 (C-F stretching), 896 (C-S stretching); ^{1}H NMR (DMSO-d_6) δ ppm: 3.22 (s, 9H, OCH_3), 6.19 (s, 1H, CH (Chiral)), 7.13-7.16 (t, 1H, Ar-H (Thiophene)), 7.30 (s, 2H, Ar-H), 7.67-7.71 (dd, 1H, Ar-H (Thiophene)), 7.81-7.84 (dd, 1H, Ar-H (Thiophene)), 8.29 (s, 1H, Ar-H (Triazole)), 10.13 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 33.54, 54.15, 56.84, 57.01, 103.74, 111.45, 114.12, 118.52, 120.61, 126.74, 134.54, 149.49, 154.45, 157.10, 171.78; MS: m/z 466; Anal. Calcd. for $C_{20}H_{17}F_3N_4O_4S$: C, 51.50; H, 3.67; N, 12.01. Found: C, 51.51; H, 3.65; N, 12.04%.

(7-(4-chlorophenyl)-5-(trifluoromethyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-27)

Yield: 85%; mp: 223-225 ºC; IR (cm^{-1}): 3156 (N-H stretching of secondary amine), 3086 (C-H stretching of aromatic ring), 2970 (C-H asymmetrical stretching of CH_3 group), 2921 (C-H asymmetrical stretching of CH_3 group), 1686 (C=N stretching), 1602 (N-H deformation of pyrimidine ring), 1508, 1468 and 1405 (C=C stretching of aromatic ring), 1349 (C-H asymmetrical deformation of CH_3 group), 1303 (C-H symmetrical deformation of CH_3 group), 1252 (C-N stretching), 1230 (C-F stretching), 899 (C-S stretching), 821 (C-H out of plane bending of p-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 6.17 (s, 1H, CH (Chiral)), 7.12-7.15 (t, 1H, Ar-H (Thiophene)), 7.22-7.26 (d, 2H, Ar-H), 7.32-7.36 (d, 2H, Ar-H), 7.71-7.74 (dd, 1H, Ar-H (Thiophene)), 7.54-7.58 (dd, 1H, Ar-H (Thiophene)), 8.30 (s, 1H, Ar-H (Triazole)), 10.10 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 54.47, 103.74, 111.12, 121.37, 125.58, 126.27, 128.78, 134.24, 149.10, 154.08, 157.74, 169.74; MS: m/z 410; Anal.

Calcd. for $C_{17}H_{10}ClF_3N_4OS$: C, 49.70; H, 2.45; N, 13.64. Found: C, 49.70; H, 2.46; N, 13.61%.

(7-(3-chlorophenyl)-5-(trifluoromethyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-28)

Yield: 81%; mp: 270-272 ºC; IR (cm^{-1}): 3172 (N-H stretching of secondary amine), 3092 (C-H stretching of aromatic ring), 2975 (C-H asymmetrical stretching of CH_3 group), 2920 (C-H asymmetrical stretching of CH_3 group), 1689 (C=N stretching), 1602 (N-H deformation of pyrimidine ring), 1505, 1468 and 1402 (C=C stretching of aromatic ring), 1353 (C-H asymmetrical deformation of CH_3 group), 1304 (C-H symmetrical deformation of CH_3 group), 1252 (C-N stretching), 1220 (C-F stretching), 885 (C-S stretching), 782 (C-H out of plane bending of m-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 6.04 (s, 1H, CH (Chiral)), 6.20-6.22 (d, 1H, Ar-H), 6.57-6.60 (m, 2H, Ar-H), 7.09-7.12 (t, 1H, Ar-H (Thiophene)), 7.20-7.23 (s, 1H, Ar-H), 7.70-7.73 (dd, 1H, Ar-H (Thiophene)), 7.67-7.71 (dd, 1H, Ar-H (Thiophene)), 8.41 (s, 1H, Ar-H (Triazole)), 10.02 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 54.12, 104.11, 112.75, 120.02, 126.75, 128.47, 129.51, 134.79, 149.54, 154.21, 158.12, 171.04; MS: m/z 410; Anal. Calcd. for $C_{17}H_{10}ClF_3N_4OS$: C, 49.70; H, 2.45; N, 13.64. Found: C, 49.70; H, 2.46; N, 13.61%.

