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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME NOVEL BENZO THIENO PYRIMIDINES

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ABSTRACT

Cyclization and chlorination of 2-amino-5-benzyl-4, 5, 6, 7-tetrahydro hydro thieno [3, 2c] pyridine-3-carboxamide yielded (3 a-b). Reaction with different substituted pyridines of [3 a-b] yielded 4a (1-4) and 4b (1-2). However reaction of 3a with different substituted 2-amino phenols yielded 4a (5-6). Further 3a yields 4a (7) & 4a (8) from different substituents like o-phenylene diamine and 4-chloro-2-triflouro acetyl aniline. Reaction of 3a & 3b with 2-amino Benzimidazole & 2-amino tetrazole yields 4a (9) & 4b (3), 4a (10) & 4b (4). All the synthesized compounds were tested against bacteria (Gram-positive and Gram–negative).

Keywords: Thieno pyrimidines, pyridines, Benzimidazole, tetrazole, antimicrobial activity.

INTRODUCTION

In an era of increasing bacterial resistance to classical antibacterial agents. It has been postulated that the development of resistance to known antibiotics could be overcome by identifying new drug targets via genomic, improving existing antibiotics and most importantly by identifying new antibacterial agents[1] with novel structures and mode of action. This will always remain the primary goal.

Pyrimidine derivative and heterocyclic annulated pyrimidines continue to attract great interest due to the wide variety of interesting biological activities observed for these compounds, such as anticancer[2], antiviral[3], antitumor[4], anti-inflammatory[5], antimicrobial[6], antifungal[7], antihistaminic[8] and analgesic[9] activities. Aromatic and heteroaromatic compounds are useful substrates for the preparation of various condensed pyrimidine heterocyclic systems[10]. In this present work, interest is expressed in synthesizing some new thieno pyrimidine derivatives 4a (1-10) and 4 b (1-4) and evaluated for their antimicrobial activity.

EXPERIMENTAL

Melting points (^oC, uncorrected) were recorded on an Electro thermal I A 9100 Digital Melting Point Apparatus. IR spectra (Vmax in Cm^{-1}) were recorded on a Shimadzu FT-IR 8300 Spectrophotometer using KBr pellets technique. ^1H NMR Spectra were recorded using Bruker WM-400 spectrophotometer using DMSO-d_6 or $CDCl_3$ as the solvent and TMS as the internal reference (Chemical Shifts in ppm). TLC using silica gel G60 (Merck, Germany) routinely checked the purity of the compounds and the spots were exposed in iodine vapour for visualization.

Synthesis of compounds:

2-amino-5-benzyl-4, 5, 6, 7-tetrahydrothieno [3, 2-c] pyridine-3-carboxamide (1)[11]: N-Benzyl-4-Piperidone (0.01 mol, 1.89 g), Cyanoacetamide[12] (0.01 mol, 0.84 g), Sulphur powder (0.01 mol, 0.32 g) and diethyl amine (10 ml) in absolute ethanol (30 ml) was stirred for 3 hrs. After the completion of the reaction time the mixture is poured on crushed ice. The separated solid was filtered, washed with water and recrystallized from alcohol to furnish compound (**1**). Yield 80%; m.p.: 230 ^oC. Anal.: Calculated for $C_{15}H_{17}N_3SO$: C, 62.71; H, 5.92; N, 14.63. Found: C, 62.67; H, 5.95; N, 14.61; IR: ν (cm^{-1}) 3377 (-$CONH_2$), 3202 (NH_2), 3008 (Ar & CH_2), 1653, 1646 (C=O), 546 (C-S); ^1H NMR: δ (ppm) 7.4 (m,

5H, Ar-H), 6.7 (s, 2H, NH_2), 4.4 (d, 2H, CO-NH_2) 4.0 (s, 2H, CH_2N), 3.5 (s, 2H, piperidine), 3.3 (t, 2H, piperidine), 3.0 (t, 2H, piperidine); LCMS (m/z): 288 [M^+]

