SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF BENZENESULPHON AMIDE BASE DERIVATES

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Abstract

A series of eighteen N-benylidene-4-(2-benzylidenehydrazinyl) benzenesulfone amide was synthesized using , aromatic aldehydes and 2-phenyl hydrazinyl-benzene sulfonamide. As starting material .Furthermore, there has been some additional work investigating the effect of these derivatives on biological activity .Aiming to obtain novel compounds that exhibit biological activities. They were characterized using FTIR, ^{1}HNMR, ^{13}CNMR & elemental analysis. The compounds show anti fungal and anti bacterial (minimal inhibitory concentration) activities.

Keywords: N-benylidene-4-(2-benzylidene hydrazinyl) benzene sulfonamide derivatives
Anti-bacterial activity, antifungal activity.

Introduction :

Heterocyclic compounds are used in agriculture,photography, biocideformulation, polymer science,Antibiotic (insecticide, herbicide). Hugo Schiff (26 April 1834-8 September 1915) was the person who first discovered Schiff Bases. He was interested in research on aldehydes which further lead to development of Schiff Test. The compound having general formula $R_2C=NR'$ ($R' \neq H$) is called Schiff Base. Primary amine and an aldehyde on condensation in the presence of solvent such as methanol, tetrahydrofuran(THF), 1,2-dicholoro ethane (DCE) forms Schiff base. Recently the Schiff base also have been formed by using a microwave. Schiff bases are also known as versatile ligands. They have been used as catalyst in various biological systems, polymers,dyes,medicines and pharmaceutical field. They are also useful in food packages , O_2detector and also in birth control. K-10 Montmorillonite mediated condensation of aldehyde 1 with arylamine 2 affords chroman-2,4-dione 5 which gives tricoumarol 8 by acid hydrolysis, 4-arylamino-3-formylcoumarin 11 and 1-benzopyrano[4,3-b]quinoline 12 on heating with $POCl_3$[[1]. Schiff bases derived from various heterocyclic compounds displayed broad range of biological activities such as anticancer, antiviral, antimicrobial,

anticonvulsant, antidepressant, angiotension-II receptor antagonist, antiinflammatory and anti-glycation activity. So far, modifications of the Schiff bases have proven highly effective with improved potency and lesser toxicity. The present review highlights the recently synthesized Schiff bases possessing important biological activities[2]. Herein we reported a transition metal free strategy for the synthesis of 4-quinolones, benzopyran derivatives and other fused systems by the domino reaction of 3-benzoyl-chromones, containing a leaving group in the position-2 of the benzoyl moiety, with aliphatic amines, anilines and different binucleophiles. The developed strategy is suitable for a broad range of substrates, namely according to the applied nucleophile the reaction provides different final products with excellent chemoselectivity. The mechanistic studies resulted in the detection and isolation of several intermediates[3] .2,2-Dimethoxypropane reacts with a variety of o-hydroxybenzaldimines in the presence of a catalytic amount of scandium triflate at ambient temperature to afford a series of new compounds, 3,4-dihydro-4-amino-2-methoxy-2-methyl-2H-1-benzopyrans, in high yields, with good diastereoselectivity. BF3. OE2, is also found to mediate this transformation under mild reaction conditions[4].A series of 7-(2-substituted phenylthiazolidinyl)-benzopyran-2-one derivatives have been synthesized by reaction of 7-amino-4-methyl-benzopyran-2-one (1) with an appropriate substituted aldehydes to obtain various Schiff bases (3a-k) which on treatment with thioglycolic acid afforded the title compounds (4a-k). Structure of these compounds were established on the bases IR, 1H NMR, 13C NMR and Mass spectral data. Schiff bases and title compounds were evaluated for antibacterial and antifungal activities against various bacterial and fungal strains[5]

