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Synthesis, Characterization and Antimicrobial Evaluation of Azetidinone and Tetrazole Derivatives of Benzo[b]thiophene

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ABSTRACT

Different 3-chloro-1-benzothiophene-2-carbonyl chloride reacted with hydrazine hydrate to give compounds 3-chloro-1-benzothiophene-2-carbohydrazide (1a-d).Further indole-3-carboxaldehyde reacted with compounds (1a-d) in the presence of glacial acetic acid and methanolic media to produce Schiff bases 3-chloro-N'-[1H-indol-3-ylmethylidene]-1-benzothiophene-2-carbohydrazid (2a-d). Cyclization reaction between compound (2a-d), chloroacetylchloride and trimethylamine in the presence of 1,4-dioxane as solvent, yields azetidinone derivatives 3-chloro-N-[3-chloro-2-(1H-indol-3-yl)-4-oxoazetidin-1-yl]-1-benzo thiophene-2-carboxamide (3a-d). In an another route compounds (2a-d) were refluxed with sodiumazide to give corresponding tetrazole derivatives3-chloro-N-[5-(1H-indol-3-yl)-2,5-dihydro-1H-tetrazol-1-yl]-1-benzothiophene-2-carboxamide(4a-d).The constitution of all the synthesized products has been supported by elemental analysis and spectral studies. The synthesized compounds (3a-d) and (4a-d) were screened for their antimicrobial activity. They were found toexhibit potent antibacterial activity.

Keywords: 3-chlorobenzo[b]thiophene-2-carbonylchloride, azetidinone, tetrazole, antibacterial and antifungal activity.

INTRODUCTION

Heterocyclic ring systems are important constituent of majority of naturally occurring and synthetic drugs. These ring systems received great attention because of their versatile utility in various aspects of medicinal chemistry.

Being a heterocyclic compound, benzothiophene finds use in research as a starting material for the synthesis of larger, usually bioactive structures. It is found within the chemical structures of pharmaceutical drugs such as raloxifene, zileuton and sertaconazole. Benzo[b]thiophene is class of fused heterocycles that is of considerable interest because of the diverse range of their biological activities such as anti-cancer[1-3], anti-inflammatory[4,5], antiviral[6], anti-microbial[7,8], antimalarial[9], anti-tuber cular[10], antioxidant[11]etc.

The β-lactam heterocycles are still the most prescribed antibiotics used in medicine. They are considered as an important contribution of science to humanity. The most widely used antibiotics such as the

penicillins, cephalosporins, carumonam, aztreonam, thienamycine and the nocardicins all contain β-lactam rings. The long-term use of β-lactam antibiotics exerts selective pressure on bacteria and permits the proliferation of resistant organisms. The development of several synthetic and semi-synthetic β-lactam antibiotics by the pharmaceutical industry was due to the growing resistance of bacteria towards the β-lactam antibiotics and the need for medicines with a more specific antibacterial activity. Number of N-substituted and unsubstituted β-lactam derivatives have been reported to show antimalarial activity[12], Anti-tubercular activity[13,14], Anti-inflammatory activity[15], anticancer activity[16], anti-oxidant activity [17], antimicrobial[18,19], antifungal[20].

The synthesis of heterocyclic rings containing nitrogen atoms became of great importance in medicinal chemistry. Interest in tetrazole chemistry over the past few years has been increasing rapidly because of its wide range of applications, mainly as a result of the role played by this heterocyclic functionality in medicinal chemistry. The major area of interest has been the application of tetrazoles in pharmacological compounds with antibacterial[21-23], antifungal[24,25], analgesic[26-28], antinociceptive[29], antican cer[30], anticonvulsant[31], antidiabetic[32], antiulcer[33] and antitubercular[34,35], glycosidase inhibit ory[36], antihypertensive[37], anti-inflammatory[38-41], antipyretic[42] activities.

