DOI:10.7598/cst2018.1436
ISSN:2278-3458

Chemical Science Transactions
2018, **7(1),** 47-54

RESEARCH ARTICLE

Synthesis, Characterization and Antimicrobial Screening of Fe(II)-Glycine Schiff Base

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Received 27 July 2017 / Accepted 14 August 2017

Abstract: Fe(II) complex of (*E*)-2-((2-hydroxynaphthalene-1-yl)methyleneamino)acetic acid was synthesized by reacting $Fe(OAc)_2$with Schiff base ligand in stoichiometric 1:1 ratio and was characterized by elemental analysis, IR, Mass and conductance measurement. Furthermore, this complex was screened for antimicrobial activity against *E. coli, S. aureus, A. niger* and *C. albicans.*

Keywords: 2-Hydroxy-1-naphthaldehyde, Glycine, Schiff Base, Fe(II) complex, Antimicrobial activity

Introduction

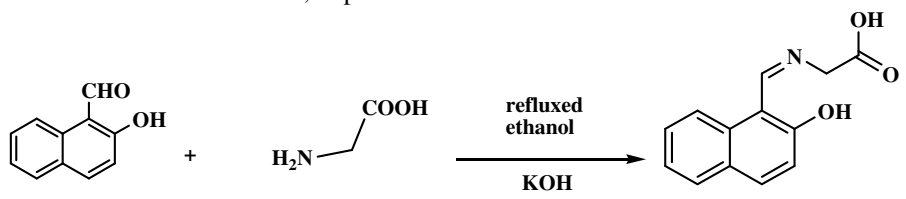
In 1864, German chemist Hugo Schiff developed a new class of organic compounds[1]. The active and well-designed Schiff base ligands are considered as ''Privileged Ligands'' by Cozzi[2]. Schiff base ligands were synthesized by condensation of α-amino acid with aldehyde to form azomethine (–RC=N–) linkage. The metal complexes with Schiff bases play important role in biology[3,4], analytical chemistry[5,6] and industry[7,8]. The complexes of amino acid Schiff bases prepared from *o*-hydroxy aryl aldehydes were used as radiotracers in nuclear medicine, antibacterial and anticancer agents[4,9-11]. Bioinorganic chemistry is important and has great impact in coordination chemistry[12]. Haemoglobin is Fe(II) containing complex acts as a oxygen carrier. Ca(II) complexes is basic constituents of bone, Zn^{2+} ions found in three-dimensional structural framework of proteins are good examples of metal complexes in biological systems[13]. Metal ions act as redox transfer and hence metal complexes showed medicinal applications like organic compounds which could be used in drug discovery efforts[14]. They were used as therapeutic agents since 3500 BC[15]. Over the past

several decades, Sb(III) complexes were used for treatment of leishmaniasis. Pt(II) complexes are the important constituent of anti-tumour drug cisplatin[16]. Ag(I) complexes commonly used as anti-microbial agents, Bi(III) complexes for anti-ulcer treatments, Au(I) complexes as anti-arthritic agents, Gd(III), Mn(II) and Fe(III) complexes as magnetic resonance imaging (MRI) contrast agents, Sc(I) and Tc(III) as radiopharmaceutical agents[17]. Hodnett and Willie[18] prepared Schiff base complexes of cobalt such as trans-dichlorotetrapyridinocobalt(II) and fluropentamine cobalt(III) nitrate which showed antitumor activity. Complexes prepared from Schiff bases and metals such as cobalt, nickel, copper *etc*. play role in the metabolic processes in body. Musavi *et al.*[19] synthesized various Schiff base of *N, N'*- bis(4-fluorobenzaldehydene) with 1,2-diaminoethane. Later on they have synthesized complexes of this Schiff bases with various metal salts such as MLX_2 (where, M= Zn(II), Cd(II), Hg(II) and X=chloride, bromide, iodide, thiocyanate and azide *etc*.). Mohammed and co-workers[20] synthesized Schiff bases by condensation of acrolein with 2-aminophenol, 2-aminophenol and phenylenediammine with cinnamaldehyde and used as inhibitors for corrosion of carbon steel in acidic media 0.5 N HCl. Aliyu *et al*.[21] has prepared Schiff base metal complexes showed higher antibacterial activity than ligand. Asadi *et al.*[22] derived Schiff base from benzoyl chloride and potassium thiocynate in acetone. Then benzoyl isothiocyanate was condensed with diethylamine to form Schiff base which on condensation with metallic salts form metal complexes. These complexes conductivity and found maximum value 1.23×10^{-4} ohm^{-1} cm^{-1} after doping I_2. Vergheese and Nair[23] synthesized Schiff base of 2-hydroxybenzilidene and 3-aminophenol and studied antimicrobial activity of synthesized complexes. Sharif *et al*.[24] prepared many Schiff bases by condensation reaction of certain aromatic amines with aromatic aldehyde derivatives and determined the fluorescence properties of these Schiff bases in acidic and basic media.

