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Archives of Applied Science Research, 2010, 2 (3): 153-161

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ISSN 0975-508X
CODEN (USA) AASRC9

Microwave assisted environmentally benign approach to the synthesis and antimicrobial activity of some novel Mannich's bases of 3-sulfamerazinyl substituted spiro (indolo-4-thiazolidinone) derivatives

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Abstract

An elegant microwave assisted environmentally benign approach to the synthesis of novel 3'-[4'-N-{ 4-methyl-2-pyrimidinyl }-benzene suphonamido]-spiro-(3H-indol-3,2'-thiazolidin)-1H-2,4' (5H) dione (5) and their Mannich's bases 6(a-g) has been described. Treatment of isatin (1) with sulphamerazine (2) yielded 4-[1, 2-dihydro-2-oxo-3H-indol-3-ylidene] amino]-N (4-methyl-2-pyrimidinyl) benzene sulfonamide (3). Cyclocondensation of its azomethine function with mercaptoacetic acid (4) over basic alumina afforded 3,-[4-N {4-methyl-2-pyrimidinyl}-benzene sulphonamido]-spiro-(3H-indol-3, 2'-thiazolidin)-1H-2, 4' (5H') dione) (5) which reacted smoothly with secondary amines and formaldehyde to give Mannich's bases 6(a-g) in excellent yield. Mannich's bases of sulphamerazinyl substituted [spiro-indolo-4-thiazolidinone] 6(a-g) were screened for their in-vitro antimicrobial activities against bacterial species (E.coli and B.substilis) and fungal species (A.niger and A.flavus) by Agar-well assay method against the standard drugs (ciprofloxacin for bacteria and flucanazol for fungi).

Key words: MW assisted organic synthesis, isatin, suphamerazine, mercaptoacetic acid, Mannich's bases.

INTRODUCTION

Sulfonamides are well known for their antibacterial, [1-3] antitumor, [4] diuretic, [5] anti-carbonic anhydrase, [6, 7] hypoglycemic, [8] antithyroid [9] and protease inhibiting[10] activities. Isatin shows a varying degree of the reactivity of its carbonyl groups towards nucleophilic reagents and this property has been extensively employed in the literature, [11] in the synthesis of a wide variety of heterocyclic compounds of medicinal interest. Out of the large number of isatin derivatives which have been tested against the AIDS virus, aminopyrimidino isatin derivatives have emerged as the most potent molecules exhibiting inhibitory effect on the replication of HIV-I virus in MT-4 cells [12-14]. Condensed heterocyclic systems containing the thiazolidinone moieties have attracted the attention of the chemists owing to this nuclei having

been identified in the literature [15] as the most promising pharmacophores in drug design and synthesis. Spiroheterocyclics containing thiazolidine moiety have been recently shown to exhibit a wide array of interesting biological activities. It has been observed that incorporation of certain bioactive pharmacophores in the existing drug molecules sometimes exert a profound influence on the biological profile of that molecule. Based on these observations, it could be anticipated that incorporation of the bioactive sulphonamide moiety on one side of the spiro-indolo-thiazolidinone nucleus and the Mannich's base fragments containing the cyclic amino methyl group on its other side could produce interesting series of compounds with enhanced biological activity. Ubiquity of indoles, [16] thiazolidinones, [15] sulphonamides, [17] and Mannich's bases [18] in the chemical literature is undoubtedly a consequence of multifarious biological response, which they elicit in combating a variety of body ailments. The recent demonstrations [19] that some of their derivatives can serve as potential agents in the control and treatment of AIDS has stimulated further interest in these molecules from yet another perspective and prompted us to synthesize some novel compounds containing these pharmacophores, on the premise that their presence in tandem in a single molecular framework can contribute significantly to the biological activity in the resulting molecules. As a part of an on going endeavour to create novel heterocyclic scaffolds with anticipated biological activity from easily accessible starting materials, herein we report the preliminary results of our studies on the synthesis of the novel 3-sulphamerazinyl substituted tricyclic systems containing spiro-indolo-4-thiazolidone nucleus.