MATERIALS AND METHODS

The reagent grade chemicals were purchased from commercial sources and purified either by distillation or recrystallization before use. Melting points of all synthesized compounds were taken in open capillaries and are uncorrected. The IR spectra were recorded using KBr discs on a Perkin Elmer - Spectrum RX-FTIR Spectrophotometer. The NMR spectra were carried out on a BRUKER Avance II Spectrophotometer at 400 MHz, using TMS as an internal reference and DMSO as solvent. The mass spectra were recorded on Waters, Micromass Q-TOF micro Separation. Elemental analysis was done on "Thermo Scientific (FLASH 2000) CHN Elemental Analyser." Purity of synthesized compounds was checked by TLC using silica gel plates; toluene and ethyl acetate as developing solvent, and the spots were exposed in an iodine chamber.

Synthesis of *3-chloro-1-benzothiophene-2-carbohydrazide (1a):* To a solution of benzo[b]thiophene (0.01mol) in methanol, hydrazine hydrate (99%) in excess was added and the reaction mixture was reflux for 4 h. The completion of the reaction was monitored by TLC. After completion, the reaction mixture was cooled and poured into ice. The solid separated was filtered, washed with water, dried and recrystallized by using methanol. Similarly the compounds (1b-d) were synthesized.
IR (KBr cm^{-1}):3106 (-CH str., ArH), 728 (C-Cl str.), 1727 (-C=O str.), 1572(characteristic of C-N str.) cm^{-1}, 3318 (-NH_2str.). 1H-NMR (400MHz, DMSO-d6)δ:7.23-7.78 (m,4H, ArH),8.34 (t,1H,NH-N),3.18(d, 2H,N-NH_2). Mass (m/z): 226$[M]^{+\cdot}$, 228$[M+2]^{+\cdot}$.

3, 6-dichloro-1-benzothiophene-2-carbohydrazide (1b):IR (KBr cm^{-1}): 3134 (-CH str., ArH), 749 (C-Cl str.), 1739 (-C=O str.), 1589 (characteristic of C-N str.), 3352 (-NH_2 str.). 1H-NMR (400MHz, DMSO-d6)δ: 7.38-7.92 (m,3H, ArH), 8.56 (t,1H,NH-N), 3.45 (d, 2H,N-NH_2). Mass (m/z): 226$[M]^{+\cdot}$, 228$[M+2]^{+\cdot}$, 230$[M+4]^{+\cdot}$.

3-chloro-6-fluoro-1-benzothiophene-2-carbohydrazide (1c):IR (KBr cm^{-1}): 3168 (-CH str., ArH), 781 (C-Cl str.), 1767 (-C=O str.), 1612 (characteristic of C-N str.), 3389 (-NH_2 str.), respectively. 1H-NMR(400MHz, DMSO-d6)δ: 7.49-8.12 (m,4H, ArH), 8.78 (t,1H,NH-N), 3.62 (d, 2H,N-NH_2). Mass (m/z): 226$[M]^{+\cdot}$, 228$[M+2]^{+\cdot}$.

3-chloro-6-hydroxy-1-benzothiophene-2-carbohydrazide (1d):IR (KBrcm^{-1}): 3088 (-CH str., ArH), 703 (C-Cl str.), 1711 (-C=O str.), 1548 (characteristic of C-N str.), 3289 (-NH_2 str.). 1H-NMR (400MHz,

DMSO-d6)δ: 7.05-7.52 (m,4H, ArH), 8.21 (t,1H,NH-N), 2.98 (d, 2H,N-NH_2). Mass (m/z): 226$[M]^{+\cdot}$, 228$[M+2]^{+\cdot}$.

