Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 5, Suppl 2, 2013

Research Article

SYNTHESIS, CHARACTERISATION AND ANTIMICROBIAL ACTIVITY OF SOME NOVEL SCHIFF BASES DERIVED FROM SULPHA DRUGS

VALARMATHY GOVINDARAJ*, SUBBALAKSHMI RAMANATHAN

PG and Research Department of Chemistry, Seethalakshmi Ramaswami College Tiruchirappalli 620002, Tamil Nadu, India.
Email: valarchola@gmail.com; subhavijay2008@g.mail.com

Received: 08 Mar 2013, Revised and Accepted: 19 Apr 2013

ABSTRACT

Considerable amount of research has been carried out in the field of sulpha drugs. The present study is aimed to prepare new Schiff bases from 2-Sulfanilamidopyridine, 2-Sulphanilamidopyrimidine, 2-sulphanilamidothiazole and 4,6-Dimethyl-2-Sulfanilamidopyrimidine with 2-hydroxy-3methoxy benzaldehyde in ethanolic media.

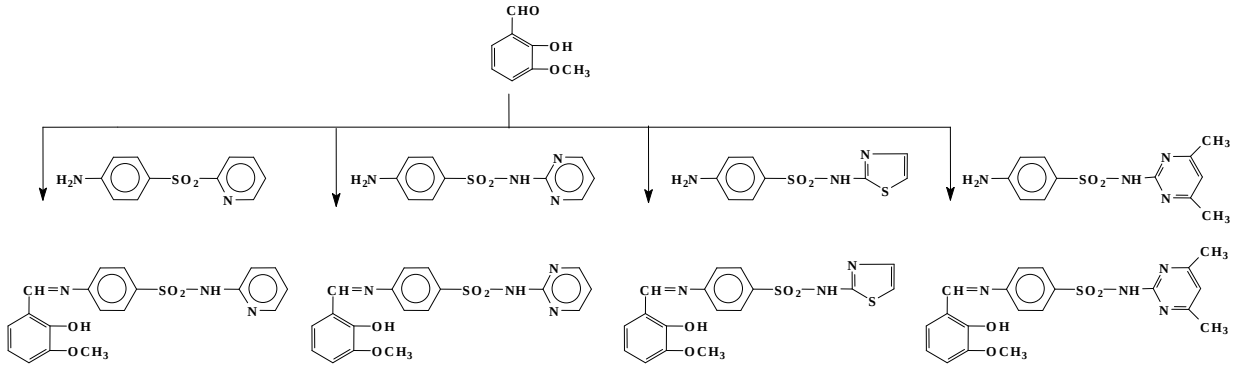
The synthesized Schiff base ligands were characterized by Elemental Analysis, IR, UV, ^{1}H-nmr and ^{13}C-nmr. Compounds were screened for antimicrobial activity against strains of gram positive, gram negative and fungal stains. All compounds exhibited good antibacterial and antifungal activity.

Keywords: 2-Sulfanilamidopyridine, 2-Sulphanilamidopyrimidine, 2-Sulphanilamidothiazole, 4,6-Dimethyl-2-Sulfanilamidopyrimidine, 2-hydroxy-3methoxy benzaldehyde, antimicrobial activity

INTRODUCTION

Sulpha drugs are chemotherapeutic agents whose molecular structures contain a 4-aminobenzene sulfonamide moiety. The antimicrobial activity of these drugs is believed from the structural resemblance between sulfanilamide group and p-amino benzoic acid where the sulpha drug mimics this metabolite and block folic acid synthesis in bacteria, thereby causing cell death. Many sulpha drugs like sulphadiazine, sulphamethoxazole, sulphamerazine possess-SO_2NH moiety as an important toxophoric function [1]. A number of Schiff's base molecules show biological activities including antibacterial, antifungal, antidiabetic, antitumour, antiproliferative, anticancer, anti-corrosion and anti-inflammatory activities [2-5]. Schiff bases are important class of compounds due to their flexibility, structural similarities with natural biological substances and also due to presence of imine (-N=CH-) which imparts in elucidating the mechanism of transformation and resamination reaction in biological system [6].

