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Synthesis of novel Sultams containing thiazolidin-4-one heterocycles

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ABSTRACT

*Novel Thiazolidin-4-one Synthesis of 3-(2-(1,1-dioxido-1,2- thiazetidin-2-yl)ethyl)-2-phenylthiazolidin-4-one **8 (a-f)** were synthesized by condensation reaction between synthesis of 2-(2-(4-substituted benzylideneamino)ethyl)-1,2-thiazetidine 1,1-dioxide **6(a-f)** and a mixture of mercaptoacetic acid and anhydrous Zinc chloride. Synthesis of 2-(2-(4-substituted benzylideneamino)ethyl)-1,2-thiazetidine 1,1-dioxide **6(a-f)** was condensed with 4-substituted benzaldehyde in absolute alcohol. The synthesis of 2-(2-aminoethyl)-1,2-thiazetidine 1,1-dioxide**(4)** was synthesized by condensation of synthesis of 1,2-thiazetidine 1,1-dioxide (β-Sultam)**(3)** a mixture of K2CO3, TEBA , Acetonitile and 2-chloro ethanamide. Synthesis of 1,2-thiazetidine-1,1-dioxide**(β-Sultam) (3)** was synthesized with Taurinesulfonylchloride **(2)** with Na2CO3, Ethyl acetate. Taurinesulfonylchloride **(2)** was synthesized by S-S bond cleavage Cystaminedihydroxychloride **(1)** with mixture of Chlorine gas, Chloroform and Ethanol solvent mixture.*

Key words: Sultam, Thiazolidin-4-one, Cylization, Antibacterial and antifungal activity.

INTRODUCTION

Thiazolidine moiety is associated with broad spectrum of biological activities including antibacterial[102-102], antifungal[105], anti-inflammatory[106-108], hypnotic, anticonvulsant, antitubercular[109], antiviral[104,112], antihistaminic[114], anthelmintic, cardiovascular and anticancer[111].

Cyclic sulfonamides (sultams) although not found in nature [1] have also found applications in drug development. Examples of biologically active sultams include the antiepileptic agent Sulthiame, [2] the antiinflamatory agent Ampiroxicam, [3] Brinzolamide [4, 5] for the treatment of glaucoma, S-2474, [6] a new anthiarthritic drug candidate that is now under clinical trials, HIV-1 inhibitors [7, 8] selective inhibitors of Calpain I, [9] and most recently PBTD's [10] which are a new class of candidates for the treatment of chronic myelogenous leukemia (CML).

In addition to their medicinal value, sultams have been successfully used as chiral auxiliaries,[11, 12] reagents, [13-15] artificial sweeteners (i.e. saccharin), [16] and agricultural agents.[17] For example, the well known Oppolzer sultam has been utilized in numerous asymmetric reactions,[11,12] sultams has been used as a stereoselective oxidizing agent [15] and sultam has also found application as an electrophilic fluorinating agent to provide monofluorinated ketones. [13, 14] In agriculture, sultams have been used as herbicides.[17]

EXPERIMENTAL SECTION

All the chemicals were used as received without further purification. Melting points were measured on a gallenkamp electro thermal melting point apparatus and are uncorrected. Reactions were carried out using household micro oven (power consumption 1200w, microwave frequency 2450MHz) and monitored by thin layer chromatography (TLC) on silica gel plates (60F254) visualizing with ultraviolet light or iodine spray. 1H NMR spectra were determined inDMSO- d6 solution on JOEL AL300 spectrometers. Proton chemical shifts are relative to tetramethylsilane as internal standard and expressed in ppm.

taurine sulfonyl chloride (2)

A suspension of cystamine dihydrochloride (1) (10.0 g, 44.4 mmol) was mixed in drychloroform (250 mL) and dry ethanol (125 mL). Chlorine was passed into the solution at -10°C under an atmosphere of nitrogen until complete saturation, noted by a permanent pale green colouration (1 hour). The system was purged with nitrogen, and dry diethyl ether (60 mL) was added to the mixture, which was stirred for a further 1 hour at room temperature. The reaction mixture was stored at 4°C overnight. The white precipitate was filtered off under vacuum and washed with dry diethyl ether to give taurine sulfonyl chloride (2) the product as a white solid (13.82 g, 94%). The yield of taurinesulfonylchloride (2) was found to be (94%, 13.82g) with M.P.141-143^{0}C. The structure of taurinesulfonylchloride (2) was established by IR. The IR spectrum of taurinesulfonylchloride (2) was recorded in the 4000-400 cm^{-1} range in KBr pellets reflect the molecular structure and showed the characteristic bonds around. The IR spectra of taurinesulfonylchloride (2) recorded in the 4000-450 cm^{-1} range in KBr pellets reflect the molecular structure and showed the characteristic bands around 2995 (w), 2912 (w), 2910 (bs, NH3), 1599 (w), 1558 (w), 1515 (w), 1399 (w)1371 (s, SO2), 1279 (w), 1173 (m), 1159 (s, SO2) groups respectively; The elemental analysis C2H7NO2S Cl2 (180); found % C, 13.33; H, 3.88; N, 7.77 agreed well with the calculated % C, 13.38; H, 3.93; N, 7.82.