In the present research reference study on 2- benzylidene hydrazinyl-benzene sulfonamide . Derivatives were synthesized and evaluated invitro for their preliminary anti bacterial activities against four different pathogenic bacterial strains such as Staphylococcusaureus , Escherichia coli , Bacillus subtilis and Pseudomonas aeruginosa. Anti bacterial activity of each compound was compared with standard drug, Ampicillin. The compounds were interpreted by UV, IR, 1HNMR, mass spectroscopy and X-ray diffraction studies. Solvato chromic behavior of these compounds was also investigated by UV-vis spectra .Zone of inhibition and minimum inhibitory concentration revealed that all the products exhibited greater anti bacterial potential against all bacterial strains. 3- Thiazolylazo and 3-(4-phenyl thiazolyl azo) of phenyl hydrazine and their Sulphonamides are well known as Intermediate , which have been exhibiting good zone of inhibition against both gram + ve strains and gram – vestrains , whereas the compound pyrazoloneazoanalogue 4e (reported analoguein literature) has tremendous anti bacterial activity. Finally we concluded that the compounds having thiazole , pyrazole and triazole nucleus in individual molecular structure club bed with potent ant-ibacterial harmacophore of 2 –benzylidene hydrazinyl – benzene sulfonamide showed anti bacterial activities. Chemists have long sought a patented molecule for the treatment of numerious Infections, a compound that will selectively activate toward the various bacterial and fungal strains without affecting the normal cells.

Chemicals :

General method for the synthesis of Schiff bases (A1 to A19): Preparation of Schiff base A1 mixture of benzaldehyde(11.77m.mol,1.20mL)and 2-phenylhydrazinyl-benzenesulfonamide(12.07m.mol, 2.08g) were taken in a twoneck flask. After adding one drop of acetic acid simple put this flask on magnetic stirrer with using magnetic stirr bar for 5 to 6 hr to completereaction.The reaction development was observed by taking TLC after half and our to initiate the reaction and control by interval of every one 1hr.The reaction masswas solidified and the attained residue was washed through water and dried. The obtained product was re-crystallized from alcohol and gave the pure Schiff base A1. The same procedure wasutilized to synthesize Schiff bases (Scheme-1).

Bioassay protocol :

Assortment of pathogensMicrobiology DepartmentAPMS campus affiliated with Sardar Patel University provided all fungal and bacterial strains.

Culture preparation:

To culture bacterial stains for media, Muller Hinton broth and Muller Hinton agar and for fungal strains Sabourd dextrose agar (SDA) plates were used.

Antibacterial activity:

Antibacterial activity of the synthetic compounds (sp-1 to sp-24) was determined by disc diffusion method (Bauer et al., 1966). Bacterial pathogens were maintained for 2 h in log phase by using Autoclaved Muller Hinton broth with constant mixing. Pure compounds were dissolved in DMSO to prepare 100mg/mL of stock solution. For screening, sterile filter discs (7 mm in diameter) were used which contain 10 □L of stock solution. 24 h old culture developed in Mueller Hinton broth (Oxoid) was utilized to seed the Mueller Hinton agar (Oxoid) plates. The ready discs were attuned on to the surfaces at numerous locations and plates were placed for incubation at 37 °C for 24 h. Outcomes were noted by finding the inhibition zone in mm. Negative control was DMSO and gentamycin was utilized as positive control.

Antifungal activity:

Antifungal activity of synthetic products (sp-1 to sp-24) was also obtained by disc diffusion strategy as defined previously (Bauer et al., 1966). A homogeneous blend of fungal culture was readied and the SDA plates were sowed with this suspension. Germ-free filter discs which contain 10 □L volume of stock solution were put on to the surfaces at various positions. Plates were placed for incubation for one week at room. After incubation distance across of zone of inhibitions was noted in mm. The gresiofulvin was utilized as standard.

Finding of Minimum inhibitory concentration (MIC) :

Those synthesized derivatives demonstrating antibacterial activity were also investigated to calculate MIC values by disc diffusion method (Bauer et al., 1966). For this reason sterile discs of various concentrations (µg/mL) of compounds and standard were set. The MIC was obtained at the lowest concentration of test compounds indicating zone of inhibition. Results were recorded in an average of triplicate.

