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Synthesis, characterization and antimicrobial evaluation of tetrahydrothiazolo[5,4-c]pyridine derivatives

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Abstract

A series of 5-((aryl/heteroaryl)sulfonyl)-2-(1H-pyrrol-1-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine have been synthesized. The structures of all synthesized compounds have been confirmed by elemental analyses and ^{1}H NMR, Mass and IR spectral studies. All the synthesized compounds were screened for their in-vitro antimicrobial activity.

Key words: Tetrahydrothiazolo[5,4-c]pyridine**,** Gewald reaction**,** Antimicrobial activity

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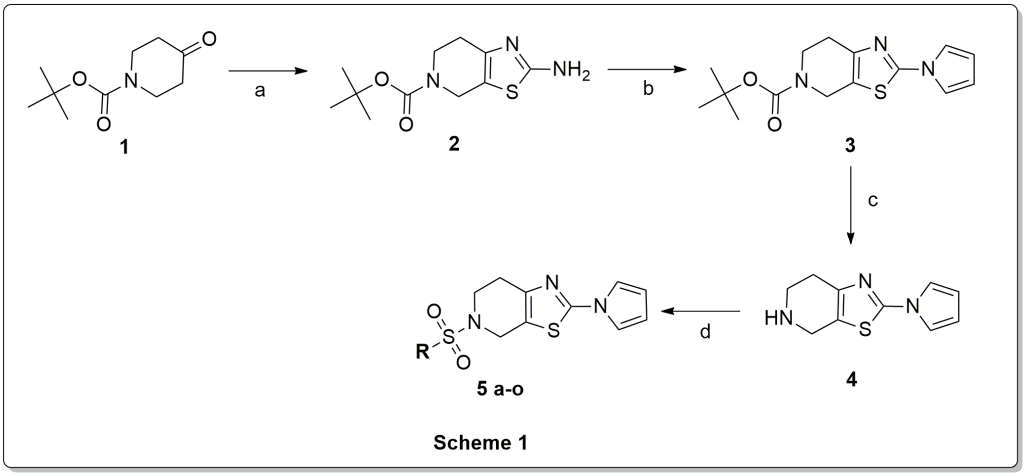
INTRODUCTION

The attention of the organic chemists has been directed towards the field of heterocyclic chemistry, because their valuable utilities in the synthesis of variety of biologically active derivatives. Heterocyclic compounds occur very widely in nature and are essential to life. Nitrogen-containing heterocyclic entities exist in many natural products and chemotherapeutic agents.

Over the years, much attention has been devoted towards thiazolopyridine derivatives due to their array of pharmaceutical and therapeutic properties. They have emerged as phosphatidylinositol 3-kinase [1], mitotic kinase inhibitor [2], neuropeptide FF receptor [3], FXa inhibitor [4], etc. According to literature survey some thiazolopyridine derivative showed biological activity such as histamine H3 receptor [5], MGluR5 receptor [6], RHO kinase inhibitor [7], steroid sulfatase inhibitor [8], 5HT3 receptor agonists [9] and useful to inhibiting ulcer and gastric secretion [10] and tumor growth in breast cancer [11]. In addition, numerous sulfonamide derivatives have been reported as carbonic anhydrase inhibitors [12-16], anti-cancer [17] and shows good antimicrobial activity [18]. In view of these findings we herein report the synthesis of sulfonamide analogue of tetrahydrothiazolo[5,4-c]pyridine derivatives and their biological activity.

MATERIALS AND METHODS

All chemicals were LR grade and used without further purification. The progress of the reaction was monitored by TLC on pre coated plates (silica gel 60, F254) and visualized with UV light. Melting points were determined using Lab India V10 apparatus and are uncorrected. Flash column chromatography was performed with silica gel 60 (60-120 mesh). NMR spectra (^{1}H at 400 MHz) were recorded using $CDCl_3$/DMSO-d^6 as a solvent and chemical shifts are expressed in parts per million (ppm) related to internal TMS. Infrared spectra were determined on a Shimadzu FT-IR. The elemental analysis was carried out by using a Perkin-Elmer 2400 series-II elemental analyzer. The specifications of the LC/MS are as follows: electrospray (+) ionization, mass range 100-1500 Da, 20-V cone voltage, and Xterra MS C18 column (2.1 mm x 50 mm x 3.5 µm).



