

SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL STUDIES OF MACROCYCLIC SCHIFF BASE DERIVED FROM MALONIC ACID AND O-PHENYLENEDIAMINE AND ITS CD (II), CO (II), CU (II), NI (II), AND ZN (II) COMPLEXES

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ABSTRACT

The condensation of Malonic acid with o-phenylenediamine have yielded the Schiff Base 7,16-dihydrodibenzo[1,4,8,11]tetraazacyclotetradecine-6,8,15,17-tetraol (89.39%). Its metal (II) complexes were prepared from the chloride salts of Cd²⁺, Co²⁺, Cu²⁺, Ni²⁺ and Zn²⁺. Solubility, melting/decomposition temperature, FT-IR, molar conductance and magnetic moments were used to determine the ligands and its complexes. The FT-IR result indicates a band at 1633cm⁻¹ which corresponds to azomethine and confirms the formation of the ligand. There was a bathochromic shift in the peak to 1607cm⁻¹, 1596cm⁻¹, 1611cm⁻¹, 1573cm⁻¹ and 1566cm⁻¹ in the spectra of Cd²⁺, Co²⁺, Cu²⁺, Ni²⁺ and Zn²⁺ complexes respectively which is attributed to the binding of the nitrogen of azomethine to the metal ions. The compounds were tested for their antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* using agar cup-plate method. The ligand and its complexes were found to be active against both *Staphylococcus aureus* and *Escherichia coli*. The Ni (II) complex displayed an enhanced activity with the highest zone of inhibition (45mm).

Keywords: Synthesis, Characterization, Ligand, Complexes, Antibacterial

INTRODUCTION

Schiff bases are condensation products of primary amine with an aldehyde or a ketone. The carboxyl group of the aldehyde produces aldimines while that of ketone produces ketoinimes (Aliyu and Adamu, 2009).

Lately, studies on biological and catalytic activities of Schiff Base derived compounds is becoming an area of research interest (El-hendawy *et al.*, 2001). Recently, transition metal complexes with ligands containing both hard and soft donor groups have been used extensively in coordination and organometallic chemistry (Prabhakaran *et al.*, 2013).

The simultaneous similarity of macrocyclic compounds with enzymes and its ability to mimic enzymes as well makes it a point of research interest internationally. The active search for new types of macrocycles and their applications has systematically increased since their discovery (Lindoy, 1989).

Several synthetic and natural macrocyclic compounds have been investigated, their chemistry has attracted the interest of both inorganic and bioinorganic chemists in recent years because of

their importance in the area of coordination chemistry. They are interesting ligand system due their ability to anchor metal ions, neutral molecules and organic cation (Singh *et al.*, 2010). The tetraaza macrocyclic ligand and their metal complexes have specifically attracted interest among the coordination and bioinorganic chemist (Tas *et al.*, 2010). Macrocyclic Schiff base ligands have received special attention because of their mixed soft-hard donor character, versatile coordination behaviour (Comba *et al.*, 2003, Puhilbhai *et al.*, 2009 & Sengupta *et al.*, 2003) and their pharmacological properties, i.e. antifungal, antibacterial, anticancerous, antitumor (Tyagi *et al.*, 2011). Transition metals of macrocyclic complexes have received much attention due to their active part that is mimicking the activities of metalloenzymes (Canadas *et al.*, 2000) as biomimic model compounds resembling natural proteins like hemerythrin and enzymes (Chaudhary, 2002). The family of these complexes with aza-macrocyclic ligands has remained a focus of scientific attention for many decades (Singh *et al.*, 2010).