II.EXPERIMENTAL

2.1MaterialsandInstrumentation

All reagents were of analytical reagent grade and were used with further purification by their purification process. Here in this work we have extended the results and research on synthesis method development toward the minimum us of non polar solvents as per the green chemistry point of view and visionary approach towards there scale up valuable standard chemical derivatization . Solvents employed were purified by standard procedure before to use. 4- hydroxyl coumarin , was purchased from S D fine chem. . Pvt Ltd . Catalyst was prepared by standard process and supported material for catalyst was purchase from S D fine Chem Pvt .Ltd. The melting points were determined in open capillary on electronic apparatus and are considering precise record of data. To monitor the reactions, as well as, to establish the identity and purity of reactants and products , thin layer chromatography was performed on microscopic glass slides (2 x 7.5 cm) coated with silica gel- G, using chloroform- methanol , as the solvent systems , Rf values and spots were visualized under UV radiation. Elemental analysis (C,H,N) were performed using a Perkin Elmer, USA 2400 – II CHN analyser . FTIR spectra (4000-400 cm – 1) recorded on Simadzu 8400 –spectrophoto meter using KBr disk. Nuclear magnetic resonance spectra were recorded on Bruker 400 MHz model spectro meter using DMSO as a solvent and TMS as internal reference (Chemical shifts in δppm).We have synthesized nineteen compounds in our labolatory. We have have carried out NMR, IF , Antimicrobial , Antifungal activities for this compounds .

Results and discussion

Schiff bases (A1 to A19) were synthesized by the condensation of hydrazinyl SULPHONAMIDE with appropriate aromatic aldehydes by using veryminute aceticacid as a normal promoter acid catalyst. All the synthesized compounds (A1 to A19) are listed.

All the prepared imines or Schiff bases were investigated for their microbial activity (Table 2) against standard gentamycin. Fourteen gram positive (+ve) and twenty-two gram negative (-ve) bacterial pathogens were used. On the basis of diameter of inhibited zone in mm outcomes were reported that was appeared around the disc (7mm).Compound**A-1** showed anti microbial activities on one bacterial strain ***Pseudomonas aeruginosa*** (Human pathogenic and Ciprofloxacin resistant). **A- 1** showed positive anti microbial activity against ***Pseudomonas aeruginosa*** (Human pathogenic and Ciprofloxacin resistant strain) which was 57.44% potency compared to Norfloxacin. Compound **A-3** showed anti microbial activities on one bacterial strain ***Pseudomonas aeruginosa***

(Human pathogenic and Ciprofloxacin resistant) . **A-3** showed positive anti microbial activity against ***Pseudomonas aeruginosa*** (Human pathogenic and Ciprofloxacin resistant strain) which gave 70.71% potency compared to Chloramphenicol.

All the synthesized products (A1 to A19) were tested for their in vitro antifungal activity (Table 2) taken gresiofulvin as standard against nineteen fungal strain. A**-11** showed positive anti microbial activity against ***Aspergillus flavus*** which was 51.00% potency compared to Griseofulvin.

Conclusion

Synthesis of Schiff bases by utilizing minute amount of acetic acid as a catalyst was found to be most effective method having few advantages over classical procedure such as short reaction time, high yield and greener reaction conditions. The biological investigations of the above synthesizedsuch imines or Schiff base revealed that compounds A 1 & A 3 shows considerable antimicrobial activity and A **– 11** showed positive anti fungal activity against ***Aspergillus flavus*** which was 51.00% potency compared to Griseofulvin . It is concluded that these products have potential of curing numerous microbial infections and can have opportunity in pharmaceuticalresearch.