In this paper we have focused on the synthesis and characterization of Schiff base complexes derived from (*E*)-2-((2-hydroxynapthalene-1-yl)methyleneamino)acetic acid and their antimicrobial activities. Bidentate Schiff bases obtained from glycine and 2-hydroxy-1-naphthaldehyde has been used to obtain Fe(II) and Pd(II) complexes. The metal complexes obtained were well characterized by via IR, Mass, elemental analysis and conductivity measurement.

Experimental

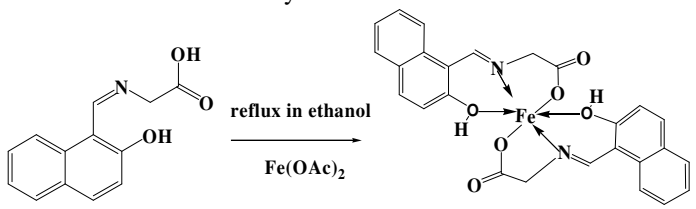
2-Hydroxy-1- napthaldehyde (1.72 g, 0.01 mol) was dissolved in 50 mL ethanol and stirred at room temperature for 5 minutes. Then it was added to stirring solution of glycine (0.0751 g, 0.01 mol, 25 mL) containing (0.56 g, 0.01 mol) KOH. The reaction mixture was refluxed for about 3 h (Scheme 1). A yellow grain mass separated, filtered, washed with anhydrous ethanol. It was recrystallized with methanol and then dried in vacuum over fused $CaCl_2$.The structure of ligand was determined on the basis of spectral and analytical data and compared to literature values[29]. Yield 88%; m.p.240 ^oC.



Scheme 1. Synthesis of 2-hydroxy-1-napthaldehyde based Schiff base

Synthesis of complex $C_{26}H_{20}Fe(NO_3)_2$

Iron acetate (0.01 mol) in anhydrous ethanol (15 mL) was added in stirring solution of solution of Schiff base (0.01 mol) in 15 mL anhydrous ethanol. The resulting solution was stirred overnight at 70 ^oC (Scheme 2). The dark brown precipitate obtained was filtered, washed with ethanol and then with diethyl ether and dried in air



Scheme 2. Complex Formation Reaction of Schiff's base with transition metal

Spectral data for complex ($C_{26}H_{20}Fe(NO_3)_2$)

IR(KBr) ν cm^{-1}: 1610(C=N), 1367(COO^-), 561(M-N), 488(M-O) MS(m/z): 512 *Anal.* Calcd. for C-60.96, H-3.94, N- 5.47, Fe-10.90, found C- 63.60, N-4.30, Fe- 10.77