6-benzyl-2-phenyl (4-substituted or unsubstituted)-5, 6, 7, 8-tetrahydro pyrido thieno [2, 3-d] pyrimidine-4(4H)-one (2a-b): Compound 1 (0.01 mol, 2.87 g), Benzaldehyde or 4-Chloro benzaldehyde (0.01mol) in ethanol (30 ml) and few drops of conc. HCl were refluxed for 4 hrs. The Yellowish solid is separated after cooling to room tempt. and then filtered, the dried product is recrystallized from DMF. **2a**: Yield 70% m.p: 318. Anal.: Calculated for $C_{22}H_{19}N_3SO$: C, 70.77; H, 5.09; N, 11.26. Found: C, 70.74; H, 5.07; N, 11.28; IR: ν (cm^{-1}) 3086 (NH), 2949 (CH of Aromatic), 2759 (CH_2), 1653 (C=O), 1540 (C-N), 694 (mono substituted benzene), 547 (C-S); ^{1}H NMR: δ (ppm) 11.2 (s, 1H, NH of Pyrimidine), 7.8 (m, 10H, Ar), 3.8 (d, 2H, CH_2 of piperidine), 3.2 (t, 2H, CH_2 of piperidine), 3.0 (t, 2H, CH_2 of piperidine); LCMS (m/z): 374 [M^+]. **2b:** Yield 78%; m.p.: 324. Anal.: Calculated for $C_{22}H_{18}N_3SOCl$; C, 64.78; H, 4.45; N, 10.30. Found: C, 65.74; H, 4.78; N, 10.28; IR: ν (cm^{-1}) 2980 (NH), 3011 (CH of Aromatic), 2719 (CH_2), 1699 (C=O), 1586 (C-N), 580 (C-S), 618 (C-Cl); ^{1}H NMR: δ (ppm) 11.45 (s, 1H, NH of Pyrimidine), 7.1-7.7 (m, 9H, Ar), 3.6 (d, 2H, CH_2 of piperidine), 3.2 (t, 4H, CH_2 of piperidine), 3.0 (t, 2H, CH_2 of N-alkyl chain); LCMS (m/z): 374 [M^+].

6-benzyl-4-chloro-2-(4-chloro (substituted or unsubstituted) benzyl) - 5, 6, 7, 8-tetrahydro pyrido thieno [2, 3-d] pyrimidine (3 a-b): Compound 2(a-b) (0.1 mol) and 25 ml of $POCl_3$ is refluxed for 8-10 hrs. After completion of the reaction (monitored by TLC), the excess of $POCl_3$ is removed by distillation and the reaction mixture is poured over crushed ice. The precipitate formed was filtered, dried and then recrystallized with DMF. **3a**: Yield 90%; m.p: 285-290. Anal.: Calculated for $C_{22}H_{18}N_3SCl$; C, 67.43; H, 4.59; N, 10.72 Found: C, 67.45; H, 4.57; N, 10.73; IR: ν (cm^{-1}) 2945 (CH of Aromatic), 2806, 2762 (CH of CH_2), 1540 (C-N), 697 (mono substituted benzene), 575 (C-S); ^{1}H NMR: δ (ppm), 7.7 (m, 10H, Ar), 3.6 (Broad s, 2H, CH_2-N and CH_2 of piperidine), 3.3 (t, 2H, CH_2 of piperidine), 2.9 (t, 2H, CH_2 of piperidine); LCMS (m/z): 392 [M^+]. **3b**: Yield 70%; m.p: 170. Anal.: Calculated for $C_{22}H_{17}N_3SCl_2$; C, 61.82; H, 3.98; N, 9.83 Found: C, 61.80; H, 3.95; N, 9.86; IR: ν (cm^{-1}) 2941, 2897 (CH of Aromatic), 2825 (CH of CH_2), 1548 (C-N), 843 (1,4 disubstituted benzene), 698 (mono substituted benzene), 508 (C-S); ^{1}H NMR: δ (ppm), 8.0 (m, 9H, Ar), 3.5 (Broad s, 4H, CH_2-N and CH_2 of piperidine), 3.2 (t, 2H, CH_2 of piperidine), 3.0 (t, 2H, CH_2 of piperidine); LCMS (m/z): 428 [M^+].