Synthesis of *3-chloro-N'-[1H-indol-3-ylmethylidene]-1-benzothiophene-2-carbohydrazide(2a):* A mixt ure of equimolar quantities (0.01 mol each) of Indole-3-carboxaldehyde and compound **(1a)** were refluxed for 6 h in ethanol with few drops of glacial acetic acid. The reaction mixture was cooled at RT and pour into ice cold water. The separated product was filtered out. The Schiff bases obtained was used for next step to form compounds (3a) and (4a). The compounds (2b-d) were synthesized by the same method.
IR (KBr cm^{-1}): 3114 (-CH str., ArH), 732 (C-Cl str.), 1728 (-C=O str.), 1578 (characteristic of C-N str.), 1636 (-C=Nstr.), 3218 (NH str.). 1H-NMR (400MHz, DMSO-d6) δ: 7.28-7.84(m, 8H, ArH), 8.43 (s,1H,NH-N), 8.75 (s, 1H, H-C=N). Mass (m/z): 226$[M]^{+\cdot}$, 228$[M+2]^{+\cdot}$.

3,6-dichloro-N'-[1H-indol-3-ylmethylidene]-1-benzothiophene-2-carbohydrazide(2b): IR(KBrcm^{-1}):3132 (-CH str., ArH), 748 (C-Cl str.), 1742 (-C=O str.), 1591 (characteristic of C-N str.), 1652 (-C=Nstr.), 3229 (NH str.). 1H-NMR (400MHz, DMSO-d6)δ: 7.39-7.94 (m,8H, ArH), 8.54 (s,1H, NH-N), 8.89 (s, 1H, H-C=N). Mass (m/z): 226$[M]^{+\cdot}$, 228$[M+2]^{+\cdot}$.

***3-chloro-6-fluoro-N'-[1H-indol-3-ylmethylidene]-1-benzothiophene-2-carbohydrazide (2c)*:** IR(KBrcm^{-1}): 3149 (-CH str., ArH), 768 (C-Cl str.), 1771 (-C=O str.), 1610 (characteristic of C-N str.), 1674 (-C=Nstr.), 3249 (NH str.). 1H-NMR (400MHz, DMSO-d6)δ: 7.48-8.16 (m,8H, ArH), 8.72 (s,1H, NH-N), 9.12 (s, 1H, H-C=N). Mass (m/z): 226$[M]^{+\cdot}$, 228$[M+2]^{+\cdot}$.

***3-chloro-6-hydroxy-N'-[1H-indol-3-ylmethylidene]-1-benzothiophene-2-carbohydrazide(2d)*:**IR(KBrcm^{-1}): 3088 (-CH str., ArH), 708 (C-Cl str.), 1713 (-C=O str.), 1552 (characteristic of C-N str.), 1619 (-C=Nstr.), 3192 (NH str.). 1H-NMR (400MHz, DMSO-d6)δ: 7.11-7.62(m,8H, ArH), 8.14 (s,1H,NH-N), 8.48 (s, 1H, H-C=N). Mass (m/z): 226$[M]^{+\cdot}$, 228$[M+2]^{+\cdot}$.

Synthesis of *3-chloro-N-[3-chloro-2-(1H-indol-3-yl)-4-oxoazetidin-1-yl]-1-benzothiophene-2-carbo xamide(3a):* A solution of compound **(2a)** (0.01mol) in dioxane was added to a well-stirred mixture of monochloroacetyl chloride (0.01 mol) and triethyl amine (0.01 mol) at 0-5^oC. The reaction mixture was stirred at RT for an hour and then refluxed for 8 h. The reaction mixture was then poured into crushed ice, filtered and washed with water. The solid product was dried and recrystallized from suitable solvents. Similarly the compounds (3b-d) were synthesized.
IR (KBrcm^{-1}): 3130 (-CH str., ArH), 732 (C-Cl str.), 1739 (-C=O str.), 1570 (characteristic of C-N str.), 3210 (NH str.). ^{1}H-NMR (400MHz, DMSO-d6)δ: 7.20-7.71(m,8H, ArH), 8.39 (s,1H,NH-N),10.4 (s, 1H, NH proton of benzopyrole).4.81 proton of azatedine ring bearing substituted phenyl, 5.51 proton of azatedine ring bearing (Cl), Mass (m/z): 226$[M]^{+\cdot}$, 228$[M+2]^{+\cdot}$.^{13}C- NMR (400 MHz, DMSO-d6) δ: 122.3-135.8 (12C, Ar–C), 129.8-141.6 (2C, thiophene ring) 160.5 (1C, C=O), 163.6(1C, C=O of azetidinone ring), 67.8 (1C, C-Cl–Azetidinone ring), 130.2-116.9 (2C, pyrole ring).