Scheme 1

Reagents and conditions: *(a) Morpholine, cyanamide, EtOH, reflux; (b) 2,5-dimethoxytetrahydrofuran, AcOH, reflux; (c) TFA, DCM, rt; (d) Aryl/heteroaryl sulfonyl chloride, DIPEA, DMF, rt.*

Synthesis of tert-butyl 2-amino-6,7-dihydrothiazolo[5,4-c]pyridine-5(4H)-carboxylate (2). To a stirred solution of N-boc-4-piperidone 1 (10.0 g, 50 mmol), cyanamide (2.53 g, 60 mmol), and sulfur(1.92 g, 60 mmol) in ethanol (100 mL) was added morpholine (6.07 mL, 65 mmol) over period of 30 min at room temperature. The reaction mixture was heated at reflux temperature for 3 h. The reaction was monitored by TLC. Cooled the reaction mixture at RT. The reaction mixture was then poured into ice cold water (200 mL). The solid product, so formed, was collected by filtration and recrystallized by ethanol as yellow solid **2**. Yield: 11.7 g (87%). MP: 92-94 °C. ^{1}H NMR (DMSO-d6): δ 1.29(s, 9H), 2.68(t, 2H), 3.49(t, 2H), 4.39(s, 2H), 7.69(s, 2H); MS: m/z 256 (M+1). Anal. Calcd. (%) For $C_{11}H_{17}N_3O_2S$: C, 51.74; H, 6.71; N, 16.46; O, 12.53; S, 12.56. Found: C, 51.68; H, 6.75; N, 16.41; O, 12.45; S, 12.51.

Synthesis of tert-butyl 2-(1H-pyrrol-1-yl)-6,7-dihydrothiazolo[5,4-c]pyridine-5(4H)-carboxylate. (3). To a solution of compound **2** (11.7 g, 46 mmol) and 2,5-dimethoxytetrahydrofuran (7.27 g, 55 mmol) in acetic acid (100 mL) was heated at 100 °C for overnight. After completion of reaction, evaporated the solvent under reduced pressure. The residue was dissolved in EtOAc (200 mL), washed with water (2 x 100 mL) and brine (1 x 100 mL). The organic layer was dried over sodium sulfate and evaporated under reduced pressure to give tert-butyl 2-(1H-pyrrol- 1-yl)-6, 7-dihydrothiazolo[5,4-c]pyridine-5(4H)-carboxylate **3**. Yield: 10.9 g (78%). MP: 135-37 °C. MS: m/z 306 (M+1). ^{1}H NMR (DMSO-d6): δ 1.32(s, 9H), 2.67(t, 2H), 3.48(t, 2H), 4.42(s, 2H), 6.31(d, 2H), 7.31(d, 2H); MS: m/z 306 (M+1). Anal. Calcd. (%) For $C_{15}H_{19}N_3O_2S$: C, 58.99; H, 6.27; N, 13.76; O, 10.48; S, 10.50. Found: C, 58.91; H, 6.34; N, 13.72; O, 10.36; S, 10.57.

Synthesis of 2-(1H-pyrrol-1-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine (4). To a stirred solution of compound **3** (10.9 g, 36 mmol) in dichloromethane (30 mL) was added TFA (30 mL) at 20 °C for 4 h. After concentration to dryness, the residue was partitioned between saturated aqueous $NaHCO_3$ solution (50 mL) and CH_2Cl_2. The organic layer washed with water and once with brine. The organic layer was dried over sodium sulfate and then evaporated under reduce pressure to give preparation of 2-(1H-pyrrol-1-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine **4**. Yield: 6.01 g (82%). MP: 160-162°C. ^{1}H NMR (DMSO-d6): δ 2.63(t, 2H), 3.47(t, 2H), 4.41(s, 2H), 6.29(d, 2H), 7.33(d, 2H); MS: m/z 206 (M+1). Anal. Calcd. (%) For $C_{10}H_{11}N_3S$: C, 58.51; H, 5.40; N, 20.47; S, 15.62. Found: C, 58.57; H, 5.31; N, 20.43; S, 15.65.

