Special Conference Edition, November, 2017
http://dx.doi.org/10.4314/bajopas.v10i1.90S
Bayero Journal of Pure and Applied Sciences, 10(1): 468 - 476
ISSN 2006 – 6996

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL STUDIES OF Ru(II) COMPLEXES WITH SCHIFF BASE CO-LIGAND DERIVED FROM 5,6-DIAMINO-1,10-PHENANTHROLINE AND BENZENE-1,4-DICARBALDEHYDE

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ABSTRACT
Two novel biologically active Ru(II) complexes with coordinating Schiff base were synthesized and characterized by elemental analysis, FT-IR, UV-visible and mass spectral analyses. On the basis of analytical and spectral data, octahedral geometry was assigned to both complexes and structural formulae have been tentatively proposed. The complexes were found to be coloured and readily dissolved in DMSO, DMF, MeOH, EtOH andCH_3CN. Molar conductivity measurement in dimethyl sulphoxide (DMSO) solutions shows the electrolytic nature of both complexes in 1:2 ratios suggesting the presence of chloride ions in the outer sphere of the complexes. The Schiff base and metal complexes were screened for their antibacterial and antifungal activities.
Keywords: Metal Complexes, Schiff base, Outer sphere, antibacterial and antifungal activities

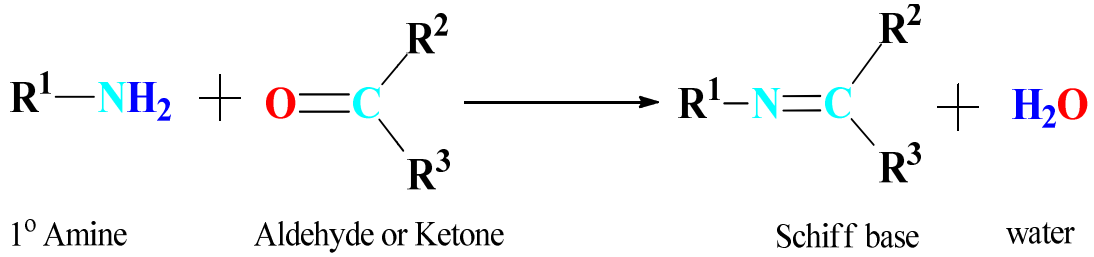
INTRODUCTION

Schiff bases

Schiff base compounds are condensation products of primary amines and carbonyl compounds (aldehydes and ketones) and were discovered by a German chemist (Nobel Prize winner) Hugo Schiff in 1864 (Ashraf *et al*,. 2011, Brodowska *et al*,. 2014).

Schiff base possess functional group containing carbon-nitrogen double bond with the nitrogen atom linked to an aryl or alkyl group, with the exception of hydrogen (Kostova and Sasa, 2013).

Schiff bases in a broad sense are compounds containing azomethine group (**>C=N**) and have the general structure $R^1R^2C{=}NR^3$, where R^1, R^2 and R^3 are aryl, alkyl, cycloalkyl or heterocyclic groups that are of different substitutes. Present day chemists still prepare diverse Schiff base ligands referred to as ''fortunate ligands'' Cozzi, 2004). Schiff base ligands and their metal complexes have been established as biochemically active chemotherapeutic agents with antibacterial, antifungal, anticancer, antioxidant, anti-inflammatory, antimalarial, antiviral activities and also as catalyst in several reactions such as polymerization reaction, reduction of thionyl chloride, oxidation of organic compounds, etc (Lashanizadegan and Jamshidbeigi, 2011). Presence of aryl substituents usually eases the synthesis and stability of Schiff bases while those containing alkyl are relatively unstable. The reactivity of aldehydes are generally faster than those of ketones in condensation reaction, thereby resulting in the formation of Schiff bases with a centre that are less steric, relatively unstable and freely polymerizable. Schiff bases of aliphatic aldehydes are relatively unstable and are readily polymerizable while those of aromatic aldehydes, having an effective conjugation system, are more stable (Hine and Yeh, 1967). Considerable attention is given to the study of Schiff bases with functionalization and modification in the chemical structure of the compound to improve its chemotherapeutic properties.



Metal complexes of Schiff bases as model of bioactive compounds

Transition metals have initiated the development of metal based drugs with promising pharmacological application and may offer unique therapeutic opportunities. Research has shown significant progress in utilization of transition metal complexes as drugs to treat several human diseases like carcinomas, lymphomas, infection control, anti-inflammatory and neurological disorders (Chohan and Sheazi, 1999).

The recognition of Schiff base complexes as models for biologically active compounds has brought rapid advancement within the field of coordination and bio-inorganic chemistry and spawned extensive research on their synthesis and applications (Chohan and Sheazi, 1999). Schiff's bases and their complexes continue to attract many researchers because of their wide applications in food industry, dye industry, analytical chemistry, catalysis and pharmacological application like antitumor, antifungal, antibacterial (Ashraf *et al,*. 2011, Brodowska *et al,*. 2014). It has been confirmed that some Schiff bases show increased bio-activity when given out as metal complexes (El-Sherif*et al,*.2012) and a number of metal chelates with anticancer activity have also been reported (Dwyer *et al,*. 1965).