6-benzyl-2-phenyl (4 chloro substituted or unsubstituted) -4-amino (substituted pyridine)-5, 6, 7, 8-tetrahydropyrido thieno [2, 3-d] pyrimidine 4a (1-4) & 4b (1-2): Compound 3a or 3b (0.01 mol), 2-amino substituted pyridine (0.01 mol) was heated under reflux with sufficient quantity of pyridine solution for 24 hrs. After the completion of the reaction (monitored by TLC) the mixture is poured over crushed ice. The precipitate formed was filtered, dried and then recrystallized with methanol. **4a (1):** Yield 65% m.p: 260. Anal.: Calculated for $C_{27}H_{23}N_5S$: C, 72.16; H, 5.12; N, 15.59. Found: C, 72.19; H, 5.13; N, 15.60; IR: ν (cm^{-1}) 3105 (NH), 2900 (CH of Aromatic), 2758 (CH_2), 1545 (C-N), 688 (mono substituted benzene), 546 (C-S); ^{1}H NMR: δ (ppm) 2.9 (m, 4H, CH_2 of piperidine), 3.4 (t, 2H, CH_2 of alkyl chain), 3.7 (t, 2H, CH_2 of piperidine), 7.5-8.1 (m, 14H, Ar), 11.39 (s, 1H, NH); LCMS (m/z): 450 [M^+]

4a (2): Yield 58% m.p: 260. Anal.: Calculated for $C_{28}H_{25}N_5S$: C, 72.57; H, 5.39; N, 15.11. Found: C, 72.55; H, 5.41; N, 15.16; IR: ν (cm^{-1}) 3158 (NH), 2888 (CH of Aromatic), 2689 (CH_2), 1502 (C-N), 613 (mono substituted benzene), 630 (C-S); ^{1}H NMR: δ (ppm) 3.1 (t, 4H, CH_2 of piperidine), 3.3 (t, 2H, CH_2 of alkyl chain), 3.8 (t, 2H, CH_2 of piperidine), 7.1-7.9 (m, 14H, Ar), 11.33 (s, 1H, NH); LCMS (m/z): 464 [M^+]

4a (3): Yield 58% m.p: 260. Anal.: Calculated for $C_{28}H_{25}N_5S$: C, 72.57; H, 5.39; N, 15.11. Found: C, 72.49; H, 5.45; N, 15.12; IR: ν (cm^{-1}) 2899 (NH), 2933 (CH of Aromatic), 2820 (CH_2), 1515 (C-N), 609 (mono substituted benzene), 555 (C-S); ^{1}H NMR: δ (ppm) 2.9 (d, 4H, CH_2 of piperidine), 3.2 (t,

3H of CH_3), 3.4 (d, 2H, CH_2 of piperidine), 3.6 (t, 2H, CH_2 of piperidine), 7.0- 7.8 (m, 13H, Ar), 11.09 (s, 1H, NH); LCMS (m/z): 464 [M^+]

4a (4): Yield 58% m.p: 260. Anal.: Calculated for $C_{28}H_{25}N_5S$: C, 72.57; H, 5.39; N, 15.11. Found: C, 72.53; H, 5.47; N, 15.18; IR: v (cm^{-1}) 3150 (NH), 2799 (CH of Aromatic), 2811 (CH_2), 1522 (C-N), 639 (mono substituted benzene), 566 (C-S); ^{1}H NMR: δ (ppm) 2.3 (d, 4H, CH_2 of piperidine), 3.15 (t, 3H of CH_3), 3.3 (d, 2H, CH_2 of piperidine), 3.7 (t, 2H, CH_2 of piperidine), 7.0- 7.9 (m, 13H, Ar), 11.66 (s, 1H, NH); LCMS (m/z): 464 [M^+]

4b (1): Yield 65%, m.p: 230. Anal.: Calculated for $C_{27}H_{22}N_5SCl$: C, 67.01; H, 4.55; N, 14.47. Found: C, 67.04; H, 4.57; N, 14.49; IR: v (cm^{-1}) 3161 (NH), 2890 (CH of Aromatic), 2778 (CH_2), 1495 (C-N), 598 (mono substituted benzene), 514 (C-S); ^{1}H NMR: δ (ppm) 3.0 (m, 4H, CH_2 of piperidine), 3.2 (t, 2H, CH_2 of alkyl chain), 3.6 (t, 2H, CH_2 of piperidine), 7.2-8.2 (m, 13H, Ar), 11.44 (s, 1H, NH); LCMS (m/z): 485 [M^+]

