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Research Article

SYNTHESIS, SPECTROSCOPIC, MOLECULAR MODELLING AND ANTIMICROBIAL STUDIES OF FIUORINE CONTAINING SCHIFF BASE

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ABSTRACT

A new bi-dentate ON type of Schiff base ligand obtained by condensation of salicylaldehyde (2-hydroxy-benzaldehyde) and 2-fluoroaniline (1-amino-2-fluorobenzene) have been synthesized. The structure of the ligand was characterized by elemental analysis, infra-red, LC-MS, electronic spectra, ^{1}H-NMR and powder XRD studies. By using Argus labs molecular modeling studies of the ligand was carried out. The Schiff base ligand was tested for antimicrobial activity against bacterial and fungal strains such as Gram positive bacteria (Staphylococcus aureus and Bacillus subtilis), Gram negative bacteria (Escherichia coli and Pseudomonas aeruginosa) and fungal strains such as Sclerotium rolfsii and Macrophamina phaseolina. The experimental data signifies that the ligand exhibited good biological activity.

Keywords: Schiff base, spectral characterization, powder XRD studies, molecular modelling, biological activity.

INTRODUCTION

Schiff bases are the class of ligands exhibiting interesting coordination modes towards metal ions[1-6] and they exhibit very important role in coordination chemistry as they form stable complexes[7]. Schiff bases are some of the most widely used organic compounds. They are used as dyes and pigments, catalysts, intermediates in organic synthesis and as polymer stabilizers. Schiff bases have number of applications such as, preparative use, identification, detection and determination of aldehydes and ketones, purification of carbonyl or amino compounds. Schiff bases appear to be important intermediates in a number of enzymatic reactions involving interaction of an enzyme with an amino or a carbonyl group of the substrate. Schiff bases have also been shown to exhibit a broad range of biological activities[8-10], including antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral and antiviral and antipyretic properties[11]. Imine or azomethine groups are present in various natural, natural-derived and non-natural compounds. The imine group present in such compounds has been shown to be critical to their biological activities[12-14]. The azomethine linkage in Schiff base (-C=N-) is responsible for the biological activity and coordinates with the metal ions to form complexes. Transition metal complexes with Schiff bases have expanded enormously and embraced wide and diversified subjects comprising vast areas of organometallic compounds and various aspects of bio coordination chemistry.

Fluorine containing compounds constitute a class of compounds with a unique pharmacological property[15-17]. Fluorinated Schiff bases are equally important because of the effects of fluorine substitution on inter and intra molecular forces which affect binding of ligands, and thus introduce receptor subtype selectively in the body[18, 19]. Fluorine – based aromatic compounds are of increasing interest as building blocks for the production of drugs and pharmaceuticals and as fine chemicals of industrial relevance including applications in the production of thermosetting plastics and lubricating materials. In addition, fluorine – based polymers and copolymers are of interest owing to their unusual optical and electrical properties and for that reason commonly used in organic light – emitting diodes, flat panel displays and in solar cells[20 - 22]. Fluorine- 2 derivatives introduced in 1960 were used in relief of the pain. Fluorine compounds have medical and biological importance and they have medicinal and pharmaceutical applications. Fluorine compounds are found to be effective against malaria and bacteria and some of the fluorine derivatives were considered as medical drugs against the diseases[23]. Numerous drugs containing fluorine include antipsychotics such as fluphenazine, HIV protease inhibitors, such as fipranavir, antibiotics such as Oflaxacin and trovafloxacin and anasthetics such as halothane[24, 25]. More and Rama reported fluorinated propanediones as anti-inflammatory[26] compounds. Fluroquinoline[27, 28] are commonly used family of broad – spectrum antibiotics. Due to these observations in view and continuation of our work a new fluoro Schiff base was synthesized and studied for antimicrobial activity. In the present work, we report the synthesis of Schiff base derived from condensation of salicylaldehyde(2-hydroxy-benzaldehyde) and 2-fluoroaniline(1-amino-2-fluorobenzene) and its characterization by elemental analysis, IR, Mass, ^{1}H-NMR and electronic spectroscopy. The ligand was screened for antimicrobial activity.