3,6-dichloro-N-[3-chloro-2-(1H-indol-3-yl)-4-oxoazetidin-1-yl]-1-benzothiophene-2-carboxamide(3b):
IR (KBr cm^{-1}): 3150 (-CH str., ArH), 747 (C-Cl str.), 1761 (-C=O str.), 1588 (characteristic of C-N str.), 3221 (NH str.). 1H-NMR (400MHz, DMSO-d6)δ: 7.33-7.90 (m,8H, ArH), 8.55 (s,1H,NH-N), (s, 1H, NH proton of benzopyrole). 4.95 proton of azatedine ring bearing substituted phenyl, 5.66 proton of azatedine ring bearing (Cl), Mass (m/z): 226$[M]^{+\cdot}$, 228$[M+2]^{+\cdot}$.^{13}C- NMR (400 MHz, DMSO-d6) δ: 118.6-141.8 (12C, Ar–C), 126.8-144.1 (2C, thiophene ring) 162.1 (1C, C=O), 165.1(1C, C=O of azetidinone ring), 68.2 (1C, C-Cl–Azetidinone ring), 123.2-119.7 (2C, pyrole ring).

3-chloro-N-[3-chloro-2-(1H-indol-3-yl)-4-oxoazetidin-1-yl]-6-fluoro-1-benzothiophene-2-carboxamide (3c):IR (KBr cm^{-1}): 3165 (-CH str., ArH), 760 (C-Cl str.), 1788 (-C=O str.), 1608 cm^{-1} (characteristic of C-N str.), 3239 (NH str.). 1H-NMR (400MHz, DMSO-d6)δ: 7.49-8.21(m,8H, ArH), 8.71 (s,1H,NH-N), (s,

1H, NH proton of benzopyrole). 5.18 proton of azatedine ring bearing substituted phenyl, 5.86 proton of azatedine ring bearing (Cl), Mass (m/z): 226[M]$^{+\cdot}$, 228[M+2]$^{+\cdot}$.^{13}C- NMR (400 MHz, DMSO-d6) δ: 114.9-143.9 (12C, Ar–C), 125.1-147.7 (2C, thiophene ring) 164.5 (1C, C=O), 166.3(1C, C=O of azetidinone ring), 69.8 (1C, C-Cl–Azetidinone ring), 121.3-114.9 (2C, pyrole ring).

3-chloro-N-[3-chloro-2-(1H-indol-3-yl)-4-oxoazetidin-1-yl]-6-hydroxy-1-benzothiophene-2-carboxamide (3d): IR (KBr cm^{-1}): 3080 (-CH str.,ArH), 705 (C-Cl str.), 1690 (-C=O str.), 1555 (characteristic of C-N str.), 3187 (NH str.). 1H-NMR (400MHz, DMSO-d6)δ: 7.0-7.62(m,8H, ArH), 8.10 (s,1H,NH-N), (s, 1H, NH proton of benzopyrole) 4.62 proton of azatedine ring bearing substituted phenyl, 5.34 proton of azatedine ring bearing (Cl), Mass (m/z): 226[M]$^{+\cdot}$, 228[M+2]$^{+\cdot}$.^{13}C- NMR (400 MHz, DMSO-d6) δ: 109.3-151.1 (12C,Ar–C), 121.1-149.2 (2C, thiophene ring) 165.9 (1C, C=O), 167.1(1C, C=O of azetidinone ring), 63.8 (1C, C-Cl–Azetidinone ring), 125.2-110.9 (2C, pyrole ring).