4b (2): Yield 60%, m.p: 230. Anal.: Calculated for $C_{28}H_{24}N_5SCl$: C, 67.52; H, 4.86; N, 14.06. Found: C, 67.09; H, 4.88; N, 14.23; IR: v (cm^{-1}) 2989 (NH), 2907 (CH of Aromatic), 2688 (CH_2), 1549 (C-N), 688 (mono substituted benzene), 556 (C-S); ^{1}H NMR: δ (ppm) 3.0 (t, 4H, CH_2 of piperidine), 3.4 (t, 2H, CH_2 of alkyl chain), 3.6 (t, 2H, CH_2 of piperidine), 6.9-7.7 (m, 14H, Ar), 11.67 (s, 1H, NH); LCMS (m/z): 500 [M^+].

6-benzyl-2-phenyl-4-amino (hydroxy, methyl substituted or unsubstituted-1-phenyl) - 5, 6, 7, 8-tetrahydropyrido thieno [2, 3-d] pyrimidine 4a (5-6): Compound 3a (0.01 mol), 2-amino substituted phenols (0.01 mol) was heated under reflux with sufficient quantity of pyridine solution for 24 hrs. After the completion of the reaction (monitored by TLC) the mixture is poured over crushed ice. The precipitate formed was filtered, dried and then recrystallized with methanol.

4a (5): Yield 43%, m.p:259. Anal.: Calculated for $C_{29}H_{26}N_4SO$: C, 72.80; H, 5.43; N, 11.71. Found: C, 72.82; H, 5.45; N, 11.73; IR: v (cm^{-1}) 3245 (NH), 3180 (CH of Aromatic), 2820 (CH_2), 1541 (C-N), 680 (mono substituted benzene), 650 (C-S); ^{1}H NMR: δ (ppm) 2.8-2.9 (m, 4H, CH_2 of piperidine), 3.6 (s, 2H, CH_2-N), 3.8 (s, 2H of Piperidine), 6.7-8.1 (m, 14H, Ar), 11.24 (s, 1H, NH); LCMS (m/z): 479 [M^+].

4a (6): Yield 39%, m.p. 251; Anal.: Calculated for $C_{28}H_{24}N_4SO$: C, 72.41; H, 5.17; N, 12.06. Found: C, 72.44; H, 5.15; N, 12.05; IR: v (cm^{-1}) 3163(N-H stretching), 3005, 2980 (C-H of Ar-H and CH_2 of Aliphatic stretching), 1515 (C=N stretching), 638 (mono substituted benzene), 647(C-S stretching), 790 (C-N stretching), 1380 (CH_3); ^{1}H NMR: δ (ppm) 1.7(s, 3H of CH_3), 2.6 (m, 4H of Piperidine), 3.2 (s, 2H of CH_2 of alkyl chain), 3.6 (s, 2H of Piperidine), 6.9- 8.2 (m, 13H of aromatic ring), 8.3 (s, 1H of OH), 11.47 (s, 1H, NH); LCMS (m/z): 460 [M^+].

6- benzyl -2- phenyl- 4- amino (2'– amino- 1-phenyl)- 5, 6, 7, 8- tetrahydropyrido thieno [2, 3-d] pyrimidine 4a (7): Compound 3a (0.01 mol), O-phenylene diamine (0.01 mol) was heated under reflux with sufficient quantity of pyridine solution for 24 hrs. After the completion of the reaction (monitored by TLC) the mixture is poured over crushed ice. The precipitate formed was filtered, dried and then recrystallized with methanol. **4a (7):** Yield 42%, m.p. 250; Anal.: Calculated for $C_{28}H_{25}N_5S$: C, 72.50; H, 5.39; N, 15.11. Found: C, 72.70; H, 5.41; N, 15.13; IR: v (cm^{-1}) 3189 (N-H stretching), 3122, 2835(C-H of Ar-H and CH_2 of Aliphatic stretching), 1585 (C=N stretching), 615 (mono substituted benzene), 547 (C-S stretching), 688 (C-Cl stretching), 1655 (C=O stretching), 1225 (C-F stretching); ^{1}H NMR: δ (ppm) 2.7 (m, 4H of Piperidine), 3.1 (s, 2H of CH_2 of alkyl chain), 3.6 (s, 2H of piperidine), 7.1- 8.2 (m, 13H of Aromatic ring), 11.44 (s, 1H, NH); LCMS (m/z): 251 [M^+].