Aims and objectives

This research is aimed at the synthesis and characterization of ruthenium (II)complexes derived from $[Ru(phen)_2Cl_2].2H_2O$ and $[Ru(bpy)_2Cl_2].2H_2O$ and to evaluate their antibacterial and antifungal activities. The proposed targets may result in the development of a drug with increased cytotoxicity compared to commercially available drugs.

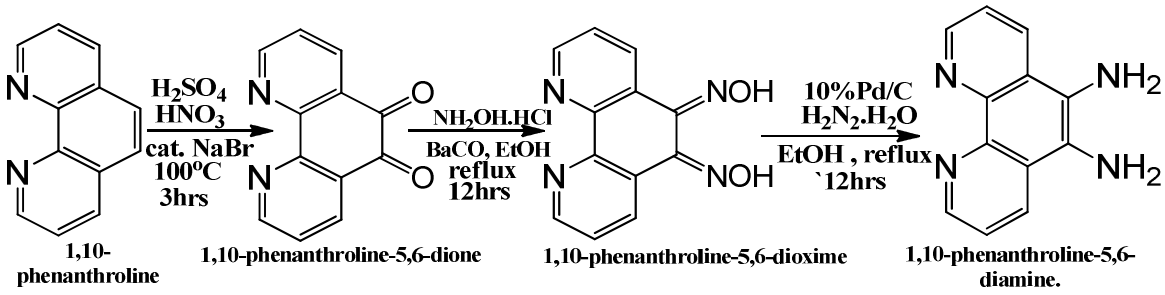
Experimental

Materials and Methods

All chemicals were obtained from Sigma-Aldrich and used without purification. Tetrabutyl ammonium chloride (TBACl) and palladium on activated charcoal 10%Pd/C were purchased from E. Merck (India).All the reactions were monitored by checking TLC of the reaction mixture. The complexes were purified by column chromatography. The ligand and the complexes were characterized by standard analytical techniques (FT-IR, Mass, UV-visible spectroscopy and Elemental analysis).

Preparation of the starting materials

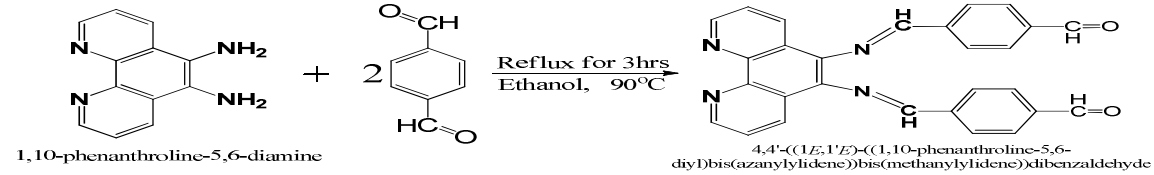
The following precursor molecules that are necessary for the synthesis of new ligand investigated in this study have been prepared by adopting the published procedures.



Scheme 1: Synthesis of 5,6-diamino-1,10-phenanthroline. Yamada *et al,*.(1992), Bodige and MacDonnell (1997)

Synthesis of 4,4-((1E,1E)-((1,10-phenanthroline-5,6-diyl)azanyllylidene))bis(methanyl lylidene))dibenzaldehyde Schiff base ligand (PDB)

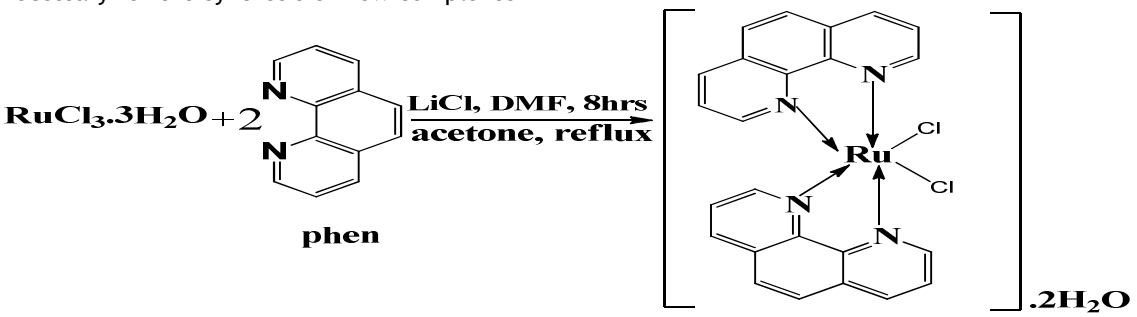
The Schiff base (PDB) was synthesized by adding Benzene-1,4-dicarbaldenhyde (0.89g, 2mmol) in 20 ml of ethanol to ethanolic solution of 5,6-diamino-1,10-phenanthroline (0.21g, 1mmol). The mixture was refluxed for 3hours. Then solution of the ligand was kept for slow evaporation and coloured precipitate was collected and dried over $CaCl_2$ for 2days in a desiccator. Yield: (78%). Anal. Calc. for $C_{28}H_{18}N_4O_2$: C, 76.02; H, 4.07; N, 12.67. Found: C, 76.10; H, 4.04; N, 12.46; FAB-MS (m/z): 443 $(M)^+$; UV-Vis., (nm); (CH_3CN + MeOH (9:1): 246, 276, 390.