General Procedure for preparation of 2-(1H-pyrrol-1-yl)-5-(4-aryl/heteroaryl sulfonyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine (5a-o). Aryl/heteroaryl sulfonyl chloride (2.4 mol) and DIPEA (4 mmol) were successively added to a solution of 2-(1H-pyrrol-1-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine **4** (0.3 g, 2 mmol) in anhydrous DMF (3 mL). The mixture was stirred at 20 °C for 5 h and then diluted with EtOAc (25 mL) and washed with saturated aqueous $NaHCO_3$ (25 mL) and brine (25 mL). The aqueous layer was re-extracted with EtOAc (25 mL), and the combined organic layer were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed on silica gel, eluting with a gradient of 10-50% EtOAc/Hexane to give 2-(1H-pyrrol-1-yl)-5-(4-aryl/heteroaryl sulfonyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine (**5a-o)**.

5-(2-chloro-5-(trifluoromethyl)phenylsulfonyl)-2-(1H-pyrrol-1-yl)- 4,5,6,7 tetrahydrothiazolo [5,4-c]pyridine (5a). IR: -SO_2- 1330, 1167 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 2.54(t, 2H), 3.43(t, 2H), 4.37(s, 2H), 6.31(s, 2H), 7.39(d, 2H), 7.45(d, 1H), 7.69(d, 1H), 7.89(s, 1H); MS: m/z 448 (M+1). Anal. Calcd. (%) For $C_{17}H_{13}ClF_3N_3O_2S_2$: C, 45.59;

H, 2.93; Cl, 7.92; F, 12.73; N, 9.38; O, 7.14; S, 14.32 found: C, 45.63; H, 2.89; Cl, 7.97; F, 12.65; N, 9.31; O, 7.19; S, 14.29.

2-(1H-pyrrol-1-yl)-5-(4-(trifluoromethoxy)phenylsulfonyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine (5b). IR: -SO_2- 1334, 1160 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 2.50(t, 2H), 3.49(t, 2H), 4.38(s, 2H), 6.30(s, 2H), 7.35(d, 2H), 7.45(d, 2H), 7.67(d, 2H); MS: m/z 430 (M+1). Anal. Calcd. (%) For $C_{17}H_{14}F_3N_3O_3S_2$: C, 47.55; H, 3.29; F, 13.27; N, 9.78; O, 11.18; S, 14.93 found: C, 47.59; H, 3.34; F, 13.21; N, 9.75; O, 11.10; S, 14.83.

5-(3,4-difluorophenylsulfonyl)-2-(1H-pyrrol-1-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine (5c). IR: -SO_2- 1337, 1154 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 2.53(t, 2H), 3.47(t, 2H), 4.36(s, 2H), 6.31(s, 2H), 7.36(d, 2H), 7.58(d, 2H), 7.63(d, 1H); MS: m/z 382 (M+1). Anal. Calcd. (%) For $C_{16}H_{13}F_2N_3O_2S_2$: C, 50.38; H, 3.44; F, 9.96; N, 11.02; O, 8.39; S, 16.81 found: C, 50.31; H, 3.49; F, 9.89; N, 11.08; O, 8.31; S, 16.79

2-(1H-pyrrol-1-yl)-5-(3-(trifluoromethyl)phenylsulfonyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine (5d). IR: -SO_2- 1345, 1169 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 2.56(t, 2H), 3.49(t, 2H), 4.38(s, 2H), 6.34(s, 2H), 7.31(d, 2H), 7.42(d, 2H), 7.59(d, 1H), 7.79(s, 1H). MS: m/z 414 (M+1). Anal. Calcd. (%) For $C_{17}H_{14}F_3N_3O_2S_2$: C, 49.39; H, 3.41; F, 13.79; N, 10.16; O, 7.74; S, 15.51 found: C, 49.43; H, 3.47; F, 13.73; N, 10.19; O, 7.69; S, 15.42

2-(1H-pyrrol-1-yl)-5-(4-(trifluoromethyl)phenylsulfonyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine (5e). IR: -SO_2- 1340, 1161 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 2.53(t, 2H), 3.46(t, 2H), 4.39(s, 2H), 6.32(s, 2H), 7.34(d, 2H), 7.45(d, 2H), 7.75(d, 2H). MS: m/z 414 (M+1). Anal. Calcd. (%) For $C_{17}H_{14}F_3N_3O_2S_2$: C, 49.39; H, 3.41; F, 13.79; N, 10.16; O, 7.74; S, 15.51 found: C, 49.36; H, 3.59; F, 13.66; N, 10.12; O, 7.75; S, 15.54.