Our present study deals with condensation of 2-Sulfanilamidopyridine, 2-Sulphanilamidopyrimidine, 2-sulphanilamidothiazole and 4,6-Dimethyl-2-Sulfanilamidopyrimidine with 2-hydroxy-3methoxy benzaldehyde in ethanolic media(Figure 1). The synthesized Schiff base ligands were characterized by Elemental Analysis, IR, UV, ^{1}H-nmr and ^{13}C-nmr. Compounds were screened for antimicrobial activity against strains of gram positive, gram negative and fungal strains. All compounds showed good antibacterial and antifungal activity.



(L_1) **(L_2)** **(L_3)** **(L_4)**

MATERIALS AND METHODS

IR spectra of the complexes were recorded in KBr pellets with a Perkin Elmer RX1 FT-IR Spectrophotometer in the 4000-400cm^{-1} range. The electronic spectra were recorded in DMF on a Perkin Elmer Lambda 35 spectrophotometer in the 190-1100 nm range. The ^{1}H& ^{13}C NMR spectra were recorded on a Bruker 400MHz FT-PMR spectrometer (DMSO-d_6). Elemental analysis of the ligand and complexes were obtained using Elementar Vario EL CHN rapid analyser. Melting points were determined using melting point apparatus (Elico) and are uncorrected.

Synthesis of Schiff base ligand: (L_1)

E-4-(2-hydroxy-3-methoxybenzlideneamino)-N-(pyridine-2-yl)benzenesulfonamide

The Schiff base was prepared by the condensation of equimolar amounts of 2-sulphanilamidopyridine (0.01mole) and 2-hydroxy-3-methoxy benzaldehyde (0.01mole) in minimum quantity of ethanol. The resulting mixture was then refluxed on a water bath for 4 hours and magnetically stirred for 2 hours. A dark orange coloured solid mass separated out on cooling was filtered, washed and dried over

anhydrous $CaCl_2$ in a desiccator. The purity of the ligand was checked by melting point, TLC and spectral data. The ligand is insoluble in some common organic solvents viz.acetone, benzene and soluble in polar solvents viz.DMF, DMSO.

Yield= 80%, Melting point =180°C, Molecular Formula=$C_{19}H_{17}O_4N_3S$, Molecular Weight=384.15

Found(Calculated) (%): C=59.38 (59.48); H=4.01 (4.42); N=10.94 (10.93); S=8.30 (8.33)

IR (KBr max) (cm^{-1}): 1618 ν(C=N), 3426 ν(O-H), 1374 $\nu_{as}(SO_2)$, 1130 $\nu_s(SO_2)$

UV (bands,cm^{-1}): 31,347 and 39,524 (n → n* and π → π* transitions)

^{1}H-NMR (ppm): δ 8.94 (CH=N), δ 6.93-8.0 (aromatic protons), δ 12.6 (phenolic OH)

^{13}C-NMR (ppm): δ165.2(CH=N), δ115.9-128.8 (aromatic ring carbons), δ153.2 (C-OH)

Synthesis of Schiff base ligand: (L_2)

E-4-(2-hydroxy-3-methoxybenzlideneamino)-N-(pyrimidin-2-yl)benzenesulfonamide

The Schiff base was prepared by the condensation of equimolar amounts of 2-sulphanilamidopyrimidine (0.01mole) and 2-hydroxy-3-methoxy benzaldehyde (0.01mole) in minimum quantity of ethanol. The resulting mixture was then refluxed on a water bath for 5 hours and magnetically stirred for 2 hours. A pale orange coloured solid mass separated out on cooling was filtered, washed and dried over anhydrous $CaCl_2$ in a desiccator. The purity of the ligand was checked by melting point, TLC and spectral data. The ligand is insoluble in organic solvents viz.acetone, benzene and soluble in polar solvents viz.DMF, DMSO.

