Synthesis, Characterization and Biological Activity of New Schiff Bases of Sulpha Drugs

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Abstract

A series of 2-hydroxy, 3- azo- (4'sulphonamoyl) benzalidene N-pyridine-2yl-amine was synthesized by condensation of unsubstituted /substituted 2-hydroxy, 3-azo-(4'suphonamoyl) benzeldehyde and amino pyridine. The newly synthesized Schiff bases were characterized on the basis of elemental analysis and spectral studies like UV-Visible, IR and NMR. Biological activities of newly synthesized Schiff bases (HASBP) were evaluated against Staphylococcus aureus, Escherichia coli and Aspergillus Niger.
Keywords: Schiff Base, antibacterial activity.

Introduction

Compounds containing azomethine group (–HC=N–) are typically known as Schiff bases. Schiff bases form a significant class of compounds in medicinal and pharmaceutical chemistry with several biological applications that include antibacterial [1-2], antifungal [3-6], and antitumor activity [7-8]. They have been synthesized by the condensation of primary amines with active carbonyls. Sulphonamides had attracted special attention due to their therapeutic importance as they were used against a wide spectrum of bacterial ailments and application against most of the gram positive and some of the gram negative bacteria. They inhibit some enzyme reactions vital to bacteria and this hinders the formation of bacterial wall [9-10].

These drugs were the first used as efficient treatment to be employed systematically for the prevention and cure of bacterial infections. In most instances, they are bacterial static that is, they inhibit the growth and multiplication of the bacteria, but do not kill them [11-13].Several metal based sulphonamides have been reported as potentially biologically active [14]. The biological importance of sulphonamides and Schiff base has prompted us to synthesize some new Schiff base having sulphonamoyl azo moiety.

Experimental

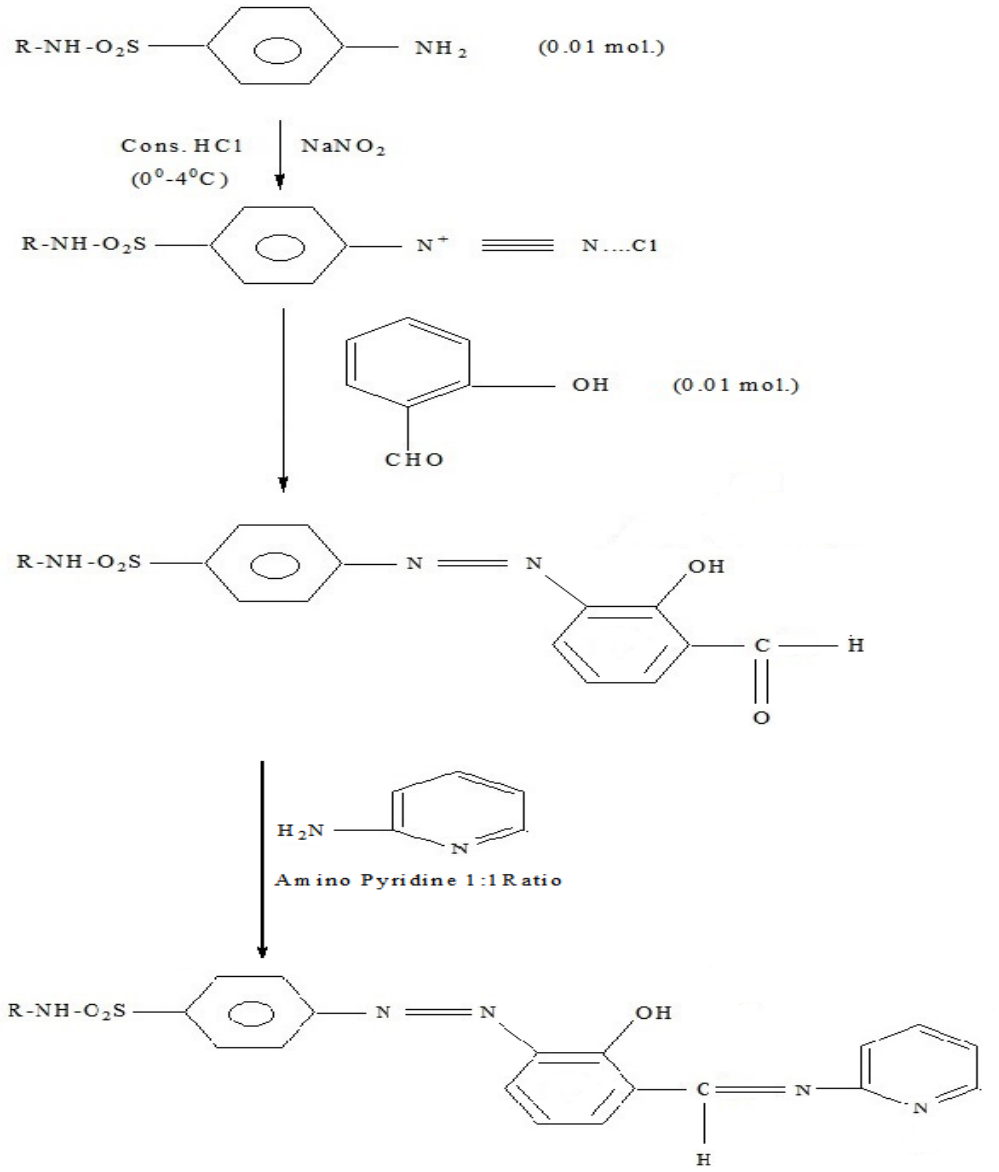
All the chemicals were used of AR Grade. IR spectra were scanned on a Perkin Elmer 883 spectrophotometer P.M.R. Spectra were recorded in (DMSO), on a Varian 270 Hz using TMS as an internal standard and UV-Vis Spectra was recorded on a UV-160 a Shimadzu spectrophotometer- All the melting points were determined in an open capillary tube and are uncorrected. Completion of the reaction was monitored by TLC on silica gel G. Plates.