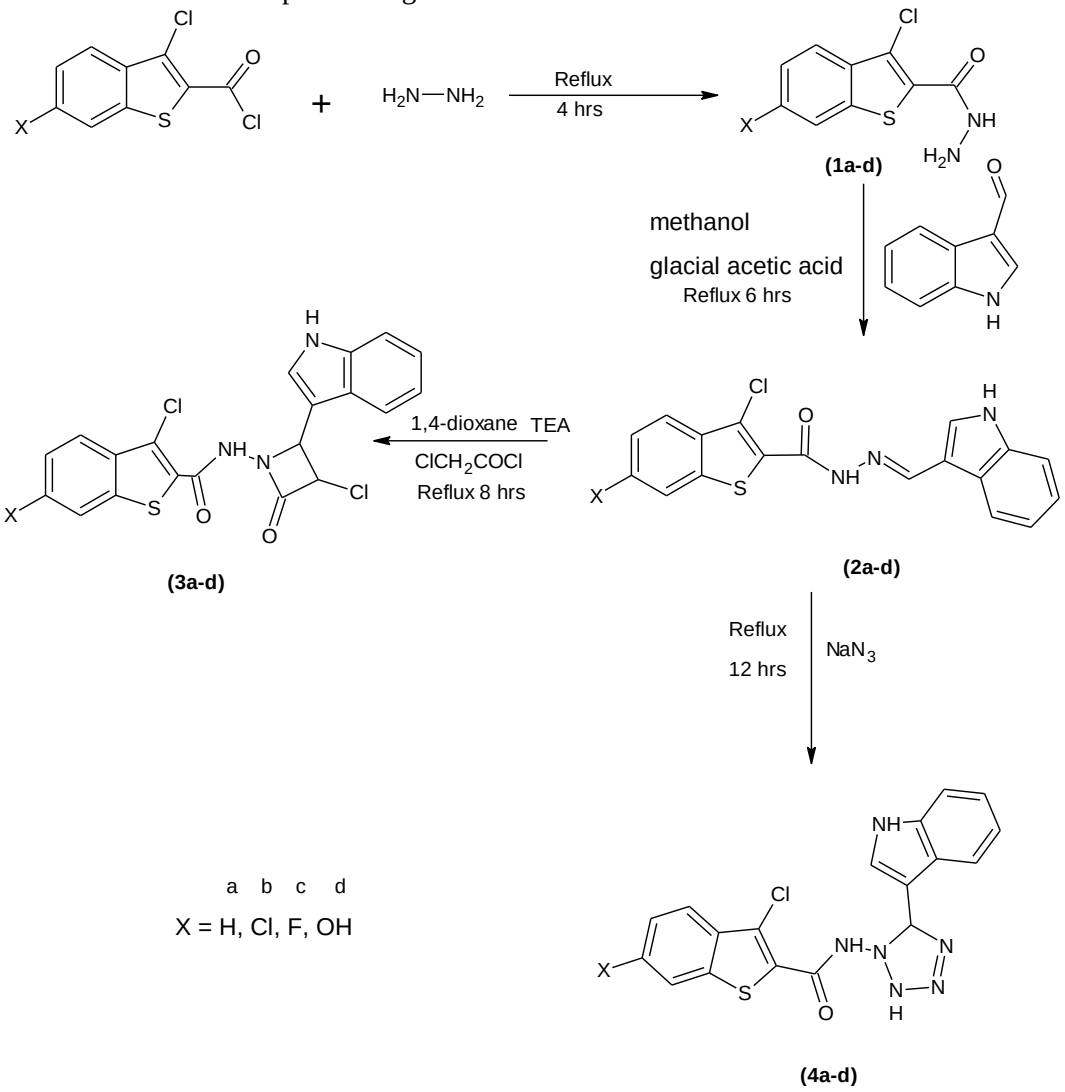
Synthesisof*3-chloro-N-[5-(1H-indol-3-yl)-2,5-dihydro-1H-tetrazol-1-yl]-1-benzothiophene-2-carboxamide (4a):*To a stirring solution of Schiff-base **(2a)** (0.01mol) in tetrahydrofuran, sodium azide (0.01mol) was mixed. The mixture was refluxed for (12 hr). The completion of reaction was checked by TLC. Then cooled the mixture at room temperature and the precipitate was filtered, washed with cold water,dried and recrystallized with suitable solvent. The compounds (4b-d) were synthesized by the same method.
IR (KBr cm^{-1}): 3119 (-CH str., ArH), 721 (C-Cl str.), 1740 (-C=O str.), 1563 (characteristic of C-N str.), 1482 (-N=Nstr.), 3218 (NH str.). 1H-NMR (400MHz, DMSO-d6)δ: 7.20-7.79(m,8H, ArH), 8.41 (s,1H, NH-N), 8.75 (s, 1H, H-C=N). Mass (m/z): 226[M]$^{+\cdot}$, 228[M+2]$^{+\cdot}$.^{13}C- NMR (400 MHz, DMSO-d6) δ: 122.1-135.2 (12C, Ar–C), 128.2-142.7 (2C, thiophene ring) 161.3 (1C, C=O), 94.8 (1C, C-tetrazole ring), 123.2-112.1 (2C, pyrole ring).

