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Synthesis, spectral investigation and biological evaluation of novel non-cytotoxic tetrahydrothieno[3, 2-c]pyridine hydrazide derivatives

Visha P. Modi, Paresh N. Patel and Hasmukh S. Patel*

Department of Chemistry, Sardar Patel University, Vallabh Vidyanagar, Gujarat (India)

ABSTRACT

*In the current research work, a series of novel title compounds, N-(3-(4-chloro phenyl)-2,5-diphenyl-3,3a-dihydro-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)-2-(6,7-dihydrothieno-[3,2-c]pyridine-5(4H)-yl) acetamide **(7a-h)** were synthesized by reaction of N-(5-(4-chlorobenzylidene)-4-oxo-2-phenylthiazolidin-3-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamide **(6a-h)** with phenyl hydrazine in presence of acetic acid. Their structures were characterized by elemental and spectral analysis. All the synthesized compounds were screened for their in-vitro antimicrobial activity, also MIC values of these compounds were determined. The investigation of antimicrobial screening data revealed that most of the compounds tested have demonstrated congruent activity. In summary, preliminary results indicate that, the compounds **6g**, **6f** ,**7g** and **7f** found to possess better antibacterial activity than Tetracycline (Reference standard) in MIC(Minimum inhibitory concentration), also compounds **6f** ,**7f** and **7h** found to possess better antifungal activity against Trichphyton longifusus and Candida glabrata than Miconazole (Reference standard).*

Keywords: Antimicrobial activity, Pyrazole, Substituted acetohydrazides, Spectral studies and Thiazolidone.

INTRODUCTION

Resistance to antimicrobial agents is nowadays recognized as a major global public health problem, so that the discovery of new antibacterial and antifungal compounds has become increasingly critical to fighting infectious disease.

The literature survey revealed that hydrazides and their heterocyclized products belong to an important structural class and display diverse biological activities including antibacterial, ant fungicidal, analgesic and anti-inflammatory properties [1-9]. Secondly acylhydrazides derivatives are of significant interest due to their chemotherapeutic history [10, 11]. 4-thiazolidinones and its arylidene compounds possess good pharmacological properties [12, 13].

Also these compounds are known to exhibit antitubercular [14], antibacterial [15] and antifungal [16] activities. These heterocyclic systems find wide use in medicine, agriculture and industry. 4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine and its various derivatives such as clopidogrel [17,18] and ticlopidine [19,20] are well acknowledged to show non-cytotoxic and complement inhibition properties. Also a series of substituted 4, 5, 6, 7-tetrahydrothieno[3, 2-*c*]pyridines (THTPs) were synthesized and evaluated for their human phenyl ethanolamine *N*-methyltransferase (hPNMT) inhibitory potency and affinity for the α_2-adrenoceptor [21].

From literature survey it was observed that N-acylhydrazide derivatives of 4, 5, 6, 7-tetrahydrothieno[3, 2-*c*]pyridines has not been reported, thus it is important for synthesis of its post heterocyclic products. So looking to the Heterocyclization of various hydrazide derivatives of 4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine and their pharmaceutical activities, it was thought of interest to merging both 4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine and thiazolidinone moieties which may enhance the antimicrobial activity of compounds to some extent or they might possess some of the above mentioned biological activities. From this point of view, the objective of the present communication comprises the synthesis of series of new compounds .The synthetic approach is shown in scheme-1.

MATERIALS AND METHODS

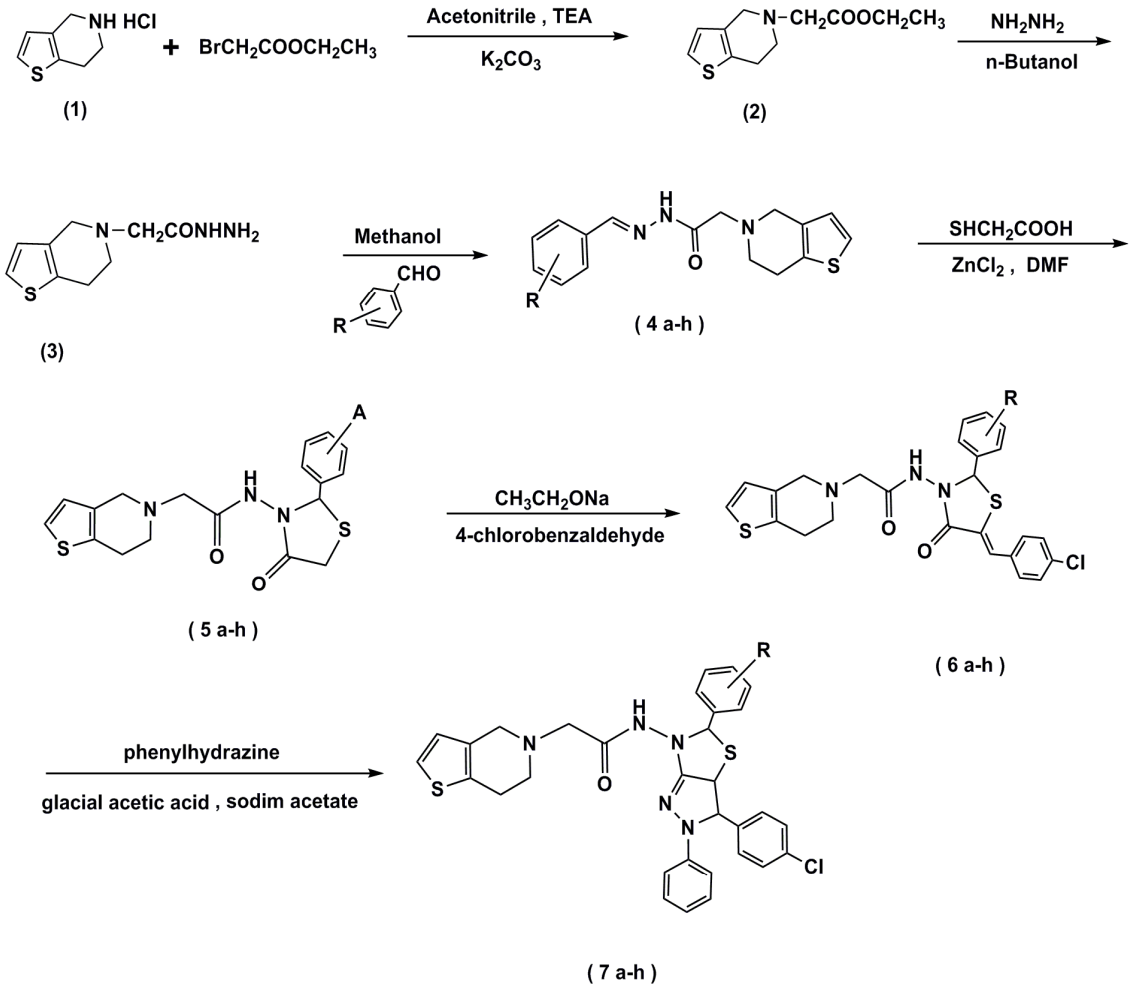
Most of the reagents, chemicals, solvents and catalyst were of analytical grade and used directly, some of them are purified by reported methods [22]. All the melting points were determined using a PMP-DM scientific melting point apparatus and are uncorrected. The purity of all the synthesized compounds were checked by thin layer chromatography (TLC) using silica gel-G coated Al-plates (0.5mm thickness, Merck) and spots were visualized by exposing the dry plates to iodine vapor or UV chamber and they were purified by column chromatography using proper solvent system. IR spectra (υ_{max} in cm^{-1}) were recorded on a Shimadzu FT-IR 8300 spectrophotometer using KBr pellets. ^{1}H NMR and ^{13}C NMR spectra were acquired on a Bruker 400 MHz NMR spectrometer using $CDCl_3$ or DMSO-d_6 as the solvent and TMS as the internal reference (chemical shifts in ppm). The elemental analysis (C, H, N, S) of all compounds were performed on Carlo Erba-1108 elemental analyzer. Their results were found to be in good agreement with the calculated values.

