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RESEARCH ARTICLE
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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF NOVEL PYRIMIDINE DERIVATIVES

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Abstract: Benzenesulfonohydrazide **(1)** on reaction with Ethyl acetoacetate **(2)** yield N'-(3-oxobutanoyl) benzene sulfonohydrazide**(3)**. Then the compound**(3)** reacted with various aromatic aldehydes **(4a-g)** and Urea **(5)** yielded N'-(6-methyl-2-oxo-4-aryl-1,2,3,4-tetrahydropyrimidine-5-carbonyl)benzenesulfonohydrazide **(6a-g)**. The compounds **(6a-g)** further reacted with 5-nitro furfural **(7)** yields N'-(3-(hydroxy(5-nitrofuran-2-yl)methyl)-6-methyl-2-oxo-4-aryl-1,2,3,4-tetrahydropyrimidine-5-carbonyl)benzenesulfonohydrazide **(8a-g)**. The structures of both the series of compounds **(6a-g)** and **(8a-g)** were characterized structurally by spectral features. The compounds were also monitored for anti microbial activity.

Keywords: Benzenesulfonohydrazide, Tetrahydropyrimidone, 5-nitro furfural, antimicrobial activity and spectral studies.

1. Introduction

In recent years lots of research was done to synthesis anti-microbial actives compounds for various microorganisms, particularly for bacteria and several fungi. The numerous derivatives of pyrimidine heterocycle moiety and natural products have been synthesized for their antibacterial, Insecticidal, anti-HIV, antifungal,anticancer and anti-inflammatory activities[1-7]. Some pyrimidines containing drugs are sulfadiazine, trimethoprim (antibacterial), trifluridine, idoxuridine (antiviral), sulfadoxine (anti-malarial), Retrovir (anti-HIV), viomycin (anti-tuberculosis) [8–12].

Sulfonyl-hydrazide ($-SO_2NHNH_2$) is a class for Organic synthesis of biological value. More particularly aryl sulfonyl hydrazide received Pharmaceutical activities [13-19]. Some of phenyl sulfonyl hydrazide based heterocyclic derivatives found as anti T. B. and Anti cancer drugs [19-23]. Thus in view of excellent biological properties of pyrimidone and aryl sulfonyl hydroxy the present paper comprises.

Hence, pyrimidine and furfural containing compounds into one molecule may have good medicinal property. Thus, it was thought to explore this type of merge molecules. The present communication deals with the pyrimidone sulfohydrazide couple derivatives. The research route is shown below.