3,6-dichloro-N-[5-(1H-indol-3-yl)-2,5-dihydro-1H-tetrazol-1-yl]-1-benzothiophene-2-carboxamide (4b): IR (KBr cm^{-1}): 3130 (-CH str., ArH), 738 (C-Cl str.), 1770 (-C=O str.), 1572 (characteristic of C-N str.), 1493 (-N=Nstr.), 3241 (NH str.). 1H-NMR (400MHz, DMSO-d6)δ: 7.31-7.96(m,8H, ArH), 8.60 (s,1H,NH-N), 8.91 (s, 1H, H-C=N). Mass (m/z): 226[M]$^{+\cdot}$, 228[M+2]$^{+\cdot}$.^{13}C- NMR (400 MHz, DMSO-d6) δ: 120.7-139.8 (12C, Ar–C), 125.3-143.4 (2C, thiophene ring) 162.9 (1C, C=O), 95.4 (1C, C-tetrazole ring), 124.8-109.9 (2C, pyrole ring).

3-chloro-6-fluoro-N-[5-(1H-indol-3-yl)-2,5-dihydro-1H-tetrazol-1-yl]-1-benzothiophene-2-carboxamide (4c):IR (KBr cm^{-1}): 3155 (-CH str., ArH), 766 (C-Cl str.), 1789 (-C=O str.), 1590 (characteristic of C-N str.), 1518 (-N=Nstr.), 3268 (NH str.). 1H-NMR (400MHz, DMSO-d6)δ: 7.51-8.22(m,8H, ArH), 8.81 (s,1H,NH-N), 8.99 (s, 1H, H-C=N). Mass (m/z): 226[M]$^{+\cdot}$, 228[M+2]$^{+\cdot}$.^{13}C- NMR (400 MHz, DMSO-d6) δ: 117.1-144.2 (12C, Ar–C), 122.6-145.9 (2C, thiophene ring) 164.3 (1C, C=O), 96.1 (1C, C-tetrazole ring), 121.1-108.3 (2C, pyrole ring).

3-chloro-6-hydroxy-N-[5-(1H-indol-3-yl)-2,5-dihydro-1H-tetrazol-1-yl]-1-benzothiophene-2-carboxamide (4d): IR (KBr cm^{-1}): 3101(-CH str., ArH), 698 (C-Cl str.), 1717 (-C=O str.), 1538 (characteristic of C-N str.), 1416 (-N=Nstr.), 3188 (NH str.). 1H-NMR (400MHz, DMSO-d6)δ: 7.07-7.56(m,8H, ArH), 8.20 (s,1H,NH-N), 8.47 (s, 1H, H-C=N). Mass (m/z): 226[M]$^{+\cdot}$, 228[M+2]$^{+\cdot}$.^{13}C- NMR (400 MHz, DMSO-d6) δ: 108.8-148.9 (12C, Ar–C), 121.2-146.3 (2C, thiophene ring) 165.1 (1C, C=O), 95.2 (1C, C-tetrazole ring), 127.2-110.1 (2C, pyrole ring).