5-(4-isopropylphenylsulfonyl)-2-(1H-pyrrol-1-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine (5f). IR: -SO_2- 1345, 1171 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 1.21(s, 6H), 2.54(t, 2H), 2.82(m, 1H), 3.46(t, 2H), 4.37(s, 2H), 6.38(s, 2H), 7.29(s, 2H), 7.64(d, 2H), 7.71(d, 2H). MS: m/z 388 (M+1). Anal. Calcd. (%) For $C_{19}H_{21}N_3O_2S_2$: C, 58.89; H, 5.46; N, 10.84; O, 8.26; S, 16.55 found: C, 58.95; H, 5.371; N, 10.81; O, 8.14; S, 16.67.

5-(phenylsulfonyl)-2-(1H-pyrrol-1-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine (5g). IR: -SO_2- 1342, 1168 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 2.50(t, 2H), 3.49(t, 2H), 4.39(s, 2H), 6.30(s, 2H), 7.35(d, 2H), 7.82(t, 1H), 7.69(d, 2H), 7.84(d, 2H). MS: m/z 345 (M+1). Anal. Calcd. (%) For $C_{16}H_{15}N_3O_2S_2$: C, 55.63; H, 4.38; N, 12.16; O, 9.26; S, 18.56 found: C, 55.75; H, 4.41; N, 12.06; O, 9.13; S, 18.63.

2-(1H-pyrrol-1-yl)-5-(m-tolylsulfonyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine (5h). IR: -SO_2- 1345, 1174 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 2.23(s, 3H), 2.61(t, 2H), 3.43(t, 2H), 4.37(s, 2H), 6.29(s, 2H), 7.15(d, 2H), 7.39(t, 2H), 7.51(d, 1H); 7.59(s, 1H); MS: m/z 360 (M+1). Anal. Calcd. (%) For $C_{17}H_{17}N_3O_2S_2$: C, 56.80; H, 4.77; N, 11.69; O, 8.90; S, 17.84 found: C, 56.76; H, 4.83; N, 11.61; O, 8.98; S, 17.74.

5-(3,4-dimethoxyphenylsulfonyl)-2-(1H-pyrrol-1-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine (5i). IR: -SO_2- 1351, 1168 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 2.63(t, 2H), 3.57(t, 2H), 3.81(s, 6H), 4.46(s, 2H), 6.31(d, 2H), 7.35(d, 2H), 7.41(d, 2H), 7.48(s, 1H); MS: m/z 406 (M+1). Anal. Calcd. (%) For $C_{18}H_{19}N_3O_4S_2$: C, 53.32; H, 4.72; N, 10.36; O, 15.78; S, 15.82 found: C, 53.39; H, 4.65; N, 10.42; O, 15.61; S, 15.74.

4-(2-(1H-pyrrol-1-yl)-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-ylsulfonyl)-3,5-dimethylisoxazole (5j) IR: -SO_2- 1347, 1159 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 2.18(s, 3H), 2.35(s, 3H), 2.66(t, 2H), 3.58(t, 2H), 4.47(s, 2H), 6.33(d, 2H), 7.39(d, 2H); MS: m/z 365 (M+1). Anal. Calcd. (%) For $C_{15}H_{16}N_4O_3S_2$: C, 49.43; H, 4.43; N, 15.37; O, 13.17; S, 17.60 found: C, 49.51; H, 4.55; N, 15.41; O, 13.22; S, 17.71**.**

Methyl 3-(2-(1H-pyrrol-1-yl)-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-ylsulfonyl)thiophene-2-carboxylate (5k). IR: -SO_2- 1352, 1167 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 2.59(t, 2H), 3.49(t, 2H), 3.83(s, 3H), 4.42(s, 2H), 6.29(d, 2H), 7.31(d, 2H),7.49(d,1H), 7.65(s, 1H); MS: m/z 410 (M+1). Anal. Calcd. (%) For $C_{16}H_{15}N_3O_4S_3$: C, 46.93; H, 3.69; N, 10.26; O, 15.63; S, 23.49 found: C, 46.91; H, 3.59; N, 10.21; O, 15.71; S, 23.59.