1,2-thiazetidin-1,1-dioxide (*β*-sultam) (3)

Taurine sulfonyl chloride (2) 13.54 g, 81.5 mmol) was added to finely ground anhydrous Sodium carbonate (17.28 g, 163.0 mmol, 2 eq.) in dry ethyl acetate (370 mL) and stirred at RT for 46 hours. The reaction mixtutre was filtered through Celite®. The solvent was removed *in vacuo* to give the product as a white solid (2.62-5.29 g, 14-60 %, m.p.= 50-52°C, lit: m.p.=53°C29). The structure of 1,2-thiazetidin-1,1-dioxide (3) was established by IR, ^{1}H-NMR and ^{13}C NMR. The IR spectrum of 1,2-thiazetidin-1,1-dioxide (3) was recorded in the 4000-400 cm^{-1} range in KBr pellets reflect the molecular structure and showed the characteristic bonds around 3581 (br), 3297 (br, NH), 3048 (w), 2987 (w), 2919 (w), 1629 (w), 1485 (w),1415 (w), 1300 (s, SO2), 1252 (s), 1150 (s, SO2), 1114 (m), 992 (w), 963 (m), 917 (w), 763 (m), 654 (m) respectively; The ^{1}H NMR structure of the compound 1,2-thiazetidin-1,1-dioxide (3) in CDCl3 showed the following signals at δppm (400 MHz, CDCl3) 5.32 (1H, bs, NH), 4.25 (2H, dt, *J*=7.0 CH2SO2), 3.33 (2H, dt, *J*=7.0 and 3.9 Hz, CH2NH). ^{13}C NMR δppm (400 MHz, CDCl3); The ^{13}C NMR δppm (400 MHz) data of the compound 1,2-thiazetidin-1,1-dioxide (3) was recorded in CDCl3 showed the following signals at 60.93 (CH2SO2), 28.14 (CH2NH); The elemental analysis C2H5NO2S (107); found % C, 22.42; H, 4.67; N, 13.08 agreed well with the calculated % C, 22.47; H, 4.72; N, 13.13.

Synthesis of 2-(2-aminoethyl)-1,2-thiazetidine 1,1-dioxide (4)

To a solution of sultam (0.25 mmol) and TEBA (5,7 mg, 0.025 mmol) in dryacetyonitrile (1 mL) at 25^{0}C, anhydrous potassium carbonate (51.8 mg, 0.375 mmol) was added. The resulting heterogeneous mixture was stirred for 10 min, then the alkylating agent RX (0.375 mmol) was added and the reaction was monitored by TLC until completion. The mixture zwas filtered through a celite pad and, after evaporation of the solvent (RV), the crude was purified by Flash Column Chromatography. The structure of 2-(2-aminoethyl)-1,2-thiazetidine 1,1-dioxide (4) was characterized by IR, (KBr), ^{1}H NMR spectra and Elemental analysis. The IR spectra of 2-(2-aminoethyl)-1,2-thiazetidine 1,1-dioxide (4) recorded in the 4000-450 cm^{-1} range in KBr pellets reflect the molecular structure and showed the characteristic bands around 3581 (br), 3297 (br, NH), 3048 (w), 2987 (w), 2919 (w), 1629 (w), 1485 (w),1415 (w), 1300 (s, SO2), 1252 (s), 1150 (s, SO2), 1114 (m), 992 (w), 963 (m), 917 (w), 763 (m),654 (m); The ^{1}H NMR structure of the compound 2-(2-aminoethyl)-1,2-thiazetidine 1,1-dioxide (4) in DMSO d6 showed the following signals at δppm^{1}H NMR δ (400 MHz, DMSO d6): 5.11 (1H, bs, NH2), 4.25 (2H, dt, *J*=7.0 and 1.7 Hz, CH2SO2),3.33 (2H, dt, *J*=7.0 and 3.9 Hz, CH2NH2), 3.11 (2H, dt, *J*=7.0 and 3.9 Hz, CH2N), 2.81 (2H, dt, *J*=7.0 and 3.9 Hz, CH2); The elemental analysis C4H10N2O2S (150); found % C, 32.00; H, 6.66; N, 32.00 agreed well with the calculated % C, 32.05; H, 6.71; N, 32.05.