6-benzyl-2-phenyl-4-amino (2'triflouro carbonyl-4-chloro-1-phenyl)- 5, 6, 7, 8- tetrahydro pyrido thieno [2, 3-d] pyrimidine 4a (8): Compound 3a (0.01 mol), 4-chloro-2 triflouro acetyl aniline (0.01 mol) was heated under reflux with sufficient quantity of pyridine solution for 24 hrs. After the completion of the reaction (monitored by TLC) the mixture is poured over crushed ice. The precipitate formed was

filtered, dried and then recrystallized with methanol. **4a (8):** Yield 41%, m.p. 230; Anal.: Calculated for $C_{30}H_{22}N_4SOF_3Cl$: C, 62.22; H, 3.80; N, 9.68. Found: C, 62.25; H, 3.82; N, 9.69; IR: ν (cm^{-1}) 3123 (N-H stretching), 3213, 2825 (C-H of Ar-H and CH_2 of Aliphatic stretching), 1541(C=N stretching), 611 (mono substituted benzene), 514 (C-S stretching), 825 (C-N stretching), 3315 (NH_2); ^{1}H NMR: δ (ppm) 2.7 (m, 4H, CH_2 of piperidine), 3.1 (m, 2H of CH_2 of alkyl chain), 3.6 (t, 2H, CH_2 of piperidine), 7.3- 8.2 (m,13H, Aromatic ring), 11.65 (s, 1H, NH); LCMS (m/z): 231 [M^+].

6-benzyl-2-(Chloro substituted or unsubstituted phenyl) -4-amino (5'-tetrazolyl)-5, 6, 7, 8-tetrahydropyrido thieno [2, 3-d] pyrimidine 4a (9) & 4b (3): Compound 3a or 3b (0.01 mol), 5 amino-1, 2, 3, 4-tetrazole hydrate (0.01 mol) was heated under reflux with sufficient quantity of pyridine solution for 24 hrs. After the completion of the reaction (monitored by TLC) the mixture is poured over crushed ice. The precipitate formed was filtered, dried and then recrystallized with methanol.
4a (9): Yield 46%, m.p. 250; Anal.: Calculated for $C_{23}H_{20}N_8S$: C, 62.72; H, 4.54; N, 25.45. Found: C, 62.75; H, 4.52; N, 25.48; IR: ν (cm^{-1}) 3163 (NH), 2930, 2820 (CH of Aromatic and CH_2), 1541 (C=N), 698 (mono substituted benzene), 547 (C-S); ^{1}H NMR: δ (ppm) 2.6 (m, 4H, CH_2 of piperidine), 3.2 (m, 2H of CH_2 of alkyl chain), 3.9 (t, 2H, CH_2 of piperidine), 7.1- 8.1 (m,10H, Aromatic ring), 11.33 (t, 2H, NH & NH of tetrazole); LCMS (m/z): 441 [M^+].
4b (3): Yield 49%, m.p. 243; Anal.: Calculated for $C_{23}H_{19}N_8SCl$: C, 58.16; H, 4.00; N, 23.59. Found: C, 58.17; H, 4.03; N, 23.64; IR: ν (cm^{-1}) 3163 (NH), 2930, 2820 (CH of Aromatic and CH_2), 1541 (C=N), 698 (mono substituted benzene), 547 (C-S); ^{1}H NMR: δ (ppm) 1.9 (m, 4H, CH_2 of piperidine), 3.2 (m, 2H of CH_2 of alkyl chain), 4.0 (t, 2H, CH_2 of piperidine), 7.1- 8.2 (m,10H, Aromatic ring), 11.65 (t, 2H, NH & NH of tetrazole); LCMS (m/z): 476 [M^+].