MATERIALS AND METHODS

All the chemicals and solvents used were of AR grade (Merck, Mumbai, India) except o-vanillin (Fluka, Switzerland) 2-fluroaniline (Sigma, USA). Melting points of all the compounds were determined in open glass capillaries and are uncorrected. Elemental analysis (C, H and N) was carried out on PERKIN ELMER, Series II, 2400 CHNS/O Analyzer. Infrared spectra were recorded on a Fourier transform infrared (FTIR), GX FT-IR

PERKIN ELMER, in the range 4000-400 cm-1 by making a KBr pellet of the compound. The electronic spectra of samples were recorded on UV Lambda 19 PERKIN ELMER spectrophotometer. The mass spectra are obtained using API QSTAR Pulsar LC-MS quadruple and TOF based single mass spectrometer. The antibacterial activities of both ligand and its metal complexes were studied by disc diffusion method against Escherichia coli, (gram negative), Staphylococcus aureus, (gram positive) bacteria.

Synthesis of Schiff base

The Schiff base (HL") was prepared (Figure 1) by refluxing a mixture of equimolar quantities of salicylaldehyde (1.09g,0.01M) and 2-fluoroaniline (1.52g,0.01M) in hot ethanol[29]. After 6-8h of refluxing, the reaction mixture was kept at room temperature overnight and then a solid product was formed which was filtered, washed with ethanol and ether. The product was recrystallization from hot ethanol. The elemental analysis (S: 2) was carried out for the newly synthesized ligand and analytical data was tabulated in Table-1.

Table 1: Physical and Analytical data of Schiff base

Ligand (molecular Formula)	$C_{14}H_{12}O_2NF$		
Molecular weight	215		
Melting point	147˚C		
Colour	Pale yellow		
Yield	80%		
Elemental analysis	C%	calculated	72.89
		observed	72.75
	H%	calculated	4.65
		observed	4.61
	N%	calculated	6.61
		observed	6.58

Table 2: Molecular modeling studies

Energy	Schiff base (kcal/mol)	HOMO (kcal/mol)	LUMO (kcal/mol)
Self-consistent energy	-59703.2049	-59701.2536	-59701.2436
Heat of formation	-13.8833	-11.9320	-11.9321

Table 3: Antibacterial activity of Schiff base

Bacteria Species	Anti-bacterial sensitivity results (Zone of inhibition in cm)	Minimum inhibitory concentration level of the ligand (Zone of inhibition in cm)				
		Conc 50µg	Conc 100µg	Conc 200µg	Conc 250µg	Streptomycin
Bacillus subtilis	0.3	0	0	0.1	0.2	1
Staphylococcus aureus	0.4	0	0	0	0.1	1
Escherichia coli	0.2	0	0	0	0.1	1
Pseudomonas aeruginosa	0	0	0	0	0	1

Table 4: Antifungal activity of Schiff base

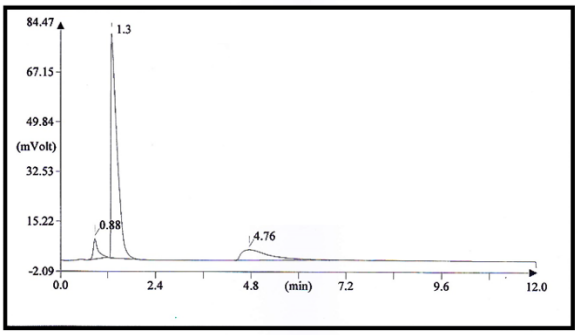
Fungal species	Anti-fungal sensitivity results	Minimum inhibitory concentration level of the ligand (zone of Inhibition in cm)			
		Conc 50 µg	Conc 100 µg	Conc 200 µg	Conc 250 µg
Sclerotiumr olfsii	1.6	0	0	0.5	0.5
Macrophamina phaseolina	0.5	1.2	1.3	1.5	1.7,