Considering this growing research interest in the macrocyclic complexes, this work/article concentrate on the synthesis, characterization and antibacterial studies of 7,16-dihydrodibenzo[1,4,8,11]tetraazacyclotetradecine-6,8,15,17-tetraol Ligand and its complexes of Cd²⁺, Co²⁺, Cu²⁺, Ni²⁺ and Zn²⁺

MATERIALS AND METHODS

All the chemicals used were of analytical grade, procured from Qualikems and used without further purifications. Melting point/decomposition temperature were determined using IA9000 series digital melting point apparatus while conductivity measurements were conducted using HI-2300 conductivity meter. IR measurements were recorded using shimadzu FTIR spectrophotometer at the range of 4000-400cm⁻¹. The magnetic moments of the complexes were determined on MSB MKI at 25°C

Preparation of the Ligand

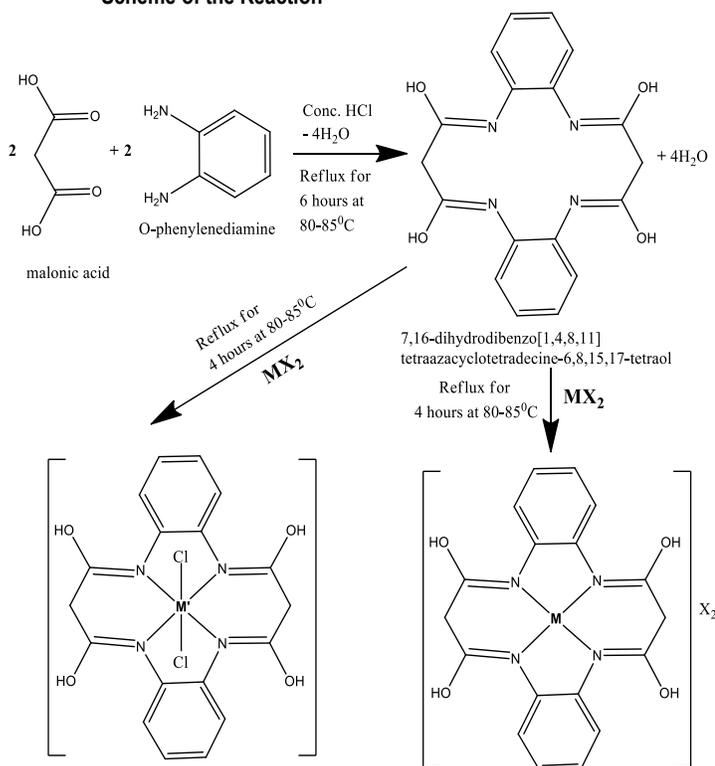
A hot ethanolic solution (20ml) of malonic acid (2.08g, 0.02mol) and an ethanolic solution (20ml) of o-phenylenediamine (2.16g, 0.02mol) were mixed with constant stirring. The mixture was refluxed at 80-85°C for 6 hours in the presence of few drops of concentrated HCl (pH-3-4). The resulting solution was kept overnight at room temperature. The precipitate formed was

separated out, filtered, washed and recrystallized with methanol/ethanol (60:40) and dried over P₄O₁₀ in vacuum.

Preparation of Metal Complexes

An ethanolic solution (20ml) of the corresponding metal salts (0.001mol) and a hot ethanolic solution (20ml) of the ligand (0.59g, 0.001mol) were mixed together with constant stirring. The reaction mixture was refluxed for 4 hours at 80-85°C. The corresponding product formed was cooled, filtered, washed and recrystallized with methanol/ethanol (60:40) and dried over P₄O₁₀ in vacuum.

Scheme of the Reaction



Scheme 1: Synthesis of the ligand and its metal complexes

Where M=Ni (II), M'= Cd (II), Co (II), Cu (II), and Zn (II) and X = chloride ions

RESULTS AND DISCUSSION

The condensation of malonic acid and o-phenylenediamine yields 7,16-dihydrodibenzo[1,4,8,11]tetraazacyclotetradecine-6,8,15,17-tetraol ligand. The Ligand solution (in methanol) was used to prepare the metal (II) complexes under reflux condition with metal chlorides (scheme 1) and were obtained in high yields (89.39%) as shown in figure 1.

