SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF THAIZOLE- PYRIMIDINE DERIVATIVES

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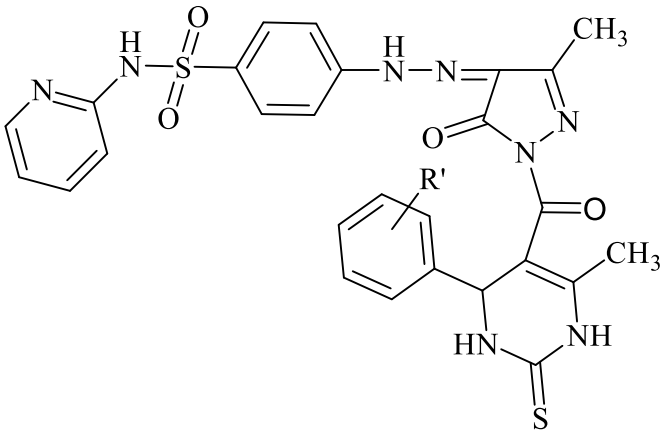
ABSTRACT

4-(2-(1-(7-aryl-5-methyl-3,7,8,8a-tetrahydro-2H-thiazolo[3,2-a]pyrimidine-6-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(pyridin-2-yl)benzenesulfonamide (B1-5) synthesised by the reaction of 4-(2-(1-(4-aryl-6-methyl-2-thioxo-1,2,3,4-tetra hydro pyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(pyridin-2-yl) benzene sulfonamide(A1-5) with dibromoethane. The structures of all the compounds series (B1-5) were characterized analytically. The compounds were also monitored for anti microbial activity.

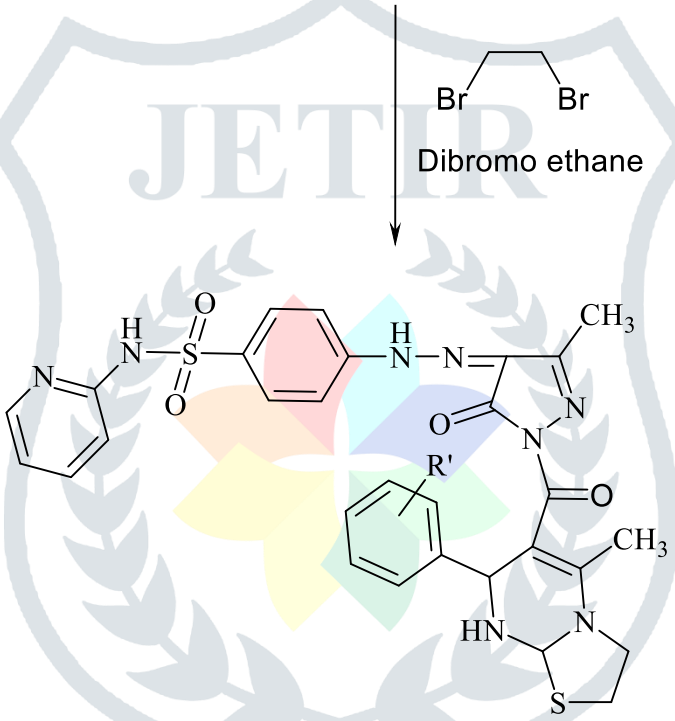
Key words: Fused heterocyclic derivatives, thaizole-pyrimidine derivatives, antimicrobial activity and spectral studies.

INTRODUCTION

Nowadays chemist are interesting to synthesis novel heterocyclic compounds.[1] Among them the fused heterocyclic compounds like, Thiazolopyrimidines are an interesting group of heterocyclic compounds. The compounds having thiazolo-pyrimidine derivatives reported for various pharmaceutical activities like, antioxidant, antihuman cytomegalovirus activity,anticancer,anti-inflammatory,antiparkinsonian,antimicrobial,antitumor and antiviral [2-10]. In connection of our previous research work on synthesis of fused heterocyclic compounds [11,12], present research article reported for the synthesis and characterization of various thiazolo-pyrimidines derivatives.