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References:

1.**Bandyopadhyay, C., Sur, K.R., Patra, R. and Sen, A.**, Tetrahedron, 56(22), pp.3583-3587,**2000.**

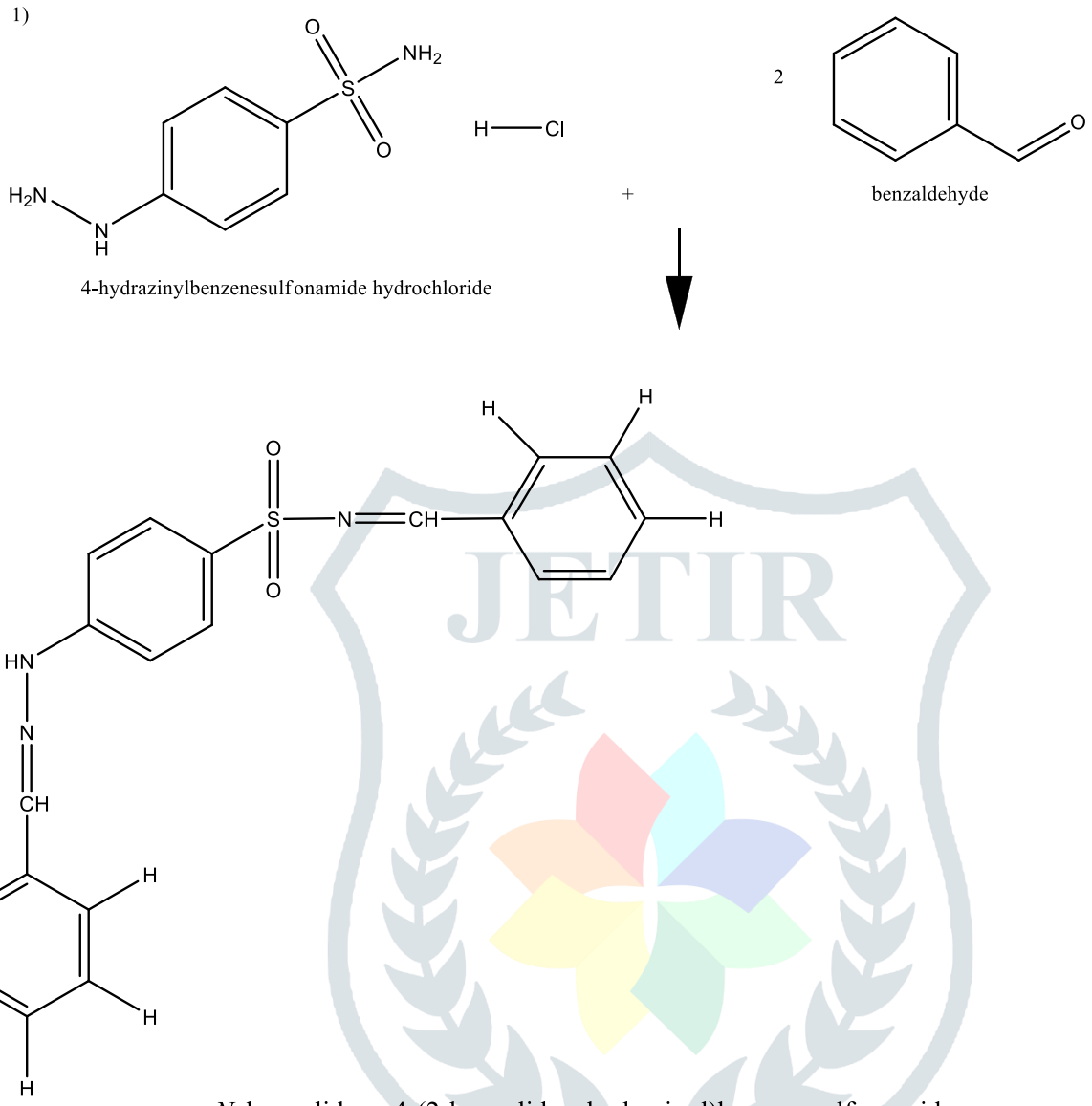
2.**Anand, P., Patil, V.M., Sharma, V.K., Khosa, R.L. and Masand, N**. Schiff bases: A review on biological insights. Int. J. Drug Des.Discov, 3, pp.851-868,**2012.**