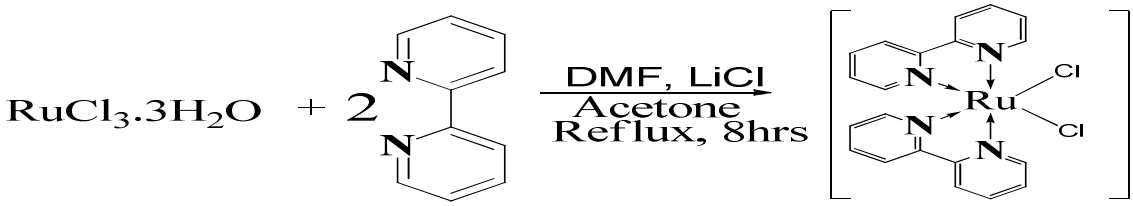
Scheme 2: Synthesis of Schiff base

Synthesis of Precursor Complexes

The following precursor complexes that are necessary for the synthesis of new complexes in this study have been prepared by adopting the published procedures.



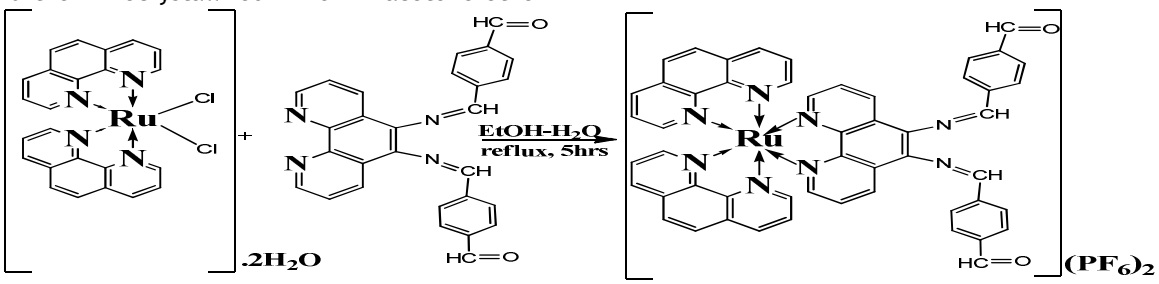
Scheme 3: Synthesis of $[Ru(phen)_2Cl_2].2H_2O$ Sullivan and Salmon (1978)



Scheme 4: Synthesis of $[Ru(bpy)_2Cl_2]$ Sullivan and Salmon (1978)

Synthesis of bis(1,10-phenanthroline)(PDB)ruthenium(II) hexaflurophosphate, $[Ru(Phen)_2(PDB)](PF_6)_2$

The complex was synthesized by refluxing PDB (0.44g, 1mmol) with $[Ru(phen)_2Cl_2].2H_2O$ (0.97g, 1mmol) in C_2H_5OH-H_2O (2:1, v/v; 225mL) mixture for 5hrs. The reddish-brown coloured crude complex was obtained on adding saturated solution of NH_4PF_6. It was purified by column chromatography (alumina, CH_3CN – Toluene (3:2, v/v) mixture) and was further recrystallized from acetone-ether mixture (1:5, v/v). Yield = 0.67g (75%).The chloride salt of $[Ru(phen)_2(ptz)]^{2+}$ was obtained by dissolving the above hexafluorophosphate complex in minimum amount of acetone and by precipitating upon addition of a saturated solution of TBACl in acetone. Analytical data: Yield: (75%). Anal. Calc. for $C_{52}H_{34}N_8O_2RuCl_2$: C, 64.06; H, 3.49; N, 11.50. Found: C, 64.01; H, 3.42; N, 11.00. MS (FAB) *m/z* Calc. $[M]^+$, 974.07; Found: $[M]^+$, 974.75.UV-Vis: (CH_3CN, nm): 225, 265, 449.

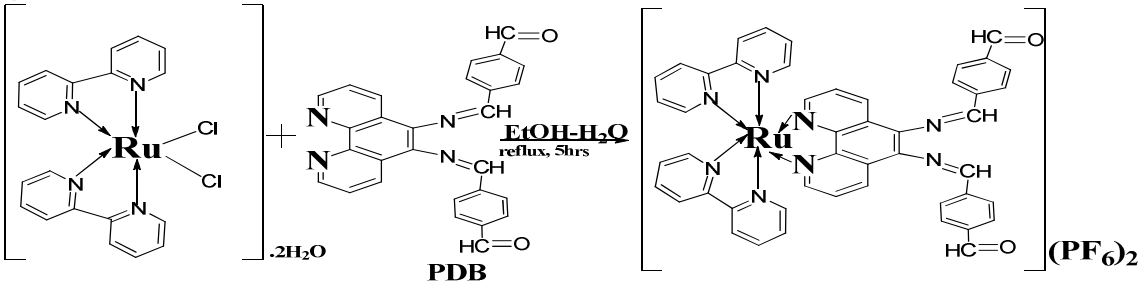


Scheme 5: Synthesis of $[Ru(phen)_2(PDB)](PF_6)_2$

Synthesis of bis(2,2-bipyridine)(PDB)ruthenium(II) hexaflurophosphate, $[Ru(bpy)_2(PDB)](PF_6)_2$