(a) Synthesis of Precursors; 2-hydroxy, 3-azo- (4' sulphonamoyl) benzeldehyde

This compound was synthesized by dissolving sulphanilamide (0.01 moles, 1.72 gm) in a mixture of concentrated HCl (3.0 ml) and water (4.0 ml) and cooled to 0^0C in an ice salt bath. To this cold aqueous

solution of sodium nitrite (0.01mol; 0.69 gm) was added in small portions with constant stirring. Instantaneous formation of diazonium salt was started. The diazonium salt so obtained was filtered into already cooled 0^0C solution mixture of sodium acetate (8 gm) and salicyldehyde (0.01 moles 1.22 gm.) in ethyl alcohol (25 ml) and solution was stirred vigorously. The product so obtained was filtered, washed with cold water and re-crystallized from ethanol; the color of the synthesized product was orange, Melting point was 165^0C and yield was 70%. Elemental analysis calculated for $C_{13}H_{11}N_3O_4S$, is as following. C= 51.14%, H= 3.60%, N =13.89% found C = 51.19%, H= 3.5%, N = 13.89%, KBR δ Max 3244 (NH_2 - O_2S), 1417(N=N), 3680cm^{-1} (-OH), 1660 (C=O), 1139 (SO_2) and 750 cm^{-1}. Other compounds of this series were synthesized in the similar manner by diazotizing different sulphonamides viz. Sulphanilamide, Sulphadiazene, Sulphadimidine, Sulphaguanadine, Sulphametoxazole, and Sulphathiazole.

Reaction Scheme



(b) Preparation of Schiff Base; 2-hydroxy, 3- azo- (4'sulphonamoyl) benzalidene N-pyridine-2yl-amine (HASBP)(1-6)

Take 2-hydroxy 4azo- (4' sulphonamoyl) benzaldehyde (0.01mol 3.05gm) in 30 ml toluene, and mixed it with amino pyridine (0.01mol 0.94 gm) in 30 ml of toluene. Add 10 ml of glacial acetic acid as catalyst with constant stirring. Mixture was refluxed in stark dean condenser for 4-5 hrs. After completion of reaction, solid Dark Orange colored product was formed, which was filtered and washed. The product was recrystallised by hot ethanol. Shining Orange crystals were obtained M.P. 180^0C yield 60%. Other compounds of this series were synthesized in similar manner by substitttuted precursors and their characteristics have been compiled in Table 1.