Materials and Methods

All reagents and solvents used were of analytical grade and were used without further purification. 2-Hydroxy-1-naphthaldehyde, glycine, iron acetate was purchased from Sigma Aldrich, Merck and Spectrochem chemicals. Melting points were determined on a Gallenkamp melting point apparatus (Table 1). The ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance II 500 MHz Spectrometer. Chemical shifts were reported in ppm relative to tetramethylsilane (TMS), and multiplicities are given as s(singlet), bs(broad singlet), d(doublet), t(triplet), q(quartet), or m(multiplet). Infrared spectra were recorded as KBr pellets on a Shimadzu FTIR-408 spectrophotometer. EDS analysis was performed at CIF, SPPU, Pune-7. Mass spectra were recorded on a Shimadzu LC-MS:EI QP 2010A mass spectrometer with an ionization potential of 70 eV. Molar conductivity of complexes was recorded using $1x10^{-3}$ M solutions in DMSO on Toshniwal TSM 15 conductivity meter. Reactions were monitored by thin layer chromatography (TLC), carried out on 0.2 mm silica gel 60 F_{254} Merck plates using UV light (254 and 366 nm) for detection.

Results and Discussion

Molar conductance measurements

The value of molar conductance of complex $C_{26}H_{20}Fe(NO_3)_2$ when dissolved in DMSO was observed 15.65 $\Omega^{-1}cm^2mol^{-1}$ respectively indicated the non-electrolytic nature of this complex.

Table 1. Reaction time, % yield, color and melting point of ligand and complex

Mol. formula	Ligand/Complex	Reaction time, h	Yield, %	Colour	M.P. ^oC
$C_{13}H_{11}NO_3$	Ligand	4	88	Yellow	240
$C_{26}H_{20}Fe(NO_3)_2$	Complex	12	80	Brown	242

IR Spectra

IR Spectra of ligand (Figure 1) showed band at 1641 cm^{-1} which is due to (νC=N) confirming the formation of Schiff base. The band of (νC=N) at 1641 cm^{-1} in ligand was shifted to 1610 cm^{-1} in complex which indicate the coordination of azomethine group through its nitrogen atom[25].

The band at 1604 and 1394 cm^{-1} in spectrum showed the presence of COO^-, these bands were shifted to 1427, 1367 cm^{-1} in Fe(II) complex indicated metal-oxygen coordination. In complex the difference [Δν(COO)] between $\nu_{assy}(COO)$ and $\nu_{sy}(COO)$ > 200 cm^{-1} indicated the unidentate coordination of COO^- with Fe(II) metal[26]. The band at 561 cm^{-1} indicated the coordination of azomethine through nitrogen with metal ion, while band at 488 cm^{-1} was due to (M-O) stretching in the complex[27]. The IR band at 3414-3340 cm^{-1} in complex corresponded to phenolic –OH stretching. This stretching frequency shift indicates the coordinate bonding of –OH oxygen to the metal[28]. Thus the ligand coordinated to free metal ion through its azomethine(–RC=N–) nitrogen and oxygen of (COO^-) carboxylate and O of the phenolic –OH indicated tridentate nature of ligand.