The ligand is dark brown in colour while the complexes gives variety of colours viz; brown, black, dark brown, brown and barn red colours for the different metal ions used. This colour changes were attributed to either metal-ligand or d-d electronic transitions or both. The ligand melts at a temperature of 80°C, while its metal complexes decomposed at the temperatures of 147°C, 233°C, 148°C, 169°C and 136°C for Cd (II), Co (II), Cu (II), Ni (II) and Zn

(II) complexes respectively. This indicates that the complexes have high thermal stabilities

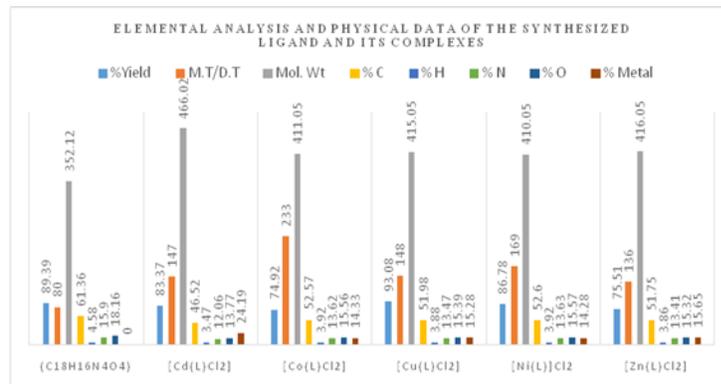


Figure 1: Elemental analysis and physical data of the synthesized ligand and its complexes

The solubility test in table 1 showed that the ligand and its metal complexes exhibit different properties in some common solvents. Most of the compounds were found to be soluble in methanol and ethanol with very few ones being slightly soluble. Both the ligand and its metal complexes were found to be soluble in dimethyl sulphoxide (DMSO). This may be due to the high dielectric constant of the solvent (Sani and Baba, 2016).

Table 1: Solubility test of the ligand and its metal (II) complexes in some common solvents

SN	Compound	Acetone	Aceto-nitrile	Chloroform	Diethyl ether	Distilled water	Ethanol	Ethyl Acetate	DMSO	Methanol	n-hexane	xylene
1	(C ₁₈ H ₁₆ N ₄ O ₄)	SS	SS	SS	IS	SS	S	SS	S	S	S	IS
2	[Cd(L)Cl ₂]	SS	IS	IS	IS	SS	SS	SS	S	S	IS	IS
3	[Co(L)Cl ₂]	IS	SS	SS	IS	SS	SS	IS	S	S	IS	IS
4	[Cu(L)Cl ₂]	IS	IS	IS	IS	SS	SS	IS	S	SS	IS	IS
5	[Ni(L)Cl ₂]	IS	IS	IS	IS	S	S	SS	S	S	S	IS
6	[Zn(L)Cl ₂]	SS	SS	SS	IS	S	S	SS	S	S	SS	IS

Where L= C₄₂H₃₂N₄

At room temperature, the Co (II), Cu (II) and Ni (II) complexes showed magnetic moments of 3.87, 1.73 and 2.83 respectively, this correspond to the 3, 1 and 2 unpaired electrons respectively. While the Cd (II) and Zn (II) complexes are diamagnetic as shown in table 3. The molar conductance values of the Ni (II) complex in DMSO was 350Ω⁻¹cm²mole⁻¹ indicating 1:2 electrolytic natures. However, the molar conductance values for the rest of the complexes falls within the range 28-167Ω⁻¹cm²mole⁻¹ as shown in table 2. An octahedral geometry has been proposed for the Cd (II), Co (II), Cu (II) and Zn (II) complexes whereas square planar geometry was expected for the Ni (II) complex.