Synthesis of 2-(2-(4-substituted benzylideneamino)ethyl)-1,2-thiazetidine 1,1-dioxide 6(a-f)

Equimolar quantities of 2-(2-aminoethyl)-1,2-thiazetidine 1,1-dioxide (4) and Benaldehyde (5a-f) were dissolved in absolute alcohol and heated at 100^0C for 5-6 hours. The progress of the reaction was monitored by TLC using hexane : ethylacetate(7:3) as mobile phase, the reaction mixture was kept overnight and evaporation of the solvent under reduced pressure with rotaevaporator afforded residue which was recrystallized from DCM(Dichloro methane) affored 2-(2-(4-substituted benzylideneamino)ethyl)-1,2-thiazetidine 1,1-dioxide **(6a)**. The yield was 70% and m.p.166-168^0C. The similar procedure was adopted with 2-(2-aminoethyl)-1,2-thiazetidine 1,1-dioxide (4) and 4-methylbenzaldehyde, 4-flourobenzaldehyde, 4-chlorobenzaldehyde, 4-triflourobenzaldehyde and 4-ntrobenzaldehyde. The structure of (6a-f) was established by IR and ^{1}HNMR and elemental analysis.

IR (KBr) pellets reflect the molecular structure and showed the characteristic bonds around 2987 & 2919 (Aliphatic C-H), 1620 (>C=N), 1300 & 1252 (SO2); ^{1}HNMR(DMSO d6) (δ ppm) : 4.25(t, 2H, J=7.0, -CH2SO2 of sultam ring), 3.33 (t, 2H, J=7.0, -CH2 attached to nitrogen sultam ring), 8.70(s,1H, -CH=N-, attached to phenyl ring),7.10-7.20(m, 5H of C6H5); The elemental analysis C11H14N2O2S (238); found % C,55.46; H,5.88; N,11.76 agreed well with the calculated % C,55.51; H,5.93; N,11.81.

2-(2-((4-methylbenzylidene)amino)ethyl)-1,2-thiazetidine 1,1-dioxide 6(b): yield 60%, m.p.172^0C; IR (KBr) pellets reflect the molecular structure and showed the characteristic bonds around 2987 & 2919 (Aliphatic C-H), 1615 (>C=N), 1300 & 1252 (SO2). ^{1}HNMR(DMSO d6) (δ ppm) : 4.25(t, 2H, J=7.0, -CH2SO2 of sultam ring), 3.33 (t, 2H, J=7.0, -CH2 attached to nitrogen sultam ring), 8.70(s,1H, -CH=N-, attached to phenyl ring),6.90-7.10(m, 4H of C6H4), 2.34(s,3H,-CH3); The elemental analysis C12H16N2O2S (252); found % C,57.14; H,6.34; N,11,11 agreed well with the calculated % C,57.19; H,6.39; N,11.16.

2-(2-((4-fluorobenzylidene)amino)ethyl)-1,2-thiazetidine 1,1-dioxide 6(c): yield 70%, m.p.159^0C; IR(KBr) pellets reflect the molecular structure and showed the characteristic bonds around 2987 & 2919 (Aliphatic C-H), 1620 (>C=N), 1300 & 1252 (SO2); ^{1}HNMR(DMSO d6) (δ ppm) : 4.25(t, 2H, J=7.0, -CH2SO2 of sultam ring), 3.33 (t, 2H, J=7.0, -CH2 attached to nitrogen sultam ring), 8.70(s,1H, -CH=N-, attached to phenyl ring),7.30-7.40(m, 4H of C6H4); The elemental analysis C11H13N2O2FS (255); found% C,51.76; H,5.09; N,10.98 agreed well with the calculated % C,51.81; H,5.14; N,11.03.

2-(2-((4-chlorobenzylidene)amino)ethyl)-1,2-thiazetidine 1,1-dioxide 6(d): yield 68%, m.p.151^0C; IR (KBr) pellets reflect the molecular structure and showed the characteristic bonds around 2987 & 2919 (Aliphatic C-H), 1617 (>C=N), 1300 & 1252 (SO2); ^{1}HNMR(DMSO d6) (δ ppm) : 4.25(t, 2H, J=7.0, -CH2SO2 of sultam ring), 3.33 (t, 2H, J=7.0, -CH2 attached to nitrogen sultam ring), 8.70(s,1H, -CH=N-, attached to phenyl ring),7.25-7.36(m, 4H of C6H4); The elemental analysis C11H13N2O2ClS (272.5); found % C,48.44; H,4.77; N,10.27 agreed well with the calculated % C,48.49; H,4.82; N,10.32.