(7-(2-chlorophenyl)-5-(trifluoromethyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-29)

Yield: 80%; mp: 261-263 ºC; IR (cm^{-1}): 3172 (N-H stretching of secondary amine), 3091 (C-H stretching of aromatic ring), 2973 (C-H asymmetrical stretching of CH_3 group), 2925 (C-H asymmetrical stretching of CH_3 group), 1690 (C=N stretching), 1600 (N-H deformation of pyrimidine ring), 1505, 1473 and 1406 (C=C stretching of aromatic ring), 1353 (C-H asymmetrical deformation of CH_3 group), 1305 (C-H symmetrical deformation of CH_3 group), 1258 (C-N stretching), 1215 (C-F stretching), 887 (C-S stretching), 752 (C-H out of plane bending of o-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 6.13 (s, 1H, CH (Chiral)), 6.77-6.82 (m, 4H, Ar-H), 7.09-7.12 (t, 1H, Ar-H (Thiophene)), 7.56-7.59 (dd, 1H, Ar-H (Thiophene)), 7.67-7.71 (dd, 1H, Ar-H (Thiophene)), 8.40 (s, 1H, Ar-H (Triazole)), 10.17 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 54.42, 103.72, 111.93, 121.24, 125.17, 126.73, 127.11, 135.14, 149.15, 154.41, 157.10, 171.45; MS: m/z 410; Anal. Calcd. for $C_{17}H_{10}ClF_3N_4OS$: C, 49.70; H, 2.45; N, 13.64. Found: C, 49.70; H, 2.46; N, 13.61%.

(7-(2,4-dichlorophenyl)-5-(trifluoromethyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-30)

Yield: 76%; mp: 256-258 ºC; IR (cm^{-1}): 3172 (N-H stretching of secondary amine), 3093 (C-H stretching of aromatic ring), 2975 (C-H asymmetrical stretching of CH_3 group), 2920 (C-H asymmetrical stretching of CH_3 group), 1694 (C=N stretching), 1600 (N-H deformation of pyrimidine ring), 1502, 1473 and 1403 (C=C stretching of aromatic ring), 1353 (C-H asymmetrical deformation of CH_3 group), 1306 (C-H symmetrical deformation of CH_3 group), 1252 (C-N stretching), 1218 (C-F stretching), 890 (C-S stretching); ^{1}H NMR (DMSO-d_6) δ ppm: 6.10 (s, 1H, CH (Chiral)), 6.37-6.41 (m, 2H, Ar-H), 6.68 (s, 1H, Ar-H), 7.10-7.13 (t, 1H, Ar-H (Thiophene)), 7.57-7.61 (dd, 1H, Ar-H (Thiophene)), 7.72-7.75 (dd, 1H, Ar-H (Thiophene)), 8.50 (s, 1H, Ar-H (Triazole)), 9.93 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 54.12, 103.75, 111.56, 119.87, 126.82, 134.91, 150.15, 153.86, 158.17, 170.42; MS: m/z 445; Anal. Calcd. for $C_{17}H_9Cl_2F_3N_4OS$: C, 45.86; H, 2.04; N, 12.58. Found: C, 45.85; H, 2.03; N, 12.59%.

(7-(2,6-dichlorophenyl)-5-(trifluoromethyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-31)

