Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 6, Issue 1, 2014

Research Article

SYNTHESIS, SPECTRAL CHARACTERIZATION AND ANTIMICROBIAL SCREENING OF NOVEL SCHIFF BASES FROM SULFA DRUGS

GOMATHI VELLAISWAMY* AND SELVAMEENA RAMASWAMY

PG and Research Department of Chemistry, Seethalakshmi Ramaswami College, Tiruchirappalli 620002, Tamil Nadu, India.
Email: vemathi@gmail.com and rsmchemsrc@gmail.com

Received: 20 Oct 2013, Revised and Accepted: 13 Nov 2013

ABSTRACT

Objective: To synthesis novel Schiff bases from sulfathiazole/sulfapyridine with 3-ethoxysalicylaldehyde/ pyridine-2-carbaldehyde/ 2-hydroxy-1-naphthaldehyde.

Method: The synthesized Schiff bases were characterized by analytical data, IR, ^{1}H NMR, ^{13}C NMR, UV-Vis spectra and screened for antibacterial activity against gram positive bacteria *Staphylococcus aureus* and gram negative bacteria *E.Coli, Klebsiella sp* and *Pseudomonas aeruginosa* and antifungal activity against *Aspergillus niger* and *Mucor* by disc diffusion method. Ciprofloxacin and Nystatin were used as standard drug for bacteria and fungus.

Results: zone of inhibition indicated that the Schiff bases possessed highly potent antibacterial and antifungal activity against gram positive and gram negative bacteria.

Conclusion: The Schiff bases were synthesized, characterized and exhibited promising antibacterial and antifungal activity.

Keywords: Sulfa drug, 3-ethoxysalicylaldehyde, pyridine-2-carbaldehyde, 2-hydroxy-1-naphthaldehyde, Schiff base, Zone of inhibition, Antibacterial activity, Antifungal activity, Ciprofloxacin, Nystatin.

INTRODUCTION

A group of synthetic organic compounds, derived from sulfanilamide, chemically similar to PABA are capable of inhibiting bacterial growth and activity, called sulfonamides (Sulfa drugs*).* Sulfonamides are compounds that contain sulfur in a -SO_2NH_2 moiety directly attached to a benzene ring[1]. Sulfa drugs, developed in the 1930s, were the first medications effective against bacterial disease. They appeared as the first "miracle drugs" at a time when death from bacterial infections such as pneumonia and blood poisoning were common [2]. Schiff base compounds which contain the azomethine (imine) group (–RC=N–) are usually prepared by the condensation of a primary amine with an active carbonyl compound [3]. The sulfonamide derivatives widely used in clinical medicine as pharmacological agents with a wide variety of biological actions [4], Schiff bases are also known as anticancer and antiviral agents [5]. Sulfonamides are well renowned for their antibacterial [6-8], antitumour [9], diuretic [10], and antithyroid [11] activities. The presence of azomethine and sulfonamide functional group is responsible for antimicrobial activity, which can be altered depending upon the type of substituent present on the aromatic rings. The condensation of sulfa drugs with aldehyde gives biologically active Schiff bases. Keeping in view of the pronounced biological activity of the Schiff bases derived from sulfa drug, it was thought of worthwhile to synthesis, characterize and to study the antimicrobial activity of Schiff bases derived from 3-ethoxysalicylaldehyde/ pyridine-2-carbaldehyde/ 2-hydroxy-1-naphthaldehyde with sulfathiazole/sulfapyridine.

MATERIALS AND METHODS

Materials and solvents

All the reagents used were of AR grade (HIMEDIA / Sigma Aldrich). Commercially available rectified spirit was dried over anhydrous quicklime for 24 hours, filtered and distilled before use (BP 78°C). Dimethylsulphoxide (MERCK) and N,N-dimethylformamide (MERCK) were used as such.

Instruments

Melting points were determined using Elico melting point apparatus. Elemental analysis (C,H,N) were performed using Elementar Vario EL III. IR spectra of the ligand and its complexes were recorded in KBr pellets with Perkin Elmer IR RXI Spectrometer in the 4000-400 cm^{-1}range. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 MHz FT- PMR Spectrometer (DMSO-d_6). The electronic spectra were recorded in Perkin Elmer Lambda 35 spectrometer in the 190-1100 nm range.

