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Synthesis and Characterization of Mixed 1,10- Phenanthroline and Penicillin G Procaine Metal (II) Complexes

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Abstract The synergetic effect of mixed ligand over single ligand for biological application is an interesting and growing area of research in coordination chemistry, especially when they contain oxygen and nitrogen donors.In this work we report the synthesis of mixed ligand metal complexes with [M (L)(L) Cl_2] where M is Ni (II), Zn (II), Mn (II) and Cu (II), while L is phenanthroline with penicillin G procaine. The structures of the synthesized complexes have been proposed based on the analytical data from Infrared spectroscopy (FTIR), UV-Visible (UV) and Atomic Absorption Spectroscopy (AAS).Conductivity, solubility of the complexes as well as their melting point were also determined. The FTIR result shows that all the basic functional groups present in the ligands were also observed in the complexes. The UV-Visible results reveal the formation of the complexes due to the observed blue shift (d-d) transition and the ligand metal charge transfer (LMCT) in the complexes. Also, the AAS result showed the presence of all the metals in the complexes. The complexes have potential applications as antifungal, antibacterial and anticancer due to the presence of the oxygen and nitrogen donors.

Keywords Synthesis, 1,10- Phenanthroline, Penicillin G, Procaine, Metal (II) Complexes

1. Introduction

The study of coordination chemistry dated back to 1798, with the Tassaert studies which is still in progress today in the field of organic and inorganic chemistry due to the wide application of these metal complexes. The structures of complexes are of great interest as they could exceed their valences as against the classical theory of valences. Research has shown that the coordination of metal center to drugs has resulted to metal ligand bioactive complexes with enhance activity, which has gained greater application in drug delivery [1-8]. The uniqueness of these metal complexes in drug delivery is attributed to their ability to deliver the bioactive functions through a selective release mechanism [9].

These metal center drugs have the ability of controlling the mechanism through which the drugs are deliver to the expected targeted site without altering the therapeutic activity of those drugs. This can in turn enhanced the activity of the parent drugs. Again, drug molecules are faced with the challenge of solubility when taken orally, hence reduced their permeability [10]. However, drugs solubility and permeability have been enhanced when coordinated to metal centers, with better bioactivity [11]. The permeability observed in the metal ligand center is attributed to the chelate effect resulting from the electron density in the bioactive ligands. While the solubility is ascribed to the hydrophilic nature of metals [12-14]. In fact, oral bioavailability can be enhanced when coordinated to metal and the

metal acting as the delivery system [15-16]. This metal coordinated drugs have also proven to reduced toxicity [17]. These metals coordinated drugs has been in market and has made great impact [18-19].

Bipyridine and analogous ligands such as phenanthroline are commonly used in the formation of different complexes with a general variety of transition metals and have antibacterial activity [20]. These studies are important in understanding electron transfer processes, mixed valence complexes, magnetic coupling and magnetic transition, photochemistry and owing to an extended π - system, non - covalent π interactions in biological process as can be simulated [21]. Type of ligands, kind of the meta ion, charge of complex, the transition metal series, electronic structure of the metal-ion and shape of the metal-ion complexes can affect the biological activity of the complex [22]. Therefore, the study of mixed ligand complexes is receiving considerable attention.

This work synthesized and characterized some mixed ligands - metal (II) complexes by using mixed ligands of 1, 10 - phenanthroline and penicillin G procaine, with some transition metal (II) Chlorides (Cu, Mn, Ni, and Zn).

2. Experimental

2.1. Materials

The drugs, chemicals and solvents used in this work were of high purity and were used as purchased from Sonitex Nigeria Enterprise without further purification.

2.2. Synthesis of [Mn(Phen) (Pen) Cl_2] H_2O

The metals were prepared following a literature procedure described by Adeyemo *et al* [23], while the synthesis of the mixed ligands – metal complexes were prepared by following a method reported in literature [24]. In brief a solution of $MnCl_2.4H_2O$ (0.593g, 0.003mole) in distilled water (30mL) was added to a solution consisting of 1, 10 Phenanthroline (0.59g, 0.003mole) in 30mL of distilled water, heated in a water bath for 5 minutes and penicillin G procaine (0.55g, 0.00mole) also in 30mL distilled water. The resulting mixture was stirred and heated for 1hour, during which clay precipitate was formed on cooling in an ice bath. The clay precipitate was filtered and dried at room temperature. The percentage yield was 64.14%. The same procedure was used for Mn, Zn and Cu mixed ligand metal complexes.

$$MnCl_2.4H_2O + (Phen)\ (Pen) \xrightarrow[\text{Heart}]{} [Mn\ (Phen)\ Cl_2]\ H_2O$$

3. Results and Discussion

Table1: Result of solubility determination for mixed 1, 10-phenanthrolineand penicillin metal complexes.