MATERIALS AND METHODS

Experimental

Melting points were determined in an open capillary and are uncorrected. The IR spectra were recorded on Schimadzu FTIR-8400S. ^{1}H-NMR spectra were recorded in $CDCl_3$ on Bruker DRX-300 MHz. spectrometer using TMS as internal reference with their values expressed in δ ppm. Purity of all the synthesized compounds were routinely checked by TLC on silica gel G in the solvent system (9:1, benzene: methanol).

General methods for the preparation of 3, 5 and 6

1. Solution phase microwave assisted method-

Isatin (0.147gm, 0.001 moles) and sulphamerazine (0.246gm, 0.001 moles) were mixed in ethanol (10ml) containing 3ml of glacial acetic acid and placed in a 100ml borosil flask fitted with a funnel as a loose top. The reaction mixture was subjected to microwave irradiation at 180 W microwave power for 2 min, 360 W for 5 min and then at 720 W for 2min with short interval of 1 min to avoid the excessive evaporation of solvents. The overheating of the solution was avoided. The reaction mixture was cooled and the resulting solid was filtered washed with dil. ethanol dried and recrystallized from ethanol chloroform (1:9) mixture to give **3**, 0.28 g (yield 68.8%) m.p. 240-241ºC.

Equimolar quantities of 3 (0.393gm, 0.001 moles) and mercaptoacetic acid (1.4) (0.092g, 0.001 moles) were mixed in dry dioxane (10ml) and the mixture was placed in a 100ml borosil flask fitted with a funnel as a loose top. The reaction mixture was subjected to microwave irradiation at 360 W for 6 min and then at 720 W for 3min with short interval of 1 min to avoid the excessive evaporation of solvents. Over heating of the solution was avoided. The reaction mixture was cooled and neutralized with 10% sodium bicarbonate solution. The resulting solid was filtered washed with water and recrystallized from dichloromethane and dried to give **5**, 0.34g (yield 70.33%) m.p. 197-198º.

Equimolar quantities of 5 (0.467gm, 0.001 mole), pyrrolidine (0.071gm, 0.001 moles) and 37 % formaldehyde (0.5 ml) were mixed in dry dioxane (10ml) and the mixture was placed in a 100ml borosil flask fitted with a funnel as a loose top. The reaction mixture was subjected to microwave irradiation at 360 W for 5 min and then at 720 W for 4 min with short interval of 1 min to avoid the excessive evaporation of solvents. The mixture, after the reaction had completed (monitored by TLC) was kept at 0ºC for 1 hour and the resulting solid obtained was recrystallized from dioxane to give **6a**, 0.38g (yield 71.12%), m.p. 143-144ºC.

Similarly, compounds 6(b-g) were prepared. (Physical and analytical data of compounds are presented in Table-1).