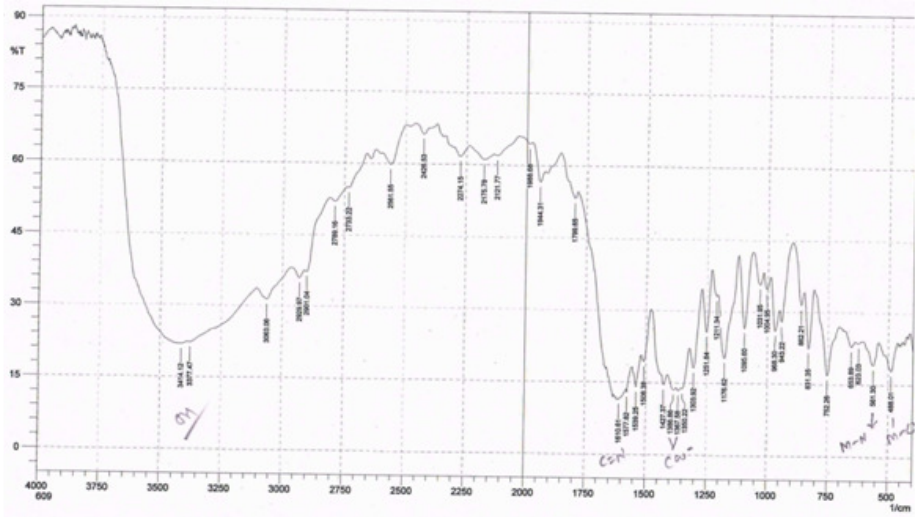


Figure 1. IR Spectra of complex, $C_{26}H_{20}Fe(NO_3)_2$

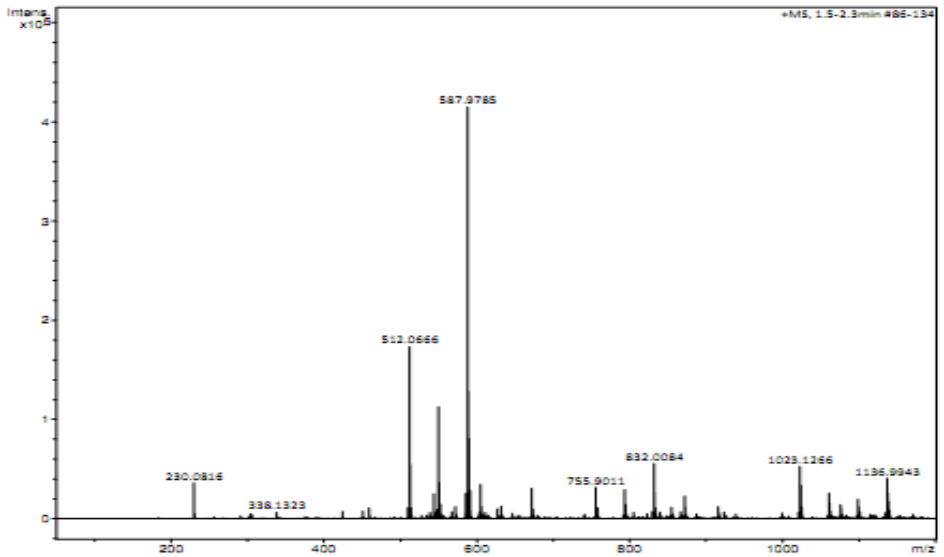


Figure 2. Mass spectrum of complex, $C_{26}H_{20}Fe(NO_3)_2$

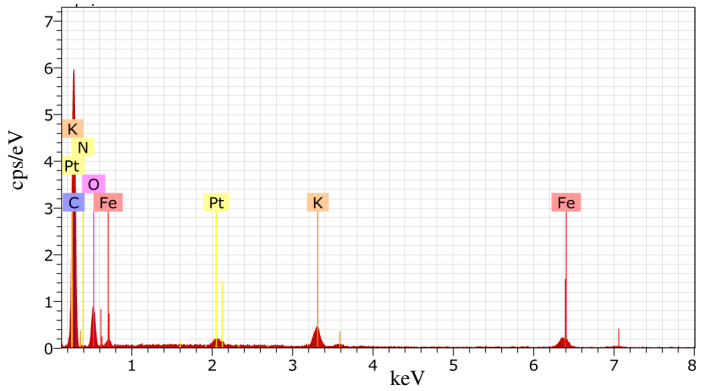


Figure 3. EDS of complex, $C_{26}H_{20}Fe(NO_3)_2$

Mass spectrum of complex

Mass spectra of complex (Figure 2) shows M+ peak at 512.06 corresponded to molecular formula $C_{26}H_{20}Fe(NO_3)_2$.