2-(2-((4-(trifluoromethyl)benzylidene)amino)ethyl)-1,2-thiazetidine 1,1-dioxide 6(e): yield 72%, m.p.184^0C; IR (KBr) pellets reflect the molecular structure and showed the characteristic bonds around 2987 & 2919***)*** (Aliphatic C-H), 1622 (>C=N), 1300 & 1252 (SO2); ^{1}HNMR(DMSO d6) (δ ppm) : 4.25(t, 2H, J=7.0, -CH2SO2 of sultam ring), 3.33 (t, 2H, J=7.0, -CH2 attached to nitrogen sultam ring), 8.70(s,1H, -CH=N-, attached to phenyl ring),7.40-7.50(m, 4H of C6H5); The elemental analysis C12H13N2O2F3S (303); found % C, 47.52; H,4.29; N,9.24 agreed well with the calculated % C,47.57; H,4.34; N,9.29.

2-(2-((4-nitrobenzylidene)amino)ethyl)-1,2-thiazetidine 1,1-dioxide 6(f) : yield 68%, m.p.193^0C; IR (KBr) pellets reflect the molecular structure and showed the characteristic bonds around 2987 & 2919 (Aliphatic C-H), 1625 (>C=N), 1622 (>C=N), 1300 & 1252 (SO2). ^{1}HNMR(DMSO d6) (δ ppm) : 4.25(t, 2H, J=7.0, -CH2SO2 of sultam ring), 3.33 (t, 2H, J=7.0, -CH2 attached to nitrogen sultam ring), 8.70(s,1H, -CH=N-, attached to phenyl ring),7.5-7.8(m, 4H of C6H4); The elemental analysis C11H13N3O4S (283); found % C,46.64; H,4.59; N,14.84 agreed well with the calculated % C,46.69; H,4.64; N,14.89.

3-(2-(1,1-dioxido-1,2- thiazetidin-2-yl)ethyl)-2-phenylthiazolidin-4-one 8 (a-f)

A mixture of 2-(2-(benzylideneamino)ethyl)-1,2-thiazetidine 1,1-dioxide **(6a)** and Mercaptoacetic acid dissolved in dioxane (20 ml) anhydrous Zinc Chloride (0.5 mg) was added and refluxed for 8 hrs. The reaction was monitored by TLC using hexane and ethyl acetate (7:3) as mobile phase. The reaction mixture was cooled and reflucting solid was washed with Sodium bicarbonate solution and recrystalized from absolute alcohol. The yield was 65% with

m.p:142-1^{0}C. Similar procedure was adopted to synthesis **8(a-f)** from **6(a-f)** with thioacetic acid. The structures of **8(a-f)** were established by IR, ^{1}H-NMR, ^{13}C-NMR, Mass Spectral analysis and the elemental analysis

IR (KBr) Spectra(υmax, cm^{-1}) of 3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-phenylthiazolidin-4-one (8a) was recorded in 4000-400 cm^{-1} range in KBr pellets reflect the molecular structure and showed signals at around 3045(Ar-H stretching),2990 & 2965(Aliphatic C-H stretching), 1675 (>C=O group of thiazolidine-2-one) and 1306 & 1160cm^{-1} (stretching of SO2 group); ^{1}HNMR(DMSO d6) (δ ppm) : 3.85(d, 1 Ha, C-Ha, of thiazolidin attached to –S, J=6.5 Hz), 3.95(d, 1 Hb, C-Hb, of thiazolidin attached to, >C=O group, J=6.5 Hz), 5.90(s, 1 H, -CH, of thiazolidine attached to, phenyl ring),7.0-7.20(m, 5H of C6H5 ring), 4.25 (t, 2H, -CH2, of 1,2-thiazetidin, J=7 Hz), 3.30 (t, 2H, -CH2-SO2 of 1,2-thiazetidin, J=7 Hz), 2.90(t, 2H, -CH2 attached to thiazetidin, J=8 Hz), 3.60(t, 2H, -CH2 attached to thiazolidine, J=8 Hz); ^{13}CNMR(CDCl3) (δ ppm): 53.3, 43.0, 33.9, 171.2, 70.5, 143.8, 126.9, 128.6, 127.1, 126.9 and the signals are ascribed to C1&C3, C2 & C4, C5, C6, C7, C8, C9, C10, C12, C11&C13; The elemental analysis C13H16N2O3S2 (312.06); found % C,49.99; H,5.12; N,8.97 agreed well with the calculated % C,50.04; H, 5.17; N,9.02.