Procedure for Synthesis

Synthesis of ESST

To a hot stirred ethanolic solution of sulfathiazole (0.0025 mol) an ethanolic solution of 3-ethoxysalicylaldehyde (0.0025 mol) was added. The reaction mixture was refluxed for 1h. The dark red coloured solid mass formed during refluxing was filtered, washed with ethanol and dried over anhydrous $CaCl_2$ in a desiccator. The purity of the Schiff base was checked by melting point, TLC and spectral data. The Schiff base is insoluble in some common organic solvents and soluble in polar solvents DMF, DMSO.

Synthesis of PCST

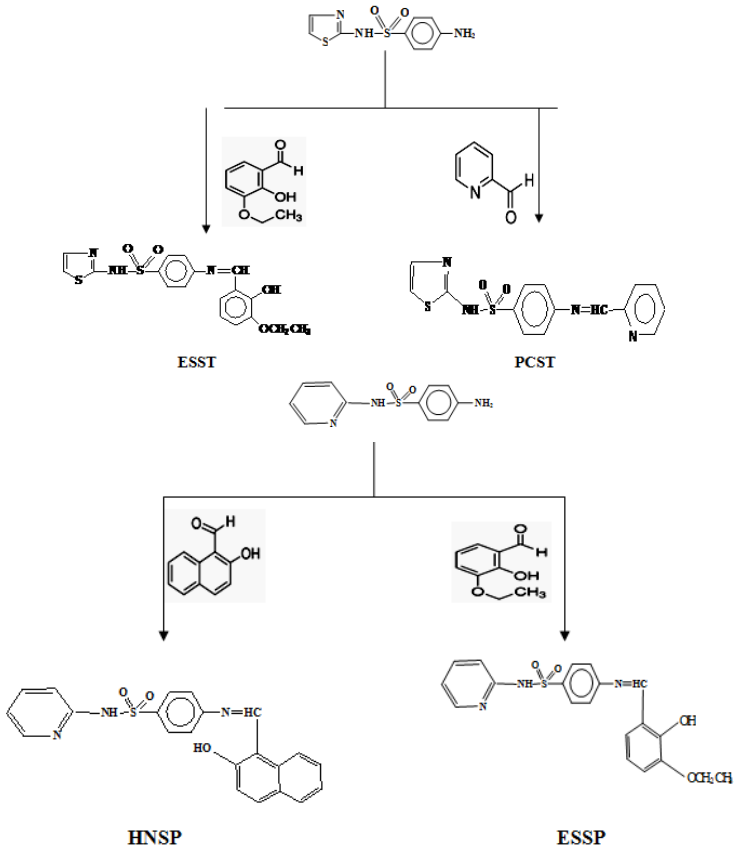
To a hot stirred ethanolic solution of sulfathiazole (0.0025 mol), pyridine-2-carbaldehyde (0.0025 mol) was added. The reaction mixture was refluxed for 4hrs. The black coloured solid mass formed during refluxing was filtered, washed with ethanol and dried over anhydrous $CaCl_2$ in a desiccator. The purity of the Schiff base was checked by melting point, TLC and spectral data. The Schiff base is insoluble in some common organic solvents and soluble in polar solvents DMF, DMSO.

Synthesis of HNSP

To a hot stirred ethanolic solution of sulfapyridine (0.0025 mol) an ethanolic solution of 2-hydroxy naphthaldehyde (0.0025 mol) was added. The reaction mixture was refluxed for 4hrs. The yellow coloured solid mass formed during refluxing was filtered, washed with ethanol and dried over anhydrous $CaCl_2$ in a desiccator. The purity of the Schiff base was checked by melting point, TLC and spectral data. The Schiff base is insoluble in some common organic solvents and soluble in polar solvents DMF, DMSO.