6-benzyl-2-(chloro substituted or unsubstituted phenyl)-4-amino (2'-benzimidazolyl) -5, 6, 7, 8-tetrahydropyrido thieno [2, 3-d] pyrimidine 4a (10) & 4b (4): Compound 3a or 3b (0.01 mol), 2 amino- Benzimidazole (0.01 mol) was heated under reflux with sufficient quantity of pyridine solution for 24 hrs. After the completion of the reaction (monitored by TLC) the mixture is poured over crushed ice. The precipitate formed was filtered, dried and then recrystallized with methanol. **4a (10):** Yield 70%, m.p. 254; Anal.: Calculated for $C_{29}H_{24}N_6S$: C, 71.31; H, 4.91; N, 17.21. Found: C, 71.35; H, 4.93; N, 17.25; IR: ν (cm^{-1}) 3112 (N-H stretching), 3130, 2768 (C-H of Ar-H and CH_2 of Aliphatic stretching), 1518 (C=N stretching), 660 (mono substituted benzene), 518 (C-S stretching); ^{1}H NMR: δ (ppm) 2.4 (m, 4H, CH_2 of piperidine), 3.6 (m, 2H of CH_2 of alkyl chain), 3.7 (t, 2H, CH_2 of piperidine), 6.7- 8.0 (m,14H, Aromatic ring), 9.35 (s, 1H of Benzimidazole), 11.22 (s,1H, NH); LCMS (m/z): 489 [M^+]
4b (4): Yield 62%, m.p. 237; Anal.: Calculated for $C_{29}H_{23}N_6SCl$: C, 66.73; H, 4.21; N, 16.10. Found: C, 66.75; H, 4.19; N, 16.13; IR: ν (cm^{-1}) 3278 (N-H stretching), 3110, 2880 (C-H of Ar-H and CH_2 of Aliphatic stretching), 1588 (C=N stretching), 722 (mono substituted benzene), 604 (C-S stretching), 618 (C-Cl stretching). 828 (C-N stretching); ^{1}H NMR: δ (ppm) 2.4 (m, 4H, CH_2 of piperidine), 2.9 (m, 2H of CH_2 of alkyl chain), 3.7 (t, 2H, CH_2 of piperidine), 7.1- 7.9 (m,13H, Aromatic ring), 9.8-10.2 (s, 1H of Benzimidazole), 11.33 (s,1H, NH); LCMS (m/z): 238 [M^+]

Antimicrobial Activity:
The antimicrobial activity[13] of representative new compounds 4a (1-10) and 4b (1-3) was investigated against a variety of micro-organisms, including the gram–positive bacteria *Bacillus Subtilis, Bacillus pumilis* and *Staphylococcus aureus*, *Escherichia coli* the gram-negative bacteria. The minimum inhibitory concentration (MIC) was determined by the Paper Disc Diffusion Method.

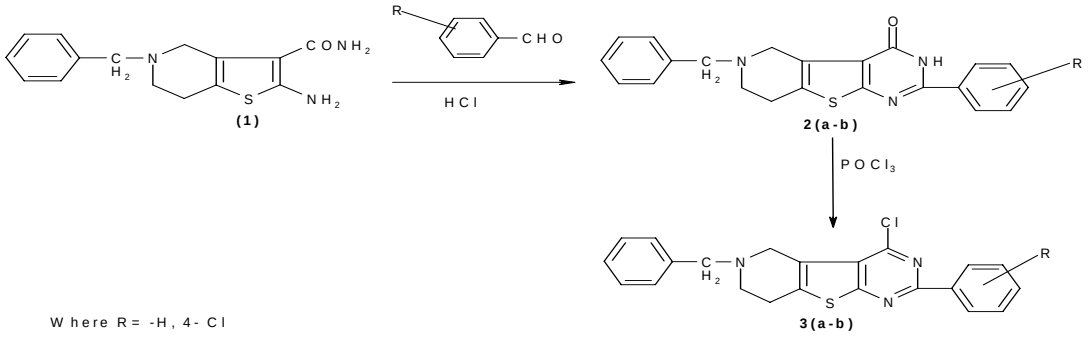
Sample preparation:
Sterilized filter paper discs (6 mm in diameter) were wetted with 10 µl each of a solution of the tested compound (50µg & 100µg/ml of the compound in DMF). The discs were then allowed to dry and placed on the surface of agar plates seeded with the test organism.