This complex was synthesized by refluxing PDB (0.44g, 1mmol) with $[Ru(bpy)_2Cl_2]$. (0.93g, 1mmol) in C_2H_5OH - H_2O (2:1, v/v; 225mL) mixture for 5hrs. The orange-brown crude complex was obtained on adding saturated solution of NH_4PF_6. It was purified by column chromatography (alumina, CH_3CN – Toluene (3:2, v/v) mixture) and was further recrystallized from acetone-ether mixture (1:5, v/v). Yield = 0.58g (76%). The chloride salt of $[Ru(phen)_2(pdb)]^{2+}$ was obtained by dissolving the above hexafluorophosphate complex in minimum amount of acetone and by precipitating upon addition of a saturated solution of TBACl in acetone.

Analytical data: Yield: (76%). Anal. Calc. for $C_{48}H_{24}N_8O_2RuCl_2$: C, 62.20; H, 2.59; N, 12.09. Found: C, 61.81; H, 5.42; N, 12.07. MS (FAB) *m/z* Calc. $[M]^+$, 926; Found: $[M]^+$, 925.70.UV-Vis: (CH_3CN, nm): 219, 288, 352, and 449.



Scheme 6: Synthesis of $[Ru(bpy)_2(PDB)](PF_6)_2$

Molar Conductivity Measurements

The molar conductance values of the complexes measured at room temperature in DMF solution with 0.001M concentration fall in the range 82-89ohm^{-1}.cm^{2}mol^{-1} indicating the electrolytic nature of the complexes, due to presence of chloride ions as a counter ions thus supports the $[Ru(phen)_2PDB]Cl_2$ and $[Ru(bpy)_2PDB]Cl_2$ formulae. The nature of complexes solutions is electrolytic in 1:2 ratios due to presence of chloride ions in the outer sphere of complexes

Antimicrobial activity

The Schiff base and its Ru(II) complexes were evaluated for antimicrobial activity by agar well diffusion method against the bacteria *Salmonella typhi, Pseudomonas aeruginosa, Escherichia coli* and *Staphylococcus aureus* and antifungal activities against the fungi *Aspergillus niger, Aspergillus flavus* nd *Rhizoctoni abataicola* cultured on potato dextrose agar as medium. The stock solution was prepared by dissolving the compounds in DMSO. The antimicrobial activities were performed in triplicate using 30µgml^{-1}concentration of the Schiff base and the complexes. The average was taken as the final reading. The well was made on the agar medium inoculated with microorganisms and filled with the test solution. The plate was incubated for 24hrs for bacteria and 72hrs for fungi at 35°C. During this period, the test solution was diffused and the growths of the inoculated microorganisms were affected. The inhibition zone was developed and it was measured in mm. Zone of inhibition of the investigated compounds against the bacteria and fungi are summarized in Table 4 and 5. Streptomycin and Nystatin were used as standard reference compounds for antibacterial and antifungal activities respectively.

RESULTS AND DISCUSSION

Table 1: Percentage yield and some physical properties of PDB and Ru(II) complexes

Properties	Schiff Base	$[Ru(phen)_2PDB]Cl_2$	$[Ru(bpy)_2PDB]Cl_2$
% yield	78%	75%	76%
Colour	greenish-yellow	Reddish-brown	Orange-brown
Appearance	Powder	Crystalline powder	Crystalline powder
Melting point	>350ºC	-	-
Decomposition temperature	-	240ºC	265ºC
Molar conductivity Measurement	-	$89\Omega^{-1}cm^2mol^{-1}$	$82\Omega^{-1}cm^2mol^{-1}$

Molar Conductivity Measurements

The molar conductance values of the complexes measured at room temperature in DMF solution with 0.001M concentration fall in the range 82-$89\Omega^{-1}cm^2mol^{-1}$. The nature of the complexes is electrolytic in 1:2 ratios due to the presence of chloride ions in their outer spheres. $[Ru(phen)_2PDB]Cl_2$ and $[Ru(bpy)_2PDB]Cl_2$

Table 2: IR data for Schiff base and Ru(II) complexes

	IR$\bar{\upsilon}$(cm^{-1})				
Compounds	υ(C=N)	υ(C=O)	υ(C=C)$_{aro}$	υ(C-H$_{st}$)$_{aro}$	υ(M-N)
PDB (Schiff base)	1561	1642	1500	3080	-
[Ru(phen)$_2$PDB](PF6)$_2$	1550	1629	1535	3050	721
[Ru(bpy)$_2$PDB](PF6)$_2$	1549	1631	1553	3046	754

The absorption bands at 1561cm^{-1}, 1550cm^{-1} and 1549cm^{-1} on the spectra of PDB ligand [Ru(phen)$_2$PDB](PF6)$_2$ and [Ru(bpy)$_2$PDB](PF6)$_2$ respectively are attributed to C=N stretching frequencies. Similarly the absorption bands at 1642cm^{-1}, 1629cm^{-1}and 1631cm^{-1} are assigned to C=O. The absorption bands at 3080cm^{-1}3050cm^{-1}and 3046cm^{-1} in al the spectra are given to (C-H) (aromatic) stretching frequency. Whereas the new absorption bands at 721cm^{-1} and 754cm^{-1} in the spectra of both complexes are assigned to M-N coordinate bonds.Arounaguiria*et al*,. (2000)