Synthesis of ESSP

To a hot stirred ethanolic solution of sulfapyridine (0.0025 mol) an ethanolic solution of 3-ethoxysalicylaldehyde (0.0025 mol) was added. The reaction mixture was refluxed for 3hrs. The orange coloured solid mass formed during refluxing was cooled, filtered, washed and dried in a desiccator. The purity of the ligand was checked by melting point, TLC and spectral data.



Antimicrobial susceptibility test by Disc diffusion Technique

Principle

Disc impregnated with known concentration of antibiotics are placed on an agar plate that has been inoculated uniformly over the entire plate with a culture of the bacterium to be tested.

The plate is incubated for 18 to 24 hours at 37°C. During this period, the antimicrobial agent diffuses through the agar and may prevent the growth of the organism. Effectiveness of susceptibility is proportional to the diameter of the inhibition zone around the disc. Organisms which grow up to the edge of the disc are resistant.

Procedure

The plate was labeled with the name of the culture, sample and standard at the bottom of the plate. Then sterile cotton swab on a wooden applicator stick was dipped into the bacterial suspension. Excess fluid was removed by rotating the swab and rubbed gently over the plate to obtain uniform distribution of the inoculums. The sterile disc was held on the inoculated plate with the help of micropipette. The sample was leveled in the sterile disc and incubated at 37°C in an incubator. After incubation the diameter of the zone of inhibition of growth was measured.

Observation	Report
Inhibition zone > 15mm	Highly active
Inhibition zone >10mm	Moderatively active
Inhibition zone > 5mm	Slightly active
Inhibition zone ≤5 mm	Inactive

RESULTS AND DISCUSTION

Physical character: The physical characteristics and analytical data of the Schiff bases are shown in Table-1

ESST: 4-(3-ethoxy-2-hydroxybenzylideneamino)-N-(thiazol-2-yl) benzenesulfonamide

FT-IR (cm^{-1}): 1591(HC=N), 1366 (S=O asym), 1139 (S=O sym)[12]

^{1}H-NMR δ **(ppm):** 12.82 (OH), 8.96 (HC=N), 6.55-7.88 (Ar-H), 1.33 (OCH_3), 4.06 (CH_2) [13]

[13]C-NMR δ **(ppm):** 165.26 (HC=N), 150.79 (phenolic C) 14.49(OCH_3) 64.36 (CH_2)[14]

UV-Vis(cm^{-1}): 24330(n →π*) 35622(π →π*), 37053(π →π*)[15]

PCST: 4-(N-pyridinyl) methyleneamino)-N-(thiazol-2-yl) benzenesulfonamide

FT-IR (cm^{-1}): 1593(HC=N), 1323 (S=O asym), 1137(S=O sym).

^{1}H-NMR δ **(ppm):** 7.5(HC=N)

[13]C-NMR δ **(ppm):** 159.7(HC=N),

UV-Vis (cm^{-1}): 33557(π →π*)

HNSP: 4-((2-hydroxynaphthalen-1-yl) methyleneamino)-N-(pyridin-2-yl) benzenesulfonamide

FT-IR (cm^{-1}): 1618(HC=N), 1358 (S=O asym), 1133(S=O sym).

^{1}H-NMR δ **(ppm):** 10.81(OH), 8.9(HC=N), 6.53 – 8.47 (Ar-H)

[13]C-NMR δ **(ppm):** 156.53 (HC=N), 170.95 (phenolic C)

UV-Vis (cm^{-1}): 22732, 25425, 26128(n → π*), 30449(π → π*), 313302(π → π*)

ESSP: 4-(3-ethoxy-2-hydroxybenzylideneamino)-N-(pyridin-2-yl)benzenesulfonamide

FT-IR (cm^{-1}): 1627(HC=N), 1381 (S=O asym), 1142(S=O sym).