Yield: 71%; mp: 192-194 ºC; IR (cm^{-1}): 3172 (N-H stretching of secondary amine), 3092 (C-H stretching of aromatic ring), 2976 (C-H asymmetrical stretching of CH_3 group), 2923 (C-H asymmetrical stretching of CH_3 group), 1695 (C=N stretching), 1600 (N-H deformation of pyrimidine ring), 1505, 1473 and 1404 (C=C stretching of aromatic ring), 1353 (C-H

asymmetrical deformation of CH_3 group), 1305 (C-H symmetrical deformation of CH_3 group), 1258 (C-N stretching), 1210 (C-F stretching), 892 (C-S stretching); ^{1}H NMR (DMSO-d_6) δ ppm: 6.24 (s, 1H, CH (Chiral)), 6.64-6.65 (m, 3H, Ar-H), 7.12-7.15 (t, 1H, Ar-H (Thiophene)), 7.30-7.35 (d, 2H, Ar-H), 7.70-7.73 (dd, 1H, Ar-H (Thiophene)), 7.81-7.84 (dd, 1H, Ar-H (Thiophene)), 8.27 (s, 1H, Ar-H (Triazole)), 10.05 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 54.97, 61.06, 111.34, 113.90, 114.29, 128.54, 128.89, 129.83, 130.56, 134.26, 139.15, 147.30, 150.01, 159. 43, 160.01, 174.60; MS: m/z 445; Anal. Calcd. for $C_{17}H_9Cl_2F_3N_4OS$: C, 45.86; H, 2.04; N, 12.58. Found: C, 45.84; H, 2.01; N, 12.60%.

(7-(4-bromophenyl)-5-(trifluoromethyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-32)

Yield: 79%; mp: 198-200 ºC; IR (cm^{-1}): 3173 (N-H stretching of secondary amine), 3092 (C-H stretching of aromatic ring), 2975 (C-H asymmetrical stretching of CH_3 group), 2924 (C-H asymmetrical stretching of CH_3 group), 1695 (C=N stretching), 1604 (N-H deformation of pyrimidine ring), 1505, 1470 and 1403 (C=C stretching of aromatic ring), 1355 (C-H asymmetrical deformation of CH_3 group), 1303 (C-H symmetrical deformation of CH_3 group), 1254 (C-N stretching), 1215 (C-F stretching), 874 (C-S stretching), 808 (C-H out of plane bending of p-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 6.17 (s, 1H, CH (Chiral)), 7.12-7.15 (t, 1H, Ar-H (Thiophene)), 7.22-7.26 (d, 2H, Ar-H), 7.32-7.36 (d, 2H, Ar-H), 7.71-7.74 (dd, 1H, Ar-H (Thiophene)), 7.54-7.58 (dd, 1H, Ar-H (Thiophene)), 8.30 (s, 1H, Ar-H (Triazole)), 10.10 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 54.12, 103.75, 111.56, 119.87, 126.82, 134.91, 150.15, 153.86, 158.17, 170.42; MS: m/z 455; Anal. Calcd. for $C_{17}H_{10}BrF_3N_4OS$: C, 44.85; H, 2.21; N, 12.31. Found: C, 44.86; H, 2.22; N, 12.33%.

(7-(3-bromophenyl)-5-(trifluoromethyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-33)

Yield: 70%; mp: 188-190 ºC; IR (cm^{-1}): 3172 (N-H stretching of secondary amine), 3095 (C-H stretching of aromatic ring), 2972 (C-H asymmetrical stretching of CH_3 group), 2925 (C-H asymmetrical stretching of CH_3 group), 1690 (C=N stretching), 1602 (N-H deformation of pyrimidine ring), 1504, 1473 and 1405 (C=C stretching of aromatic ring), 1356 (C-H asymmetrical deformation of CH_3 group), 1308 (C-H symmetrical deformation of CH_3 group), 1254 (C-N stretching), 1222 (C-F stretching), 901 (C-S stretching), 782 (C-H out of plane bending of m-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 6.28 (s, 1H, CH (Chiral)), 6.57-6.63 (m, 4H, Ar-H), 7.10-7.13 (t, 1H, Ar-H (Thiophene)), 7.17-7.21 (s, 1H, Ar-H), 7.47-7.50 (dd, 1H, Ar-H (Thiophene)), 7.67-7.71 (dd, 1H, Ar-H (Thiophene)), 8.40 (s, 1H, Ar-H (Triazole)), 10.17 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 54.12, 103.75, 111.56, 119.87, 126.82, 134.91, 150.15, 153.86, 158.17, 170.40; MS: m/z 455; Anal. Calcd. for $C_{17}H_{10}BrF_3N_4OS$: C, 44.85; H, 2.21; N, 12.31. Found: C, 44.85; H, 2.24; N, 12.28%.