Compound [A1-5]



Compound [B1-5]

Where, R' = H, 4-Cl, 4-Br, 4-F & 3-NO_2

EXPERIMENTAL

4-(2-(1-(4-aryl-6-methyl-2-thioxo-1,2,3,4-tetra hydro pyrimidine-5-carbonyl)-3-methyl- 5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(pyridin-2-yl)benzene sulfonamide **(A1-5)** were synthesis by reported method. All other reagents were used laboratory grade.

The IR spectra of all compounds were taken in KBr pellets on a Nicolet 400D spectrometer. Proton NMR spectra were recorded on a Bruker (400 MHz) spectrometer. Deutorated DMSO was used as a solvent. LC-

MS of selected samples taken on LC-MSD-Trap-SL_01046. All the compounds were checked for their purity by TLC. The characterization data of all these compounds are given in Table.1.

The antibacterial activities of both the series of compounds (B1-5) were studied against gram +Ve and –Ve bacteria shown in Table-2. The activity was measured at a conc, 50µg/ml by agar-cup plate method. The percentage inhibition of growth of bacteria by the compounds is shown in Table-2.

The antifungal activity of both the series of compounds (B1-5) were measured at 1000ppm concentration in vitro Plant pathogen shown in Table-3 have been selected for study.

Synthesis of 4-(2-(1-(7-aryl-5-methyl-3,7,8,8a-tetrahydro-2H-thiazolo[3,2-a]pyrimidine-6-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(pyridin-2-yl) benzene sulfonamide (B1-5)

In a round bottom flask 4-(2-(1-(4-aryl-6-methyl-2-thioxo-1,2,3,4-tetra hydro pyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(pyridin-2-yl)benzene sulfonamide(A1-5) (10mmol) and 1,2-dibromoethane (20mmol) in methanol was stirred by magnetic stirrer at R.T. for 5 hrs. The product was checked by TLC frequently. The obtained precipitates filtered, washed by acetone and air-dried. Finally, the characterization data of these compounds are given in Table -1.

Table-1 Physical and Analytical Data of the Compounds Synthesized (B1-5)

Comp. No.	Molecular Formula	Yield %	M.P.* ˚C	Elemental Analysis							
				C%		H%		N%		S%	
				Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
B1	$C_{29}H_{28}N_8O_4S_2$ (616)	57	154-156	56.48	56.50	4.58	4.60	18.17	18.20	10.40	10.40
B2	$C_{29}H_{27}N_8O_4S_2Cl$ (651)	58	158-160	53.49	53.50	4.18	4.20	17.21	17.20	9.85	9.90
B3	$C_{29}H_{27}N_8O_4S_2Br$ (685)	57	164-165	50.07	50.10	3.91	3.90	16.11	16.10	9.22	9.20
B4	$C_{29}H_{27}N_8O_4S_2F$ (634)	58	162-164	54.88	54.90	4.29	4.30	17.65	17.60	10.10	10.10

B5	$C_{29}H_{27}N_9O_6S_2$ (661)	60	165-167	52.64	52.60	4.11	4.10	19.05	19.00	9.69	9.70

***** *Uncorrected* LC-MS data for B1:618, B4: 637

RESULTS AND DISCUSSIONS

The 4-(2-(1-(4-aryl-6-methyl-2-thioxo-1,2,3,4-tetra hydro pyrimidine-5-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene)hydrazinyl)-N-(pyridin-2-yl)benzene sulfonamide(A1-5) on reaction with 1,2-dibromoethane yielded 4-(2-(1-(7-aryl-5-methyl-3,7,8,8a-tetrahydro-2H-thiazolo[3,2-a]pyrimidine-6-carbonyl)-3-methyl-5-oxo-1H-pyrazol-4(5H)-ylidene) hydrazinyl)-N-(pyridin-2-yl)benzene sulfonamide (B1-5).