Compound	Dist. H_2O		Ethanol		Methanol		Acetone		Chloroform		DMSO	
	C	H	C	H	C	H	C	H	C	H	C	H
1, 10-phenanthroline	**SS**	**S**	**S**	**S**	**S**	**S**	**S**	**S**	**SS**	**S**	**S**	**S**
Penicillin G	**S**	**S**	**S**	**S**	**S**	**S**	**SS**	**SS**	**NS**	**SS**	**S**	**S**
Ni (phen) (pen) Cl_2	**SS**	**S**	**NS**	**SS**	**S**	**S**	**NS**	**S**	**NS**	**NS**	**SS**	**S**
Zn (phen) (pen) Cl_2	**NS**	**SS**	**NS**	**SS**	**NS**	**S**	**SS**	**SS**	**NS**	**S**	**S**	**S**
Mn (phen) (pen) Cl_2	**SS**	**S**	**NS**	-	**NS**	-	**NS**	-	-	-	-	-
Cu (phen) (pen) Cl_2	**SS**	**S**	**SS**	**SS**	**SS**	**SS**	**NS**	**SS**	**NS**	**NS**	**SS**	**S**

Key: C-Cold, H-Hot, S-Soluble, SS-Slightly Soluble and NS-Not Soluble

Table 2: Analytical data of mixed 1, 10-phenanthroline and penicillin metal complexes

Compound	Colour	Melting Point (^oC)	% Yield	Conductivity (µs/cm)
1, 10-phenanthroline	White	125	-	01
Penicillin G	White	158	-	17
Ni (phen) (pen) Cl_2	Black	280	37.94	10
Zn (phen) (pen) Cl_2	Grey	>300	23.80	07
Mn (phen) (pen) Cl_2	Clay	195	64.14	01
Cu (phen) (pen) Cl_2	Green	200		17

Table one gives information on the solubility of the ligands: 1, 10-phenanthroline, penicillin and their metal complexes. The ligands and their complexes were dissolved in both cold and hot distilled water, ethanol, methanol, acetone, chloroform and DMSO. The solubility test shows that most of the complexes were either soluble or slightly soluble all the solvent tested especial in the hot solvent with exception of nickel and copper showing non soluble in hot chloroform.

Table 2. showed the colour, melting point, percentage yield and conductivity data of the 1, 10-phenanthroline and penicillin metal complexes.

Table 3: Selected FTIR data (cm^{-1}) of the mixed 1, 10-phenanthroline and penicillin metal complexes.

Compound	V(N-H)	V(C-N)	Aromatic substituted benzene V(C-H)	Aromatic V(C=C)	V(C-S)	V(M-L)	V(C-Cl)	V(C=O)	V(C=N)	Aromatic Ring	V(O-H)	V(C-O)	CH_3
1, 10-phenanthroline	3649.44 (m)	1346.36 (m,s)	3061.13 (s)	1587.47 (s)	-	-	-	-	1647.26 (s)	779.29 (s)	3441.12 (b)	-	-
Pennicilline G	3853.90 (w)	1361.79 (m)	3030.27 (s)	1597.11 (w)	1273.06 (m)	-	-	1782.29 (s)	1693.56 (s)	775.41 (s)	-	1273.06 (s)	1400.37 (m)
Ni (phen) (pen) Cl_2	3394.83 (w)	1383.10 (m)	3061.13 (s)	1518.03 (s)	1174.69 (s)	426.28 (s)	848.71 (s)	1649.19 (m)	1600.97 (s)	727.19 (s)	3234.73 (b)	1289.20 (s)	1425.44 (s)
Zn (phen) (pen) Cl_2	3275.24 (m)	1315.50 (s)	3063.06 (s)	1537.32 (m)	1172.76 (s)	416.64 (s)	852.58	1641.48	1600.97 (s)	769.62 (s)	-	1289.20 (s)	1442.80 (s)
Mn (phen) (pen) Cl_2	3410.26 (b)	1313.57 (m)	3061.13 (m)	1591.96 (s)	1267.27 (s)	420.50 (s)	848.71 (s)	1649.19	1624.12 (b)	731.05 (s)	3261.74 (b)	1222.19 (m)	1425.44 (s)
Cu (phen) (pen) Cl_2	3408.33 (b)	1342.50 (m)	3061.88 (m)	1519.96 (s)	1224.84 (s)	449.43 (w)	850.64 (s)	1645.33 (m)	1606.76 (s)	723.33 (s)	3257.88 (b)	1224.84 (m)	1429.30 (s)

The FTIR spectral of 1, 10-phenanthroline and penicillin G and their combination metal complexes were compared. The V(C=N) band of the 1, 10-phenanthroline molecules undergoes a shift in all the complexes. These could be attributed to the coordination site [21].