Preparation of ethyl-2(6, 7dihydrothieno [3, 2-*c*]pyridine-5(4H)-yl)acetate (2)

Ethyl-2-bromoacetate [0.01 mole /1.225gm] was added drop wise with constant starring and cooling in 4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine hydrochloride **(1)** [23] [0.01mole/1.755gm] which was dissolved in acetonitrile by using TEA [0.01 mole/0.73gm] as base then the reaction mixture was refluxed for 5 hours with water condenser then after on cooling the product **(2)** was separated out which was filtered and dried. It was purified by column chromatography technique and recrystallized from ethanol. Colour : White crystals; Yield : 86.00%; m.p. 180-182 ^{o}C; Anal. Calcd. for $C_{11}H_{15}NO_2S$(225.24) : C, 63.38; H, 7.20; N, 6.72; S, 15.36 %. Found : C, 63.41; H, 7.24; N, 6.76; S, 15.34 %; IR (ν_{max}, KBr, cm^{-1}) : 3062(C-H str, aromatic), 2884.7(C-H,str,aliphatic), 1596.7(C=C, asymmetric, str.), 1487.5,1469.7(C=C,str.ring),1224(C-N str), 981.8 (C-H bending, trans olefin), 748.4(C-H def, aromatic), 1726(>C=O str,ester),1223,1041(C-O str, ester), 721(C-S-C str, thiophene); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 3.2-3.8 (m, 4H, py.), 4.2-4.6(s, 2H, py.), 6.8-7.5(m,2H,thiophene), 1.23(t, 3H, CH_3CH_2O), 4.13(q, 2H,

CH_3CH_2O), 8.46(s, 2H, NCH_2CO); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 14.1(-CH_3), 61.0 (-CH_2O-), 168.2(RCOO-), 62.1(-CH_2COO-).

Scheme of synthesis



Scheme-1 :- Synthetic pathway for the preparation of derivatives of Acylehydrazide.

Where, R = (a) -C_6H_5, (b) 4-OCH_3-C_6H_4, (c) 4-OH-C_6H_4, (d) 2-OH-C_6H_4, (e) 4-CH_3-C_6H_4, (f) 3,4-CH_2O_2-C_6H_3, (g) 4-OH-3-OCH_3-C_6H_3, (h) 3,4-$(OC_2H_5)_2$-C_6H_3

Preparation of 2-(6,7-dihydrothieno[3,2-*c*]pyridin-5(4H)-yl)acetohydrazide (3)

A mixture of ethyl-2(6,7dihydrothieno[3,2-*c*]pyridine-5(4H)-yl)acetate **(2)** [0.01mole/2.25gm] and hydrazinehydrate [0.01mole/0.5006gm] was refluxed in 15 ml n-butanol for six hours. The solid separated was collected by filtration, dried, purified by column chromatography and recrystallized from ethanol. Colour : Yellowish white crystals; Yield : 92.02%; m.p. 220-225 °C; Anal. Calcd. for $C_9H_{13}N_3OS$ (211.43) : C, 51.08; H, 6.15; N, 19.86; S, 15.13 %. Found : C, 51.18; H, 6.17; N, 19.76; S, 15.20 %; IR (ν_{max}, KBr, cm^{-1}) : 3064(C-H str, aromatic), 2874.7(C-H str, aliphatic),1594.9(C=C, asymmetric str), 1488.4, 1468.6(C=C str.ring),1228(C-N str), 986 (C-H

bending, trans olefin),748.6(C-H def, aromatic),724(C-S-C str , thiophene), 3352, 3378(-$NHNH_2$), 1665 (>C=O of amide); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 3.4-4.0(m,4H,py.), 4.3-4.9(s,2H,py.), 6.8-7.9(m,2H,thiophene), 4.88 (s,2H,NCH_2CO), 4.40 (s, 2H, -NH_2), 7.88 (s, 1H, -CONH-); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 178.2(RCOO-),62.8(-CH_2COO-).

Preparation of N-benzylidene-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)aceto hydrazide (4a-h)

An equimolar mixture of 2-(6,7-dihydrothieno[3,2-*c*]pyridin-5(4H)-yl)acetohydrazide **(3)** [0.01mole/2.12gm] and the aromatic aldehydes **(a-h)** in ethanol (5 ml) were refluxed on a water bath for 2 hrs. The solid separated was collected by filtration, dried then it was purified by column chromatography technique and recrystallized from ethanol or chloroform.

Compound 4a: N'-benzylidene-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetohydrazide. Colour**:** Light green crystals; Yield : 78.02 %; m.p. 232-236°C; Anal. calcd. for $C_{16}H_{17}N_3OS$ (299) : C,64.21 ; H,5.68 ; N,14.05 ; S,10.70 %. Found **:** C,64.23 ; H,5.67 ; N,14.03 ; S,10.74 % . IR (ν_{max}, KBr, cm^{-1}) : 3340, 1335 (-NH-), 1668 (>C=O, amide), 1626 (-N=CH-); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 5.38(s,1H, -N=CH-), 8.07 (s, 1H,-CONH-), 6.91-7.68 (m, 5H, Ar-H); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 166.8(RCOO-), 144.8(-N=CH-).

Compound 4b: 2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)-N'-(4- methoxybenzylidene) acetohydrazide. Colour : Green crystals; Yield : 88.08 %; m.p. 240-245°C; Anal. calcd. for $C_{17}H_{19}N_3O_2S$ (329) : C,62.00 ; H, 5.77 ; N,12.76 ; S,9.72 %. Found : C,62.03 ; H,5.74 ; N,12.74 ; S,9.75 %; IR(KBr, cm^{-1}): 3350, 1345 (-NH-), 1672 (>C=O, amide), 1632 (-N=CH-), 2830 (Ar-OCH3); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 5.36(s,1H, -N=CH-), 8.12 (s, 1H,-CONH-), 6.86-7.72 (m, 4H, Ar-H), 2.26(s,3H, -OCH_3); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 166.8 (RCOO-), 146.3(-N=CH-), 64.8(-OCH_3).

