International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.3, No.1, pp 364-368, Jan-Mar 2011

Synthesis,Characterisation, and anti Microbial Screeninig of some 2-Amino,5-(Phenyl substituted)1,3,4-Thiadiazole derivatives

Bijo Mathew[1]*, A.Jerad suresh[2], Githa Elizabeth Mathew[3], Shayam Shankar[4],Shayam S. Kumar[4]

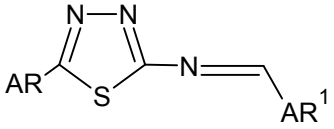
***[1]Department of Pharmaceutical Chemistry, Grace college of Pharmacy, Palakkad, Kerala.India.**
[2]Dept. of Pharmaceutical Chemistry, Madras Medical College-Chennai,India.
[3]Department of Pharmacology,Grace College of Pharmacy, Palakkad,Kerala.
[4]Grace College of Pharmacy, Palakkad, Kerala,India.

***Corres.author: bijovilaventgu@gmail.com**
Phone:09946700219

Abstract: The present study involves the reaction of various substituted aryl carboxylic acid with thiosemicarbazide in presence of conc. H_2SO_4 to yield 2-amino (5-phenyl substituted) 1,3,4-thiadiazole derivatives via cyclization. These derivatives on treatment with various aldehydes in presence of conc. H_2SO_4 formed Schiff's bases. The structures of these compounds were established on the basis of IR, ^{1}H-NMR and elemental analysis. All the compounds were screened *in vitro* for their antimicrobial activity against a variety of microbial strains such as *E.Coli, Staphylococcus* and fungi strains such as *Candida albicans. Saccharomyces cervisea* .Some of the compounds has shown antibacterial and antifungal activity when compared with the standard drugs.
Keywords:1,3, 4-Thiadiazole, Schiff's bases, antimicrobial screening.

Introduction:

The biological activity of a compound depends up on their molecular structure. The interesting biological activities of a novel heterocyclic like Thiadiazole has stimulated considerable research work[1]. There are number of five membered heterocyclic containing nitrogen and sulphur atom, have turned out to be a potential chemotherapeutic and pharmacotherapeutic agents. The biological profile of 1,3, 4-Thiadiazole derivatives is very extensive. The compounds with azomethine linkages were also shown to possess an array of biological activities such as antifungal, antibacterial, and anti-inflammatory activity [2,3]



From these findings, our attempt was to synthesis various derivatives of 2-amino, 5-(phenyl substituted) 1,3,4-thiadiazole derivatives from thiosemi carbazide and various substituted aryl carboxylic acid. The reaction involves the of cyclization the thiosemi carbazide in the presence of dehydrating agent like conc. H_2SO_4 .The resultant compounds subjected to treat with various substituted aromatic aldehydes to form corresponding Schiff's bases

Experimental

Melting points of all the synthesized compounds were determined by open capillary tube method and are uncorrected. The purity of all compounds was checked by TLC technique and iodine as the visualizing agent. IR spectra were recorded on FT-IR spectrophotometer (Shimadzu) by using KBr pellets technique. ^{1}H-NMR was recorded on DRX-300 MHz FT spectrophotometer by using DMSO as solvent and TMS as internal standard. The chemical shift was expressed in δ ppm.The physical characterization of the synthesized compounds were shown in table no:2

1) Synthesis of 2-amino, 5-(phenyl substituted) 1, 3, 4-thiadiazole

A mixture of thiosemicarbazide, 0.1mol and aryl substituted carboxylic acid 0.1mol, and conc. H_2SO_4 (5ml) in 50 ml of ethanol was refluxed for 2 hours. The resultant product was transferred in to a beaker and poured on to crushed ice. The solid separated out was filtered, washed with cold water and recrystallized from ethanol[4].

2) Synthesis 5-phenyl-*N*-[(1*E*)-phenylmethylidene]-1,3,4-thiadiazol-2-amine

The substituted Thiadiazole derivatives 0.01 mol was dissolved in 30 ml of ethanol containing few drops of sulphuric acid. The appropriate aldehyde 0.01 mol was added to the reaction mixture. It was refluxed around 45 minutes, cooled and then poured in to crushed ice. The solid obtained was filtered, washed with water and recrystallized with ethanol[5]

Mobile phase for TLC- Ethanol: Ethylacetate 9:1

Compound. 3a

IR (KBr,cm^{-1}): 3059.53(Ar-CH),1375.30(OH-bend), 1166.98(Ar-Cl),1594.23(C=N str), 690 (C-S-C linkage in thiadiazole)

Compound. 3b

IR (KBr,cm^{-1}): 3049.53(Ar-CH),1350.36(OH-bend), 1166.98(Ar-Cl),1594.95(C=N str),1461.94 (Ar-$N(CH_3)_2$,690.47 (C-S-C linkage in thiadiazole)

Compound. 3c

IR (KBr,cm^{-1}): 3023.53(Ar-CH),1296.36(OH-bend), 1614.15(C=N str),700..41 (C-S-C linkage in thiadiazole)