Yield= 75%, Melting point =203°C, Molecular Formula = $C_{18}H_{16}N_4O_4S$, Molecular Weight=384.28

Found (Calculated) (%): C=56.20 (56.25); H=4.10 (4.17); N=14.51 (14.58); S=8.30 (8.33)

IR (KBr max) (cm^{-1}): 1582 ν(C=N), 3423 ν(O-H), 1332 $\nu_{as}(SO_2)$, 1254 $\nu_s(SO_2)$

UV(bands,cm^{-1}): 33,333 and 28901 (n → n* and π → π* transitions)

^{1}H-NMR (ppm): δ 8.5 (CH=N), δ 6.8-8.1 (aromatic protons), δ 12.2 (phenolic OH)

^{13}C-NMR (ppm): δ162.2(CH=N), δ115.4-124.8 (aromatic ring carbons), δ150.4 (C-OH)

Synthesis of Schiff base ligand: (L_3)

E-4-(2-hydroxy-3-methoxybenzlideneamino)-N-(thiazol-2-yl)benzenesulfonamide

The Schiff base was prepared by the condensation of equimolar amounts of 2-sulphanilamidothiazole (0.01mole) and 2-hydroxy-3-methoxy benzaldehyde (0.01mole) in minimum quantity of ethanol. The resulting mixture was then was stirred in a magnetic stirrer and refluxed on a water bath for 5 hours. A dark orange coloured solid mass separated out on cooling was filtered, washed and dried over anhydrous $CaCl_2$ in a desiccator. The purity of the ligand was checked by melting point, TLC and spectral data. The ligand is insoluble in some common organic solvents viz.acetone, benzene and soluble in polar solvents viz.DMF, DMSO.

Yield = 75%, Melting point =160°C, Molecular Formula = $C_{17}H_{15}N_3O_4S_2$, Molecular Weight=389

Found (Calculated) (%): C=52.40 (52.44); H=3.80 (3.85); N=10.44 (10.70); S=15.35 (16.45)

IR (KBr max) (cm^{-1}): 1562 ν(C=N), 3433 ν(O-H), 1284 $\nu_{as}(SO_2)$, 1257 $\nu_s(SO_2)$

UV(bands,cm^{-1}): 39,521 and 42,105cm^{-1} (n → n* and π → π* transitions)

^{1}H-NMR (ppm): δ 8.9 (CH=N), δ 6.9-7.8 (aromatic protons), δ 12.7 (phenolic OH)

^{13}C-NMR (ppm): δ165.1(CH=N), δ116.0-124.4 (aromatic ring carbons), δ150.6 (C-OH)

Synthesis of Schiff base ligand: (L_4)

E-4-(2-hydroxy-3-methoxybenzlideneamino)-N-(4,6-dimethylpyrimidin-2-yl)benzenesulfonamide

The Schiff base was prepared by the condensation of equimolar amounts of 4,6-Dimethyl-2-Sulfanilamidopyrimidine (0.01mole) and 2-hydroxy-3-methoxy benzaldehyde (0.01mole) in minimum quantity of ethanol. The resulting mixture was then refluxed on a water bath for 6 hours. A dark orange coloured solid mass separated out on cooling in a refrigerator, filtered, washed and dried over anhydrous $CaCl_2$ in a desiccator. The purity of the ligand was checked by melting point, TLC and spectral data. The ligand is insoluble in some common organic solvents viz.acetone, benzene and soluble in polar solvents viz.DMF, DMSO.

Yield= 70%, Melting point =105°C, Molecular Formula = $C_{20}H_{20}N_4O_4S$, Molecular Weight=412

Found (Calculated) (%): C=58.06 (58.25); H=4.80 (4.85); N=12.58 (13.49); S=7.28 (7.76)

IR (KBr max)(cm^{-1}): 1600 ν(C=N), 3423 ν(O-H), 1462 $\nu_{as}(SO_2)$, 1438 $\nu_s(SO_2)$

UV(bands,cm^{-1}): 33579 cm^{-1} and 28901cm^{-1} indicate n → n* and π → π*

^{1}H-NMR (ppm): δ 8.9 (CH=N), δ 6.6-8.0 (aromatic protons), δ 12.7 (phenolic OH)

^{13}C-NMR (ppm): δ165.1(CH=N), δ115.8-127.8 (aromatic ring carbons), δ152.2 (C-OH)

Antimicrobial Activity

The synthesized compounds were subjected to antimicrobial activity. Antimicrobial activites were observed for all compounds using stains of gram positive bacteria such as (staphylococcus aureus, Klebsiella aerogenes), gram negative bacteria (pseudomonas aeruginosa, E.coli) and fungal strains (Aspergillus niger and Mucor).