2. Experimental

2.1. Materials and Methods

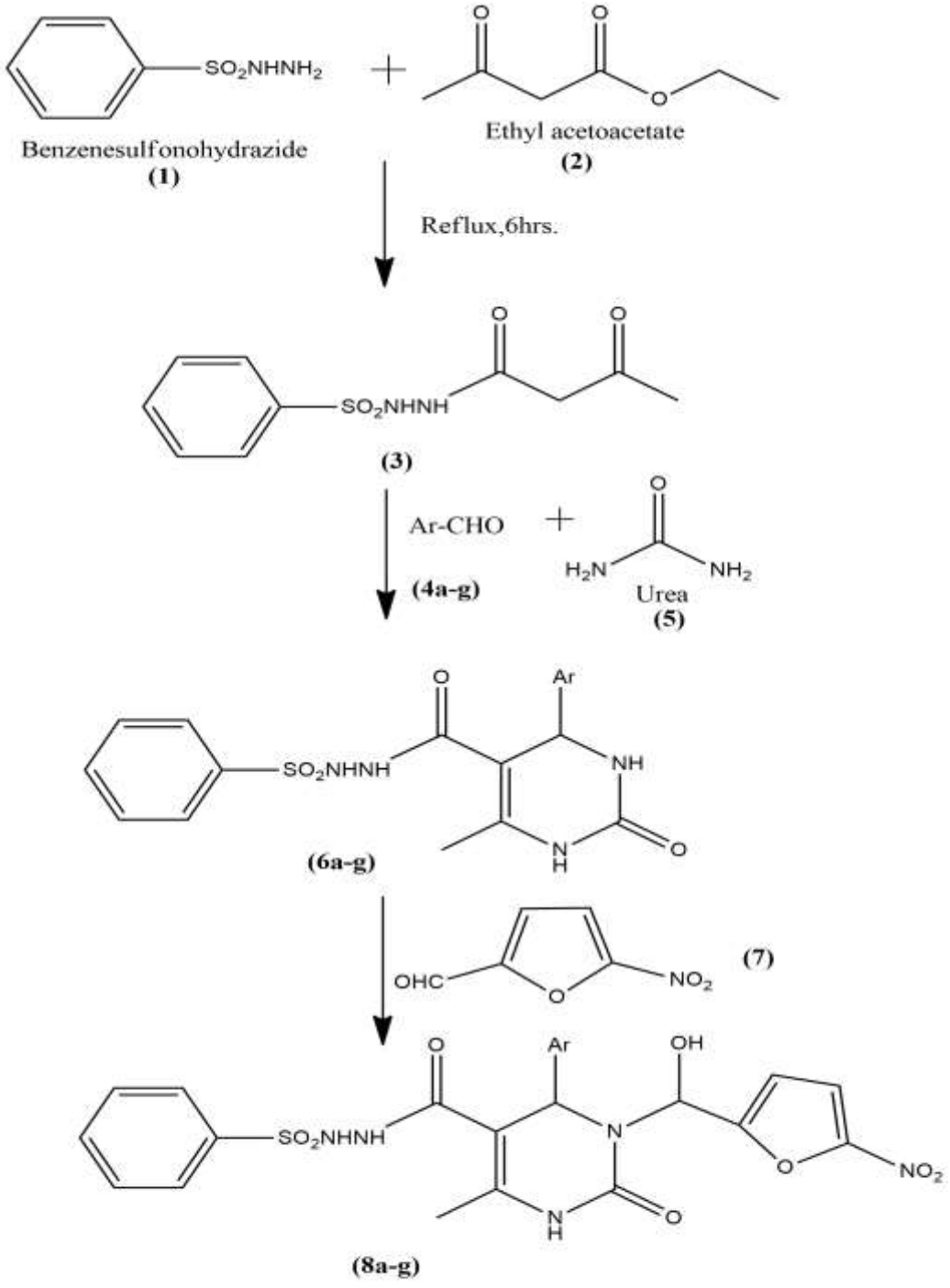
All the chemicals used were procured as pure grade.

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 antibacterial activity of both the series of compounds 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 [24-26]. The % age inhibition of growth of bacteria by the compounds is shown in Table-4.

The antifungal activity of both the series of compounds were measured at 1000ppm concentration *in vitro* Plant pathogen shown in Table-5 have been selected for study [24-26].



Where Ar= (a) Ph (b) 4-ClPh (c) 4-BrPh (d) 4-FPh

(e) 3-NO_2Ph (f) 2,4-Cl_2Ph (g) 2,4-$(NO_2)_2$Ph

2.2. Synthesis of N'-(3-oxobutanoyl) benzene sulfono hydrazide(3)

The Benzene sulfonohydrazide **(1)** (0.01 mole) refluxed with Ethyl acetoacetate (0.01 mole) in ethanol containing with catalytic amounts of piperidine (0.5 ml) for 3-4 hrs. Then cool the reaction mixture and pour in to ice, solid product formed. Filter, washed with cold water and dried it.

2.2.1. Synthesis of N'-(6-methyl-2-oxo-4-aryl-1,2,3,4-tetrahydropyrimidine-5-carbonyl) benzene sulfonohydrazide (6a-g)

Treatment of equimolar N'-(3-oxobutanoyl) benzene sulfonohydrazide **(3)** with Various aromatic aldehydes **(4a-g)** and Urea **(5)** in presence of catalytic amount of HCl was refluxed for 6-7 hrs. Then reaction mixture was cooled under tap water, then poured into ice. The solid product which precipitated was collected by filtration, washed with solid product with water, dried and crystallized from ethyl alcohol. The details are given in Table-1.