The reaction scheme of the compounds is given below



(4a-d)

Reaction Scheme

Biological Activity: The compounds (3a-d) and (4a-d) were screened for their antibacterial activity against Gram positive bacteria *Staphylococcus aureus,* Gram negative *Escherichia coli*, and fungal strain: *Candida albicans* and *Aspergillus clavatus*. Cefixime was used as a standard drug for antibacterial activity while Griseofulvin was used as a standard drug for antifungal activity. All the compounds were dissolved in dimethyl sulfoxide to give a concentration of 50 µg mL^{-1}, Muller-Hinton agar medium was used as culture medium. The method employed was agar disk diffusion method. The zones of inhibition were measured in mm.

RESULTS AND DISCUSSION

Chemistry: In the present investigation, synthesis of 3-chloro-N-[3-chloro-2-(1H-indol-3-yl)-4-oxo azetidin-1-yl]-1-benzothiophene-2-carboxamide (3a-d) and Synthesis of 3-chloro-N-[5-(1H-indol-3-yl)-2,5-dihydro-1H-tetrazol-1-yl]-1-benzothiophene-2-carboxamide (4a-d) are described. Different 3-chloro-1-benzothiophene-2-carbonyl chloride was allowed to reacts with hydrazine hydrate in methanol. Characterized by IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectral data. The IR spectra of compound (1a), showed an intense band at 3318 cm^{-1} for $NH_2$and 1572 cm^{-1}(characteristic of C-Nstr.). The 1H-NMR

spectra of these compounds displayed triplet for NH-N proton at δ 8.34 and doublet for N-NH_2proton at δ 3.1. Treatment of compound (1a-d) with indole-3-carboxaldehyde in methanol with few drops glacial acetic acid yields compound 3-chloro-N'-[1H-indol-3-ylmethylidene]-1-benzothiophene-2-carbohydrazide (2a-d) was confirmed by the appearance of intense band at 1636 cm^{-1} for -C=Nstr.,3218 cm^{-1} for NH str. and disappearance of NH_2 stretching at 3318$cm^{-1}$and 1H NMR spectra of these compounds displayed singlet for NH proton at δ 8.34 and singlet for H-C=N at δ 8.75. The absorption bands associated with other functionalities present are appeared in the expected regions. Cyclization reaction between compound (2a-d), chloroacetylchloride and trimethylamine, in the presence of 1,4-dioxane as solvent, yields compounds (3a-d),were confirmed by a new band at 728 cm^{-1} of C-Cl str.. In 1H-NMR spectra disappearance of N=CH signals of Schiff base also helped in assigning the structure of (3a-d). In alternative reaction compounds (2a-d) were allowed to reacts with sodiumazide to give corresponding tetrazole derivatives (4a-d),were confirmed by a new band at 1482 cm^{-1} of N=N str.

The results of physical and analytical data of the synthesized compounds are presented in **table 1**.