Table 4: Powder XRD data of the ligand

Pos. [°2Th.]	Height [cts]	FWHM [°2Th.]	d-spacing [Å]	Rel. Int. [%]
11.5503	120.62	0.2755	7.66153	24.50
14.6371	492.25	0.2755	6.05199	100.00
15.3325	66.31	0.2755	5.77904	13.47
19.8314	183.25	0.2755	4.47701	37.23
23.0559	33.44	0.2362	3.85766	6.79
23.6951	27.72	0.2362	3.75503	5.63
26.7752	75.10	0.2755	3.32965	15.26
27.7765	28.68	0.3542	3.21185	5.83
29.0872	31.05	0.3149	3.07003	6.31
30.3079	30.72	0.2362	2.94911	6.24
31.8205	22.35	0.2362	2.81230	4.54
33.6246	16.35	0.2362	2.66541	3.32
38.9076	13.97	0.2362	2.31480	2.84
40.7351	10.15	0.2362	2.21508	2.06
41.5639	7.13	0.2362	2.17280	1.45
42.4219	10.65	0.2362	2.13082	2.16
44.3179	9.17	0.3149	2.04396	1.86
48.0692	12.40	0.2755	1.89285	2.52
48.7791	8.18	0.4800	1.86541	1.66

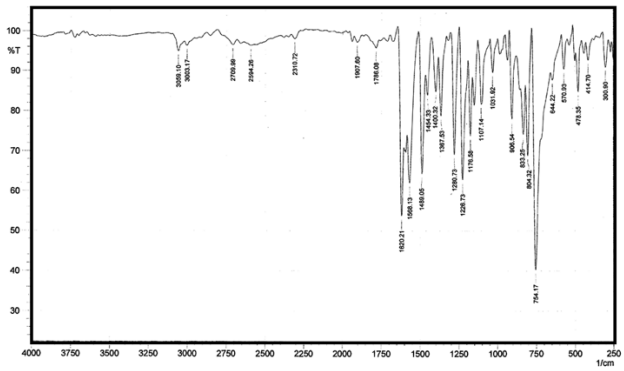
Spectra's of the Schiff base

S 1: CHN spectra of the ligand

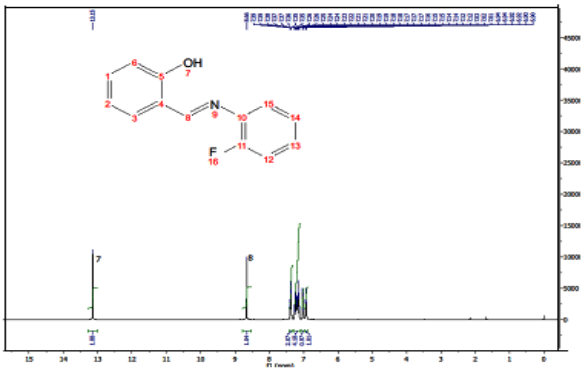


Element Name	Element %	Ret. Time
Nitrogen	5. 16	0. 88
Carbon	62. 47	1. 30
Hydrogen	4. 92	4. 76