The V(N-H) stretching frequency of the penicillin molecule undergoes a slight shift in all the complexes V(N-H) 3853.90 cm^{-1} for the complexes has shifted to various lower frequencies showing likely coordination site for the complexes. Also, V(C-S) with 1273.06 cm^{-1} of the penicillin ligand has slightly shifted to lower frequencies in most of the complexes, indicating coordination site.

Table 4: Uv-visible spectra of mixed 1, 10-phenanthroline, and penicillin metal complexes and their ligands

Compound	Wavelength (nm)	Energies (KJ/mol)	Assignment
1, 10-phenanthroline	191.40	625.40	$\pi \rightarrow \pi^*$
	286.20	418.25	$n \rightarrow \pi^*$
Penicillin G	194.20	616.40	$\pi \rightarrow \pi^*$
	299.60	399.55	$n \rightarrow \pi^*$
Ni (phen) (pen) Cl_2	217.50	550.36	$\pi \rightarrow \pi^*$
	282.50	423.73	$n \rightarrow \pi^*$
	410.50	291.60	LMCT
Zn (phen) (pen) Cl_2	214.00	559.37	$\pi \rightarrow \pi^*$
	312.50	383.05	$n \rightarrow \pi^*$
	631.50	195.78	LMCT
Mn (phen) (pen) Cl_2	196.50	609.18	$\pi \rightarrow \pi^*$
	282.50	423.73	$n \rightarrow \pi^*$
Cu (phen) (pen) Cl_2	194.00	617.03	$\pi \rightarrow \pi^*$
	283.80	414.49	$n \rightarrow \pi^*$

1, 10-phenanthroline shows two absorption bands at 19.40 nm (625.41 KJ/mol) and 286.20 nm (418.25 KJ/mol) due to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transition. While penicillin G also show two bands; 194.20 nm (616.40 KJ/mol) and 299.60 nm (399.55 KJ/mol) due to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$. The Zn (phen) (pen) Cl_2, metal complexes show bands between 196.50 - 631.50 nm, (a bathochromic shift) which are assigned to metal to ligand charge transfer (MLCT) transitions

from the filled 3d orbital to the empty π* orbital (dπ–π*) as observed in the spectra of related complexes with N,N bidentate ligands [25-26]. The bands have undergone both bathochromic and hypsochromic shift in the complexes due to complexation [26-27]. LMCT (ligand metal charge transfer) was also observed in Ni (phen) (pen) Cl_2 metal complexes but was not observed in Mn (phen) (pen) Cl_2 and Cu (phen) (pen) Cl_2 complexes.

4. Atomic Absorption Spectroscopy

The atomic absorption spectroscopy of the metal complexes was carried out in accordance with the technique recommended for determining the concentration of a particular metal element in a sample [] (Yan, Sperling, & Welz, 1999). The technique makes use of absorption spectroscopy to assess the concentration of an analyze in a sample. It relies heavily on beer – Lambert law.