Compound 4c: 2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)-N'-(4-hydroxy-benzylidene) acetohydrazide. Colour : Green crystals; Yield : 79.01%; m.p. 236-238°C; Anal. calc. for $C_{16}H_{17}N_3O_2S$ (315) : C,60.96 ; H,5.39 ; N,13.33 ; S,10.16 %, Found : C,60.94 ; H,5.35 ; N,13.32 ; S,10.14 %; IR(KBr, cm^{-1}): 3380, 1337(-NH-), 1679 (>C=O, amide), 1628 (-N=CH-), 3583 (Ar-OH); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 5.30(s,1H, -N=CH-), 8.10 (s, 1H,-CONH-), 6.85-7.71 (m, 4H, Ar-H),4.26(s,H, -OH); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 166.8(RCOO-), 148.3 (-N=CH-).

Compound 4d: 2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)-N'-(2-hydroxy-benzylidene) acetohydrazide. Colour : Light green crystals; Yield : 84.14%; m.p. 231-235°C; Anal. calcd. for $C_{16}H_{17}N_3O_2S$ (315) : C,60.96; H,5.39; N,13.33 ; S,10.16 %. Found : C,60.94; H,5.35; N,13.32; S,10.14 %; IR(KBr, cm^{-1}): 3380, 1337 (-NH-), 1684 (>C=O, amide), 1642 (-N=CH-), 3588 (Ar-OH); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 5.34(s,1H, -N=CH-), 8.12 (s, 1H,-CONH-), 6.85-7.71 (m, 4H, Ar-H), 4.32(s,H, -OH); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 169.8 (RCOO-), 156.3(-N=CH-).

Compound 4e: 2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)-N'-(4-methylbenzylidene) acetohydrazide. Colour : Dark yellow crystals; Yield : 74.33%; m.p. 238-240°C; Anal. calcd. for $C_{17}H_{17}N_3O_3S$ (313) : C,65.18 ; H,5.43 ; N,13.42 ; S,10.22 %. Found - C,65.22; H,5.41;

N,13.39; S,10.21 %; IR(KBr, cm^{-1}): 3388, 1341 (-NH-), 1678 (>C=O, amide), 1638 (-N=CH-); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 5.28(s,1H, -N=CH-), 8.10 (s, 1H,-CONH-), 6.85-7.71 (m, 4H, Ar-H), 2.85(s,3H, -CH_3); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 166.8(RCOO-), 146.3(-N=CH-), 36.8(-CH_3).

Compound 4f: N'-(benzo[d][1,3]dioxol-5-ylmethylene)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetohydrazide (4f) : Colour : Brown crystals; Yield : 82.12%; m.p. 240-244°C; Anal. calcd. for $C_{17}H_{19}N_3OS$ (343) : C,59.47 ; H,5.54 ; N, 12.25 ; S,9.33 %. Found : C,59.45 ; H,5.52 ; N,12.23 ; S,9.34 %; IR(KBr, cm^{-1}): 3350, 1345 (-NH-), 1672 (>C=O, amide), 1632 (-N=CH-); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 5.68(s,1H, -N=CH-), 8.15 (s, 1H,-CONH-), 7.15-7.75 (m, 3H, Ar-H), 6.25(s,2H, O-CH_2-O); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 172.8(RCOO-), 166.3(-N=CH-),112(O-CH_2-O).

Compound 4g: 2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)-N'-(4-hydroxy-3-methoxy benzylidene)acetohydrazide: Colour : Brown crystals; Yield : 69.17%; m.p.241-246°C; Anal. calcd. for $C_{17}H_{19}N_3O_3S$ (345) : C,59.13 ; H,5.51 ; N, 12.17 ; S,9.27 %. Found : C,59.15 ; H,5.48 ; N,12.14 ; S,9.26 %; IR(KBr, cm^{-1}): 3380,1337 (-NH-), 1684 (>C=O, amide), 1637 (-N=CH-); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 5.66(s,1H, -N=CH-), 8.12 (s, 1H,-CONH-), 6.85-7.75 (m, 3H, Ar-H), 3.75(s,3H, -OCH_3), 5.80(s, H,-OH); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 170.8(RCOO-), 164.3(-N=CH-),64.8(-OCH_3).

Compound 4h: N'-(3,4-diethoxybenzylidene)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetohydrazide: Colour : Light brown crystals; Yield : 89.54%; m.p. : 253-257°C; Anal. calcd. for $C_{18}H_{20}N_3OS$ (326) : C,66.26 ; H,6.11 ; N,12.89 ; S,9.80 %. Found : C,66.25 ; H,6.13 ; N,12.87 ; S,9.83 %; IR(KBr, cm^{-1}): 3380,1337 (-NH-), 1684 (>C=O, amide), 1639 (-N=CH-); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 5.66(s,1H, -N=CH-), 8.12 (s, 1H,-CONH-), 6.85-7.75 (m, 3H, Ar-H), 4.25(q,2H,-OCH_2CH3), 1.85(t,3H,-OCH_2CH3); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm) : 173.8 (RCOO-), 164.6 (-N=CH-).

Preparation of 2-(6,7-dihydrothieno[3,2-*c*]pyridin-5(4H)-yl)-N-(4-oxo-2-phenyl thiazolidin-3-yl)acetamide (5a-h).

A mixture of *N*'-benzylidene-2-(6,7-dihydrothieno[3,2-*c*]pyridine-5(4H)-yl)acetohydrazide **(4a-h)** [0.01mole] in THF (30ml) and mercapto acetic acid (thioglycolic acid) [0.01 mole] with a pinch of anhydrous $ZnCl_2$ [0.05gm] was refluxed for 12 hrs. The solvent was then removed to get a residue, which was dissolved in pet-ether and passed through a column of silica gel using pet-ether: chloroform (6:4; v/v) mixture as eluent. The eluate was concentrated and the product crystallized from alcohol to give 4-thiazolidinones **(5a-h)**.

Compound 5a: 2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)-N-(4-oxo-2-phenylthiazolidin-3-yl)acetamide: Colour : White crystals, Yield : 80.02%; m.p. 210-215°C; Anal. calcd. for $C_{18}H_{20}N_3O_2S_2$ (374) : C,57.75 ; H,5.35 ; N,11.23 ; S,17.11 %. Found - C, 57.73; H, 5.33; N,11.20; S,17.15%; IR(KBr, cm^{-1}): 3285, 1348 (-NH-), 1678(>C=O, amide), 1726 (>C=O, thiazolidinone); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.53 (s, 1H, -CONH-), 7.00-7.95 (m, 5H, Ar-H), 5.15 (s, 1H, -N=CH-), 4.60 (s, 2H, -CH_2-thiazolidinone); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 164.5 (>C=O, thiazolidinone), 170(>C=O, amide), 47.2 (-CH_2-, thiazolidinone), 74.60(-N=CH-).