(7-(2-bromophenyl)-5-(trifluoromethyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-34)

Yield: 74%; mp: 118-120 ºC; IR (cm^{-1}): 3172 (N-H stretching of secondary amine), 3092 (C-H stretching of aromatic ring), 2972 (C-H asymmetrical stretching of CH_3 group), 2925 (C-H asymmetrical stretching of CH_3 group), 1692 (C=N stretching), 1602 (N-H deformation of pyrimidine ring), 1503, 1474 and 1402 (C=C stretching of aromatic ring), 1350 (C-H asymmetrical deformation of CH_3 group), 1302 (C-H symmetrical deformation of CH_3 group), 1252 (C-N stretching), 1221 (C-F stretching), 893 (C-S stretching), 758 (C-H out of plane bending of o-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 6.19 (s, 1H, CH (Chiral)), 6.70-6.75 (m, 4H, Ar-H), 7.19-7.22 (t, 1H, Ar-H (Thiophene)), 7.26-7.31 (s, 1H, Ar-H), 7.500-7.53 (dd, 1H, Ar-H (Thiophene)), 7.67-7.71 (dd, 1H, Ar-H (Thiophene)), 8.32 (s, 1H, Ar-H (Triazole)), 10.11 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 54.12, 103.75, 111.56, 119.87, 126.82, 134.91, 150.15, 153.86, 158.17,

170.77; MS: m/z 455; Anal. Calcd. for $C_{17}H_{10}BrF_3N_4OS$: C, 44.85; H, 2.21; N, 12.31. Found: C, 44.86; H, 2.22; N, 12.33%.

(5-(trifluoromethyl)-7-(4-fluorophenyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-35)

Yield: 73%; mp: 194-196 ºC; IR (cm^{-1}): 3174 (N-H stretching of secondary amine), 3092 (C-H stretching of aromatic ring), 2973 (C-H asymmetrical stretching of CH_3 group), 2924 (C-H asymmetrical stretching of CH_3 group), 1695 (C=N stretching), 1602 (N-H deformation of pyrimidine ring), 1503, 1470 and 1404 (C=C stretching of aromatic ring), 1355 (C-H asymmetrical deformation of CH_3 group), 1303 (C-H symmetrical deformation of CH_3 group), 1253 (C-N stretching), 1231 (C-F stretching), 896 (C-S stretching), 815 (C-H out of plane bending of p-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 6.22 (s, 1H, CH (Chiral)), 7.02-7.04 (t, 1H, Ar-H (Thiophene)), 7.15-7.18 (d, 2H, Ar-H), 7.31-7.34 (d, 2H, Ar-H), 7.60-7.63 (dd, 1H, Ar-H (Thiophene)), 7.67-7.71 (dd, 1H, Ar-H (Thiophene)), 8.41 (s, 1H, Ar-H (Triazole)), 10.07 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 54.50 103.75, 111.56, 119.87, 126.82, 134.91, 150.15, 153.86, 158.17, 169.36; MS: m/z 394; Anal. Calcd. for $C_{17}H_{10}F_4N_4OS$: C, 51.78; H, 2.56; N, 14.21. Found: C, 51.77; H, 2.57; N, 14.26%.

(5-(trifluoromethyl)-4,7-dihydro-7-(4-hydroxyphenyl)-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-36)