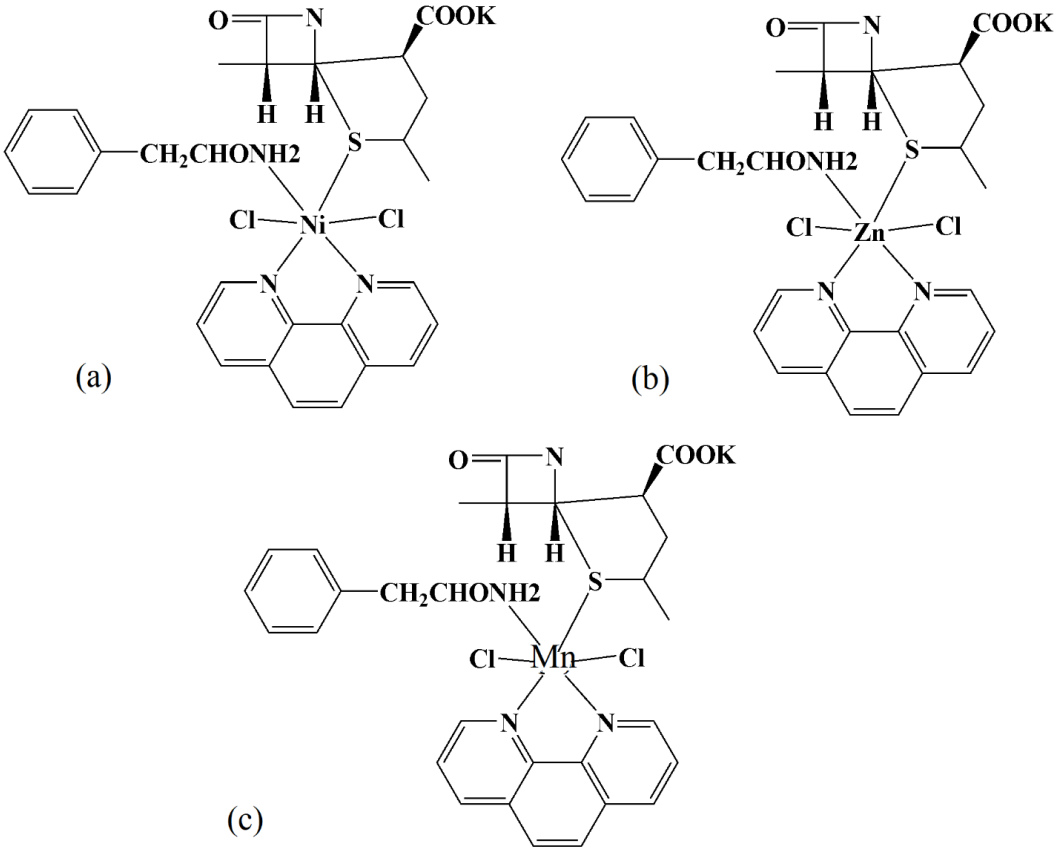
The metal analysis was carried out on Alpha Atomic Absorption spectrophotometer at Tudaka environmental consultants' limited lab, Warri. 0.1g of each complex was digested in dilute 8ml of 6M HCl and 0.8ml of conc. HNO_3 and make up to a final volume of 1 liter with distilled water (double acid method).

Table 5: Results of Atomic Absorption Spectrometer (AAS) for metal determination of mixed 1, 10-phenanthroline, and penicillin metal complexes

S/N	Sample Code	Metals AnalyzedConcentration (µg/g)
1	Nickel	174.18
2	Zinc	139.44
3	Manganese	193.32
4	Copper	159.76

From table 5 the Atomic Absorption Spectrometer (AAS) of the mixed ligands metal complexes shows that the metals were present in the complexes from the range of 159.76-193.32 µg/g.

5. Proposed structure



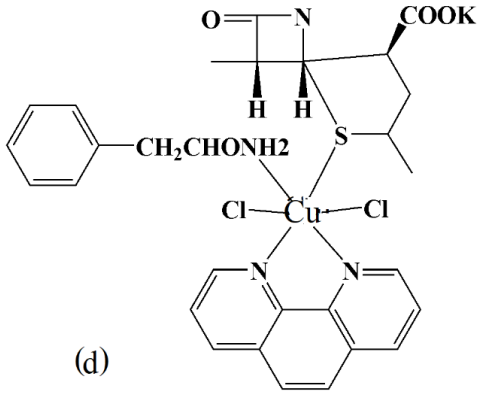


Figure 1: The proposed structure of (a) Ni (Phen) (Pen) Cl_2, (b) Zn (Phen) (Pen Asco) Cl_2,(c) Mn (Phen) (Pen) Cl_2 and (d) Co (Phen) (Pen) Cl_2

5. Conclusion

There is high mortality rate caused by microorganism despite antibiotics drugs due to new infectious diseases that leads to multi-drug resistance microbial pathogens. The coordination of organic drugs to metal ion has been proven to increase the activity of such drugs due to the strong interaction between metals complexes and DNA. Generally, metal complexes have demonstrated an essential future of antimicrobial treatment due to their ability to thwart drug resistance, increasing activity through additive or synergic effect, reduced required doses, cost, chances of toxic side effect and increases the spectrum of activity. Hence, the urgent need for new metal -based drug search continues in the field of bio inorganic chemistry. Still on this search this study was carried out to contribute to the efforts being made to search for novel metal complexes with new mechanism used against diseases.

Four mixed metal complexes were synthesized and characterized from 1, 10-Phenanthroline, penicillin G and metal and four metal (II) chloride (Ni, Zn, Mn and Co). The spectroscopic studies revealed that 1,10- Phenanthroline is a bidentate ligand and coordinated to the metal ions through (Pyridine) Nitrogen. However, Penicillin G coordinated through the Nitrogen of the secondary amine and Sulphur. The tentative metal ligand (M-L) assignments from all the spectroscopic data favors six coordination for the complexes studied. Finally, this research has provided additional results and data for mixed ligands metal complexes.

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