2. Solid phase microwave assisted method-

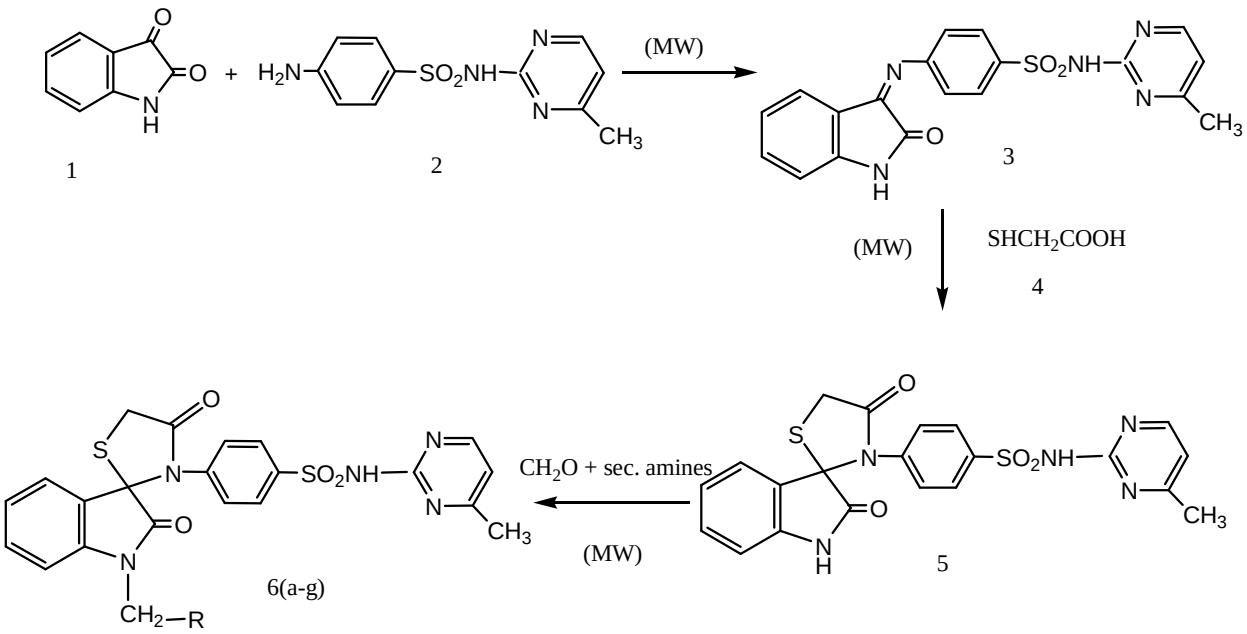
Slurry of equimolar quantities of isatin (0.147gm, 0.001 moles) and sulphamerazine (0.246gm, 0.001 moles) was adsorbed over basic alumina (0.0786 gm.) via a solution in glacial acetic acid (2ml). The dried slurry was powdered and the free flowing powder was placed in a 10ml borosil beaker and irradiated at 360 W microwave power for 5 min and then at 720 W for 2 min. The recyclable inorganic solid support was separated by extracting the product with ethanol. The solvent was evaporated and the solid obtained was recrystallized from ethanol-chloroform mixture (1:9) and dried to give **3**, 0.37g (yield 90.2%, m.p. 240-241ºC.

A slurry of equimolar quantities of 3 in (0.393gm, 0.001 moles) and mercaptoacetic acid (4) (0.092g, 0.001 moles) was adsorbed over montmorillonite KSF (.0970 gm) via a solution in dry dioxane (3ml). The dried slurry was powdered and the free flowing powder was placed in a 10ml borosil beaker and irradiated at 360 W microwave power for 5 min and then at 720 W for 2 min. The slurry was then cooled and neutralized with 10% sodium bicarbonate solution. The recyclable inorganic solid support was separated by extracting the product with ethyl acetate. The solvent was evaporated and the solid obtained was recrystallized from dichloromethane and dried to give **5**, 0.43g, (yield 90.5%), m.p. 197-198ºc.

A slurry of equimolar quantities of 5 (0.467gm, 0.001 moles), pyrrolidine (0.071gm, 0.001 mole) and 37% formaldehyde (0.5ml) was adsorbed over basic alumina (0.235 gm) via a solution in ethanol (3ml). The dried slurry was powdered and the free flowing powder was placed in a 10ml borosil beaker and irradiated at 360 W microwave power for 5 min and then at 720 W for 2 min. The recyclable inorganic solid support was separated by extracting the product with ethyl acetate. The solvent was evaporated and the solid obtained was recrystallized from dichloromethane and dried to give **6a**, 0.49g, (yield 91.4%), m.p. 143-144ºc.
Similarly, compounds 6(b-g) were prepared.