Yield: 84%; mp: 108-110 ºC; IR (cm^{-1}): 3350 (N-H stretching of secondary amine), 3090 (C-H stretching of aromatic ring), 2979 (C-H asymmetrical stretching of CH_3 group), 2881 (C-H asymmetrical stretching of CH_3 group), 1692 (C=N stretching), 1601 (N-H deformation of pyrimidine ring), 1507, 1478 and 1409 (C=C stretching of aromatic ring), 1447 (C-H asymmetrical deformation of CH_3 group), 1354 (C-H symmetrical deformation of CH_3 group), 1351 (C-N stretching), 1204 (C-F stretching), 881 (C-S stretching), 814 (C-H out of plane bending of p-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: ^{1}H NMR (DMSO-d_6) δ ppm: 6.12 (s, 1H, CH (Chiral)), 6.52 (s, 1H, OH), 6.99-7.03 (t, 1H, Ar-H (Thiophene)), 7.12-7.15 (d, 2H, Ar-H), 7.26-7.29 (d, 2H, Ar-H), 7.34-7.37 (dd, 1H, Ar-H (Thiophene)), 7.57-7.61 (dd, 1H, Ar-H (Thiophene)), 8.43 (s, 1H, Ar-H (Triazole)), 10.10 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 55.14, 103.75, 111.56, 119.87, 126.82, 134.91, 150.15, 153.86, 158.17, 171.38; MS: m/z 392; Anal. Calcd. for $C_{17}H_{11}F_3N_4O_2S$: C, 52.04; H, 2.83; N, 14.28. Found: C, 52.05; H, 2.80; N, 14.25%.

(5-(trifluoromethyl)-4,7-dihydro-7-(2-hydroxyphenyl)-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-37)

Yield: 80%; mp: 261-263 ºC; IR (cm^{-1}): 3213 (N-H stretching of secondary amine), 3080 (C-H stretching of aromatic ring), 2949 (C-H asymmetrical stretching of CH_3 group), 2918 (C-H asymmetrical stretching of CH_3 group), 1689 (C=N stretching), 1602 (N-H deformation of pyrimidine ring), 1560, 1491 and 1448 (C=C stretching of aromatic ring), 1384 (C-H asymmetrical deformation of CH_3 group), 1340 (C-H symmetrical deformation of CH_3 group), 1302 (C-F stretching), 1238 (C-N stretching), 896 (C-S stretching), 745 (C-H out of plane bending of o-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 6.19 (s, 1H, CH (Chiral)), 6.58 (s, 1H, OH), 6.87-6.94 (m, 4H, Ar-H), 7.14-7.19 (t, 1H, Ar-H (Thiophene)), 7.26-7.31 (s, 1H, Ar-H), 7.53-7.56 (dd, 1H, Ar-H (Thiophene)), 7.60-7.64 (dd, 1H, Ar-H (Thiophene)), 8.15 (s, 1H, Ar-H (Triazole)), 10.31 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 53.82, 103.75, 111.56, 119.87, 126.82, 134.91, 150.15, 153.86, 158.17, 172.12; MS: m/z 392; Anal. Calcd. for $C_{17}H_{11}F_3N_4O_2S$: C, 52.04; H, 2.83; N, 14.28. Found: C, 52.03; H, 2.82; N, 14.27%.

(5-(trifluoromethyl)-4,7-dihydro-7-(4-nitrophenyl)-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-38)

Yield: 79%; mp: 242-244 ºC; IR (cm^{-1}): 3176 (N-H stretching of secondary amine), 3095 (C-H stretching of aromatic ring), 2974 (C-H

asymmetrical stretching of CH_3 group), 2922 (C-H asymmetrical stretching of CH_3 group), 1693 (C=N stretching), 1606 (N-H deformation of pyrimidine ring), 1506, 1471 and 1400 (C=C stretching of aromatic ring), 1352 (C-H asymmetrical deformation of CH_3 group), 1307 (C-H symmetrical deformation of CH_3 group), 1255 (C-N stretching), 1228 (C-F stretching), 892 (C-S stretching), 826 (C-H out of plane bending of p-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 6.20 (s, 1H, CH (Chiral)), 7.12-7.16 (t, 1H, Ar-H (Thiophene)), 7.24-7.26 (d, 2H, Ar-H), 7.32-7.36 (d, 2H, Ar-H), 7.58-7.61 (dd, 1H, Ar-H (Thiophene)), 7.70-7.75 (dd, 1H, Ar-H (Thiophene)), 8.30 (s, 1H, Ar-H (Triazole)), 10.18 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 56.32, 103.75, 111.56, 119.87, 126.82, 134.91, 150.15, 153.86, 158.17, 170.70; MS: m/z 421; Anal. Calcd. for $C_{17}H_{10}F_3N_5O_3S$: C, 48.46; H, 2.39; N, 16.62. Found: C, 48.45; H, 2.37; N, 16.64%.