Compound 5b: 2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)-N-(2-(4-methoxyphenyl)-4-oxothiazo-lidin-3-yl)acetamide: Colour : White crystals; Yield : 78.06%; m.p. 205-210°C; Anal. calcd. for $C_{19}H_{22}N_3O_3S_2$ (404) : C,56.44 ; H,5.45 ; N,10.40 ; S,15.84 %. Found - C,56.35 ;H,5.55 ; N,10.48 ; S,15.78 %; IR(KBr, cm^{-1}): 3378,1339 (-NH-), 1675 (>C=O,amide), 1721 (>C=O, thiazolidinone), 2830 (Ar-OCH3); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.53 (s, 1H, -CONH-), 6.65-7.77 (m, 4H, Ar-H), 5.16(s, 1H, -N=CH-), 4.66 (s, 2H, -CH2-thiazolidinone), 3.89 (s, 3H, -OCH3); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 62.35(-OCH_3), 164.5 (>C=O, thiazolidinone), 170(>C=O, amide), 47.2 (-CH_2-,thiazolidinone), 74.60(-N=CH-).

Compound 5c: 2-(6, 7-dihydrothieno [3, 2-c] pyridin-5(4H)-yl)-N-(2-(4-hydroxyphenyl)-4-oxothiazolidin-3-yl)acetamide: Colour : White crystals; Yield : 67.26%; m.p. 155-158°C; Anal. calcd. for $C_{18}H_{20}N_3O_3S_2$ (390) : C,55.38 ;H, 12.5 ;N,10.76 ;S,16.41 %. Found : C,55.36 ;H,12.53 ;N,10.70 ;S,16.46 %; IR(KBr, cm^{-1}): 3390, 1337 (-NH-), 1679 (>C=O, amide),1730(>C=O, thiazolidinone), 3583 (Ar-OH); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.49 (s, 1H, -CONH-), 7.20-7.90 (m, 4H, Ar-H), 5.57 (s, 1H, -N=CH-), 4.60 (s, 2H,-CH2-thiazolidinone), 10.26 (s, 1H, -OH); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 31.5 (-S-CH2-), 175 (>C=O, thiazolidinone), 167.2 (amide, >C=O),72.6(-N=CH-).

Compound 5d: 2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)-N-(2-(2-hydroxyphenyl)-4-oxothiazolidin-3-yl) acetamide: Colour : White crystals; Yield : 85.07%; m.p. 130-135°C; Anal. calcd. for $C_{18}H_{20}N_3O_3S_2$ (390) : C,55.38 ;H, 12.5 ;N,10.76 ;S,16.41 %. Found : C,55.36 ;H,12.53 ;N,10.70 ;S,16.46 %; IR(KBr, cm^{-1}): 3290,1338 (-NH-), 1670(>C=O, amide), 1725 (>C=O, thiazolidinone), 3590 (Ar-OH); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.49 (s, 1H, -CONH-), 7.20-7.90 (m, 4H, Ar-H), 5.17 (s, 1H, -N=CH-), 4.51 (s, 2H, S-CH2-), 4.65 (s, 1H, -OH); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 31.5 (-S-CH2-), 175 (>C=O, thiazolidinone), 167.2 (amide, >C=O),62.4(-N=CH-).

Compound 5e: 2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)-N-(4-oxo-2-p-tolylthiazolidin-3-yl) acetamide : Colour : White crystals; Yield : 94.11%; m.p. 165-170°C; Anal. calcd. for $C_{19}H_{20}N_3O_4S_2$ (388): C,54.54 ; H,4.78 ; N,10.05 ; S,15.3 %. Found: C,54.58 ; H,4.83 ; N,10.15 ; S,15.34 %; IR(KBr, cm^{-1}) : 3294, 1334 (-NH-), 1675(>C=O, amide), 1720 (>C=O, thiazolidinone); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.49 (s, 1H, -CONH-), 7.20-7.90 (m, 4H, Ar-H), 5.17 (s, 1H, -N=CH-), 4.58 (s, 2H, S-CH2-), 2.9(s,3H, -CH_3); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 31.5 (-S-CH2-), 175 (>C=O, thiazolidinone), 167.2(amide, >C=O), 62.4(-N=CH-).

Compound 5f: N-(2-(benzo[d][1,3]dioxol-5-yl)-4-oxothiazolidin-3-yl)-2-(6,7-dihydrothieno [3,2-c] pyridin-5(4H)-yl)acetamide: Colour : White crystals; Yield : 88.03%; m.p. 181-183°C; Anal. calcd. for $C_{19}H_{22}N_3O_2S_2$ (418) : C,58.76; H,5.68; N,10.82; S,16.49%. Found : C,58.76 ;H,5.68 ;N,10.82 ;S,16.49 %; IR(KBr, cm^{-1}): 3290, 1338 (-NH-), 1670(>C=O, amide), 1727 (>C=O, thiazolidinone), 2367(-CH_2-O-CH_2-); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.49 (s, 1H, -CONH-), 7.20-7.90 (m, 3H, Ar-H), 5.27 (s, 1H, -N=CH-), 4.61 (s, 2H, S-CH2-), 6.2 (s, 2H, O-CH_2-O); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 101.2(O-CH_2-O), 33.5 (-S-CH2-), 172 (>C=O, thiazolidinone), 167.2(>C=O, amide), 62.6(-N=CH-).

Compound 5g: 2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)-N-(2-(4-hydroxy-3-methoxy phenyl)-4-oxothiazolidin-3-yl)acetamide: Colour : White crystals; Yield : 68.07%; m.p. 154-156°C; Anal. calcd. for $C_{19}H_{22}N_3O_4S_2$ (420) : C,54.28 ;H,5.24 ;N,10.00 ;S,15.24 %. Found : C,54.30 ; H,5.28 ;N,10.06 ;S,15.22%; IR(KBr, cm^{-1}): 3275, 1342 (-NH-), 1665(>C=O, amide), 1724 (>C=O, thiazolidinone), 3580 (Ar-OH); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.49 (s, 1H, -CONH-), 7.30-7.90 (m, 3H, Ar-H), 5.34 (s, 1H, -N=CH-), 4.63 (s, 2H, S-CH2-), 3.82 (s, 3H, -OCH_3), 4.82(s,H,-OH); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 66.8(-OCH_3),33.8 (-S-CH2-), 174(>C=O,thiazolidinone), 168.4(>C=O, amide),64.5(-N=CH-),63.45(-OCH_3).