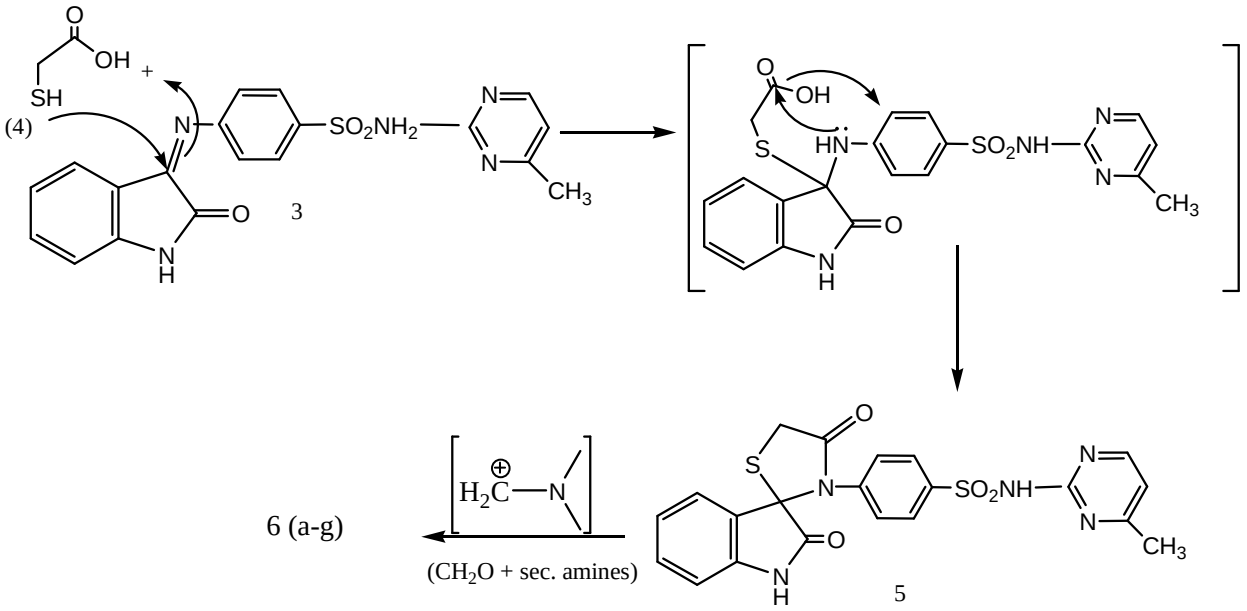
Antimicrobial activity

Mannich's bases of sulphamerazinyl substituted [spiro-indolo-4-thiazolidinone] 6(a-g) were screened for their in-vitro antimicrobial activities against bacterial species (E.coli and B.substilis) and fungal species (A.niger and A.flavus) by Agar-well assay method against the standard drugs (ciprofloxacin for bacteria and fluconazol for fungi). In antibacterial studies, the stock solution of standard and test compounds were prepared in DMF and subsequent dilutions were made with the same solvent.



R= **a**- pyrrolidinyl, **b**- piperidinyl, **c**- morpholinyl, **d**- N-methyl piperazinyl, **e**- N-ethyl piperazinyl, **f**- N-phenyl piperazinyl, **g**- N-ethoxycarbonyl piperazinyl.

Scheme-1



Mechanism of formation of 5 from 3

Scheme-2

Spectral data of compounds 5 and 6 (a-g)

5; IR (KBr) cm^{-1} 3410 (NHsymm. str.),3050 (aromatic str.),1710 (C=O) [spiroindole],1650(-C=O,str. amide), 1670 (ring skeletal vib.), 1610(C=N str), 1320(SO_2 symm.str), 1150(-C-N-str amides), 1425(C=C aromatic str.), 900-690(aromatic C-H str), 610 (C-S-C str), 1110 (C-N). **^{1}H-NMR($CDCl_3$)-** δ, 8.00 (s,1H, -NH broad)**,** 8.28 (d,1H,pyrimidine ring)**,** 7.98 (d,2H,Ar-H)**,**

7.38(d,2H,Ar-H)**,** 7.52-6.88 (m,4H,Ar-H 2-oxo indole)**,** 6.43 (d,1H,pyrimidine ring)**,** 4.0(s,1H, -NH)**,** 3.43-3.33(s,2H,CH_2 of spiro indolo-thiazolidinone)**,** 2.35 (s,3H,-CH_3).