(5-(trifluoromethyl)-4,7-dihydro-7-(3-nitrophenyl)-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-39)

Yield: 82%; mp: 252 250 ºC; IR (cm^{-1}): 3215 (N-H stretching of secondary amine), 3085 (C-H stretching of aromatic ring), 2942 (C-H asymmetrical stretching of CH_3 group), 2912 (C-H asymmetrical stretching of CH_3 group), 1678 (C=N stretching), 1615 (N-H deformation of pyrimidine ring), 1512, 1454 and 1410 (C=C stretching of aromatic ring), 1378 (C-H asymmetrical deformation of CH_3 group), 1314 (C-H symmetrical deformation of CH_3 group), 1242 (C-N stretching), 1211 (C-F stretching), 891 (C-S stretching), 778 (C-H out of plane bending of m-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 6.14 (s, 1H, CH (Chiral)), 6.20-6.22 (d, 1H, Ar-H), 6.57-6.60 (m, 2H, Ar-H), 7.09-7.12 (t, 1H, Ar-H (Thiophene)), 7.20-7.23 (s, 1H, Ar-H), 7.70-7.73 (dd, 1H, Ar-H (Thiophene)), 7.67-7.71 (dd, 1H, Ar-H (Thiophene)), 8.41 (s, 1H, Ar-H (Triazole)), 10.27 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 55.12, 103.75, 111.56, 119.87, 126.82, 134.91, 150.15, 153.86, 158.17, 169.82; MS: m/z 421; Anal. Calcd. for $C_{17}H_{10}F_3N_5O_3S$: C, 48.46; H, 2.39; N, 16.62. Found: C, 48.46; H, 2.38; N, 16.67%.

(5-(trifluoromethyl)-4,7-dihydro-7-(2-nitrophenyl)-[1,2,4]triazolo[1,5-a]pyrimidin-6-yl)(thiophen-2-yl)methanone (LK-40)

Yield: 80%; mp: 131-133 ºC; IR (cm^{-1}): 3180 (N-H stretching of secondary amine), 3105 (C-H stretching of aromatic ring), 2978 (C-H asymmetrical stretching of CH_3 group), 2910 (C-H asymmetrical stretching of CH_3 group), 1684 (C=N stretching), 1612 (N-H deformation of pyrimidine ring), 1521, 1445 and 1417 (C=C stretching of aromatic ring), 1345 (C-H asymmetrical deformation of CH_3 group), 1324 (C-H symmetrical deformation of CH_3 group), 1258 (C-N stretching), 1208 (C-F stretching), 899 (C-S stretching), 750 (C-H out of plane bending of o-disubstituted ring); ^{1}H NMR (DMSO-d_6) δ ppm: 6.24 (s, 1H, CH (Chiral)), 6.64-6.62 (m, 4H, Ar-H), 7.16-7.21 (t, 1H, Ar-H (Thiophene)), 7.38-7.42 (d, 2H, Ar-H), 7.71-7.73 (dd, 1H, Ar-H (Thiophene)), 7.78-7.81 (dd, 1H, Ar-H (Thiophene)), 8.31 (s, 1H, Ar-H (Triazole)), 10.20 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ ppm: 54.54, 103.75, 111.56, 119.87, 126.82, 134.91, 150.15, 153.86, 158.17, 169.42; MS: m/z 421; Anal. Calcd. for $C_{17}H_{10}F_3N_5O_3S$: C, 48.46; H, 2.39; N, 16.62. Found: C, 48.48; H, 2.39; N, 16.60%.