^{1}H-NMR δ (ppm): 12.72(OH), 8.95 (HC=N), 6.87-7.95(Ar-H), .34(OCH_3), 4.06 (CH_2)

[13]C-NMR δ (ppm): 153.20 (HC=N), 165.35 (phenolic C), 14.68 (OCH_3), 64.15(CH_2)

UV-Vis (cm^{-1}): 27377(n ⟶ π*), 32701(π ⟶ π*)

^{1}H NMR and UV spectrum of [ESST] are shown in Figure (1) and (2)

Antibacterial bioassay (in-vitro)

Antibacterial activity of Schiff bases were screened against bacterial species like gram positive bacteria *Staphylococcus aureus,* and gram negative bacteria *E.Coli , Klebsiella sp* and *Pseudomonas aeruginosa* by disc diffusion method [16] and the results obtained are formulated in Table-2 and Figure (3). The test was carried out in DMSO solution at a concentration of 100ppm using Muller Hinton agar media. Ciprofloxacin was used as the standard drug. ESSP is highly active against *Staphylococcus aureus* and ESST, PCST, and HNSP are moderately active against all bacterial species.

Antifungal bioassay (in-vitro)

Antifungal screening of Schiff bases were carried out against *Aspergillus niger* [17] and *Mucor* by disc diffusion method and the results obtained are formulated in Table-2 and Figure (1). The test was carried out in DMSO solution at a concentration of 100 ppm. Results were compared with standard drug Nystatin at the same concentration. ESST, PCST, HNSP and ESSP exhibit moderate antifungal activities.

Table 1: The physical characteristics and analytical data of the Schiff bases

S. No.	Schiff Base	Molecular Frormula	M.Wt	Colour	M.pt	Yield	Elemental analysis % Found (Calcd)			
							C	H	N	S
1	ESST	$C_{18}H_{17}N_3O_4S_2$	403	Dark red	175	93	53.00 (53.60)	4.02 (4.22)	11.84 (10.42)	15.00 (15.88)
2	PCST	$C_{15}H_{12}N_4O_2S_2$	344	Black	180	70	51.99 (52.33)	3.89 (3.49)	16.15 (16.28)	18.02 (18.61)
3	HNSP	$C_{22}H_{17}N_3O_3S$	403	Yellow	238	82	65.50 (65.51)	4.00 (4.22)	9.84 (10.42)	7.63 (7.94)
4	ESSP	$C_{20}H_{19}N_3O_4S$	397	Orange	185	83	60.01 (60.45)	4.12 (4.79)	11.48 (10.58)	9.02 (8.06)

Table 2: Antimicrobial Activity of Schiff bases

Name of the Organisms	Zone of Inhibition in mm				
	ESST	PCST	HNSP	ESSP	Ciprofloxacin/ Nystatin
Staphylococcus aureus	12	12	15	20	35
Klebsiella sp	15	14	14	16	30
E.Coli	12	13	15	14	38
Pseudomonas aeruginosa	14	17	14	18	35
Aspergillus niger	13	13	12	13	35
Mucor sp	12	13	13	14	32

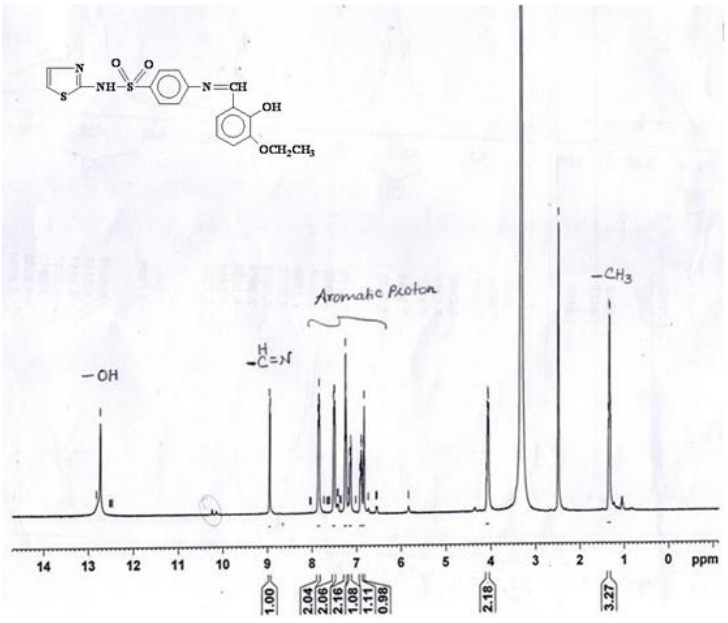


Fig. 1: ^{1}H NMR spectrum of [ESST]