6a; IR (KBr) cm^{-1} 3300 (OH), 2938 (aromatic str.), 1710 (C=O)spiroindole, 1650 (-C=O, str amide), 1590 (ring skeletal vib.),1595(C=N str), 1234 (C-O-C), 1425 (C=C aromatic str.), 900-690 (aromatic C-H str), 610 (C-S-C), 1115(C-N). **^{1}H-NMR(CDCl$_3$)-** δ, 8.28 (d,1H, pyrimidine ring), 7.98 (d,2H,-(CH_2) AR-H), 7.38 (d,2H,-(CH_2) Ar-H), 7.11-6.98 (m,4H,Ar-H of 2 oxoindole), 6.43 (d,1H,-CH pyrimidine ring), 4.0(s,1H,-NH) , 4.45 (s,2H,N-CH_2-N), 3.43-3.33 (s,2H,CH_2 spiro-indolo-thiazolidinone), 2.35 (s, 3H, -CH_3 pyrimidine ring), 2.25 (t,4H,N-(CH_2)$_2$ pyrrolidine ring.

6b; IR (KBr) cm^{-1} 3390 (NH symm.str.), 3050 (aromatic str.), 1710(C=O) spiroindole, 1675 (C=O str.), 1602 (C=N str.), 1234 (SO_2 symm.str), 1425 (C=C aromatic str.), 900-690 (aromatic C-H str.), 610 (C-S-C str.). **^{1}H-NMR(CDCl$_3$)-** δ, 8.28 (d,1H,pyrimidine ring), 7.98 (d,2H,Ar-H), 7.38 (d,2H,Ar-H), 7.11-6.98 (m,4H,Ar-H 2-oxo indole), 6.43 (d,1H, pyrimidine ring), 4.0 (s,1H,-NH), 4.45 (s,2H,N-CH_2-N), 3.43-3.33 (s,2H,CH_2 spiro-indolo-thiazolidinone), 2.35 (s,3H,-$CH_3$of pyrimidine ring), 2.24 (t,4H,N-(CH_2)$_2$ piperidine ring), 1.50(t,6H, piperidine ring).

6c; **IR (KBr) cm^{-1}** 3390 (NHsymm.str.), 3050(aromatic str.), 1710 (C=O) spiroindole, 1675 (C=O)[CONH], 1602 (C=N str.), 1160 (SO_2 symm.str.), 1425 (C=C aromatic str.), 1225 (C-O-C), 900-690 (aromatic C-H str.), 610 (C-S-C str.). **^{1}H-NMR(CDCl$_3$)-** δ, 8.28 (d,1H,pyrimidine ring), 7.98 (d,2H Ar-H),7.38 (d,2H, Ar-H), 7.11-6.98(m,4H,Ar-H 2 oxo indole), 6.43 (d,1H,pyrimidine ring), 4.0 (s,1H,-NH),4.45 (s,2H,N-CH_2-N),3.44-3.33 (s,2H,CH_2 spiro-indolo-thiazolidinone), 2.35 (s,3H,-CH_3 pyrimidine ring), 2.37 (t,4H,N-(CH_2)$_2$ of morpholine ring), 3.67 (t,4H Of CH_2) of morpholine ring.