3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-(p-tolyl)thiazolidin-4-one 8(b) :
yield,55%; m.p: 162-1^{0}C IR (KBr) pellets reflect the molecular structure and showed the characteristic bonds around 3040(Ar-H stretching), 2985 & 2960(Aliphatic C-H stretching), 1670 (>C=O group of thiazolidine-2-one) and 1305 & 1150cm^{-1} (stretching of SO2 group); ^{1}HNMR(DMSO d6) (δ ppm) : 3.85(d, 1 Ha, C-Ha, of thiazolidin attached to –S, J=6.5 Hz), 3.95(d, 1 Hb, C-Hb, of thiazolidin attached to, >C=O group, J=6.5 Hz), 5.90(s, 1 H, -CH, of thiazolidine attached to, phenyl ring),7.0-7.20(m, 5H of C6H5 ring), 4.25 (t, 2H, -CH2, of 1,2-thiazetidin, J=7 Hz), 3.30 (t, 2H, -CH2-SO2 of 1,2-thiazetidin, J=7 Hz), 2.90(t, 2H, -CH2 attached to thiazetidin, J=8 Hz), 3.60(t, 2H, -CH2 attached to thiazolidine, J=8 Hz), 2.54(t, 3H, -CH3 attached to phenyl ring), 6.90-7.10(m, 4H, C6H4 ring); ^{13}CNMR(CDCl3) (δ ppm): 53.3, 43.0, 33.9, 171.2, 70.5, 140.8, 128.6, 128.9, 136.8, 128.6, 21.3 and the signals are ascribed to C1&C3, C2 & C4, C5, C6, C7, C8, C9, C10, C12, C11&C13, C14; The elemental analysis C14H18N2O3S2 (326); found % C,51.52; H,5.52; N,8.58 agreed well with the calculated % C,51.57; H, 5.57; N,8.63.

3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-(4-fluorophenyl)thiazolidin-4-one 8(c) : yield, 60%; m.p: 190-3^{0}C IR (KBr) pellets reflect the molecular structure and showed the characteristic bonds around3055(Ar-H stretching),2993 & 2967(Aliphatic C-H stretching), 1680 (>C=O group of thiazolidine-2-one) and 1320 & 1165cm^{-1} (stretching of SO2 group); ^{1}HNMR(DMSO d6) (δ ppm) : 3.85(d, 1 Ha, C-Ha, of thiazolidin attached to –S, J=6.5 Hz), 3.95(d, 1 Hb, C-Hb, of thiazolidin attached to, >C=O group, J=6.5 Hz), 5.90(s, 1 H, -CH, of thiazolidine attached to, phenyl ring),7.0-7.20(m, 5H of C6H5 ring), 4.25 (t, 2H, -CH2, of 1,2-thiazetidin, J=7 Hz), 3.30 (t, 2H, -CH2-SO2 of 1,2-thiazetidin, J=7 Hz), 2.90(t, 2H, -CH2 attached to thiazetidin, J=8 Hz), 3.60(t, 2H, -CH2 attached to thiazolidine, J=8 Hz), 7.20-7.40(m, 4H, C6H4 ring); ^{13}CNMR(CDCl3) (δ ppm): 53.3, 43.0, 33.9, 171.2, 70.5, 139.4, 130.3, 115.4, 162.3, 130.3 and the signals are ascribed to C1&C3, C2 & C4, C5, C6, C7, C8, C9, C10, C12, C11&C13; The elemental analysis C13H15N2O3S2F (329); found % C,47.84; H,4.60; N,8.58 agreed well with the calculated % C,47.89; H, 4.65; N,8.63.

2-(4-chlorophenyl)-3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)thiazolidin-4-one 8(d) : yield, 70%; m.p: 196-1^{0}C IR (KBr) pellets reflect the molecular structure and showed the characteristic bonds around3050(Ar-H stretching),2995 & 2976(Aliphatic C-H stretching), 1670 (>C=O group of thiazolidine-2-one) and 1315 & 1165cm^{-1} (stretching of SO2 group); ^{1}HNMR(DMSO d6) (δ ppm) : 3.85(d, 1 Ha, C-Ha, of thiazolidin attached to –S, J=6.5 Hz), 3.95(d, 1 Hb, C-Hb, of thiazolidin attached to, >C=O group, J=6.5 Hz), 5.90(s, 1 H, -CH, of thiazolidine attached to, phenyl ring),7.0-7.20(m, 5H of C6H5 ring), 4.25 (t, 2H, -CH2, of 1,2-thiazetidin, J=7 Hz), 3.30 (t, 2H, -CH2-SO2 of 1,2-thiazetidin, J=7 Hz), 2.90(t, 2H, -CH2 attached to thiazetidin, J=8 Hz), 3.60(t, 2H, -CH2 attached to thiazolidine, J=8 Hz), 7.10-7.30(m, 4H, C6H4 ring); ^{13}CNMR(CDCl3) (δ ppm): 53.3, 43.0, 33.9, 171.2, 70.5, 141.9, 130.1, 128.7, 132.7, 130.1 and the signals are ascribed to C1&C3, C2 & C4, C5, C6, C7, C8, C9, C10, C12, C11&C13; The elemental analysis C13H15N2O3S2Cl (346.5); found % C,45.40; H,4.36; N,8.14 agreed well with the calculated % C,45.45; H, 4.41; N,8.19.