Table 1

S.No.	Mol. Formula	Mol. Weight	X	M.P. (^oC)	Yield (%)	% Found (Calcd.)		
						C	H	N
1a	$C_9H_7ClN_2OS$	227	H	185	85%	48.12(47.58)	2.99(3.08)	12.29(12.33)
1b	$C_9H_6Cl_2N_2OS$	262	Cl	178	84%	41.88(41.22)	2.38(2.29)	10.54(10.69)
1c	$C_9H_6ClFN_2OS$	245	F	172	79%	44.71(44.08)	2.51(2.45)	11.29(11.43)
1d	$C_9H_7ClN_2O_2S$	243	OH	182	81%	44.93(44.44)	2.83(2.88)	11.40(11.52)
2a	$C_{18}H_{12}ClN_3OS$	264	H	206	91%	61.89(61.02)	3.32(3.39)	11.81(11.86)
2b	$C_{18}H_{11}Cl_2N_3OS$	274	Cl	198	89%	56.07(55.52)	2.88(2.83)	10.63(10.80)
2c	$C_{18}H_{11}ClFN_3OS$	270	F	192	82%	58.45(58.06)	2.91(2.96)	11.18(11.29)
2d	$C_{18}H_{12}ClN_3O_2S$	262	OH	211	84%	58.89(58.54)	3.29(3.25)	11.28(11.38)
3a	$C_{20}H_{13}Cl_2N_3O_2S$	281	H	240	84%	55.13(55.81)	2.93(3.02)	09.74(09.77)
3b	$C_{20}H_{12}Cl_3N_3O_2S$	294	Cl	258	80%	51.03(51.61)	2.49(2.58)	08.98(09.03)
3c	$C_{20}H_{12}Cl_2FN_3O_2S$	288	F	247	79%	52.89(53.57)	2.63(2.68)	09.36(09.38)
3d	$C_{20}H_{13}Cl_2N_3O_3S$	278	OH	261	81%	53.38(53.81)	2.87(2.91)	09.39(09.42)
4a	$C_{18}H_{13}ClN_6OS$	304	H	278	79%	53.98(54.41)	3.22(3.27)	21.11(21.16)
4b	$C_{18}H_{12}Cl_2N_6OS$	312	Cl	282	80%	49.77(50.12)	2.69(2.78)	19.45(19.49)
4c	$C_{18}H_{12}ClFN_6OS$	294	F	270	72%	51.67(52.05)	2.83(2.89)	20.19(20.24)
4d	$C_{18}H_{13}ClN_6OS$	286	OH	292	77%	51.87(52.30)	3.09(3.15)	20.31(20.34)

APPLICATIONS

Antimicrobial Studies: From table 2, it can be concluded that compound 3d exhibited excellent anti bacterial and antifungal activities. For antibacterial activity of this series of compound 4d showed excellent activity, while compound 3c showed moderate activity against *E.Coli*. For *S. aureus* compounds 3c and 4b were excellent while 3b and 4c were good to moderately active. For antifungal activity, compound 3aexhibited excellent activity against both *C. albicans* and *A. Clavatus*. Compounds 4d, 4c and 3b were good to moderate against *A. Clavatus*.

Table 2 Antimicrobial evaluation of derivatives (3a-d) and (4a-d)

Group	***Concentration (μg mL^{-1})***	***Zone of inhibition in mm***			
		Staphylococcus aureus	***E. coli***	***Candida albicans***	***Aspergillus clavatus***
3a	50	*17 (.809)*	*13 (.520)*	20 (.909)	25 (.892)
3b	50	*19 (.904)*	*18 (.720)*	18 (81.82)	22 (.785)
3c	50	*20 (.952)*	*21 (.840)*	14 (.636)	21 (.75)

3d	50	*19 (.904)*	*23 (.920)*	21 (.954)	26 (.928)
4a	50	*17 (.809)*	*14 (.560)*	18 (.818)	21 (.75)
4b	50	*20 (.952)*	*15 (.600)*	13 (.590)	19 (.678)
4c	50	*19 (.904)*	*19 (.760)*	16 (.727)	22 (.785)
4d	50	*13 (.619)*	*22 (.880)*	19 (.863)	24 (.857)
Cefixime	50	21	25	-	-
Griseofulvin	50	-	-	22	28

CONCLUSIONS

In conclusion, synthesis of 3-chloro-N- [3-chloro-2-(1H-indol-3-yl) -4-oxoazetidin-1-yl]-1-benzothio phene-2-carboxamide (3a-d) and 3-chloro-N-[5-(1H-indol-3-yl)-2,5-dihydro-1H-tetrazol-1-yl]-1-benzo thiophene-2-carboxamide (4a-d) derivatives was accomplished from 3-chloro-1-benzothiophene. Antibacterial and antifungal activities of the newly synthesized compounds were evaluated and they exhibited well to moderate activities. The results indicate that compounds show better antibacterial activities compared to antifungal activity. Further, in general the compounds having –OH substituent have still better activities compared to other compounds, which do not have this substituent. Finally, it is concluded that these potential candidates might be useful in the future to develop an effective chemotherapeutic agents.

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