Compound 5h: N-(2-(3,4-diethoxyphenyl)-4-oxothiazolidin-3-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamide : Colour : White crystals; Yield : 72.23%; m.p. 190-194°C; Anal. calcd. for $C_{20}H_{23}N_3O_2S_2$ (401) : C,59.85 ;H,5.73 ;N,10.47 ;S,15.96 %. Found : C,59.88 ;H,5.76 ;N,10.42 ;S,15.92%; IR(KBr, cm^{-1}): 3290, 1338 (-NH-), 1670(>C=O, amide), 1728 (>C=O, thiazolidinone), 3590 (Ar-OH); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.49 (s, 1H, -CONH-), 7.30-7.90 (m, 3H, Ar-H), 5.32 (s, 1H, -N=CH-), 4.57 (s, 2H, S-CH_2-), 4.82 (q, 4H, -OCH_2CH_3),4.82(t,6H,-OCH_2CH_3); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 33.8 (-S-CH_2-),-172 (>C=O, thiazolidinone), 167.2(>C=O,amide),62.8(-N=CH-),16.24(-CH_3),66.8(-CH_2-),

Preparation of N-(5-benzylidene-4-oxo-2-phenylthiazolidin-3-yl)-2-(6,7-dihydro thieno [3,2- *c*]pyridin-5(4H)-yl)acetamide (6a-h).

An equimolar solution of 2-(6,7-dihydrothieno[3,2-*c*]pyridin-5(4H)-yl)-N-(4-oxo-2-phenylthiazolidin-3-yl)acetamide (0.01mole) **(5a-h)** and 4-chlorobenzaldehyde in dioxane (50 ml) in the presence of C_2H_5ONa were refluxed for about 3 hr. The solvent was removed in vacuum. The resulting product was purified by column chromatography technique and recrystallized from methanol to yield compounds **(6a-h).**

Compound 6a: N-(5-(4-chlorobenzylidene)-4-oxo-2-phenylthiazolidin-3-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamide : Yield : 82.01%; m.p. 214-216°C; Anal. calcd. for $C_{25}H_{24}N_3O_2S_2Cl$ (462) : C,64.93 ;H,5.19 ;N,9.09 ;S,13.85 %. Found : C,64.96 ; H,5.22 ;N,9.12 ;S,13.83%; IR(KBr, cm^{-1}): 3285, 1345 (-NH-), 1685(>C=O, amide),1738 (>C=O, thiazolidi none); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.53 (s, 1H, -CONH-), 7.00-7.58 (m, 10H, Ar-H), 4.15 (s, 1H, -N-CH-),6.86(>C=CH); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 164.5 (>C=O, thiazolidinone), 170(>C=O, amide),74.72(-N-CH-),132.5,128.4(>C=CH-).

Compound 6b: N-(5-(4-chlorobenzylidene)-2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)-2-(6,7-dihydro thieno[3,2-c]pyridin-5(4H)-yl)acetamide : Yield : 72.42%; m.p. 220-225°C; Anal. calcd. for $C_{26}H_{26}N_3O_3S_2Cl$ (492) : C,63.41 ;H,5.28 ;N,8.54 ;S,13.00 %. Found : C,63.46 ;H,5.24 ;N,8.56 ;S,13.05%; IR(KBr, cm^{-1}): 3388, 1349 (-NH-), 1684 (>C=O, amide),1734 (>C=O, thiazolidinone), 2830 (Ar-OCH_3); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.55 (s, 1H, -CONH-), 6.65-7.87 (m, 9H, Ar-H), 4.16(s, 1H, -N-CH-), 3.91 (s, 3H, -OCH3),4.20(>C=CH-); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 62.38(-OCH_3), 164.8 (>C=O, thiazolidinone), 171.8(>C=O, amide),134,129(>C=CH-),70.60(-N-CH-).

Compound 6c: N-(5-(4-chlorobenzylidene)-2-(4-hydroxyphenyl)-4-oxothiazolidin-3-yl)-2-(6,7-dihydro thieno[3,2-c]pyridin-5(4H)-yl)acetamide : Yield : 68.04%; m.p. 200-202°C; Anal. calcd. for $C_{25}H_{24}N_3O_3S_2Cl$ (478) : C,62.76 ;H,5.02 ;N,8.79 ;S,13.38 %. Found : C,62.79 ;H,5.06 ;N,8.82

;S,13.41%; IR(KBr, cm^{-1}): 3386, 1341 (-NH-), 1678 (>C=O, amide), 1733(>C=O, thiazolidinone), 3573 (Ar-OH); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.47 (s, 1H, -CONH-), 7.20-7.90 (m, 9H,Ar-H), 3.57 (s, 1H, -N-CH-), 4.68 (s, 1H, -OH),4.21(>C=CH-); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 174 (>C=O, thiazolidinone), 166.2(>C=O,amide), 70.6(-N-CH-), 134.8,128.8(>C=CH-).

Compound 6d: N-(5-(4-chlorobenzylidene)-2-(2-hydroxyphenyl)-4-oxothiazolidin-3-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamide : Yield : 62.00%; m.p. 190-194°C; Anal. calcd. for $C_{25}H_{24}N_3O_3S_2Cl$ (478) : C,62.76 ;H,5.02 ;N,8.79 ;S,13.38 %. Found : C,62.79 ;H,5.06 ;N,8.82;S,13.41%; IR(KBr, cm^{-1}): 3290,1338 (-NH-), 1670(>C=O, amide), 1725(>C=O, thiazolidinone), 3590 (Ar-OH); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.49 (s, 1H, -CONH-), 7.20-7.90 (m, 4H, Ar-H), 4.17 (s, 1H, -N=CH-), 4.31 (s, 2H, S-CH2-), 4.65 (s, 1H, -OH); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 31.5 (-S-CH2-), 175 (>C=O, thiazolidinone), 167.2 (amide, >C=O),62.4(-N=CH-).

Compound 6e: N-(5-(4-chlorobenzylidene)-4-oxo-2-p-tolylthiazolidin-3-yl)-2-(6,7-dihydrothieno [3,2-c] pyridin-5(4H)-yl)acetamide : Yield : 78.05%; m.p. 185-187°C; Anal. calcd. for $C_{26}H_{24}N_3O_4S_2Cl$ (476) : C,65.55 ;H,5.04 ;N,8.82 ;S,13.44 %. Found : C,65.58 ;H,5.06 ;N,8.85 ;S,13.48%; IR(KBr, cm^{-1}): 3294, 1334 (-NH-), 1675(>C=O, amide), 1720 (>C=O, thiazolidinone), 3595 (Ar-OH); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.49 (s, 1H, -CONH-), 7.20-7.90 (m, 4H, Ar-H), 4.17 (s, 1H, -N=CH-), 4.31 (s, 2H, S-CH2-), 4.65 (s, 1H, -OH); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 31.5 (-S-CH2-), 175 (>C=O, thiazolidinone), 167.2(amide, >C=O),62.4(-N=CH-).