Table 3:UV-Visibleand Mass spectral data for Schiff base and Ru(II) Complexes

CompoundsUV-visible λ_{max} (nm) (logε)	Mass
PDB (Schiff base)390 (3.0),246 (3.1), 276 (3.3)	444 (M^+), base peak 222
[Ru(phen)$_2$PDB](PF6)$_2$499 (2.7), 288 (3.3)974.75 $(M)^+$, base-peak 341.50	
[Ru(bpy)$_2$PDB](PF6)$_2$499 (2.6), 265 (3.3)925.70 $(M)^+$, base-peak 299.65	

*Spectra were measured in CH_3CN

As seen, the spectrum of PDB is characterized by low intensity, low energy absorption band due to $\pi\rightarrow\pi^*$ transitions at 390nm. This band is assigned to the azomethine chromophore attached to the phenanthroline moiety. The high-energy bands (PDB: 246nm and 276nm) are attributed to the $\pi\rightarrow\pi^*$ transitions corresponding to the phenanthroline moiety of the ligand. The low energy band at 449nm for both complexes is due to MLCT Ru(dπ) $\rightarrow$PDB(π^*) transition. The band centered at 265nm and 288nm for [Ru(bpy)$_2$(PDB)](PF$_6$)$_2$and [Ru(Phen)$_2$(PDB)](PF$_6$)$_2$respectively are attributed to intra-ligand$\pi\rightarrow\pi^*$ transitions.John*et al*,.(1984).

PDB ligand mass spectrum showed base-peak at 222 (M-$C_{15}H_{11}O_2$). In the case of corresponding mixed-ligand Ru(II) complexes the molecular ion peak for the complex [Ru(phen)$_2$(PDB)]Cl$_2$ peaks were seen at 974.75 $(M)^+$,The base-peak at 341.50 is for $(M - C_7H_4O)^+$. Similarly we also got the molecular ion peak for the complex [Ru(bpy)$_2$(PDB)](Cl)$_2$ at 925.70 $(M)^+$.Suma *et al*,. (2012).

Antibacterial Activity

Table 4: Antibacterial activity of the Schiff base and its Ru(II) complexes

Compounds	Zone of Inhibition (mm)			
	S. typhi	*S. aureus*	*E. coli*	*P. aeruginosa*
Schiff Base	5	6	6	7
[Ru(phen)$_2$PDB]Cl$_2$	9	9	8	10
[Ru(bpy)$_2$PDB]Cl$_2$	8	9	8	11
Streptomycin (**Control**)	13	16	15	15

Antifungal Activity

Table 5: Antifungal activity of the Schiff base and its Ru(II) complexes

Compounds	Zone of Inhibition (mm)		
	Aspergillus niger	*Aspergillus flavus*	*Rhizoctonia bataicola*
Schiff Base	4	4	5
[Ru(phen)$_2$PDB]Cl$_2$	7	7	8
[Ru(bpy)$_2$PDB]Cl$_2$	7	7	9
Nystatin (**Control**)	11	10	13

The Schiff base and the complexes show more activity against *Pseudomonas aeruginosa* and *Rhizoctonia bataicola*. Generally, the results indicate that the complexes are more potent when compared to the ligand.

CONCLUSION

We have successfully synthesized novel Ru(II) complexes with coordinating Schiff base which was characterized by elemental analysis, FT-IR, ^{1}HNMR, UV-visible and mass spectral analysis. The data of molar conductivity in dimethylsulphoxide (DMSO) solutions shows the electrolytic behavior of both complexes in 1:2 ratios suggesting the presence of chloride ions in the outer sphere of complex structures. Octahedral geometry for $[Ru(phen)_2PDB]Cl_2$and $[Ru(bpy)_2PDB]Cl_2$were proposed according to the data obtained from molar conductivity, elemental and spectral analyses. The antimicrobial activity of the ligand and the complexes were screened against four bacteria and three fungal species and the obtained inhibition zones data indicate the possibility of their applications in the treatment of diseases.

ACKNOWLEDGEMENT

We sincerely acknowledged SRM Research Institute and Faculty of Bioengineering, SRM University, Kattankulathur Campus, India for providing all the necessary facilities required for this work.