Result and Disscussion

Schiff base

The structure of above synthesized Schiff bases have been established on the basis of elemental and IR, UV-VIS, and NMR Spectral studies.

Elemental Analysis for $C_{18}H_{23}N_5O_3S$

All synthesized compounds give consistent C, H and N analysis. It is compiles in following table

S.No	Compounds	Elements					
		C		H		N	
		Theoretical	Observe	Theoretical	Observe	Theoretical	Observe
1	$C_{18}H_{23}N_5O_3S$	56.69	56.00	3.93	3.50	18.37	17.00
2	$C_{19}H_{16}N_7O_3S$	54.02	54.00	3.79	3.45	23.22	22.50
3	$C_{22}H_{17}N_7O_3S$	57.51	57.20	3.70	3.35	21.35	20.80

Spectral Analysis

UV- Visible

The broadband appears at 298 nm (-N=N-) azo group.

S. No.	λ Max Value	Assigned Structure
1	298 nm	-N=N

IR spectra and mode of bonding

IR Spectra of Schiff bases shown strong peek at 1650-1668 suggest the presence of azomethine group $H\text{-}\underset{|}{C}\text{=}N$. The broadband at 3650-3700 cm^{-1} is due to phenolic -OH group. The broadband of phenolic group indicates the presence of hydrogen bonding with azomethine group. The other important bond is at 1450-1460 cm^{-1} and at 3220-3240 cm^{-1} is due to N=N and $–NH_2O_2S$ group.

S.No	Compounds	V_{max} -C=H	V_{max} -OH	V_{max}-N=N-	V_{max} -NH2O2S
1	$C_{18}H_{23}N_5O_3S$	1658	3700	1459	3240
2	$C_{19}H_{16}N_7O_3S$	1650	3725	1465	3235
3	$C_{22}H_{17}N_7O_3S$	1652	3690	1448	3245

1H NMR spectra

The 1H NMR spectrum of the Schiff base was recorded in DMSO. In this the 1HNMR spectra of Schiff base, a singlet appears at 8.7-8.9 δ is due to azomethine protons. The multiple between 7.5-8.0 δ suggest the presence of aromatic protons.

S.No.	Signal-δ Value	Assigned Structure
1	8.7-8.9 (Singlet)	HC=N
2	7.5 8.0 (multiplet)	Aromatic protons

On the basis of above elemental and spectral studies following structure is assigned to newly synthesized Schiff bases. l

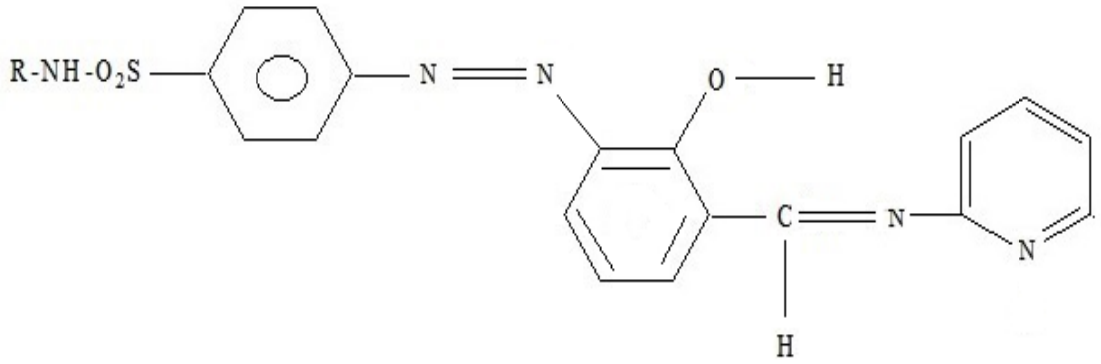
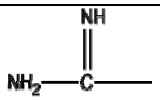
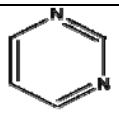
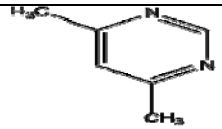
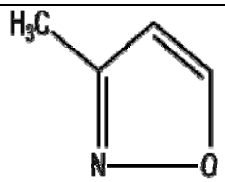
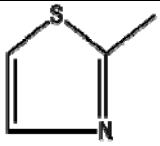