Compound 6f: N-(2-(benzo[d][1,3]dioxol-5-yl)-5-(4-chlorobenzylidene)-4-oxothiazolidin-3-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamide (6f) : Yield : 82.55%; m.p. 207-210°C; Anal. calcd. for $C_{26}H_{26}N_3O_2S_2Cl$ (506) : C,61.66 ;H,5.13 ;N,8.30 ;S,12.64 %. Found - C,61.64 ;H,5.16 ;N,8.34 ;S,12.67%; IR(KBr, cm^{-1}): 3290, 1338 (-NH-), 1670(>C=O, amide), 1725 (>C=O, thiazolidinone), 3590 (Ar-OH); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.49 (s, 1H, -CONH-), 7.20-7.90 (m, 3H, Ar-H), 4.27 (s, 1H, -N=CH-), 4.38 (s, 2H, S-CH2-), 6.2 (s, 2H, O-CH_2-O); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 101.2(O-CH_2-O), 33.5 (-S-CH2-), 172(>C=O, thiazolidinone), 167.2(amide, >C=O),62.6(-N=CH-).

Compound 6g: N-(5-(4-chlorobenzylidene)-2-(4-hydroxy-3-methoxyphenyl)-4-oxothiazolidin-3-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamide : Yield : 72.03%; m.p. 195-198°C; Anal. calcd. for $C_{26}H_{28}N_3O_2S_2Cl$ (508) : C,61.42 ;H,5.11 ;N,8.26 ;S,12.59 %. Found **:** C,61.45 ; H,5.14 ;N,8.28 ;S,12.57%; IR(KBr, cm^{-1}): 3275, 1342 (-NH-), 1665(>C=O, amide), 1745 (>C=O,thiazolidinone), 3580 (Ar-OH); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.49 (s, 1H, -CONH-), 7.30-7.90 (m, 3H, Ar-H), 4.34 (s, 1H, -N=CH-), 4.36 (s, 2H, S-CH2-), 3.82 (s, 3H, -OCH_3), 4.82(s,H,-OH); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 101.4(O-CH_2-O), 33.8 (-S-CH2-),172(>C=O,thiazolidinone), 167.2(>C=O, amide),62.8(-N=CH-), 63.45(-OCH_3).

Compound 6h: N-(5-(4-chlorobenzylidene)-2-(3,4-diethoxyphenyl)-4-oxothiazolidin-3-yl)-2-(6,7-dihydro thieno[3,2-c]pyridin-5(4H)-yl)acetamide(6h) : Yield : 64.04%; m.p. 215-218°C; Anal. calcd. for $C_{27}H_{27}N_3O_2S_2Cl$ (489) : C,63.80 ;H,5.52 ;N,8.59 ;S,13.08 %. Found : C,63.82 ;H,5.60 ;N,8.61 ;S,13.12%; IR(KBr, cm^{-1}): 3290, 1338 (-NH-), 1670(>C=O, amide), 1730 (>C=O,thiazolidinone); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.49 (s, 1H, -CONH-), 7.30-7.90 (m, 3H, Ar-H), 4.32 (s, 1H, -N=CH-), 4.38 (s, 2H, S-CH_2-), 4.82 (q, 4H, -OCH_2CH_3),

4.82(t,6H,-OCH_2CH_3); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 33.8 (-S-CH2-), 172 (>C=O, thiazolidinone),167.2(>C=O, amide),62.8(-N=CH-),16.24(-CH_3),66.8(-CH_2-).

Preparation of N-(3-(4-chlorophenyl)-2,5-diphenyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamide (7a-h).

A mixture of benzylidine derivatives **(6a-h)** (0.01, mole) and phenyl hydrazine (0.01 mole) were refluxed in glacial acetic acid (10ml) and sodium acetate (1.0gm) for 8 hrs. The hot mixture was filtered to remove any insoluble material, cooled, then water was added and boiled for few minutes, then it was cooled to give crude product. The product thus obtained was purified by column chromatography over silica gel using n-hexane: chloroform (8:2, v/v) system as eluent. The eluate was concentrated to give compounds (**7a-h).**

Compound 7a: N-(3-(4-chlorophenyl)-2,5-diphenyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)-2-(6,7-dihydro thieno[3,2-c]pyridin-5(4H)-yl)acetamide. Yield: 76.15%; m.p. 205-210°C; Anal. calcd. for $C_{31}H_{28}N_5OS_2Cl$ (586): C,63.48; H,4.78; N, 11.94; S,10.92%. Found: C,63.47; H,4.76; N,11.96; S,10.94%; IR(KBr, cm^{-1}): 3275, 1355(-NH-), 1670(>C=O, amide), 1040(N-N, pyrazole); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.50(s, 1H, -CONH-), 6.85-7.95(m, 14H, Ar-H), 4.25(s, 1H, -N-CH-); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 173(>C=O,amide), 98.60 (-N-CH-), 165.50(>C=N-, pyrazole).

Compound 7b: N-(3-(4-chlorophenyl)-5-(4-methoxyphenyl)-2-phenyl-2H-pyrazolo[3,4-d] thiazole-6(5H)-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamide. Yield: 68.62%; m.p. 225-230°C; Anal. calcd. for $C_{32}H_{30}N_5O_2S_2Cl$ (616): C,62.34; H,4.54; N,11.36; S,10.38%. Found: C,62.48; H,4.58; N,11.38; S,10.32%; IR(KBr, cm^{-1}): 3270, 1350(-NH-), 1675(>C=O, amide), 1045(N-N, pyrazole); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.52(s, 1H, -CONH-), 6.85-7.95(m, 14H, Ar-H), 4.23(s, 1H, -N-CH-); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 174 (>C=O, amide), 98.75(-N-CH-), 165.62(>C=N-, pyrazole).

Compound 7c: N-(3-(4-chlorophenyl)-5-(4-hydroxyphenyl)-2-phenyl-2H-pyrazolo[3,4-d] thiazol-6(5H)-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamide. Yield: 56.08%; m.p. 198-200°C; Anal. calcd. for $C_{31}H_{28}N_5O_2S_2Cl$ (602): C,60.39; H,4.65; N,11.62; S,10.63%. Found: C,60.48; H,4.78; N,11.64; S,10.62%; IR(KBr, cm^{-1}): 3260, 1345(-NH-), 1672(>C=O, amide), 1042(N-N, pyrazole); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.45(s, 1H, -CONH-), 6.85-7.95(m, 14H, Ar-H), 4.28(s, 1H, -N-CH-); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 176.5 (>C=O, amide), 97.20 (-N-CH-), 167.30(>C=N-, pyrazole).