6d; IR (KBr) cm^{-1} 3390 (NH symm.str.), 3050 (aromatic str.), 1710 (C=O) spiroindole, 1675 (C=O) [CONH], 1602 (C=N str.), 1160 (SO_2 symm.str.), 1425 (C=C aromatic str.), 900-690 (aromatic C-H str.), 710 (C-S-C str). **^{1}H-NMR(CDCl$_3$)-** δ, 8.28 (d,1H,pyrimidine ring),7.98 (d,2H Ar-H),7.38 (d,2H,of Ar-H),7.11-6.98(m,4H,Ar-H of 2 oxo indole),6.43 (d,1H , pyrimidine ring), 4.0 (s,1H,-NH) ,4.45 (s,2H,N-CH_2-N),3.44-3.33 (s,2H,CH_2 of spiro-indolo-thiazolidinone), 2.35 (s,3H,-CH_3 pyrimidine ring), 2.46 (m,8H,N-(CH_2)$_4$-N of N-methyl piperazine ring), 2.27 (s,3H,CH_3 N-methyl piperazine ring).

6e; IR (KBr) cm^{-1} 3390 (NH symm.str.), 3050 (aromatic str.), 1710 (C=O)spiroindole, 1675 (C=O) [CONH], 1602 (C=N str.), 1160 (SO_2 symm.str.), 1425 (C=C aromatic str.), 900-690 (aromatic C-H str.), 710(C-S-C str.). **^{1}H-NMR(CDCl$_3$)-** δ, 8.28 (d,1H,pyrimidine ring), 7,.98 (d,2H of Ar-H) ,7.38 (d, 2H, Ar-H),7.11-6.98 (m,4H,Ar-H 2 oxo indole),6.43 (d,1H,pyrimidine ring) 4.0 (s,1H,-NH) 4.45 (s,2H,N-CH_2-N),3.44-3.33 (s,2H,CH_2 of spiro-indolo-thiazolidinone),2.35 (s,3H,-CH_3 of pyrimidine ring), 2.46 (m,8H,N-(CH_2)$_4$-N piperazine ring)2.40 (q,2H,$CH_2$of n-ethylpiperazine ring),1.00 (t,3H,-CH_3 of N-ethyl piperazine), 3.5 (q, 2H,-CH_2 ethyl).

6f;IR (KBr) cm^{-1} 3300 (NH symm.str.),3050 (aromatic str.),1710 (C=O) spiroindole, 1675 (C=O) [CONH],1602 (C=N str.),1338 (SO_2 symm.str.),1425 (C=C aromatic str.),900-690 (aromatic C-H str.). 748(C-S-C str.). **^{1}H-NMR(CDCl$_3$)-** δ, 8.28 (d,1H,pyrimidine ring) 7,.98 (d,2H Ar-H) 7.38 (d,2H, Ar-H),7.11-6.98(m,4H,Ar-H of 2 oxo indole),6.43 (d,1H,pyrimidine ring) 4.0 (s,1H,-NH) 4.45 (s,2H,N-CH_2-N),3.45 (t,4H,N-CH_2 piperazine, 3.44-3.33 (s,2H,CH_2

spiro-indolo-thiazolidinone),2.59 (t,4H, N(-CH_2)$_2$ of N-phenyl piperazine ring), 2.35 (s,3H,-CH_3 of pyrimidine ring).

6g; IR (KBr) cm^{-1} 3410 (NH symm.str.), 3050 (aromatic str.), 1710 (C=O) spiroindole, 1730(C=O) [carboethoxy], 1675(C=O) [CONH], 1602 (C=N str.), 1425 (C=C aromatic str.), 1320 (SO_2 symm.str.), 900-690 (aromatic C-H str.), 748(C-S–C str.). **^{1}H-NMR($CDCl_3$)-** δ, 8.28 (d,1H,pyrimidine ring) ,7.98 (d,2H of Ar-H) ,7.38 (d,2H,of Ar-H),7.11-6.98(m,4H,Ar-H of 2 oxo indole),6.43 (d,1H,pyrimidine ring), 4.0 (s,1H,-NH), 4.45 (s,2H,N-CH_2-N),3.44-3.33 (s,2H,CH_2 of spiro-indolo-thiazolidinone),3.06 (t,4H,N-(CH_2) of piperazine,2.35 (s,3H,-CH_3 pyrimidine ring),2.62 (t, 4H,N-(CH_2)$_2$of piperazine,1.30 (t,3H,-CH_3 of $COOCH_2$-CH_3), 4.12 (q, 2H of CH_2 $COOCH_2$-CH_3).