Table 2: Magnetic moments and molar conductance of the synthesized complexes

S/N	COMPOUND	MOLECULAR FORMULA	μ_{eff} (B.M)	MOLAR CONDUCTANCE ($\Omega^{-1}\text{cm}^2\text{mole}^{-1}$)
1	[Cd(L)Cl ₂]	C ₁₈ H ₁₆ CdN ₄ O ₄ Cl ₂	Diamagnetic	138
2	[Co(L)Cl ₂]	C ₁₈ H ₁₆ CoN ₄ O ₄ Cl ₂	3.87	115
3	[Cu(L)Cl ₂]	C ₁₈ H ₁₆ CuN ₄ O ₄ Cl ₂	1.73	28
4	[Ni(L)Cl ₂]	C ₁₈ H ₁₆ NiN ₄ O ₄ Cl ₂	2.83	350
5	[Zn(L)Cl ₂]	C ₁₈ H ₁₆ ZnN ₄ O ₄ Cl ₂	Diamagnetic	167

Where L= C₄₂H₃₂N₄

Job's method of continuous variation was used for the estimation of the ligand to metal ratio. The plot of absorbance against mole fraction in each case was taken at maximum absorbance which corresponds to the ligand-metal mole fraction of 1:1 as shown in table 3.

Table 3: Job's Method Data

Mole fractions, X	1.00	0.94	0.81	0.69	0.56	0.44	0.31	0.19	0.06	0.00	
S/ N	COMPOUND	Absorbance at 450nm									
1	[Cd(L)Cl ₂]	0.24	1.03	1.80	2.61	3.36	3.14	2.25	1.43	0.64	0.00
2	[Co(L)Cl ₂]	0.27	1.05	2.02	2.66	3.51	3.27	2.29	1.56	0.64	0.00
3	[Cu(L)Cl ₂]	0.28	1.08	1.93	2.72	3.52	3.26	2.30	1.47	0.69	0.00
4	[Ni(L)Cl ₂]	0.26	1.05	1.87	2.71	3.50	3.30	2.32	1.46	0.68	0.01
5	[Zn(L)Cl ₂]	0.27	1.05	1.87	2.75	3.35	3.07	2.33	1.44	0.65	0.00

Where L= C₄₂H₃₂N₄

The important IR bands and their assignment in the ligand and its complexes are shown in table 4. The IR spectrum of the ligand does not exhibit any band corresponding to a free primary diamine or a free keto group which suggest the complete condensation of the amino groups with the keto groups. The ligand showed absorption peak at 1633cm⁻¹ that is assignable to azomethine and confirms the formation of the ligand. Upon complexation, the peak shifted towards the lower frequencies of 1607cm⁻¹, 1596cm⁻¹, 1611cm⁻¹, 1573cm⁻¹ and 1566cm⁻¹ for Cd (II), Co (II), Cu (II), Ni (II), Zn (II) complexes respectively. This manifested that the nitrogen atoms of the azomethine groups are coordinated to the central metal ions. The absorption peaks at 415cm⁻¹, 430cm⁻¹, 448cm⁻¹, 440cm⁻¹ and 415cm⁻¹ can be ascribed to ν (M-N) for Cd (II), Co (II), Cu (II), Ni (II), Zn (II) complexes respectively.

Table 4: Infrared Absorption Frequencies (cm⁻¹) of the Ligand and its Metal Complexes

S/N	COMPOUND	MOLECULAR FORMULA	ASSIGNMENTS		
			ν (C=N)	ν (M-N)	ν (O-H)
1	L	(C ₁₈ H ₁₆ N ₄ O ₄)	1633	-	3454
2	[Cd(L)Cl ₂]	C ₁₈ H ₁₆ CdN ₄ O ₄ Cl ₂	1607	415	3342
3	[Co(L)Cl ₂]	C ₁₈ H ₁₆ CoN ₄ O ₄ Cl ₂	1596	430	3220
4	[Cu(L)Cl ₂]	C ₁₈ H ₁₆ CuN ₄ O ₄ Cl ₂	1611	448	3350
5	[Ni(L)Cl ₂]	C ₁₈ H ₁₆ NiN ₄ O ₄ Cl ₂	1573	440	3290
6	[Zn(L)Cl ₂]	C ₁₈ H ₁₆ ZnN ₄ O ₄ Cl ₂	1566	415	3208