EDS of complex

EDS of complex shows 10.77% of Fe(II), which is in good agreement with elemental analysis (Figure 3).

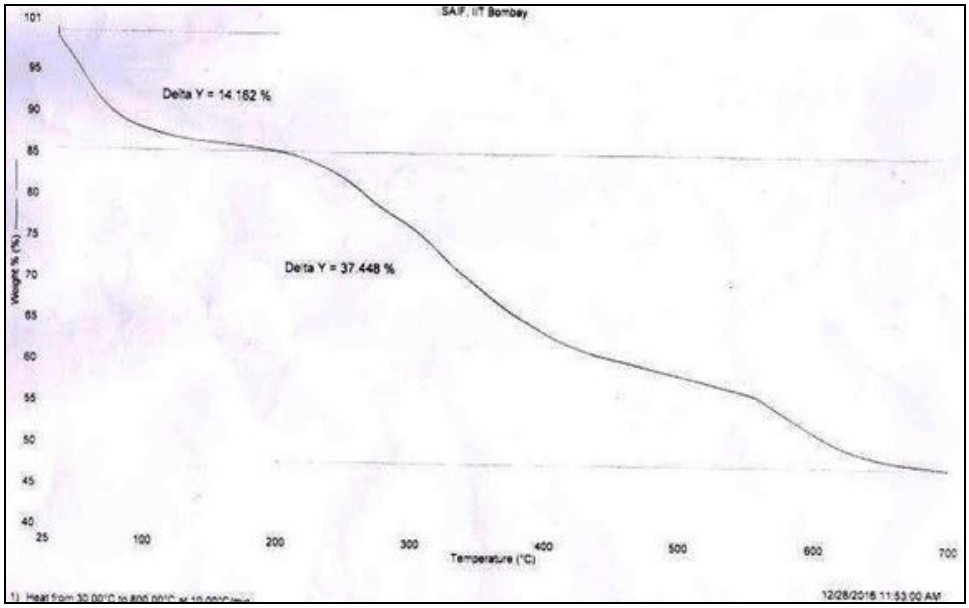


Figure 4. TGA of complex $C_{26}H_{20}Fe(NO_3)_2$

TGA

The TGA curve of synthesized Fe complex (Figure 4) reveals weight loss occurring in two stages. The first small weight loss is due to absorbed moisture which is found at 100 °C and the second exothermic loss of 37.448% due to decomposition of Fe complex and crystallization of FeO particles. The theoretical weight loss calculated by conversion of

complex precursor to FeO is in good agreement with the measured value. The process accounts for one third of total weight loss in the whole decomposition process from 100 to 600 °C according to TGA results, with the major loss occurring between 200 to 500 °C. The TGA result shows that complex is highly stable up to 225 °C.

Antimicrobial assay

The antimicrobial assay of Fe metal complex was done using agar well plate method (Figure 5). The antibacterial and antifungal assays were performed in Muller-Hinton broth and Crazek Dox broth[30]. The standard strains used was procured from Microbial Culture Collection, Pune, India. Antimicrobial evaluation was performed using the bacteria reseeded in Muller-Hinton broth for 24 h at 37 ^{o}C and fungi reseeded in Crazek Dox broth[30] for 48 h at 25 ^{o}C. The antibacterial activity of tested samples were studied (Table 2) in triplicate against gram positive bacteria *Staphylococcus aureus* (ATCC 29737) and gram negative bacteria *Escherichia coli* (ATCC 25922). The same samples were tested for antifungal activity in triplicate against *Candida albicans* (MTCC 277) and *Aspergillus niger* (MCIM 545). The compounds were dissolved in DMSO at desired concentrations of 40, 20, 10 µg/mL. DMSO was loaded as negative control. Gentamicin (10 µg/mL) and Fluconazole (20 µg/mL) were used as standards for evaluating the antibacterial and antifungal activity. The zone of inhibition (mm) was determined from the diameter of the zone of inhibition using caliper as per National Committee for Chemical Laboratory Standards (NCCLS, M7-A5, January 2000). Both metal complexes shows good antibacterial as well as good antifungal activity.