RESULTS AND DISCUSSION

Biological Evaluation

The miscellaneous biological activity of pyrimidine and its fused derivatives inspired us to screen the newly synthesized compounds. Nowadays many antimicrobial agents have been applied for treatment; still the medical field needs extensive efforts for the development of new antimicrobial agents to overcome the highly resistant species of microbes. All the synthesized compounds (LK-21 to 40) were tested for their antibacterial and antifungal activity (MIC) *in vitro* by broth dilution method[24-26] with two bacterial strains *S. aurues MTCC-96* and *B. subtillitis MTCC-441* and two fungal strains *A. niger MTCC-282* and *C. albicans MTCC-227* taking Ampicillin,

Table 2: Antibacterial and antifungal activity of synthesized compounds LK-21 to 40

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.***
LK-21	**125**	**100**	**100**	125	**250**	1000	250
LK-22	**250**	500	250	250	**250**	200	200
LK-23	500	250	**100**	500	500	500	>1000
LK-24	**125**	125	250	200	500	>1000	1000
LK-25	**250**	500	250	500	>1000	>1000	>1000
LK-26	500	500	**62.5**	500	500	>1000	>1000
LK-27	500	**62.5**	250	**62.5**	1000	500	>1000
LK-28	**100**	250	**62.5**	500	1000	500	500
LK-29	500	500	500	125	**250**	>1000	>1000
LK-30	500	200	**100**	125	**250**	1000	250
LK-31	**125**	500	250	**100**	**250**	200	200
LK-32	500	500	**100**	250	500	500	>1000
LK-33	**250**	**62.5**	250	250	500	>1000	1000
LK-34	**125**	200	250	125	>1000	>1000	>1000
LK-35	**250**	250	**100**	**100**	500	>1000	1000
LK-36	**250**	125	250	**62.5**	1000	500	>1000
LK-37	500	200	**62.5**	500	1000	500	500
LK-38	500	500	500	125	**250**	>1000	>1000
LK-39	**100**	250	1000	250	500	1000	1000
LK-40	**125**	**62.5**	**100**	**100**	500	1000	200
Ampicillin	250	100	100	100	-	-	-
Chloramphenicol	50	50	50	50	-	-	-
Ciprofloxacin	50	50	25	25	-	-	-
Norfloxacin	10	10	10	10	-	-	-
Nystatin	-	-	-	-	100	100	100
Greseofulvin	-	-	-	-	500	100	100

Bold letters indicate that synthesized compounds are comparatively active as standard drugs.
DMF used as control and its antibacterial activity is nil or zero.

S.a.- *Staphylococcus aureus MTCC-96* ***S.p.***- *Streptococcus pyogenes MTCC 443*
E.c.- *Escherichia coli MTCC 442* ***P.a.***- *Pseudomonas aeruginosa MTCC 441*
C. a.- *Candida albicans MTCC 227* ***A. n.***- *Aspergillus Niger MTCC 282*
A.c.- *Aspergillus clavatus* MTCC 1323

Chloramphenicol, Ciprofloxacin, Norfloxacin and Griseofulvin as standard drugs. To ensure that the solvent had no effect on the bacterial growth, a control was performed with the test medium supplemented with DMF at the same dilutions as used in the experiments and it was observed that DMF had no effect on the microorganisms in the concentrations studied. The results are depicted in (Table 2).

CONCLUSION

In conclusion, we have developed a simple and efficient procedure to generate [1,2,4]triazolo[1,5-*a*]pyrimidines in excellent yields via a one-pot, solid phase, catalyst-free Biginelli like cyclocondensation.. The synthetic protocol utilizes mild reaction conditions and does not require work-up or column purification. Reaction time was considerably reduced and product yields were increased in the fusion method of synthesis. This simple and efficient synthetic protocol should be amenable to construct new substituted [1,2,4]triazolo[1,5-*a*]pyrimidine scaffolds with potential biological applications.