The antimicrobial activities of the synthesized ligands (100 ppm) were studied by disc diffusion method [7,8]. Filter paper discs of diameter 6mm were used and the diameters of zones of inhibition formed around each disc after incubating for a period of 72 hours at 25-30^0 C were recorded. Results were compared with standard drug Ciprofloxacin for bacteria and Nystatin for fungi at the same concentration(Figure 2a,2b,2c). The zone of inhibition was measured in mm (Table 1) to estimate the potency of the test compounds [9,10].

Table 1: Antimicrobial activity of Schiff base ligands (zone of inhibition in mm)

Ligand	S.aureus	Klebsiellaaerogenes	E.Coli	P.aeruginosa	Mucor	A. niger
L_1	10	12	12	12	14	14
L_2	15	19	14	17	15	14
L_3	14	25	14	16	15	16
L_4	22	20	12	12	14	15

Standard= ciprofloxacin 5 g/ disc for bacteria; Nystatin= 100 units/disc for fungi.

Highly active = +++ (inhibition zone > 15mm); Moderatively active = ++ (inhibition zone> 10mm); slightly active = + (inhibition zone >5mm); Inactive = -- (inhibition zone <5mm)

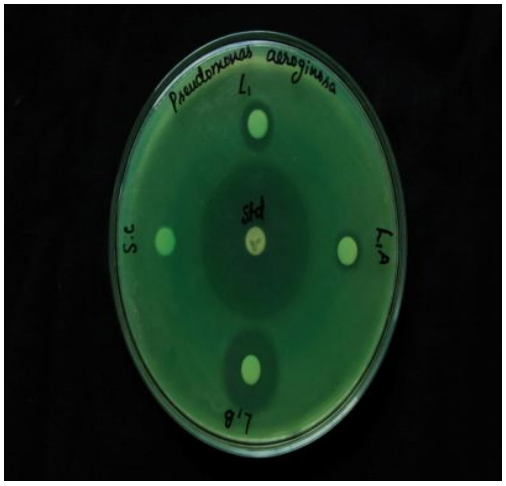


Fig. 2a: Activity of L_1 against Pseudomonas aeruginosa

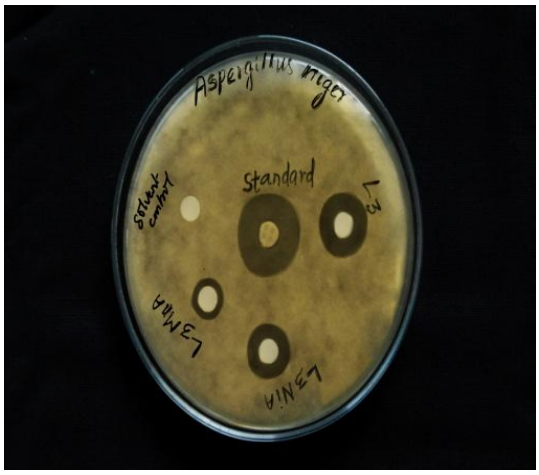


Fig. 2b: Activity of L_3 against Aspergillus niger

Fig. 2c: Activity of L_2 against Mucor

RESULTS AND DISCUSSION

The synthesized compounds were characterized through Elemental analysis,IR, 1H-NMR and^{13}C-NMR. All synthesized compounds in the present study showed expected characteristic absorption bands for azomethine, phenolic OH, ν_{as} (SO_2), ν_s(SO_2), ν (S-N) and ν(C-S). The investigation of antimicrobial screening data revealed that all the tested compounds shown good antimicrobial activity.

CONCLUSION

The synthesized compounds were subjected to antimicrobial activity. Concentrations of 100 pp. were screened for antimicrobial activity. Among the synthesized compounds L_3 and L_4 showed good antimicrobial activity in gram positive bacteria when compared to gram negative bacteria. The order of antimicrobial activity is **$L_3 > L_4 > L_2 > L_1$**

ACKNOWLEDGEMENTS

The authors express their gratitude to UGC- SERO, Hyderabad for financial assistance. The authors express their gratitude to The Secretary, Seethalakshmi Ramaswami College, Tiruchirappalli, Tamilnadu, India for providing laboratory facilities. The timely help and suggestions given by the faculty members of the PG and Research Department of Chemistry are greatly acknowledged.

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