The complex $C_{26}H_{20}Fe(NO_3)_2$ showed excellent antibacterial activity against *Escherichia coli* (ATCC25922) with MIC 20 µg/mL when compared with standard antibacterial drug gentamicin (10 µg/mL). Similarly it also showed excellent anifungal activities against *Aspergillus niger* (MCIM 545), *Candida albicans* (MTCC 277) with MIC 10 µg/mL when compared with standard antifungal drug fluconazole (20 µg/mL) (Table 3).

Table 2. Antimicrobial screening of complex $C_{26}H_{20}Fe(NO_3)_2$

Complex	Inhibition Zone Diameter, mm			
	E. coli (ATCC25922)	*S. aureus* (ATCC 29737)	*A.niger* (MCIM 545)	*C.albicans* (MTCC 277)
$C_{26}H_{20}Fe(NO_3)_2$	15±0.3	22±0.5	21±0.8	19±0.8
DMSO	11±0.7	12±0.9	12±0.6	13±0.3
Gentamicin	22±0.4	23±0.7	-	-
Fluconazole	-	-	23±0.8	24±0.5

Gentamicin (10 µg/ mL) and fluconazole (20 µg/ mL) Inhibition Zone= 9-14 mm: slight activity, 15-19 mm: moderate activity, 20 -24 mm : high activity, >25 mm: excellent activity.

Table 3. Antimicrobial screening of complex $C_{26}H_{20}Fe(NO_3)_2$

Complex	Minimum Inhibition Concentration (MIC), µg/mL			
	E.coli (ATCC25922)	*S.aureus* (ATCC 29737)	*A.Niger* (MCIM 545)	*C.albicans* (MTCC 277)
$C_{26}H_{20}Fe(NO_3)_2$	10	10	10	10
Gentamicin	10	10	-	-
Fluconazole	-	-	20	20

Gentamicin (10 µg/mL) and Fluconazole (20 µg/mL), (MIC in µg/mL)=10 µg/mL: excellent activity, 20 µg/mL: moderate activity, 40 µg /mL: slight activity

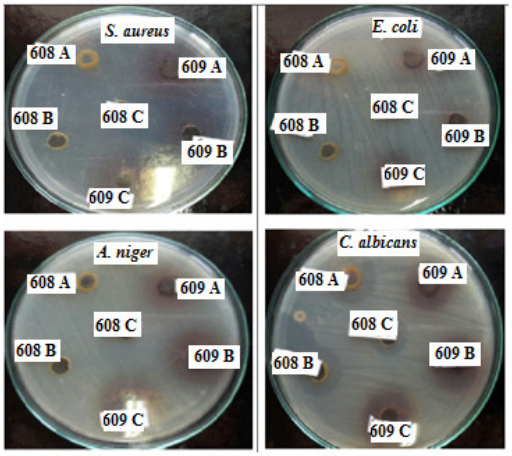


Figure 5. Antimicrobial screening of complex (609): $C_{26}H_{20}Fe(NO_3)_2$

Conclusion

The synthesis and characterization of Fe(II) Complex were studied herein in the light of elemental analysis, ^{1}H NMR, IR, electronic spectra and mass spectra. It was concluded that the Schiff base coordinating through the azomethine nitrogen and carboxylate oxygen. The synthesized complex has good antimicrobial activities.

Acknowledgement

The authors are thankful to UGC,WRO, Pune for financial support to this research project. and Savitribai Phule Pune University, Pune, SAIF, IIT Bombay, M.V.P. Samaj, Principal, K.R.T. Arts, B.H. Commerce and A. M. Science College, Shivajinagar, Gangapur Road, Nashik- 422 002, (MS), India for facilities.

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