3.**.Iaroshenko, V.O., Mkrtchyan, S., Gevorgyan, A., Grigoryan, T., Villinger, A. and Langer, P.** RSC Advan.ces, 5(36), pp.28717-28724 **, 2015.**

4. **Yadav, J.S., Reddy, B.S., Sekhar, K.C. and Geetha, V.,.** Tetrahedron letters, 42(26), pp.4405-4407, **2001.**

5. **Ronad, P.M., Noolvi, M.N., Sapkal, S., Dharbhamulla, S. and Maddi, V.S.,.** European Journal of medicinal chemistry, 45(1), pp.85-89, **2010.**

Reaction Scheme :



N-benzylidene-4-(2-benzylidenehydrazinyl)benzenesulfonamide

Scheme 1: General Synthesis for Schiff base e.g.N-benzyldene-4-(2-benzylidenehydrazinyl) benzenesulfonamide

Table 1 Detail of Synthesised compound A10 toA19 with different aldehydes.

JETIR

A10	4-sulphonylamidephenylhydrazine	Hydrochloricacid	Anisaldehdye	EA:HEXANE
A11	4-sulphonylamidephenylhydrazine	Hydrochloricacid	Iso-butyraldehyde	EA:HEXANE
A12	4-sulphonylamidephenylhydrazine	Hydrochloricacid	Acetaldehyde	EA:HEXANE
A13	4-sulphonylamidephenylhydrazine	Hydrochloricacid	4-methylbenzaldehdye	EA:HEXANE
A14	4-sulphonylamidephenylhydrazine	Hydrochloricacid	Propianoaldehyde	EA:HEXANE
A15	4-sulphonylamidephenylhydrazine	Hydrochloricacid	Cinnamaldehdye	EA:HEXANE

A16	4-sulphonylamidephenylhydrazine	Hydrochloricacid	Furfuraldehdye	EA:HEXANE
A17	4-sulphonylamidephenylhydrazine	Hydrochloricacid	2-hydroxybenzaldehdye	EA:HEXANE
A18	4-sulphonylamidephenylhydrazine	Hydrochloricacid	4-hydroxybenzaldehyde	EA:HEXANE
A19	4-sulphonylamidephenylhydrazine	Hydrochloricacid	Formaldehyde	EA:HEXANE

Table2.Anti bacterial activity of the compounds

		MinimalInhibitoryConcentrationMIC(µg/ml)		
		BacterialSpecies		
Compounds		P.aeruginosa	S.aureus	S.pyogenus
		MTCC1688	MTCC96	MTCC442
A1		125	100	125
A2		200	250	500
A3		140	200	200
A4		200	500	500
A5		500	500	500
A6		400	400	400
A7		500	500	500
A8		400	400	400
A9		400	400	400
A10		200	200	200
A11		500	500	500
A12		500	500	500
A13		500	500	500
A14		250	500	500
A15		300	300	300
A16		500	500	500
A17		300	300	300
A18				
A19				
Chloramphenicol		50	50	50

Table3 .Anti fungal activity of the compounds.

	MinimalInhibitoryConcentrationMIC(µg/ml)		
	FungalSpecies		
	C.albicans	A.clavatus	Aspergillusniger
Compounds	MTCC227	MTCC1323	MTCC2208
A1	250	500	500
A2	500	1000	1000
A3	250	200	250
A4	250	1000	500
A5	250	500	500
A6	1000	500	400
A7	500	400	1000
A8	400	500	1000
A9	250	250	400
A10	250	200	200
A11	100	100	100
A12	200	200	200
A13	250	200	500
A14	300	300	250
A15	250	250	250
A16	1000	1000	500
A17	300	300	500
A18	500	500	500
A19	500	500	500
Standarddrugs			
Nystatin	100	100	100
Griseofulvin	50	50	50