Table 1. Analysis of compounds (6a-g)

Comp. No.	Molecular Formula	M.P.* ˚C	Elemental Analysis				
			C%	H%	N%	S%	X%
			Calcd. (Found)	Calcd. (Found)	Calcd. (Found)	Calcd. (Found)	Calcd. (Found)
6a	$C_{18}H_{18}N_4O_4S$ (386)	178-179	55.95 55.9	4.70 4.6	14.50 14.4	8.30 8.2	-
6b	$C_{18}H_{17}N_4O_4SCl$ (420.5)	231-232	51.37 51.3	4.07 4.0	13.31 13.3	7.62 7.6	8.42 8.4
6c	$C_{18}H_{17}N_4O_4SBr$ (465)	245-246	46.46 46.4	3.68 3.6	12.04 12.0	6.89 6.8	17.17 17.1
6d	$C_{18}H_{17}N_4O_4SF$ (404)	227-228	53.46 53.4	4.24 4.2	13.85 13.8	7.93 7.9	4.70 4.6
6e	$C_{18}H_{17}N_5O_6S$ (431)	233-234	50.11 50.1	3.97 3.9	16.23 16.2	7.43 7.4	-
6f	$C_{18}H_{16}N_4O_4SCl_2$ (455)	234-235	47.48 47.4	3.54 3.5	12.31 12.3	7.04 7.0	15.57 15.5
6g	$C_{18}H_{16}N_6O_8S$ (476)	239-240	45.38 45.3	3.39 3.3	17.64 17.6	6.73 6.7	-

***** Uncorrected. LC-MS data for 6e:432.2

Where X= Halogen Atom

2.2.3. Synthesis of N'-(3-(hydroxy(5-nitrofuran-2-yl)methyl)-6-methyl-2-oxo-4-aryl-1,2,3,4-tetrahydropyrimidine-5-carbonyl)benzenesulfonohydrazide (8a-g)

Compounds N'-(6-methyl-2-oxo-4-aryl-1,2,3,4-tetrahydropyrimidine-5-carbonyl)benzene sulfono hydrazide **(6a-g)** refluxed with 5-nitro furfural **(7)** in (0.01 mole) alcoholic KOH solution (50ml) yieldedN'-(3-(hydroxy(5-nitrofuran-2-yl)methyl)-6-methyl-2-oxo-4-aryl-1,2,3,4-tetra hydropyrimidine-5-carbonyl)benzene sulfonohydrazide **(8a-g)**.Then reaction mixture was cooled under tap water, then poured into ice. The solid product which precipitated was collected by filtration,washed with solid product with water, dried and crystallized from ethyl alcohol. The details are given in Table-2.

Table 2. Analysis of compounds

Comp. No.	Molecular Formula	M.P.* ˚C	Elemental Analysis				
			C%	H%	N%	S%	X%
			Calcd. (Found)	Calcd. (Found)	Calcd. (Found)	Calcd. (Found)	Calcd. (Found)
8a	$C_{23}H_{21}N_5O_8S$ (527)	243-244	52.37 52.3	4.01 4.0	13.28 13.2	6.08 6.0	-
8b	$C_{23}H_{20}N_5O_8SCl$ (561.5)	258-259	49.16 49.1	3.59 3.5	12.46 12.4	5.71 5.7	6.31 6.3
8c	$C_{23}H_{20}N_5O_8SBr$ (606)	252-253	45.55 45.5	3.32 3.3	11.55 11.5	5.29 5.2	13.18 13.1
8d	$C_{23}H_{20}N_5O_8SF$ (545)	240-241	50.64 50.6	3.70 3.6	12.84 12.8	5.88 5.8	3.48 3.4
8e	$C_{23}H_{20}N_6O_{10}S$ (572)	247-248	48.25 48.2	3.52 3.5	14.68 14.6	5.60 5.5	-
8f	$C_{23}H_{19}N_5O_8SCl_2$ (596)	250-252	46.32 46.3	3.21 3.2	11.74 11.7	5.38 5.3	11.89 11.8
8g	$C_{23}H_{19}N_7O_{12}S$ (617)	253-254	44.74 44.7	3.10 3.0	15.88 15.8	5.19 5.1	-