Medium inoculation and cultivation condition:
Each plate contained 15ml of the agar medium, previously seeded with 0.2ml of an 18h old broth culture of each organism. The inoculated plates were incubated at 37 ^{o} C for 48 h with the test discs in place and the inhibition zones were measured in mm. Discs impregnated with DMF were used as controls. The antibacterial reference Ampicillin discs tested as standard.

Table-1: Physical and analytical data of the prepared compounds 4a (1-10) & 4b (1-4)

S.No.	Compound Code	Mol. Formula	Molecular Wt.	Rf Value	Melting Point (^{o}C)	Yield %
1	4a (1)	$C_{27}H_{23}N_5S$	449.0	0.68	260	47
2	4a (2)	$C_{28}H_{25}N_5S$	463.0	0.68	258	43
3	4a (3)	$C_{28}H_{25}N_5S$	463.0	0.67	250	45
4	4a (4)	$C_{28}H_{25}N_5S$	463.0	0.71	262	40
5	4a (5)	$C_{29}H_{26}N_4SO$	478.0	0.70	259	43
6	4a (6)	$C_{28}H_{24}N_4SO$	464.0	0.67	251	39
7	4a (7)	$C_{28}H_{25}N_5S$	463.0	0.62	250	42
8	4a (8)	$C_{30}H_{22}N_4SOF_3Cl$	578.5	0.69	230	41
9	4a (9)	$C_{23}H_{20}N_8S$	440.0	0.62	250	46
10	4a (10)	$C_{29}H_{24}N_6S$	488.0	0.69	254	70
11	4b (1)	$C_{27}H_{22}N_5SCl$	483.5	0.62	230	78
12	4b (2)	$C_{28}H_{24}N_5SCl$	498.5	0.65	257	56
13	4b (3)	$C_{23}H_{19}N_8SCl$	474.5	0.60	243	75
14	4b (4)	$C_{29}H_{23}N_6SCl$	522.5	0.63	237	62

Scheme-1



Where R= -H, 4- Cl

Fig-1

RESULTS AND DISCUSSION

The antimicrobial screening results presented in table-2 reveal that compounds 4a (2), 4a (6) & 4b (4) exhibited a significant activity against *Escherichia coli* Compounds 4a (1), 4a (2), 4a (6), 4a (8), 4a (10) & 4b (3) showed promising activity against *Bacillus Subtilis, Bacillus pumilis* and *Staphylococcus aureus.* While the compounds 4a (4), 4a (9) and 4b (1) showed moderate activity against all the organisms.