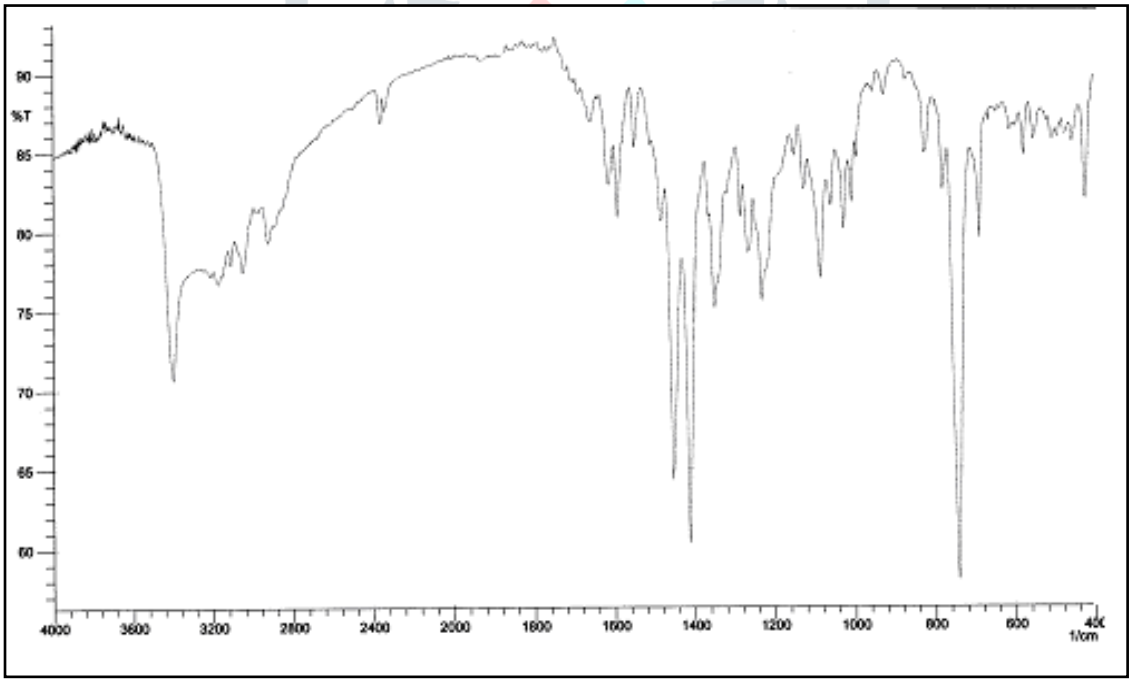


Figure 1 IR spectrum of compound B1

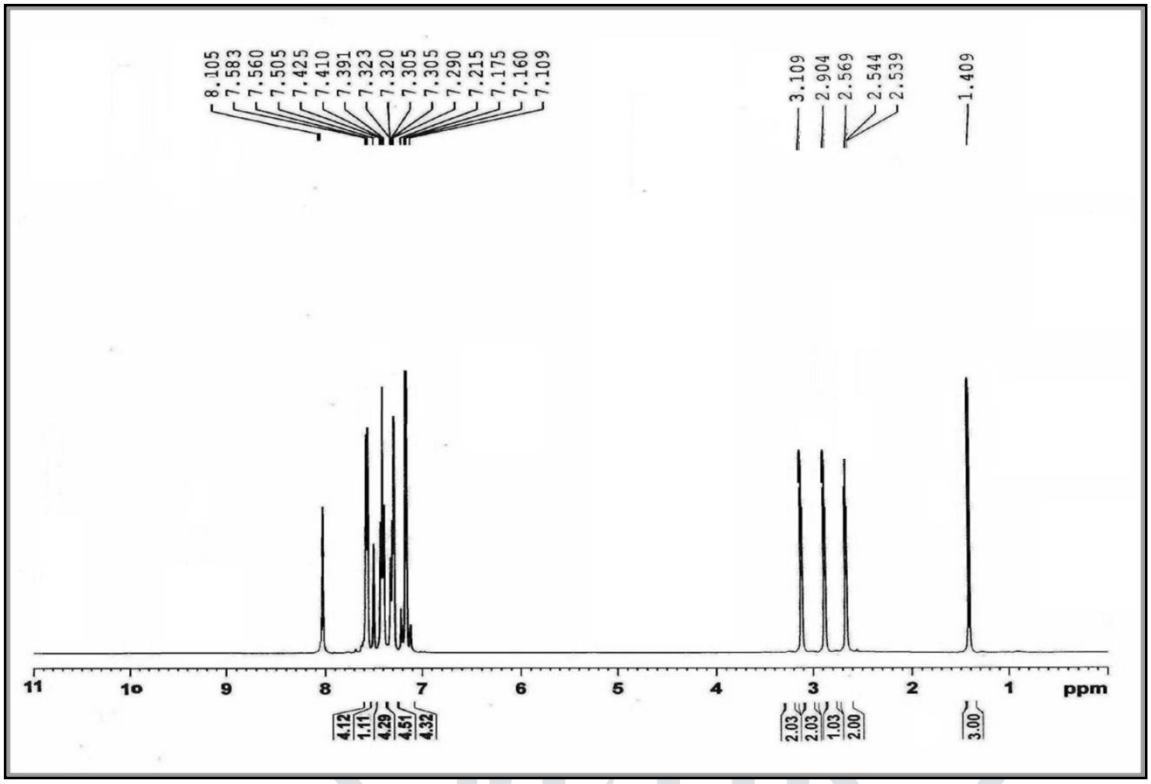


Figure 2 NMR spectrum of compound B2

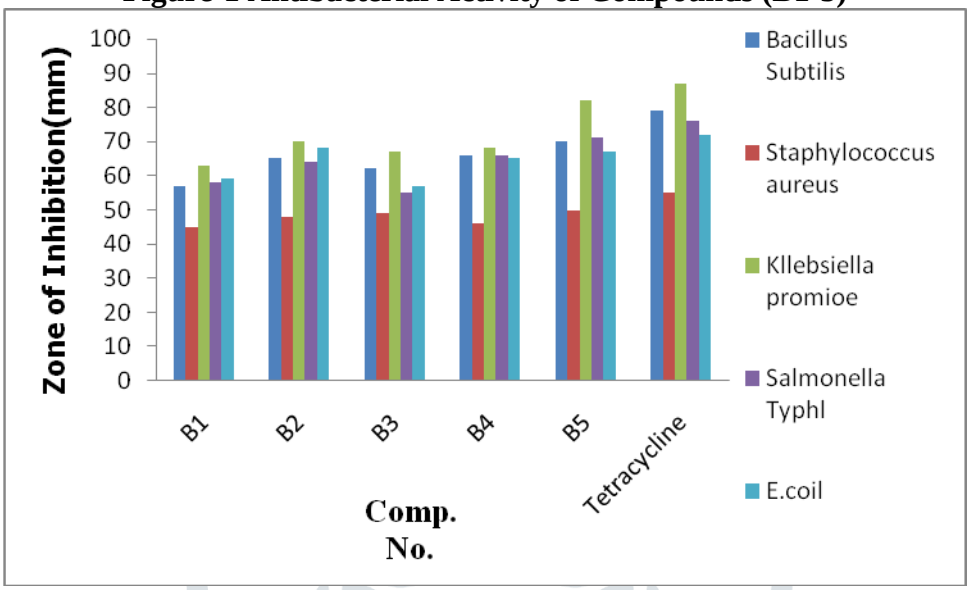
The IR spectra of **(B1-5)** are 3030-3080 cm^{-1}(C-H of Ar),3330cm^{-1}(NH),1620-1630 cm^{-1}(C=N),1680cm^{-1}(CO),2950,1370cm^{-1}(-CH_3,CH_2),680(C-S),1160(SO_2),1080(C-Cl),1555, 1375 (C-NO_2),1070 (C-Br),1150 (C-F).^{1}H NMR (400MHz,DMSO-d_6,δ/*ppm*):7.10-8.10 (multiplet, aromatic C-H protons),1.40(3H Triplet,CH_3),2.53-2.56 (3H,Singlet,CH_3), 2.90 (2H,Triplet, CH_2 Thiazolidine), 3.10(2H,Triplet,CH_2 Thiazolidine).The C, H, N analysis data of all compounds are presented in Table-1.