5-(4-tert-butylphenylsulfonyl)-2-(1H-pyrrol-1-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine (5l). IR: -SO_2- 1345, 1159 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 1.24(s, 9H), 2.69(t, 2H), 3.48(t, 2H), 4.37(s, 2H), 6.30(d, 2H), 7.31(d, 2H), 7.60(d, 2H), 7.74(d, 2H); MS: m/z 402 (M+1). Anal. Calcd. (%) For $C_{20}H_{23}N_3O_2S_2$: C, 59.82; H, 5.77; N, 10.46; O, 7.97; S, 15.97 found: C, 59.79; H, 5.85; N, 10.31; O, 7.95; S, 15.84.

4-(2-(1H-pyrrol-1-yl)-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-ylsulfonyl)benzonitrile (5m). IR: -SO_2- 1343, 1164 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 2.67(t, 2H), 3.45(t, 2H), 4.39(s, 2H), 6.28(d, 2H), 7.32(d, 2H), 7.69(d, 2H),

7.79(d, 2H); MS: m/z 371 (M+1). Anal. Calcd. (%) For $C_{17}H_{14}N_4O_2S_2$: C, 55.12; H, 3.81; N, 15.12; O, 8.64; S, 17.31 found: C, 55.22; H, 3.74; N, 15.09; O, 8.74; S, 17.22.

4-(4-(2-(1H-pyrrol-1-yl)-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-ylsulfonyl)benzyl)morpholine (5n). IR: -SO_2- 1339, 1171 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 2.26(d, 4H), 2.64(s, 2H), 3.49-3.52(m, 8H), 4.58(s, 2H), 6.30(s, 2H), 7.30(s, 2H), 7.49(d, 2H), 7.78(d, 2H); MS: m/z 445 (M+1). Anal. Calcd. (%) For $C_{21}H_{24}N_4O_3S_2$: C, 56.73; H, 5.44; N, 12.60; O, 10.80; S, 14.43 found: C, 56.83; H, 5.39; N, 12.65; O, 10.71; S, 14.51.

2-(1H-pyrrol-1-yl)-5-(2-(trifluoromethoxy)phenylsulfonyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine (5o). IR: -SO_2- 1339, 1164 cm^{-1}; ^{1}H NMR (DMSO-d6): δ 2.49(t, 2H), 3.45(t, 2H), 4.37(s, 2H), 6.29(s, 2H), 7.33(d, 2H), 7.41(d, 1H), 7.48(d, 1H), 7.67(d, 2H); MS: m/z 430 (M+1). Anal. Calcd. (%) For $C_{17}H_{14}F_3N_3O_3S_2$: C, 47.55; H, 3.29; F, 13.27; N, 9.78; O, 11.18; S, 14.93 found: C, 47.43; H, 3.21; F, 13.32; N, 9.83; O, 11.24; S, 14.81.

RESULTS AND DISCUSSION

Chemistry: General methods used for the synthesis of the aryl/heteroaryl sulfonamide are illustrated in **scheme 1.** As shown in **scheme 1**, the synthetic route involves the Gewald reaction of boc-piperidone with cyanamide and sulfur in presence of morpholine in refluxing ethanol to obtain 2-amino thiazole derivative **2**. Compound **2** reacted with 2,5-dimethoxy teterahydrofuran in refluxing acetic acid furnished pyrrole derivative **3**. The hydrolysis of carbamate group by TFA furnished secondary amine derivative **4**. The target compounds were obtained with good yield, by reacting secondary amine **4** with various aryl or heteroaryl sulfonyl chloride in presence of DIPEA as base. The structures of all the synthesized compounds were confirmed by elemental analyses and ^{1}H NMR, MS & IR spectral studies. The mass spectrum of all the synthesized compounds showed a molecular ion peak as M+1. The physical characterization data are listed in **Table 1**.