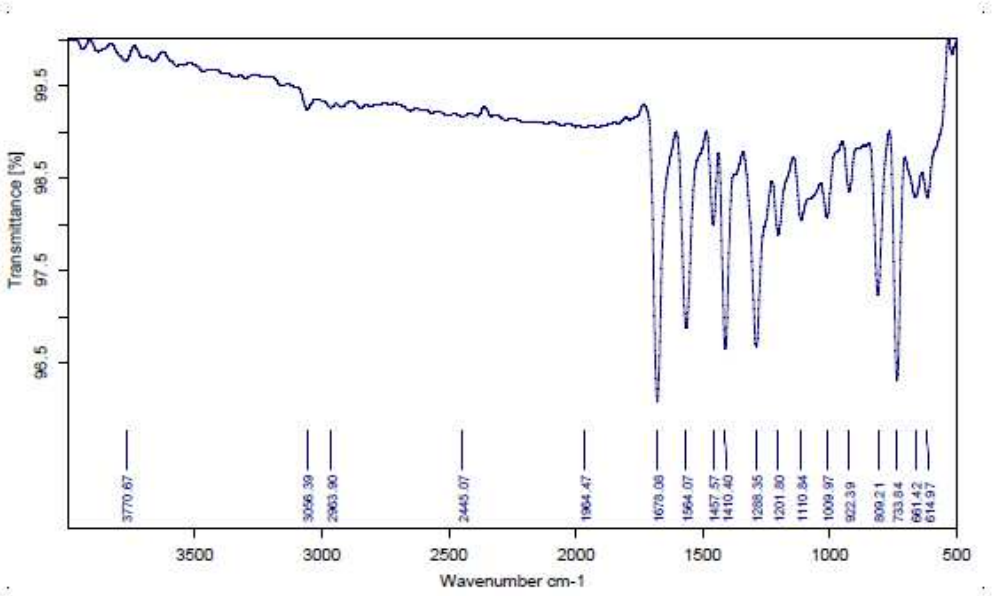


Fig.1: IR Spectrum of PDB

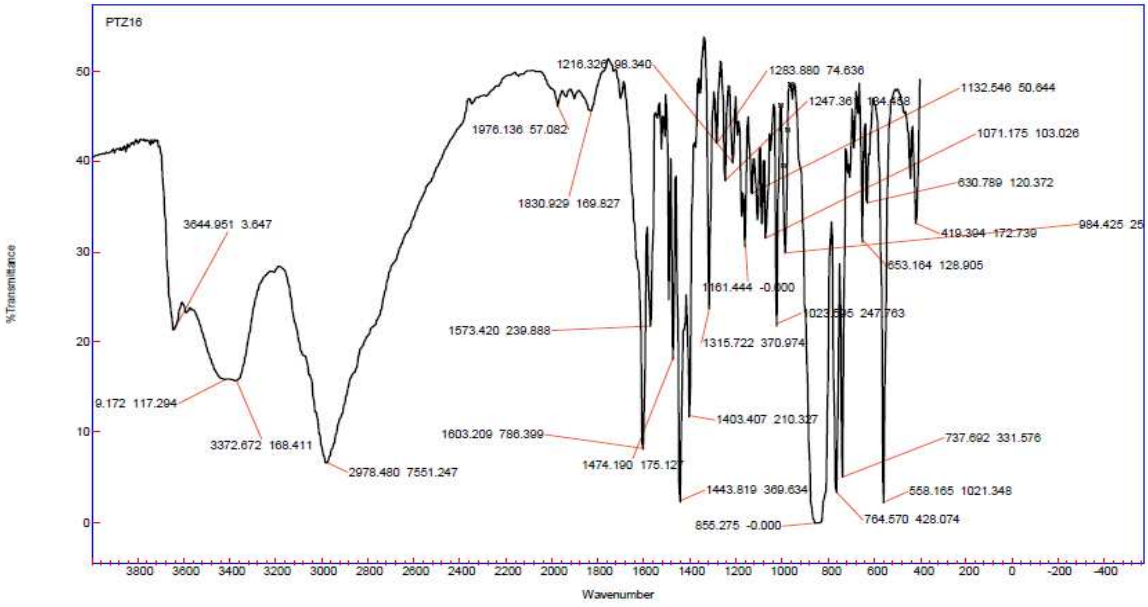


Fig.2: IR Spectrum of $[Ru(phen)_2PDB](PF_6)_2$

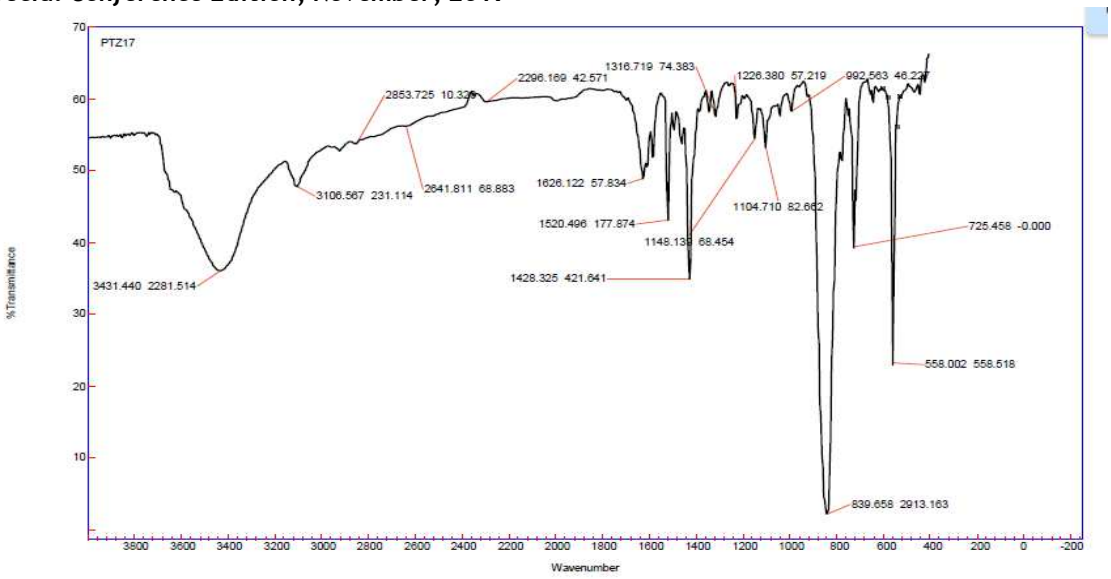


Fig.3: IR Spectrum of $[Ru(bpy)_2PDB](PF6)_2$

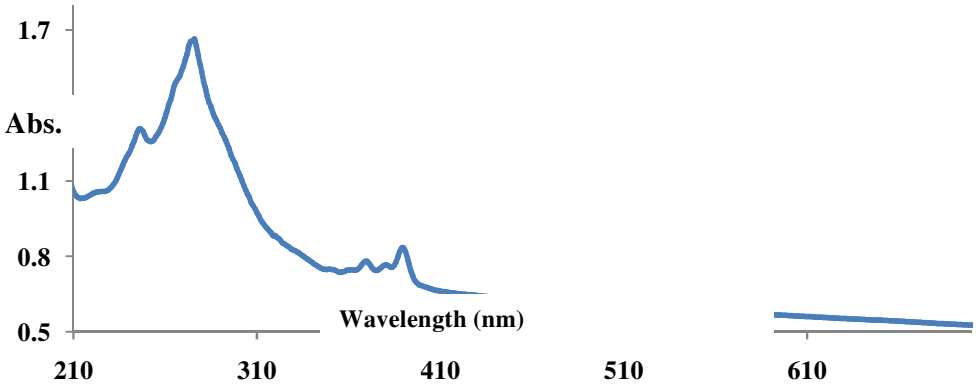


Fig.4:UV-Vis absorption spectrum of Schiff base(PDB)