Compound. 3d

IR (KBr,cm^{-1}): 3039.53(Ar-CH),1281.33(C-O str), 2921.96(Methyl CH str), 1244.0(Asymmetric C-O-C str)694.33(C-S-C linkage in thiadiazole)

Compound. 3e

IR (KBr,cm^{-1}): 3026.58(Ar-CH),1358.36(OH-bend), 1166.85(Ar-Cl),1600.42(C=N str),1527.52 (Ar-NO_2),679.68 (C-S-C linkage in thiadiazole)

^{1}H NMR(DMSO):4.5(1H,s,-OH),1.5(1H,s, N=CH), 7.1-7.8(4H.d,CH-Aryl).8.4-8.9(4H,d,CH-Aryl$_2$)

Compound. 3f

IR (KBr,cm^{-1}): 3046.22(Ar-CH),1614.13(C=N str), 1533.30 (Ar-NO_2),668.78 (C-S-C linkage in thiadiazole)

^{1}H NMR(DMSO):2.3(1H,s,N=CH),7.5-7.89 (4H.d, CH-Aryl).8.3-8.9(4H,d,CH-Aryl$_2$)

Compound. 3g

IR (KBr,cm^{-1}): 3023.26(Ar-CH),1591.16(C=N str), 668.78 (C-S-C linkage in thiadiazole)

Compound. 3h

IR (KBr,cm^{-1}): 3086.58(Ar-CH),1165.05(Ar-Cl), 1597.34(C=N str),1545.59 (Ar-NO_2),695.78 (C-S-C linkage in thiadiazole)

^{1}H NMR(DMSO):1.81H,s, N=CH),7.5-8.2(4H.d,CH-Aryl).8.4-8.9(4H,d,CH-Aryl$_2$)

Compound. 3i

IR (KBr,cm^{-1}): 3066.58(Ar-CH),,1593.38(C=N str), 1565.39 (Ar-NO_2),669.68 (C-S-C linkage in thiadiazole)

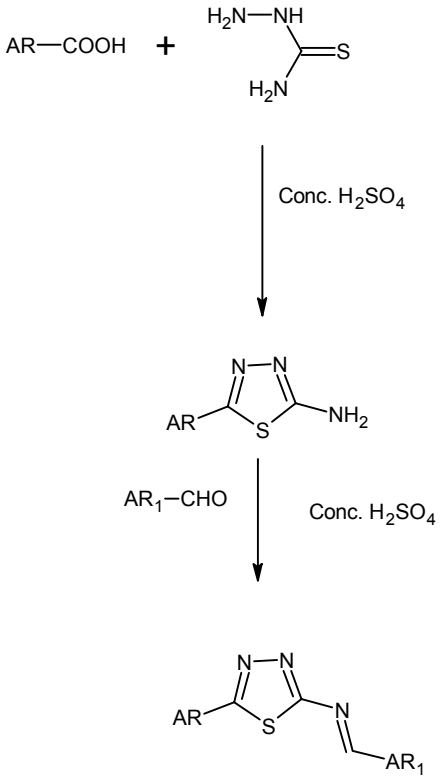
^{1}H NMR(DMSO):4.4(1H,s,-OH),1.6(1H,s, N=CH), 7.6-7.9(4H.d,CH-Aryl).8.4-8.8(4H,d,CH-Aryl$_2$)

Compound. 3j

IR (KBr,cm^{-1}): 3064.58(Ar-CH),,1614.13(C=N str), 1549.39 (Ar-NO_2),662.68 (C-S-C linkage in thiadiazole)

^{1}H NMR(DMSO):2.3 (1H,s, N=CH),7.5-7.9(4H.d,CH-Aryl).8.3-8.9(4H,d,CH-Aryl$_2$).

SCHEME OF THE PRESENT STUDY



DETAILS OF SYNTHESISED COMPOUNDS

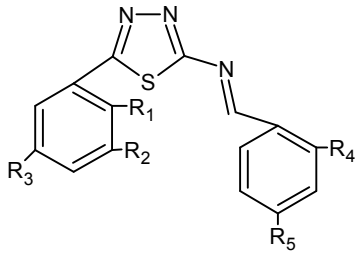


Table no: 1

Compound	R_1	R_2	R_3	R_4	R_5
3a	OH	H	H	H	Cl
3b	OH	H	H	H	CH_3NCH_3
3c	OH	H	H	OH	H
3d	OH	H	H	H	OCH_3
3e	OH	NO_2	NO_2	H	Cl
3f	$OCOCH_3$	H	H	H	Cl
3g	H	H	H	H	H
3h	H	NO_2	H	H	Cl
3i	H	NO_2	H	OH	H
3j	H	NO_2	H	H	H