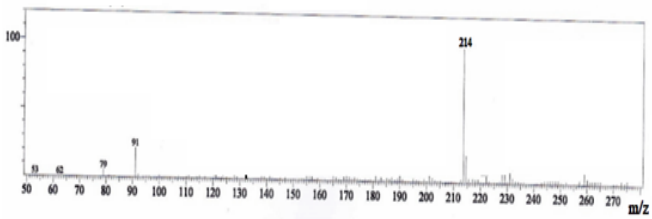
S 2: IR spectra of the ligand



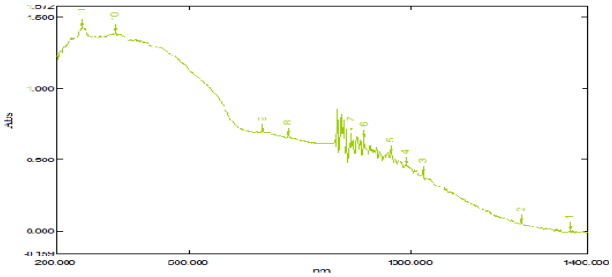
S 3: ^{1}H-NMR spectra of the ligand



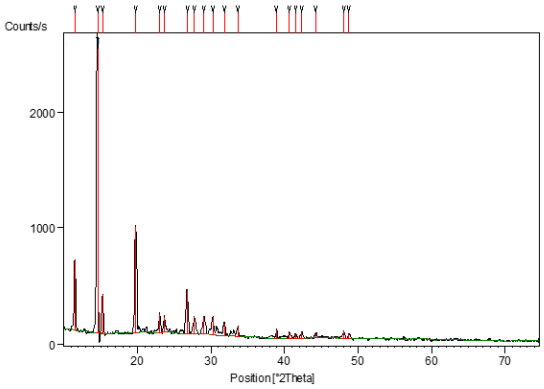
S 4: LCMS spectra of the ligand



S 5: Electronic spectra of the ligand



S 6: XRD spectrum of the ligand



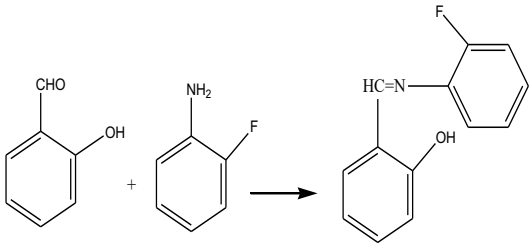
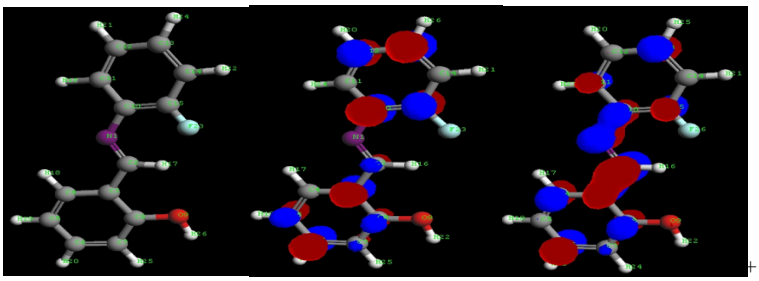


Figure 1: Formation of Schiff base ligand



Ligand **HOMO** **LUMO**

Figure 2: Molecular modeling structures of the ligand, HOMO, LUMO

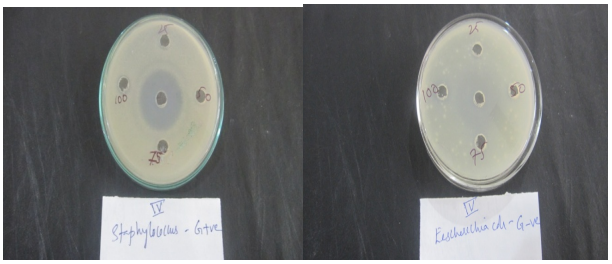


Figure 3: Zone of inhibition against Staphylococcus and E. coli

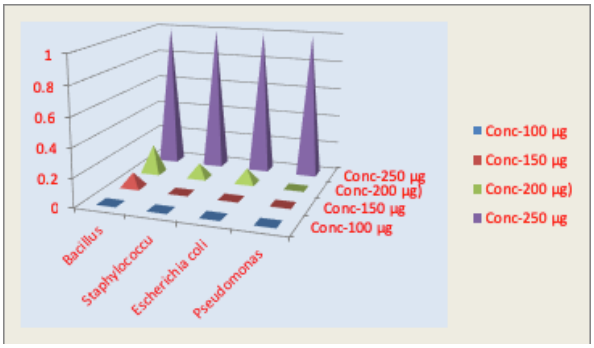


Figure 4: Comparative antibacterial activities of the Ligand with standard

RESULTS AND DISCUSSION

Physical Properties and Elemental Analysis

The physical properties and results obtained from C.H.N. analysis (S: 1) of the synthesized ligand was described in Table 1. The analytical data was almost agreeable with calculated values with some deviations attributed to incomplete combustion or technical errors. The molecular formula of the ligand was suggested according to these data together with those obtained from spectral analyses. The proposed structures of Schiff base in Figure 1.