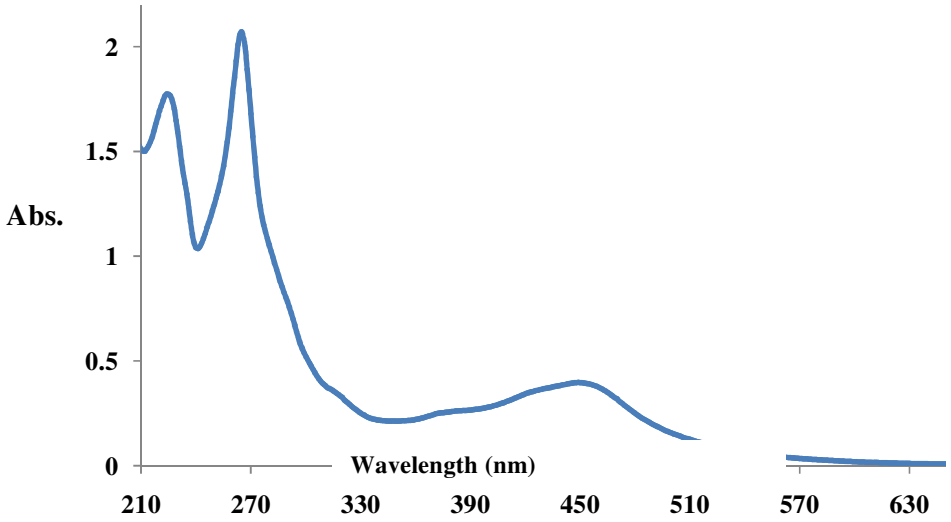


Fig.5: UV-Vis absorption spectrum of $[Ru(phen)_2(PDB)](PF_6)_2$

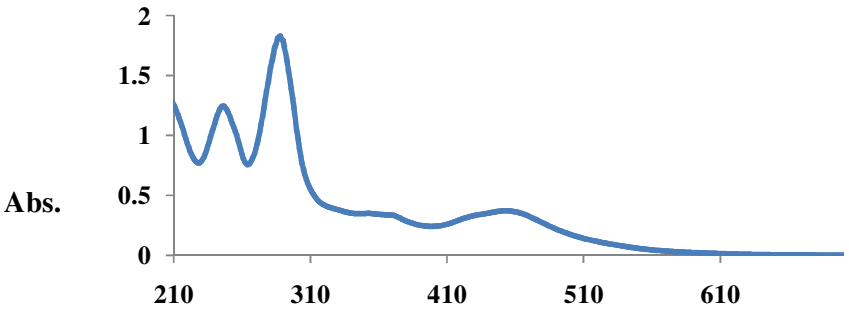


Fig.6:U' 'DB)](PF$_6$)$_2$

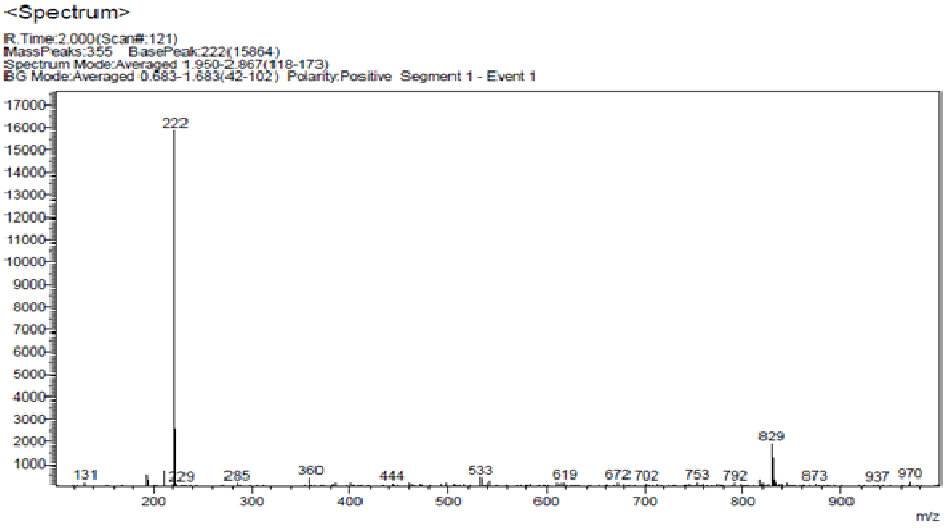


Fig.7: mass spectrum of Schiff base(PDB)