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REFERENCES

1. Fischer, G. (1993). *Adv. Heterocyclic Chemistry*, 57, 81.
2. Shaban, M. A. E., & Morgan, A. E. A. (2000). *Advance in Heterocyclic Chemistry*, 77, 345.
3. Shaban, M. A. E., & Morgan, A. E. A. (2000). *Advance in Heterocyclic Chemistry*, 73, 131.
4. Shaban, M. A. E., & Morgan, A. E. A. (2000). *Advance in Heterocyclic Chemistry*, 75, 243.
5. Zhang, N., Semiramis, A. K., & Thai N. (2007). *Journal of Medicinal Chemistry*, 50, 319.
6. Havlicek, L., Fuksova, K., Krystof, V. (2005). *Bioorganic and Medicinal Chemistry*, 13, 5399.
7. Fraley, M. E., Hoffman, W. F., Rubino, R. S. (2002). *Bioorganic and Medicinal Chemistry Letters*, 12, 2767.
8. Chen, Q., Zhu, X. L., Liu, Z. M. (2008). *European Journal of Medicinal Chemistry*, 43, 595.
9. Cheng, C. C., Robins, R. K. J. (1956). *Org. Chem., 21*, 1240-1256.
10. Ismail, Z. H., Abdel-Gawad, S. M., Abdel-Aziem, A., Ghorab, M. M. (2003). *Phosphorus, Sulfur and Silicon*, 178, 1795-1805.
11. Carraro, F., Naldini, A., Pucci, A., Locatelli, G. A., Maga, G., Schenone, S., Bruno, O., Ranise, A., Bondavalli, F., Brullo, C., Fossa, P., Menozzi, G., Mosti, L., Modugno, M., Tintori, C., Manetti, F., Botta, M. J. (2006). *Med. Chem., 49*, 1549-1561.
12. El-Enany, M. M., Kamel, M. M., Khalil, O. M., El-Nassan, H. B. (2010). *Eur. J. Med. Chem., 45*, 5286-5291.
13. Abd El Hamid, M. K., Mihovilovic, M. D., El-Nassan, H. B. (2012). *Eur. J. Med. Chem., 57*, 323-328.
14. Kandeel, M. M., Mohamed, L. W., Abd El Hamid, M. K., Negmeldin, A. T. (2012). *Sci Pharm., 80*, 531-545.
15. Peat, A. J., Garrido, D., Boucheron, J. A., Schweiker, S. L., Dickerson, S. H., Wilson, J. R., Wang, T. Y., & Thomson, S. A. (2004). *Bioorg. Med. Chem. Lett. 14*, 2127-2130.
16. Kim, D. C., Lee, Y. R., Yang, B. S., Shin, K. J., Kim, D. J., Chung, B. Y., & Yoo, K. H. (2003). *Eur. J. Med. Chem. 38*, 525-532.

17. Schenone, S., Brullo, C., Bruno, O., Bondavalli, F., Mosti, L., Maga, G., Crespan, E., Carraro, F., Manetti, F., Tintori, C., Botta, M. (2008). *Eur. J. Med. Chem., 43,* 2665-2676.

18. Schenone, S., Bruno, O., Bondavalli, F., Ranise, A., Mosti, L., Menozzi, P., Fossa, G., Manetti, F., Morbidelli, L., Trincavelli, L., Martini, C., Lucacchini, A. (2004). *Eur. J. Med. Chem., 39,* 153-160.

19. Adib, M., Mohamadi, A., Sheikhi, E., Ansari, S., Bijanzadeh, H. R. (2010). *Synlett, 11,* 1606-1608.

20. Reid, J., Calvin, M. (1950). *Journal of the American Chemical Society, 72 (7),* 2948-2952.

21. Kappe, C. O. (1997). *J. Org. Chem., 62,* 7201.

22. Shaban, M. A. E., Morgaan, A. E. A. (1999). *Adv. Heterocycl. Chem., 73,* 131.

23. Babichev, F. S., & Kovtunenko, V. A. (1977). *Khim. Geterotsikl. Soedin. 2,* 147.

24. National Committee for Clinical and Laboratory Standards, Method for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically Approved Standard, *fourth ed. NCCLS, Villanova, Italy, 1997*, Document M 100-S7. S100-S157.

25. Isenberg, D. H. (1998). *Essential Procedure for Clinical Microbiology, American Society for Microbiology*, Washington, 1998.

26. Zgoda, J. R., & Porter, J. R. (2001). *Pharm. Biol.,* 39, 221.