Table 1 Characteristics of 2-hydroxy, 3 azo (4' sulphonamoyl) benzalidene N-pyridine-2yl-amine (HASBP)

S. No.	-R	Molecular Formula	Melting Point	Colour	Yield %
1.	—H	$C_{18}H_{15}N_5O_3S$	180	Dark Orange	60
2.		$C_{19}H_{16}N_7O_3S$	190	Light Orange	65
3.		$C_{22}H_{17}N_7O_3S$	185	Dark Brown	59
4.		$C_{24}H_{21}N_7O_3S$	200	Dark Orange	67
5.		$C_{22}H_{18}N_6O_4S$	220	Orange	64
6.		$C_{22}H_{17}N_5O_4S_2$	215	Dark Orange	70

All compounds gave consistent C, H, N, and Analysis.

Biological Activity

The biological l activity of all the synthesized compounds (1-6) were examined against Gram-positive (*Staphylococcus aureus)* , Gram-negative (*Escherichia coli*) and fungal strains (*Aspergillus niger)* species by measuring zone of inhibition. The antimicrobial activity was performed by Agar diffusion method at the concentration level of 200µg/ml.. Nutrient agar was used as culture media for antimicrobial activity and Sabouraud dextrose agar was used as culture media for antifungal activity and DMSO as control. Ofloxacin and etoconazole as standard drug at a concentration of 200µg/ml the results of the biological activity are shown in Table II.

Table 2 Zone of inhibition (mm) data of synthesized compounds (1-6)

Compound	Antibacterial activity	Antibacterial activity	Antifungal activity
	S.aureus	E.Coli	A.Niger
	Gram +ve	Gram –ve	Antifungal
Control	-	-	-
1	12	11	13
2	13	12	14
3	14	15	15
4	11	13	13
5	14	12	15
6	12	18	15
Ofloxacin	18	22	-
Ketoconazole	-	-	20