***** Uncorrected. LC-MS data for 8e:572.9

Where X= Halogen Atom

3. Results and discussions

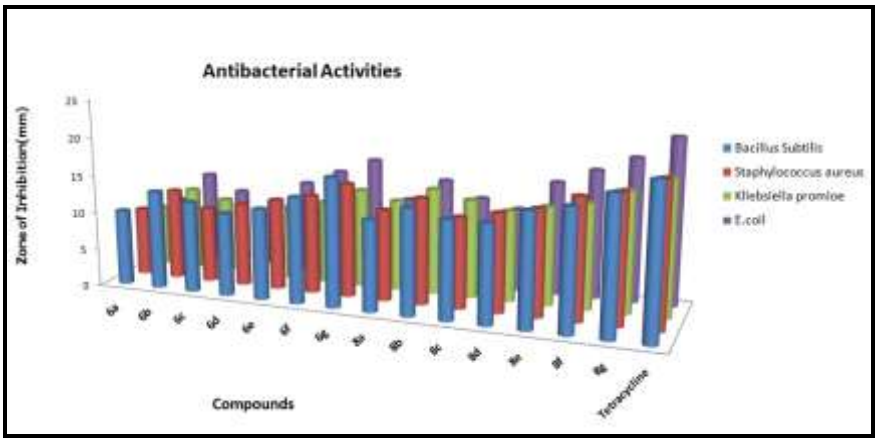
The N'-(3-oxobutanoyl) benzene sulfono hydrazide **(3)** was synthesised from Benzene sulfono hydrazide **(1)** on reaction with Ethyl acetoacetate **(2)**. The elemental characterization of compound **(3)** shows mol. formula: $C_{10}H_{12}N_2O_4S$ (mol.wt. 256.28 gm/mole),(Cal./ Found) %C, 46.87/46.8; %H, 4.72/4.7: %N, 10.93/10.9 and %S, 12.51/12.5. The IR spectra shows bands at 3330-3350 cm^{-1} (N-H), 2980 cm^{-1} (C–H), 1650 cm^{-1} (C=O), 1160-1150, 1330- 1340cm^{-1} (SO_2NH) and NMR peak at 7.60-7.90 multiple for aromatic proton, 8.48,5.20 for NH, 3.75 singlet for CH_2 and 2.30 for CH_3 proton.

The compound **(3)** react with Various aromatic aldehydes **(4a-g)** and Urea **(5)** yielded N'-(2-oxo -6-aryl -1,2,3,4-tetrahydro pyrimidine-5-carbonyl)benzene sulfono hydrazide **(6a-g)**. Its IR spectrum revealed absorption bands due to NH,C=O and SO_2NH groups near 3330-3350 cm^{-1}, 1650 cm^{-1} and 1160-1150, 1330- 1340cm^{-1}, respectively. And also, 1080 cm^{-1} (C-Cl), 710 cm^{-1} (C-Br), 1260 cm^{-1} (C-F) and 1550,1370 cm^{-1} (-NO_2). The 1H NMR spectrum revealed 7.30-8.20 multiple for aromatic proton, 8.48, 6.52,6.48,5.20 for NH, 2.30 singlet for CH_3 proton.