3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one 8(e) : yield,60%; m.p: 172-1^{0}C IR (KBr) pellets reflect the molecular structure and showed the characteristic bonds around 3060(Ar-H stretching), 2993 & 2965(Aliphatic C-H stretching), 1680 (>C=O group of thiazolidine-2-one) and 1325 & 1160cm^{-1} (stretching of SO2 group); ^{1}HNMR(DMSO d6) (δ ppm) : 3.85(d, 1 Ha, C-Ha, of thiazolidin attached to –

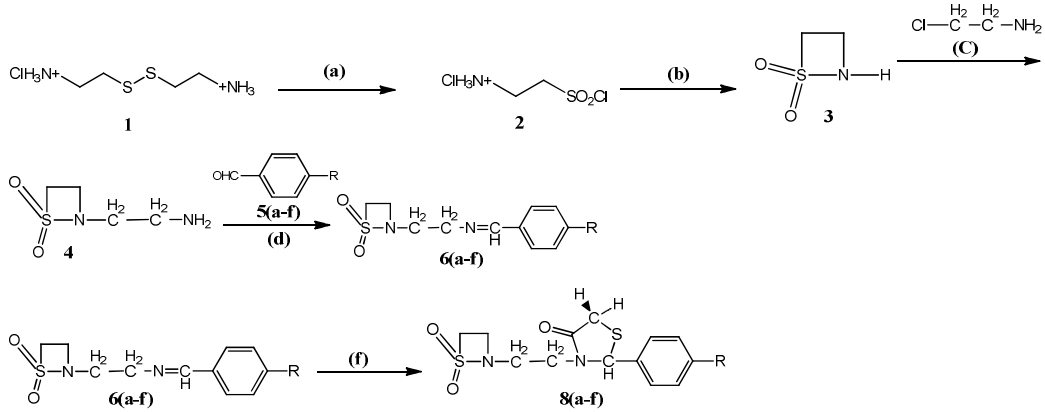
S, J=6.5 Hz), 3.95(d, 1 Hb, C-Hb, of thiazolidin attached to, >C=O group, J=6.5 Hz), 5.90(s, 1 H, -CH, of thiazolidine attached to, phenyl ring),7.0-7.20(m, 5H of C6H5 ring), 4.25 (t, 2H, -CH2, of 1,2-thiazetidin, J=7 Hz), 3.30 (t, 2H, -CH2-SO2 of 1,2-thiazetidin, J=7 Hz), 2.90(t, 2H, -CH2 attached to thiazetidin, J=8 Hz), 3.60(t, 2H, -CH2 attached to thiazolidine, J=8 Hz), 7.30-7.50(m, 4H, C6H4 ring); ^{13}CNMR(CDCl3) (δ ppm): 53.3, 43.0, 33.9, 171.2, 70.5, 147.1, 129.0, 125.0, 129.4, 125.0, 124.1 and the signals are ascribed to C1&C3, C2 & C4, C5, C6, C7, C8, C9, C10, C12, C11&C13, C14; The elemental analysis C14H15N2O3S2F3 (377); found % C,44.91; H,4.01; N,7.48 agreed well with the calculated % C,44.96; H, 4.06; N,7.53.

3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-(4-nitrophenyl)thiazolidin-4-one 8(f) : yield, 55%; m.p: 215-1^{0}C IR (KBr) pellets reflect the molecular structure and showed the characteristic bonds around 3065(Ar-H stretching), 2995&2967(Aliphatic C-H stretching), 1685 (>C=O group of thiazolidine-2-one) and 1325 & 1150cm^{-1} (stretching of SO2 group); ^{1}HNMR(DMSO d6) (δ ppm) : 3.85(d, 1 Ha, C-Ha, of thiazolidin attached to –S, J=6.5 Hz), 3.95(d, 1 Hb, C-Hb, of thiazolidin attached to, >C=O group, J=6.5 Hz), 5.90(s, 1 H, -CH, of thiazolidine attached to, phenyl ring),7.0-7.20(m, 5H of C6H5 ring), 4.25 (t, 2H, -CH2, of 1,2-thiazetidin, J=7 Hz), 3.30 (t, 2H, -CH2-SO2 of 1,2-thiazetidin, J=7 Hz), 2.90(t, 2H, -CH2 attached to thiazetidin, J=8 Hz), 3.60(t, 2H, -CH2 attached to thiazolidine, J=8 Hz), 7.40-7.60(m, 4H, C6H4 ring); ^{13}CNMR(CDCl3) (δ ppm): 53.3, 43.0, 33.9, 171.2, 70.5, 149.9, 129.6, 123.8, 146.3, 123.8, and the signals are ascribed to C1&C3, C2 & C4, C5, C6, C7, C8, C9, C10, C12, C11&C13; The elemental analysis C13H15N3O5S2 (357); found % C,44.06; H,4.23; N,11.86 agreed well with the calculated % C,44.11; H, 4.28; N,11.91.