Table-2 Antibacterial Activity of Compounds (B1-5)

Comp. No.	Zone of Inhibition(mm)				
	Gram +ve		*Gram –ve*		
	Bacillus Subtilis	***Staphylococcus aureus***	***Kllebsiella promioe***	***Salmonella Typhl***	***E.coil***
B1	57	45	63	58	59
B2	65	48	70	64	68
B3	62	49	67	55	57

B4	66	46	68	66	65
B5	70	50	82	71	67
Tetracycline	79	55	87	76	72

Figure-1 Antibacterial Activity of Compounds (B1-5)

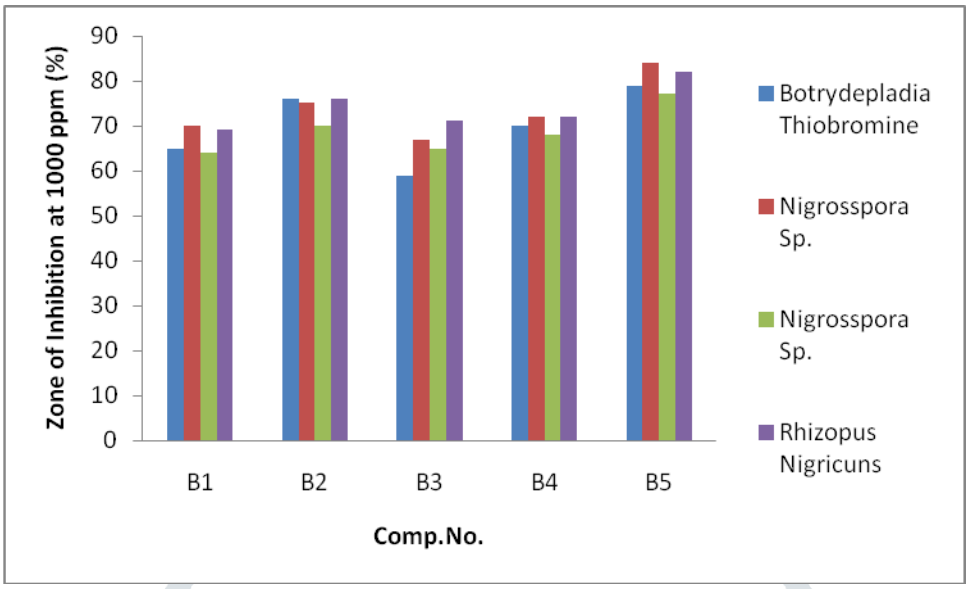


All the elemental and spectral features suggest that the data are consistent with the predicted structure shown in Scheme-1. The LC-MS of selected compounds shows the peak of M^+ ion which is consistent of their molecular weight. All these facts confirm the structures B1-5.

Table-3 Antifungal Activity of Compounds (B1-5)

Zone of Inhibition at 1000 ppm (%)				
Comp. No.	***Botrydepladia Thiobromine***	***Nigrosspora Sp.***	***Penicillium Expansum***	***Rhizopus Nigricuns***
B1	65	70	64	69
B2	76	75	70	76
B3	59	67	65	71
B4	70	72	68	72
B5	79	84	77	82

Figure-3 Antifungal Activity of Compounds (B1-5)



The examination of antibacterial activity data reveals that all compounds toxic against microbes and the compounds **B5** found more active against the gram-positive and gram-negative bacteria.

ACKNOWLEDGEMENT

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