Compound 7d: N-(3-(4-chlorophenyl)-5-(2-hydroxyphenyl)-2-phenyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamide : Yield **:** 68.15%; m.p. 212-214°C; Anal. calcd. for $C_{31}H_{28}N_5O_2S_2Cl$ (602) : C,60.39; H,4.65; N,11.62; S,10.63%. Found **:** C,60.36; H,4.69; N,11.58; S,10.65%; IR(KBr, cm^{-1}): - 3273, 1352 (-NH-), 1668(>C=O, amide),1038(N-N,pyrazole); ^{1}H NMR(400 MHz, DMSO-d_6, δ / ppm): - 8.62 (s, 1H, -CONH-), 6.85-7.95 (m, 14H, Ar-H), 4.40 (s, 1H, -N-CH-); ^{13}C NMR(400 MHz, DMSO-d_6, δ / ppm): - 176.45 (>C=O, amide),97.68 (-N-CH-),167.45(>C=N-, pyrazole).

Compound 7e: N-(3-(4-chlorophenyl)-2-phenyl-5-p-tolyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamide : Yield : 72.08%; m.p. 185-187°C; Anal.

calcd. for $C_{32}H_{30}N_5OS_2Cl$ (600) : C,64.00; H,5.00; N, 11.66; S,10.66%. Found : C,64.08; H,5.03; N,11.69; S,10.58%; IR(KBr, cm^{-1}) : 3277, 1358 (-NH-), 1676(>C=O, amide), 1043(N-N,pyrazole); ^{1}H NMR(400 MHz, DMSO-d_6, δ / ppm) : 8.57(s, 1H, -CONH-),6.87-7.98(m, 14H,Ar-H), 4.29 (s, 1H, -N-CH-); ^{13}C NMR(400 MHz, DMSO-d_6, δ / ppm) : 178.5 (>C=O ,amide),98.60 (-N-CH-), 167.68(>C=N-, pyrazole).

Compound 7f: N-(5-(benzo[d][1,3]dioxol-5-yl)-3-(4-chlorophenyl)-2-phenyl-2H-pyrazolo-[3,4-d]thiazol-6(5H)-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamid. Yield: 68.45 %; m.p. 203-204°C; Anal. calcd. for $C_{32}H_{28}N_5O_3S_2Cl$ (630): C,60.95; H,4.44; N,11.11; S,10.15%. Found: C,60.93; H,4.46; N,11.15; S,10.17%; IR(KBr, cm^{-1}): 3276, 1362(-NH-), 1670(>C=O, amide), 1042 (N-N,pyrazole); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.56(s, 1H, -CONH-), 6.85-7.95(m,14H,Ar-H), 4.29(s, 1H, -N-CH-); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 174.5 (>C=O, amide), 98.68 (-N-CH-), 165.58(>C=N-, pyrazole).

Compound 7g: N-(3-(4-chlorophenyl)-5-(4-hydroxy-3-methoxyphenyl)-2-phenyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamid. Yield: 78.32 %; m.p. 218-220°C; Anal. calcd. for $C_{32}H_{30}N_5O_3S_2Cl$ (632): C,60.95; H,4.75; N,11.08; S,10.13%. Found: C,60.89; H,4.78; N,11.11; S,10.15%; IR(KBr, cm^{-1}): 3278, 1356(-NH-), 1675(>C=O, amide) , 1047(N-N, pyrazole); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.52(s, 1H, -CONH-), 6.85-7.95(m, 14H, Ar-H), 4.28(s, 1H, -N-CH-); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 178 (>C=O, amide), 98.74 (-N-CH-), 165.72(>C=N-, pyrazole).

Compound 7h: N-(3-(4-chlorophenyl)-5-(3,4-diethoxyphenyl)-2-phenyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)-2-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl)acetamide. Yield: 58.20%; m.p. 228-230°C; Anal. calcd. for $C_{35}H_{36}N_5O_3S_2Cl$ (674): C,62.31; H,5.34; N,10.38; S,9.19%. Found: C,62.38; H,5.38; N,10.44; S,9.25%; IR (KBr, cm^{-1}): 3278, 1357 (-NH-), 1667(>C=O, amide), 1043(N-N,pyrazole); ^{1}H-NMR(400 MHz, DMSO-d_6, δ / ppm): 8.57 (s, 1H, -CONH-), 6.85-7.95 (m, 14H, Ar-H), 4.22 (s, 1H, -N-CH-); ^{13}C-NMR(400 MHz, DMSO-d_6, δ / ppm): 176 (>C=O,amide), 98.74 (-N-CH-), 165.68(>C=N-, pyrazole).

Biological Screening

Antibacterial Activities

All the newly synthesized compounds have been tested *in vitro* for their antibacterial activity against gram-positive and gram-negative bacteria *Staphylococcus aureus* (ATCC-25923), *Bacillus subtilis* (recultured), Escherichia *coli* (ATCC-25922), *Pseudomonas picketti* (recultured) and *Micrococcus luteus* (recultured) at a concentration of 50µg/ml by agar well diffusion method[24]. DMSO was used as a control solvent. Under similar conditions Tetracycline was used as a standard drug for comparison. After 24 hr of incubation at 37°C, the zone of inhibition was measured in mm.Their results show that almost all compounds are active against bacteria, twenty of them are shown in Table -1.

Antifungal Activities

Selected representatives of newly synthesized compounds were screened *in vitro* for their antifungal activity against six species like *Trichphyton longifusus*, *Candida albicans*, *Aspergillus flavus*, *Microsporum Canis*, *Fusarium Solani*, *Candida glabrata* by using agar plate technique [25]. The linear growth of the fungus were obtained by measuring the diameter of the fungal

colony after seven days. The amounts of growth of inhibition in each case were calculated as percentage inhibition. The screening results are given in Table 2.

RESULTS AND DISCUSSION

The IR spectra of the compound **(2)** display a strong absorption band at 1726 cm^{-1} for >C=O of ester and ^1H NMR spectra, shows triplet-quartet pair at 1.23 and 4.13 ppm for ethoxy group which indicate the formation of compound **(2)**.In the IR spectra of the compound **(3)** the absorption bands due to >C=O of ester was disappeared and a new strong band at 1665 cm^{-1} of (-CONH-) amide clearly indicated the formation of the respective amide, also the triplet–quartet pair at 1.23 and 4.13 ppm for ethoxy group was disappear and two singlet peaks at 4.40 and 7.88 for free $–NH_2$ and –NHCO- show the formation of amide with hydrazine. The strong absorption band at ~1638 $cm^{-1}$for –N=CH- in IR spectra of all the **(4a-h)** compounds and disappearance of peak at 4.40 for free $–NH_2$ in ^1H NMR spectra of compounds **(3)** reveals the formation of Schiff's base. In IR spectra of compounds **(5a-h),** the band at ~1638 $cm^{-1}$for –N=CH- was disappeared and new band at 1725 cm^{-1} for (>C=O, thiazolidinone) carbonyl was appear which show the formation of cyclic thiazolidinone ring **(5a-h)**, also in 1H-NMR (400 MHz, DMSO-d6, δ/ppm):peak at 4.51-4.66 for (s,2H,-CO-CH_2-S-). Presence of strong absorption band at (840-870) cm^{-1} for >C = CH- in IR spectra of all the **(6a-h)** compounds and in ^1H NMR spectra, peak around 6.86 for (s,1H,>C = CH-Ar) reveals the formation of compounds **(6a-h)**.In IR spectrum of **(7a-h)** compounds, the band at ~1725 cm^{-1} for carbonyl of thiazolidinone ring was disappear and new band at 1038-1047 cm^{-1} (N-N, pyrazole) was appear which show the formation of pyrazole ring, in ^1H NMR spectra peak at 3.46,4.80 (s,2H,>CH-CH<, pyrazole) conform the formation of pyrazolo ring. All these compounds were also conformed by ^{13}C NMR and elemental analysis as show in experimental section.