RESULTS AND DISCUSSION

The development of sultam-thizolidin-4-one heterocycles was described in the scheme-1 of synthetic sequence. The different steps involve simple reaction conditions and good yield procedure. Compounds 6(a-f) were allowed to react with 4-substituted benzaldehyde 5(a-f) to afford 8(a-f) in good yield. The IR spectrum of 8a revealed the appearance of bands characteristics of 3045(Ar-H stretching),2990 & 2965(Aliphatic C-H stretching), 1675 (>C=O group of thiazolidine-2-one) and 1306 & 1160cm^{-1} (stretching of SO2 group); ^{1}HNMR(DMSO d6) (δ ppm) : 3.85(d, 1 Ha, C-Ha, of thiazolidin attached to –S, J=6.5 Hz), 3.95(d, 1 Hb, C-Hb, of thiazolidin attached to, >C=O group, J=6.5 Hz), 5.90(s, 1 H, -CH, of thiazolidine attached to, phenyl ring),7.0-7.20(m, 5H of C6H5 ring), 4.25 (t, 2H, -CH2, of 1,2-thiazetidin, J=7 Hz), 3.30 (t, 2H, -CH2-SO2 of 1,2-thiazetidin, J=7 Hz), 2.90(t, 2H, -CH2 attached to thiazetidin, J=8 Hz), 3.60(t, 2H, -CH2 attached to thiazolidine, J=8 Hz); ^{13}CNMR(CDCl3) (δ ppm): 53.3, 43.0, 33.9, 171.2, 70.5, 143.8, 126.9, 128.6, 127.1, 126.9 and the signals are ascribed to C1&C3, C2 & C4, C5, C6, C7, C8, C9, C10, C12, C11&C13; The elemental analysis C13H16N2O3S2 (312.06); found % C,49.99; H,5.12; N,8.97 agreed well with the calculated % C,50.04; H, 5.17; N,9.02. conformed the formation of sultam-thiazolidin-4-one(8a).

Scheme-1



	6a	**6b**	**6c**	**6d**	**6e**	**6f**
Compound	**8a**	**8b**	**8c**	**8d**	**8e**	**8f**
R	**-H**	**-CH3**	**-F**	**-Cl**	**-CF3**	**-NO2**

Anti- Microbial Activity

The anti-microbial activity of (8a-f) was determined by the disc diffusion method with Amoxicillin and Griseofulvin as the reference antibiotics [18]. The newly synthesised compounds were examined, respectively, against *Staphylococcus aureus*, *Bacillus Cereus*, *Escherichia Coli* and *Pseudomonas aeruginosa*bacteria. The test results were presented in the table-1, suggest that –Nitro, -Chloro and –Flouro exhibit high activity against the tested bacteria, the rest of the compounds were found to be either slightly active or inactive against the tested microorganisms. The order of anti-bactirial activity was found to be 8f>8d>8e>8b>8a>8c.

Table 1. Antibacterial Activity by the disc diffusion method

S.No.	Compound	Zone of Inhibition			
		***Staphylococcus aureus* NCCS2079**	***Bacillus Cereus* NCCS2106**	***Escherichia Coli* NCCS2065**	***Pseudomonas aeruginosa* NCCS2200**
1	*3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-phenylthiazolidin-4-one 8(a)*	07	08	06	06
2	*3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-(p-tolyl)thiazolidin-4-one 8(b)*	05	07	05	06
3	*3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-(4-fluorophenyl)thiazolidin-4-one 8(c)*	06	07	06	07
4	*2-(4-chlorophenyl)-3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)thiazolidin-4-one 8(d)*	06	07	06	05
5	*3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one 8(e)*	09	09	07	09
6	*3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-(4-nitrophenyl)thiazolidin-4-one 8(f)*	08	08	06	07
7	*Amoxycillin*	21	22	24	27

Antifungal activity

Antifugal activity of final compounds 3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-phenylthiazolidin-4-one 8(a-f) were screened against Aspergillus niger, Helminthosporium Oryzae. The compounds 8(a-f) showed more fungal activity while 8(a-c) exhibited low activity. The fungal activity thiazolidin-4-one 8(a-f) was shown in the (Table-2). Here Griseofulvin [19-20] is tested as reference compound to compare the activity.