RESULTS AND DISCUSSION

The synthesis of 5 consisted of treating isatin (1) with sulfamerazine (2) to give the Schiff's base (3). Literature is replete with examples demonstrating the cyclocondensation of an azomethine function with mercaptoacetic acid to form the 4-thiazolidinone nucleus. This strategy was applied on 3 and 4 under microwave conditions to give 5 .In an alternate procedure MW reaction was applied in dry media using basic alumina as a solid support to give almost a quantitative yield (90-95 %) of 5 from 3 . Almost the same yield of 5 from the reaction of 3 and 4 was also observed in the MW induced reaction of mercaptoacetic acid (4). when the reaction was carried out using montomorillonite KSF as a solid support. Isatin nitrogen of 4 reacted smoothly with formaldehyde and secondary amines viz- pyrrolidine, piperidine, morpholine, 1-methyl piperazine, 1-ethyl piperazine, 1-phenyl piperazine, 1-benzyl piperazine and 1-ethoxy carbonyl piperazine under microwave conditions to give 6 (a-g) **scheme-1** in excellent yield. **(Table-1).**

All the synthesized compounds gave satisfactory results of S and N analysis. IR and ^{1}H-NMR spectral data were found to be consistent to the assigned structures. The physical and analytical data of the compounds are presented in Table-1.

In accord to the generally accepted mechanism of the formation of thiazolidinone nucleus from the reaction of mercaptoacetic acid on azomethine function, we suggest that the formation of 5 from 3 takes place through the pathway shown in **scheme-2.**

The antibacterial activity was evaluated against two pathogenic strains (*E.coli*. and *B.subtilis*).The zone of inhibition and activity index were determined by comparison with the standard drug ciprofloxacin. The outcome of this study is presented in table-2. The antibacterial screening against *B.subtilis* showed that amongst the compounds 6(a-g), the compound 6b displayed highest activity. The compound 6e showed minimum activity amongst all the compound. The remaining compounds 6a, 6d, 6e, 6f and 6g showed only moderate activity. Contrary to this observation, compound 6a showed highest activity amongst all the compounds screened for this activity against *E.coli*.

The antifungal activity was evaluated against two pathogenic strains (*A.niger* and *A.flavus).*The zone of inhibition and activity index were determined by comparison with the standard drug fluconazol. The outcome of this study is presented in table-2. The antifungal screening against *A.niger* showed that amongst the compounds 6(a-g), the compound 6f exhibited highest activity. The compound 6a showed minimum activity amongst all the compounds. The remaining compounds 6b, 6c, 6d, 6e and 6g showed only moderate activity.Contary to this observation,

compound 6g showed highest activity amongst all the compounds screened for this activity against *A.flavus.*

Table-1 Physical and analytical data of 3, 5 and 6 (a-g)-

S. No.	Comp No.	Molecular Formula	M.W.	M.P. °C	Yield (%)		Elemental analysis (Calcd./ Found)	
					MW Solvent phase	MW Solid phase	N	S
1.	3	$C_{19}H_{15}N_5O_3S$	393	240-241	68.8	90.2	17.50/ 17.67	8.15/ 8.28
2.	5	$C_{21}H_{17}N_5O_4S_2$	467	197-197	70.3	90.5	14.98/ 15.23	13.72/13.92
3.	6a	$C_{21}H_{21}N_6O_4S_2$	550	143-144	71.12	91.4	15.26/ 15.38	11.65/ 11.81
4.	6b	$C_{27}H_{28}N_6O_4S_2$	564	152-153	71.4	92.3	14.88/ 15.15	11.36/ 11.42
5.	6c	$C_{26}H_{26}N_6O_5S_2$	566	181-182	72.3	93.2	14.83/ 14.96	11.32/ 11.43
6.	6d	$C_{27}H_{29}N_7O_4S_2$	579	130-132	68.5	90.5	16.91/ 17.23	11.06/ 11.31
7.	6e	$C_{28}H_{31}N_7O_4S_2$	593	142-143	70.3	93.3	16.51/ 16.62	10.80/ 10.96
8.	6F	$C_{32}H_{31}N_7O_4S_2$	641	151-152	68.5	90.1	15.28/ 15.34	9.99/ 10.26
9.	6g	$C_{29}H_{31}N_7O_6S_2$	637	186-187	72.4	93.4	15.37/15.42	10.06/10.18