Biological Evaluation

From Table -1, we can see that almost all the compounds are active against *Escherichia coli* except **5c,5g** and **6a**. It is worth noting here that compounds **6h,7b** and **7g** showed moderate (9.5 mm) to significant activity (18.4 mm) against all the bacteria except *Pseudomonas picketti*, also compound **6g** significantly active against all the bacteria except *Micrococcus luteus.* The compounds **6f, 7f** and **7h** are significantly (maximum) active against all the bacteria. The other compounds showed none to low activity as displayed in Table-1. The investigation on the structure-activity relationship (SAR) shows that in general, compounds **(7a-h)** are significantly more active than that of the compounds **(6a-h)**, this is due to pyrazole ring. Also the presence of chlorine, dioxole ring, diethoxy group and methoxy-hydroxy groups on benzene ring in addition to thiazolidone and pyrazole moiety enhanced the antibacterial activity of synthesized compounds. Minimum Inhibitory Concentration (MIC) values of all the twenty four synthesized compounds were determined by agar well diffusion method [24] and results are shown in Table-1.

In addition, Selected representatives of newly synthesized compounds were screened for antifungal activities. From table 2 we can see that most of the compounds are significantly (maximum) active against *Trichphyton longifusus* and *Candida glabrata*.Compounds **5f** and **7c** exhibit moderate activity against some fungus where as compounds **6f**, **7f** and **7h** shows significant activity against all the fungus. It is worthwhile to note that compounds **6f** and **7f** exhibits significant (maximum) antifungal activities against all fungus, possibly due to the presence of dioxole ring moiety on benzene in addition to thiazolidone and pyrazole ring. While, in case of compounds **6h** and **7h** the substitution of diethoxy

group on benzene ring, in addition to thiazolidone and pyrazole ring improve the antifungal activity as given in Table- 2.

Table 1. Antibacterial activities and minimum inhibitory conc. (MIC)

Comp No.	*Eschericha Coli (MIC)*	*Pseudomoas picketti (MIC)*	*Bacillu Subtilis (MIC)*	*Staphylococcs aureus (MIC)*	*Micrococcluteus (MIC)*
5b	08.40 (0.4)	--	--	--	--
5c	--	10.00 (0.5)	--	--	--
5g	--	--	0.85 (0.6)	--	06.78 (0.8)
5h	11.35 (0.4)	13.45 (0.5)	--	--	--
6a	--	--	--	09.05 (0.8)	11.30 (0.8)
6b	10.00 (0.7)	09.25 (0.8)	--	--	--
6c	12.00 (0.7)	--	11.65 (0.7)	--	--
6d	10.50 (0.7)	12.55 (0.8)	--	08.35 (0.8)	--
6e	09.00 (0.7)	--	--	--	08.75 (0.8)
6f	14.40 (0.7)	18.85 (0.8)	22.70 (0.7)	17.36 (0.8)	16.00 (0.8)
6g	13.25 (0.7)	18.50 (0.8)	21.50 (0.7)	18.40 (0.8)	--
6h	12.55 (0.7)	13.00 (0.8)	--	15.60 (0.8)	11.30 (0.8)
7a	06.85 (0.8)	--	04.60 (0.9)	08.74 (0.8)	--
7b	11.50 (0.8)	12.05 (1.0)	10.05 (0.9)	--	09.56 (1.0)
7c	13.00 (0.8)	11.45 (1.0)	12.50 (0.9)	--	--
7d	11.25 (0.8)	13.35 (1.0)	--	10.05 (0.8)	--
7e	10.45 (0.8)	--	11.35 (0.9)	--	--
7f	17.60 (0.8)	19.25 (1.0)	23.25 (0.9)	18.35 (0.8)	15.20 (1.0)
7g	16.45 (0.8)	18.60 (1.0)	--	17.65 (0.8)	16.45 (1.0)
7h	13.75 (0.8)	16.00 (1.0)	13.45 (0.9)	15.78 (0.8)	14.85 (1.0)
Tetracyclie (Standard)	14.00	18.46	23.50	17.85	15.00

a). Zone diameter of growth inhibition (mm) after 24 hours,<10 mm concentration, 1 mg/ml in Methanol.
b). ( ) Minimum Inhibitory Concentrations (MIC) in mg/mL
c). The data represents the mean values of two replicates
d). (--) – Not Active or Very minor active

Table 2. Antifungal activity of the newly synthesized compounds

Name of Fungi	Compd. No. and Inhibition Zones 1000 ppm(%)									Standard drug (%)
	5f	**6f**	**6g**	**6h**	**7b**	**7c**	**7f**	**7g**	**7h**	
Trichphyton longifusus	30	96	--	78	--	--	92	--	88	Miconazole (90)
Candida albicans	--	54	64	--	--	48	57	--	64	Miconazole (90)
Aspergillus flavus	45	36	--	72	82	--	38	68	75	Amphotericin (90)
Microsporum Canis	58	60	74	--	--	26	62	74	34	Miconazole (90)
Fusarium Solani	--	69	--	62	74	--	72	--	68	Miconazole (90)
Candida glabrata	--	88	--	84	--	58	84	78	92	Miconazole (90)

CONCLUSION

A series of some new 2-(6,7-dihydrothieno[3,2-*c*]pyridin-5(4H)-yl)-acetohydrazide **(3)** derivatives were synthesize through a facile reaction in good yields. This synthetic strategy allows the construction of relatively complicated nitrogen and sulfur containing heterocyclic system as well as the introduction of various substitutions into 4- and 6- positions of benzene.

Their structures were characterized by IR, ^{1}H-NMR, ^{13}C-NMR and elemental analysis. The antibacterial and antifungal activities of the newly synthesized compounds were evaluated. The results of bioassays indicated that some of these title compounds exhibited excellent fungicidal and antibacterial activities, which were comparable to the commercial becteriocides and fungicides. The modification of the heterocyclic ring of the parent compounds offers a promising prospect and highly active analogues are expected to be found by further work.

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