Table 2. Antifungal Activity by the disc diffusion method

S.No.	Compound	Zone of Inhibition	
		***Aspergillus niger* NCCS 1196 250(µg/disc)**	***Helminthosporium Oryzae* 250(µg/disc)**
1	*3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-phenylthiazolidin-4-one 8(a)*	9	8
2	*3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-(p-tolyl)thiazolidin-4-one 8(b)*	10	9
3	*3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-(4-fluorophenyl)thiazolidin-4-one 8(c)*	8	6
4	*2-(4-chlorophenyl)-3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)thiazolidin-4-one 8(d)*	18	19
5	*3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-(4-(trifluoromethyl)phenyl)thiazolidin-4-one 8(e)*	16	17
6	*3-(2-(1,1-dioxido-1,2-thiazetidin-2-yl)ethyl)-2-(4-nitrophenyl)thiazolidin-4-one 8(f)*	17	18
7	*Griseofulvin*	28	26

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REFERENCES

[1] Hanessian, S.; Sailes, H.; Therrien, E. *Tetrahedron* **2003**, *59*, 7047- 7056.
[2] Tanimukai, H.; Inui, M.; Harigushi, S.; Kaneko, J. *Biochem. Pharmacol.* **1965**, *14*, 961-970.
[3] Ampiroxicam. *Drugs Future* **1992**, *17*, 451-454.
[4] Brinzolamide. *Drugs Future* **1998**, *23*, 365-369.

[5] Conrow, R. E.; Dean, D.; Zinke, P. W.; Deason, M. E.; Sproull, S.J.; Dantanarayan, A. P.; DuPriest, M. T. *Org. Proc. Res. Dev*. **1999**, *3*, 114- 120.
[6] Inagaki, M.; Tsuri, T.; Jyoyama, H.; Ono, T.; Yamada, K.; Kobayashi, M.; Hori, Y.; Arimura, A.; Yasui, K.; Ohno, K.; Kakudo, S.; Koizumi, K.; Suzuki, R.; Kato, M.; Kawai, S.; Matsumoto, S.Novel *J. Med. Chem.* **2000**, *43*, 2040-2048.
[7] Zhuang, L.; Wai, J. S.; Embrey, M. W.; Fisher, T. E.; Egbertson, M.S.; Payne, L. S.; Guare, Jr., J. P.; Vacca, J. P.; Hazuda, D. J.; Felock, P. J.; Wolfe, A. L.; Stillmock, K. A.; Witmer, M. V.; Moyer, G.; Schleif, W. A.; Gabryelski, L. J.; Leonard, Y. M.; Lynch,Jr., J. J.; Michelson, S. R.; Young, S. D. *J. Med. Chem.* **2003**, *46*, 453-456.
[8] Brzozowski, Z.; Saczewski, F.; Neamati, N. *Bioorg. Med. Chem. Lett*. **2006**, *16*, 5298-5302.
[9] Wells, G. J.; Tao, M.; Josef, K. A.; Bihovsky, R. *J. Med. Chem.* **2001**, *44*, 3488-3503.
[10] Silvestri, R.; Marfe, G.; Artico, M.; La Regina, G.; Laveccchia, A.;Novellino, E.; Morgante, M.; Di Stefano, C.; Catalano, G.; Filomeni,G.; Abruzzese, E.; Ciriolo, M. R.; Russo, M. A.; Amadori, S.; Cirilli, R.; La Torre, F.; Salimei, P. S. *J. Med. Chem.* **2006**, *49*, 5840-5844.
[11] Oppolzer, W. *Pure Appl. Chem.* **1988**, *60*, 39-48.
[12] Oppolzer, W. *Pure Appl. Chem.* **1990**, *62*, 1241-1250.
[13] Differding, E.; Lang, R. W. *Helv. Chim. Acta* **1989**, *72*, 1248-1252.
[14] Differding, E.; Rüegg, G. M.; Lang, R. W. *Tetrahedron Lett*. **1991**, *32*, 1779-1782.
[15] Davies, F. A.; Chen, B-C. *Chem. Rev.* **1992**, *92*, 919-934.
[16] Cohen, S. M. Saccharin: Past, Present and Future. *J. Am. Diet. Assoc.* **1986**, *86*, 929-931.
[17] Pasteris, R. J., Eur. Patent **1984**, 107, 979.
[18] H.M.Hassan and A.Farrag, *J. Chem. Pharm. Res.*, **2011**, 3(2), 776-785.
[19] R.A.Bnjara; S.K.Jadhav and S.A.Bhoite, *J. Chem. Pharm. Res.*, **2012**, 4(1), 648-652.[46] E. Dadapeer,.I.Reddi Mohan Naidu; M. Ramesh; C. Naga Raju and M. Nagalaskshmi Devamma, *J. Chem. Pharm. Res.*, **2011**, 2(3), 109-116.
[20] Rishi Pratap Singh; D.V. Singh, S.P. Tripathi and Shailendra Singh, *J. Chem. Pharm. Res.*, **2012**, 4(4):2055-2060.