Table-2 Antimicrobial activity of 6 (a-g)

Comp. no.	Conc. In (µg/ml)	E.coli Zone of inhibition (mm)	% activity compared to the standard	B.subtilis Zone of inhibition (mm)	% activity compared to the standard	A.niger Zone of inhibition (mm	% activity compared to the standard	A.flavus Zone of inhibition (mm	% activity compared to the standard
6 a	400	15.2	57.59	13.0	72.22	11.0	39.28	8.0	26.66
	200	14.0	54.61	12.6	70.0	10.6	37.27	7.5	25.0
	100	13.0	50.0	11.3	62.77	9.3	33.21	6.3	21.0
6 b	400	14.0	53.84	15.0	83.33	17.0	60.71	13.0	43.33
	200	12.8	49.23	14.4	80.0	16.6	59.28	12.7	42.33
	100	11.6	44.61	13.2	73.33	15.2	54.28	11.4	38.0
6 c	400	12.0	46.15	9.0	50.0	12.0	42.85	18.0	60.0
	200	11.5	44.23	8.5	47.22	11.4	40.71	17.4	58.0
	100	10.0	38.46	7.2	40.0	10.2	36.42	16.3	54.33
6 d	400	13.0	50.0	11.0	61.11	16.0	57.14	16.0	53.33
	200	12.3	47.30	10.7	59.44	15.5	55.35	15.7	52.33
	100	12.0	46.15	9.0	50.0	14.4	51.42	14.4	48.0
6 e	400	9.0	34.61	11.0	61.11	14.0	50.0	11.0	36.66
	200	8.0	30.76	10.7	59.44	13.6	58.57	10.6	35.33
	100	7.3	28.07	9.0	50.0	12.2	43.57	9.4	31.33
6 f	400	11.0	42.30	13.0	72.22	18.0	64.28	14.0	46.66
	200	10.5	40..38	12.5	69.44	17.6	62.84	13.3	44.33
	100	10.0	38.46	11.0	61.11	16.3	58.21	12.2	30.66
6 g	400	12.0	46.15	14.0	77.77	22.0	78.57	28.0	93.33
	200	11.7	45.0	13.5	75.0	21.5	76.78	27.6	92.0
	100	10.2	39.23	12.0	66.66	20.2	72.14	26.2	87.33
Ciprof loxacin	400	26	100.0	18	100.0	--	--	--	--
	200	26	100.0	18	100.0				
	100	26	100.0	18	100.0				
Fluconazole	400	--	--	--	--	28	100.0	30	100.0
	200					28	100.0	30	100.0
	100					28	100.0	30	100.0

CONCLUSION

In conclusion, several novel 3-sulphamerazinyl substituted spiro-indolo-thiazolidinones 6(a-g) displaying potential antibacterial and antifungal activities were synthesized from the commercially available sulphamerazine, Isatin and mercaptoacetic acid under the solvent free microwave conditions. The study showed that MW provided an elegant method for the synthesis of their Mannich's bases of biological interest.

Acknowledgement
Authors are grate-ful to the Director CDRI Lucknow for providing the ^{1}H-NMR data of the compounds and to the Head Department of Bioscience and Biotechnology,of Banasthali University for providing the antimicrobial screening of the compounds.

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