Table 1. Characteristics physical data of tetrahydrothiazolo[5,4-c]pyridine derivatives (5a-o)

Sr. No.	Compound Code	R	M.P. (°C)	Yield (%)
1	5a	2-Chloro 5-Trifluromethylphenyl	139-141	75
2	5b	4- trifluoromethoxyphenyl	280-282	83
3	5c	3,4-difluorophenyl	168-170	85
4	5d	3-trifluoromethyl phenyl	141-143	69
5	5e	4-trifluoromethyl phenyl	211-213	81
6	5f	4-isopropyl	161-163	87
7	5g	phenyl	210-212	81
8	5h	m-tolyl	160-162	76
9	5i	3,4-dimethoxy phenyl	284-286	86
10	5j	3,5-di methyl isooxazole 4-sulfonyl	175-177	71
11	5k	2-carbomethoxy 3-thiophene sulfonyl	169-171	79
12	5l	4-t-butyl phenyl	223-225	83
13	5m	4-Cyano	189-191	88
14	5n	4-(morpholin-4-ylmethyl)benzenesulfonyl	203-205	68
15	5o	2-trifluoromethoxy phenyl	261-263	81

Biological activities

Antibacterial and antifungal activities: The newly synthesized derivatives were evaluated for their *in vitro* antibacterial activity against gram negative Escherichia coli and pseudomonas aeruginosa, gram positive Bacillus cereus and Bacillus megaterium and antifungal activity against aspergillus niger and Aspergillus flavus by micro broth dilution method. The standard strains used for screening antibacterial and antifungal activities were procured from institute of microbial technology (IMTECH), Chandigarh, India. The MIC values are given in **Table-2**. The standard drugs used for antibacterial activity were Streptomycin, Ampicillin and Nystatin for antifungal activity. Mueller Hinton Broth was used as nutrient medium for bacteria and Sabouraud Dextrose Broth for fungal to grow. Inoculums size for test strain was adjusted to 10^8 CFU/mL by comparing the turbidity. The serial dilutions were prepared in primary and secondary screening. The target compounds and standard drugs were dissolved in DMSO-water at a concentration of 2.0 mg/ml. In primary screening, 500 µg/mL, 250 µg/mL, and 125 µg/mL concentrations of the synthesized drugs were taken. Data were not taken for the initial solution because of the high DMSO concentration (10%). The actively synthesized drugs found in this primary screening were further tested in a second set of dilution against all microorganisms. In secondary screening, the drugs found active in primary screening were similarly diluted to obtain 100 µg/mL, 50 µg/mL, and 25 µg/mL, 12.5 µg/mL, and 6.25 µg/mL concentrations. The inoculated wells were incubated overnight at 37ºC in a humid atmosphere overnight. The highest dilution showing at least 99% inhibition zone is taken as MIC [19].

The MIC values revealed that the synthesized compounds showed moderate to good inhibition. Compound **5f** shows excellent activities against bacterial and fungal strains. Compounds **5i** and **5j** exhibited good activities against

bacterial strains. Compound **5h** and **5k** shown good activity against E. coli and B. megaterium respectively. The MIC values of antifungal activity shown that compound **5a** and **5b** exhibited good activity against all fungal strain. Compound **5k** and **5l** shows good activity against A. flavus and compound **5h** shows good activity against A. niger.

Table 2: Antibacterial and antifungal activity of tetrahydrothiazolo[5,4-c]pyridine derivatives (5a-o)

	Antibacterial MIC (µg/mL)				Antifungal MIC (µg/mL)	
Compounds	**E. coli**	**P. aeruginosa**	**B. cereus**	**B. megaterium**	**A. niger**	**A. flavus**
Streptomycin	50	-	-	-	-	-
Ampicillin	-	100	100	100	-	-
Nystatin	-	-	-	-	100	100
5a	1000	1000	1000	1000	500	500
5b	1000	1000	1000	1000	500	500
5c	1000	1000	1000	1000	1000	1000
5d	1000	1000	1000	1000	1000	1000
5e	1000	1000	500	1000	1000	1000
5f	125	500	125	500	1000	1000
5g	1000	1000	1000	1000	1000	1000
5h	500	1000	1000	1000	500	1000
5i	500	500	500	500	1000	1000
5j	250	500	500	500	1000	1000
5k	1000	1000	500	1000	1000	500
5l	1000	1000	500	1000	1000	500
5m	500	500	500	500	500	500
5n	500	500	500	500	1000	1000
5o	1000	500	1000	500	1000	1000

CONCLUSION

we have devised a small library of structurally diverse tetrahydrothiazolo[5,4-c]pyridine derivatives in good to excellent yield and screened for their *in-vitro* biological activity with the aim of discovering innovative lead molecule as potent antimicrobial agents and potential privileged medicinal scaffold.

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