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Scheme-1

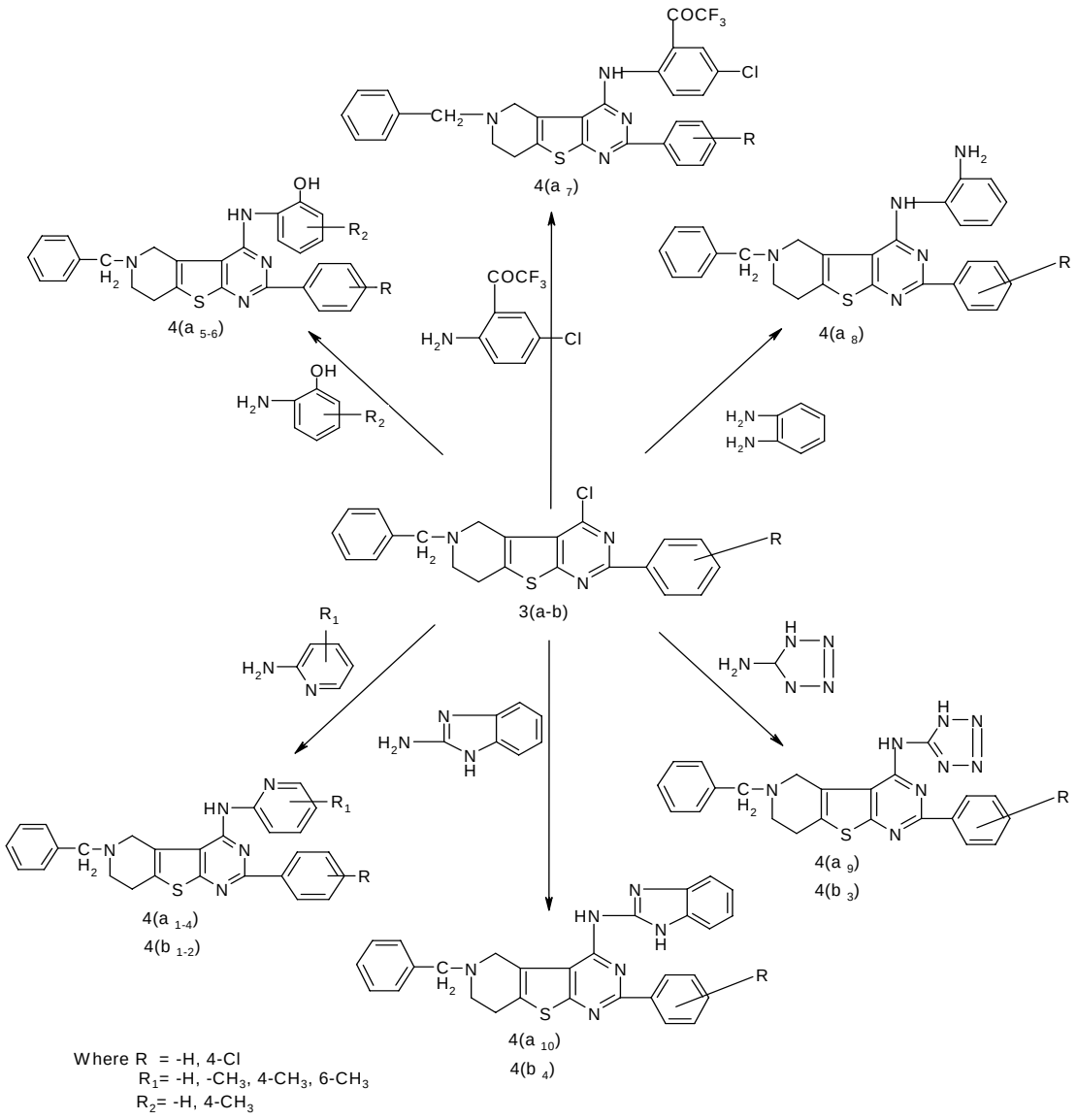

Fig-2

Table-2: Antimicrobial activity of compounds 4a (1-10) & 4b (1-4)

S.No.	Compound	Gram +ve				Gram -ve			
		B.Subtilis		*B.pumilis*		*S.aureus*		*E.coli*	
		50 µg	100 µg	50 µg	100 µg	50 µg	100 µg	50 µg	100 µg
01	4a (1)	-	++	+	+	-	++	+	++
02	4a (2)	+	++	+	++	-	+	++	+++
03	4a (3)	+	+	+	+	-	+	-	++
04	4a (4)	-	++	-	+	+	++	+	+

05	4a (5)	-	+	-	+	-	-	-	+
06	4a (6)	+	++	++	+++	+	++	++	+++
07	4a (7)	+	+	+	++	-	+	+	++
08	4a (8)	++	+++	+	+++	+	++	+	++
09	4a (9)	+	++	+	++	+	++	+	++
10	4a (10)	++	+++	+	++	+	++	+	+
11	4b (1)	+	++	+	++	+	+	+	+
12	4b (2)	-	+	-	+	+	+	-	+
13	4b (3)	+	+	++	+++	++	+++	+	++
14	4b (4)	+	++	+	++	+	++	++	+++
DMF (Control)		-	-	-	-	-	-	-	-
	ZONE OF INHIBITION OF STANDARD DRUG								
Ampicillin		+++	++++	+++	++++	+++	++++	+++	++++

Zone of Inhibition: (-) 6 mm; (+) 6-15 mm, (++) 15-20 mm, (+++) 20-25mm, (++++) 25-30mm

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