Table no: 2
Physical Parameters and Elemental Analysis of Synthesised Compounds

Compound	MF	MW	MP(^{0}C)	Rf	Elemental analysis calculated(found)		
					C	H	N
3a	$C_{15}H_{10}ON_3SCl$	315.78	138	0.31	57.05 (57.21)	3.19 (3.23)	13.31 (13.27)
3b	$C_{17}H_{16}ON_4S$	324.40	143	0.34	62.94 (62.54)	4.97 (4.61)	17.27 (17.02)
3c	$C_{15}H_{11}O_2N_3S$	297.33	162	0.41	60.59 (60.99)	3.73 (3.89)	14.13 (14.27)
3d	$C_{16}H_{13}O_2N_3S$	311.36	136	0.22	61.72 (61.93)	4.21 (4.51)	13.50 (13.37)
3e	$C_{15}H_8O_5N_5SCl$	405.77	154	0.51	44.40 (44.62)	1.99 (1.92)	17.26 (17.39)
3f	$C_{17}H_{12}O_2N_3SCl$	357.81	112	0.54	57.06 (57.23)	3.38 (3.31)	11.74 (11.61)
3g	$C_{15}H_{11}N_3S$	265.33	98	0.46	67.90 (67.63)	4.18 (4.09)	15.84 (15.70)
3h	$C_{15}H_9O_2N_4SCl$	344.78	60	0.42	52.25 (52.05)	2.63 (2.41)	16.25 (16.41)
3i	$C_{15}H_{10}O_3N_4S$	326.33	108	0.48	55.21 (55.38)	3.09 (3.18)	17.17 (17.32)
3j	$C_{15}H_{10}O_2N_4S$	310.33	94	0.38	58.05 (58.33)	3.25 (3.16)	18.05 (18.22)

in vitro Antimicrobial Screening

The synthesized compounds were subjected to antimicrobial screening by cup plate method for zone of inhibition. The antibacterial activity was tested against various Gram positive and Gram negative bacteria and antifungal activity against various fungal strains compared with standard drug (Gentamycin and Griseofulvin) .The concentration of the synthesized compounds and standard drug were taken as (100µg/ml). All the compounds were dissolved in DMSO. In order to account for the effect due to DMSO, a blank was also performed[6, 7].The results were shown in the table no :3

Result & Discussion

All the synthesized compounds were characterized by recrystallization, TLC, Melting point, elemental analysis, IR, ^{1}HNMR analysis. All the synthesized structures showed satisfactory result. Analysis indicated by the symbols of elements are within ±0.4% of theoretical values. The IR data of the compounds clearly showed a strong C=N stretching band around 1614.31cm^{-1} and a C-S-C linkage in thiadiazole of absorption band around 690.47cm^{-1}.This indicates that the formation of 1,3, 4 thiadiazole derivatives along with a. azomethine linkage The ^{1}HNMR also confirms the presence of shift value at 1.8-2.3and 7.8-8.3 for CH=N,(CH-Aryl) groups respectively.

In the antimicrobial activity, Gentamycin (standard drug) showed a zone of inhibition 14,16mm in concentration 100µg/ml against the organism *E.coli & Bacillus* respectively . Out of the synthesized compounds **3c,3e,3f,and 3i** exhibit a good activity against *E.coli*. The compounds like **3e,3f,3i and3j** exhibit good activity against *Bacillus* organism. In the antifungal activity , Griseofulvin (standard drug) showed a zone of inhibition 15 and21 mm in concentration 100µg/ml against the organism *Candida albicans & Saccharomyces cervisea* respectively . Out of the synthesized compound **3f,3i,and 3j** exhibit a appreciable activity against both the organism.With the suitable molecular modification , we can make good antibacterial agent from this synthesized compounds.

Table no: 3
Antimicrobial Study of Synthesised Compounds

Compounds	Zone of inhibition(mm)			
	Bacteria		Fungi	
	E.Coli	Bacillus	Saccharomyces	Candida
3a	5	6	5	6
3b	6	6	5	5
3c	10	7	6	5
3d	7	6	5	6
3e	10	10	7	7
3f	12	10	10	12
3g	3	5	6	5
3h	3	5	5	6
3i	10	12	12	13
3j	5	13	12	10
Standard(100µg/ml)	14	14	14	14
Solvent Control(DMSO)	-	-	-	-

(-) indicates no activity

References

1. Kudari S M, Sajjanshetty AS, Lagali KH. Indian journal of hetrocyclic chemistry;1992 , 11, 221-224.
2. Mahadev BT, Shoba RD, Yallappa SS ,Subash CM and Shankar CB. Indian journal of hetrocyclic chemistry; 1996 , 5, 215-218.
3. Silver stenin RM, Bassler and Morrd TC "spectrometric identification of organic compounds "; 1979,5,328.
4. Arun KP, Nag Vl, Panda CS, Indian journal of chemistry; 1999, 38B , 998-1001.
5. Patel RB, Desai PS and Chukbalia Indian journal of chemistry; 2006, 42B, 773-778.
6. Prescott LM, Harley JP, Klein DA. Text book of microbiology; 1990,2,328.
7. Cremer. A microbiological methods; 1991,6, 235.

*****