The compound **(6a-g)** further react with 5-nitro furfural **(7)** yields N'-(3-(hydroxy(5-nitrofuran-2-yl)methyl)-6-methyl-2-oxo-4-aryl-1,2,3,4-tetrahydropyrimidine-5-carbonyl) benzene sulfono hydrazide **(8a-g)**. The IR spectrum revealed absorption bands similar to compound (6a-g) in addition they show band of –OH,-NO_2 and furan C-O at 3400-3450,1550,1370 and 1120-1080 cm^{-1}. The 1H NMR spectrum revealed 7.00-8.20 multiple for aromatic proton, 8.48, 6.52, 5.20 for NH, 2.30 singlet for CH_3 proton, 3.80 for hydroxyl group and 6.90 for CH proton .

Table 3. Antibacterial Activity of Compounds (6a-g) and (8a-g)

Comp. No.	*Zone of Inhibition(mm)*			
	Gram +ve		*Gram -ve*	
	Bacillus Subtilis	*Staphylococcus aureus*	*Kllebsiella promioe*	*E.coil*
6a	10	9	8	8
6b	13	12	11	12
6c	12	10	10	10
6d	11	11	9	9
6e	12	12	10	12
6f	14	13	11	14
6g	17	15	13	16
8a	12	12	12	11
8b	14	14	14	14
8c	13	12	13	12
8d	13	13	12	11
8e	15	14	13	15
8f	16	16	14	17
8g	18	17	16	19
Tetracycline	20	19	18	22

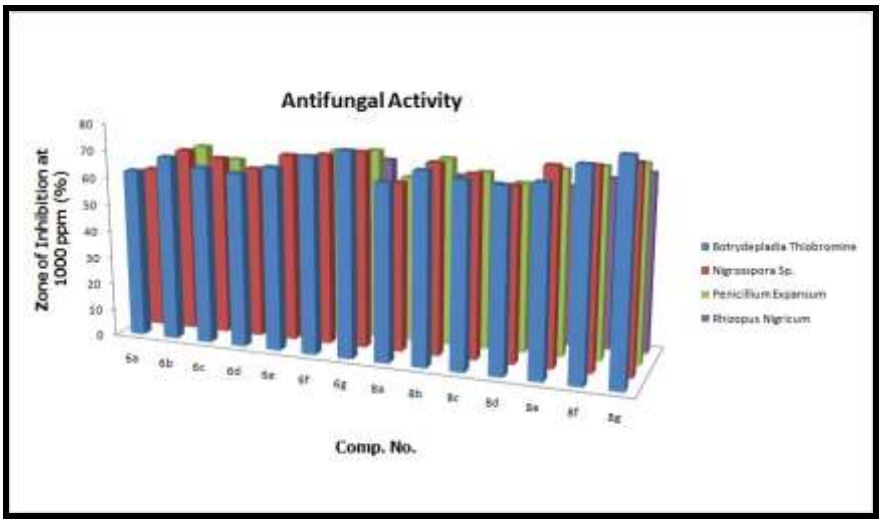


All the elemental and spectral features suggest that the data are consistent with the predicted structure shown in Scheme-1. The LC-MS of selected compounds shows the peak of M^+ ion which is consistent of their molecular weight. All these facts confirm the structures **(6a-g)** and **(8a-g)**.

Table 4. Antifungal Activity of Compounds (6a-g) and (8a-g)

Comp. No.	*Zone of Inhibition at 1000 ppm (%)*			
	Botrydepladia Thiobromine	*Nigrosspora Sp.*	*Penicillium Expansum*	*Rhizopus Nigricuns*
6a	62	60	59	52
6b	68	68	67	58
6c	65	66	63	56
6d	64	63	61	55
6e	67	69	66	58
6f	72	70	69	61
6g	75	72	70	64
8a	65	62	61	55
8b	70	70	69	60

8c	68	67	65	58
8d	67	64	62	56
8e	69	72	68	59
8f	76	73	70	63
8g	80	75	72	66



The examination of antibacterial and antifungal activities data reveals that all compounds toxic against microbes and the compounds **8g , 8f** and **6g** found more active against the gram-positive and gram-negative bacteria as well as fungi.

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