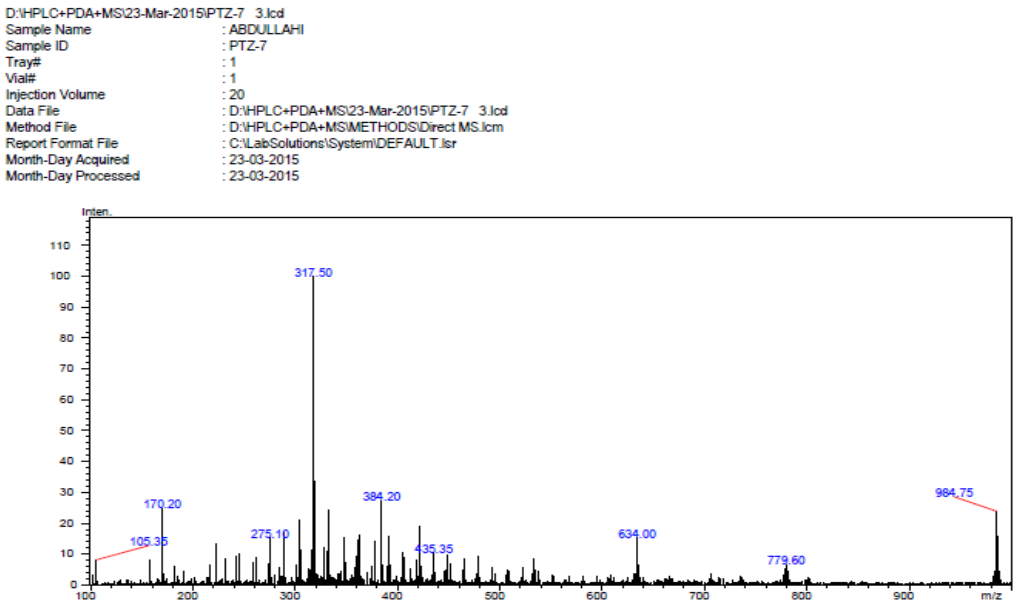


Fig.8: Mass spectrum of [Ru(phen)$_2$PDB]Cl$_2$

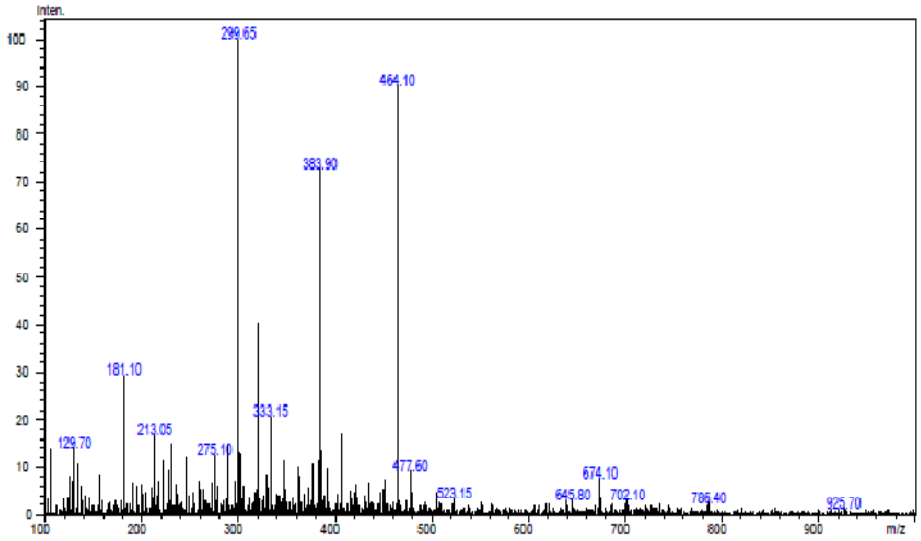


Fig.9: Mass spectrum of $[Ru(bpy)_2PDB]Cl_2$

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