FT-IR studies

IR spectrum of the Schiff base ligand (S: 2) showed a sharp band at 1570cm^{-1} which is assigned to υ(C=N) mode of the azomethine group[30]. A broad band at 1226cm^{-1} due to υ(C-O) phenolic group. The band at 3061cm^{-1}(s) is assigned to phenolic υ(OH) and a strong band appearing at 1151cm^{-1} has been assigned to –OCH_3[31].

NMR and Mass studies

The NMR spectra of the ligand (S: 3) showed broad singlet at 13.15 ppm due to phenolic hydroxyl proton in the aldehyde moiety of the ligands[32]. On the other hand, the azomethine proton, HC=N, appeared as a strong singlet at 8.66 ppm, The purity of the ligands was indicated by the disappearance of the aldehyde and the amino protons; CHO (δ = 9 - 10 ppm) and NH_2 (δ = 3 – 4 ppm); in the ligands spectra and lastly all the aromatic protons were accounted for and absorbed at 6.50 - 7.50 ppm. The mass spectra of the ligand (S: 4) was carried out in a polar aprotic solvent, acetonitrile as ESI-MS. The spectra showed the peak attributed at m/z of 214(M-1) and this peak was in line with the proposed structure of the ligand.

UV- Visible studies

The electronic transition study of the ligand (S: 5) was carried out in methanol. Three distinct bands were observed at 280 - 275nm; 350 - 334nm and 450 - 421nm. The first two bands correspond to the π → π* and n → π *transitions of the azomethine chromophore respectively.

Molecular modelling studies

The possible structure of the Schiff base was evaluated using molecular calculation with Argus Lab software[33]. The structure was built using quantum mechanics, molecular orbital calculations were performed with AM1 (Austin Model 1) approximation, for the synthesized ligand. The electron density surfaces of highest occupied molecular orbitals (HOMO) and lowest unoccupied molecular orbitals (LUMO), are also generated for the ligand (Figure 2). The Self consistent field (SCF) energy value and heat of formation ΔH_f for the optimized structure are reported for the ligand, HOMO and LUMO (Table 2)

Powder XRD studies

X-ray powder diffraction analysis: Growth of single crystals of azomethine compounds from various solvents including DMF, ethyl alcohol, chloroform etc. failed and so they were characterized by powder XRD. X- ray powder diffraction analysis of the ligand was carried out to determine the type of crystal system, lattice parameters and cell volume[34, 35]. As shown in the S: 6, the XRD patterns indicate a crystalline nature for the ligand. Indexing of the diffraction patterns was performed using High score plus software. It is found that the ligand have monoclinic structure. Moreover, using the diffraction data, the mean crystallite size of the ligand D, were determined according to the Scherrer equation (D = 0.9□/□cos□□, where □□is the X-ray wave length (1.5406A^0), □□is Bragg diffraction angle, and □ is the full width at half maximum of the diffraction peak. The XRD data of the Schiff base is given in the Table 3.

Antimicrobial studies

In-vitro biological activities of Schiff base ligand in DMSO medium were screened against few bacterial and fungal strains using standard agar as the medium by a well diffusion method. Fresh bacterial culture having 5x10^{-5} colonies was mixed with nutrient agar medium and poured in to plates. Wells were made in the cooled agar plates (1cm). The compounds 10mg were dissolved in 2mL DMSO and 100µL was loaded in the well. The activity or sensitivity was observed after 24 - 48h incubation at 37^{o}C. In MIC range of concentrations were tested. The zone of inhibition was recorded in centimeter's [36, 37] (Figure 3). The obtained zone of inhibition (in cm) of the Schiff base was compared with commercially available controls (Figure 4)[38]. The antimicrobial data of ligand is given in Table 3 & 4. Based on the data it is very clear that the ligand exhibited good antimicrobial activity.

CONCLUSION

A simple and efficient method has been developed for the synthesis of Schiff base which is obtained by the condensation of salicylaldehyde and 2-fluoroaniline respectively. This ligand is characterized by elemental analysis, IR, H^1-NMR, mass spectra and electronic spectral studies. The in vitro antimicrobial results showed that the ligand showed good biological activity against Gram +ve, Gram –ve and fungal strains.

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