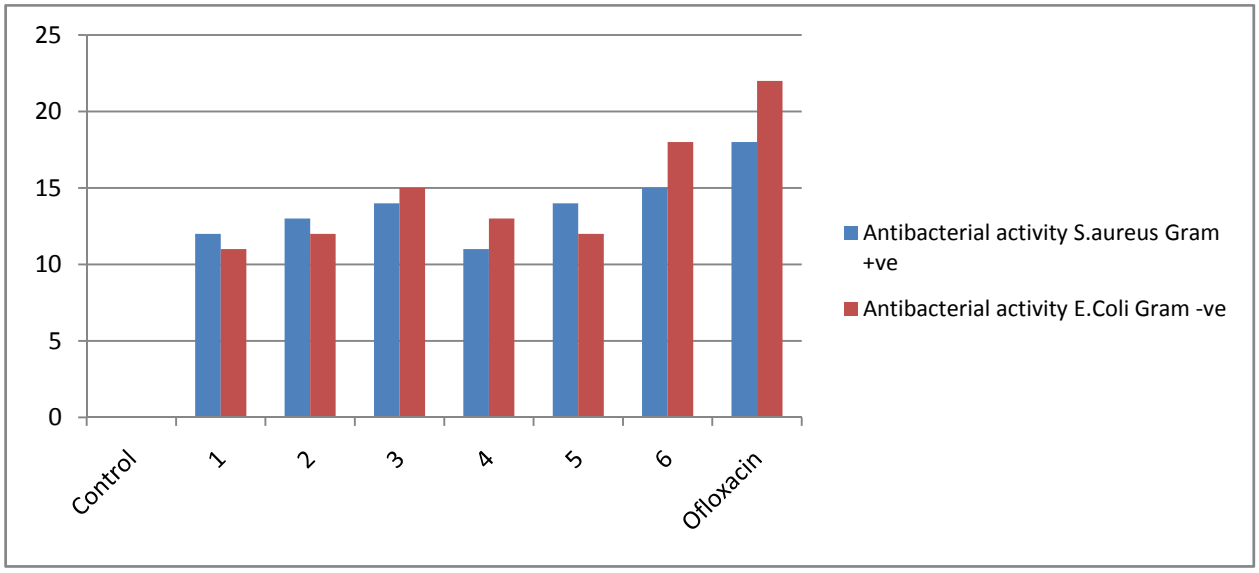


Fig.1: Antibacterial activity (Gram +ve), Antibacterial activity (Gram -ve) of synthesized compounds.

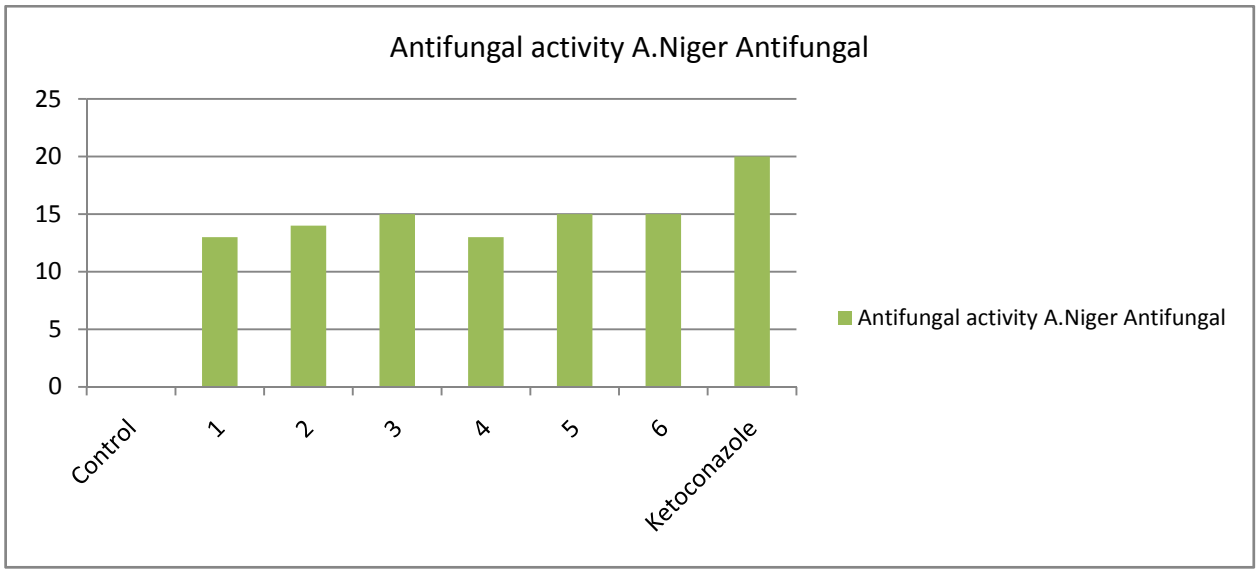


Fig.2: Antifungal activity of synthesized compounds.

Conclusion

The structures of newly synthesized Schiff bases have been established on basis of spectral studies Antibacterial and antifungal activity of the synthesized derivatives (1-6) was done in comparison with ofloxacin and ketoconazole as standard dare to reveal the potency of synthesized derivatives. All the 4 selected strains of bacteria and fungi namely *S. Aureus, E. Coli*, and *A. Niger* showed sensitivity to all derivatives at higher concentration (200µg/ml) and no sensitivity at lower concentration among these.

Referances

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