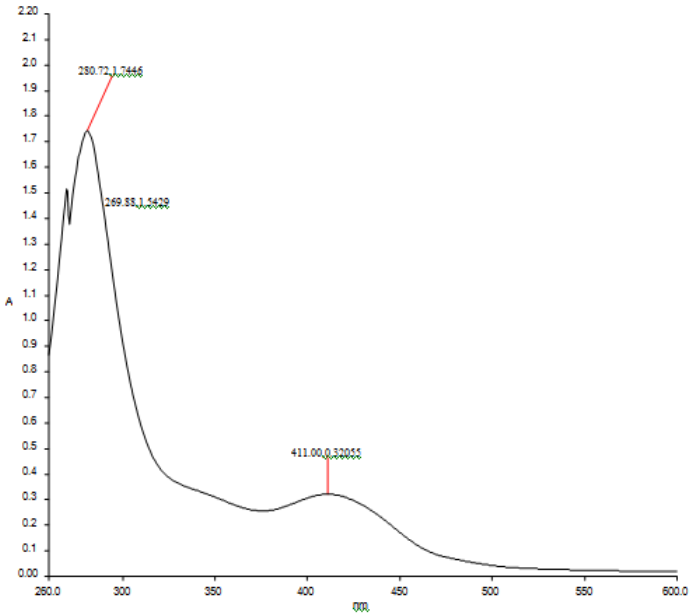


Fig. 2: UV Spectrum of [ESST]

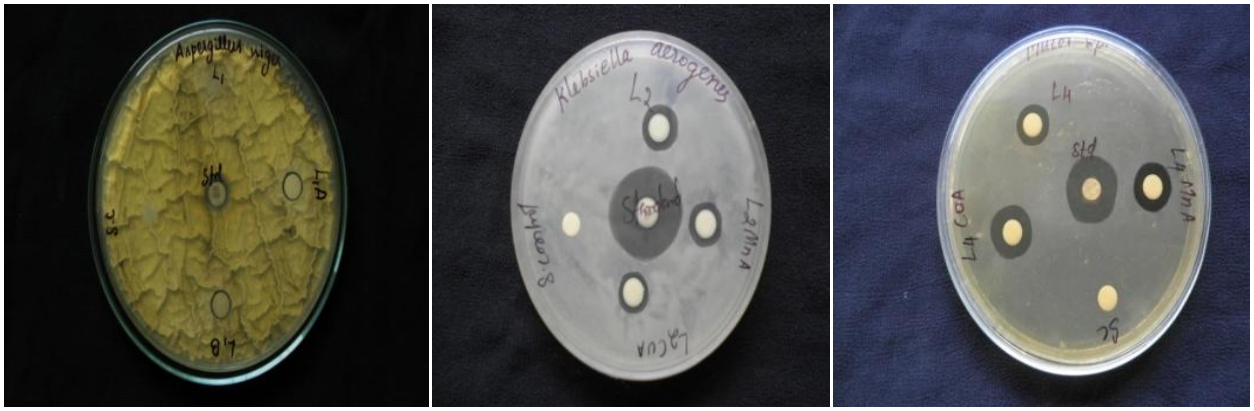


Fig. 3: HNSP against *Aspergillus niger* ESSP against *Klebsiella sp* and ESST against *Mucor.*

CONCLUSION

The synthesized Schiff bases are screened against bacterial and fungal species. ESSP is highly active against *Staphylococcus aureus.* ESST, PCST, and HNSP are moderately active against all bacterial and fungal species.

ACKNOWLEDGEMENTS

The authors are thankful to the University Grants Commission, Hyderabad, India, for the financial support. Laboratory facilities provided by the Management and all the Faculties, PG and Research Department of Chemistry, Seethalakshmi Ramaswami College, Tiruchirappalli are gratefully acknowledged.

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