Where L= C₄₂H₃₂N₄

Synthesis, Characterization and Antibacterial Studies of Macrocyclic Schiff Base derived from Malonic acid and o-phenylenediamine and its Cd (II), Co (II), Cu (II), Ni (II), and Zn (II) complexes

The synthesized compounds were also tested for their antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* using agar cup-plate method at three different concentrations. The results are listed in table 5 as determined by measuring the zone of inhibition (mm). The result showed that the Ni (II) complex has highest zone of inhibition (45mm) at the concentration of 50,000 $\mu\text{g/ml}$, while Cd (II) complex showed the lowest zone of inhibitions (32mm) at the same concentration against *Staphylococcus aureus*. The ligand was also found to be active against both *Staphylococcus aureus* and *Escherichia coli* though most of its complexes displayed enhanced activity. This was ascribed to the presence of metal ions in the lattice which makes it more powerful and effective bactericidal agents (Morad *et al.*, 2007).

Table 5: Antibacterial screening of the ligand and its complexes

S/ N	Compounds	Concentrations and zone of inhibition					
		50,000 $\mu\text{g/ml}$		5,000 $\mu\text{g/ml}$		500 $\mu\text{g/ml}$	
		S. Aureus	E. Coli	S. Aureus	E. Coli	S. Aureus	E. Coli
1	L	30 mm	34mm	16mm	22mm	11mm	-
2	[Cd(L)Cl ₂]	32mm	-	22mm	-	17mm	-
3	[Co(L)Cl ₂]	33mm	31mm	20mm	20mm	12mm	10mm
4	[Cu(L)Cl ₂]	34mm	34mm	17mm	25mm	10mm	10mm
5	[Ni(L)Cl ₂]	45mm	26mm	-	16mm	-	-
6	[Zn(L)Cl ₂]	36mm	35mm	20mm	24mm	17mm	15mm

Where L= C₄₂H₃₂N₄

Conclusion

7,16-dihydrodibenzo[1,4,8,11]tetraazacyclotetradecine-6,8,15,17-tetraol has been synthesized by the condensation of malonic acid and o-phenylenediamine. Its metal (II) complexes were prepared from Cd (II), Co (II), Cu (II), Ni (II) and Zn (II) chlorides respectively. The ligand and its complexes were characterized on the basis of solubility, melting/decomposition temperature, FT-IR, molar conductance and magnetic susceptibility measurements. The ligand acts in a tetradentate manner coordinating through the four nitrogens of the azomethine groups. An octahedral geometry has been proposed for the Cd (II), Co (II), Cu (II) and Zn (II) complexes, whereas square planar geometry has been proposed for the Ni (II) complex. Moreover, the antibacterial data revealed that the ligand was also found to be active against both *Staphylococcus aureus* and *Escherichia coli* with an enhanced activity in its complexes. Thus the compounds can be potential antibacterial agents upon further investigations.

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REFERENCES

- Aliyu H. N. and Adamu H. (2009): synthesis and characterization of n-(i-morpholinobenzyl) semicarbazide Manganese (II) And Iron (II) Complexes. *Bayero Journal of pure and applied Sciences*. Volume 2 (2), 143-148
- Canadas, M., Lopez-Torres, E., Arias, A. M., Mandioca, M. A., and Sevilla, M. T. (2000): spectroscopic and electrochemical properties of nickel(II), iron(II) and cobalt(II) complexes with benzilbisthiosemicarbazone. *Polyhedron*,

- 19(18-19), 2059-2068
- Chaudhary, A., Dave, S., Swaroop, R., and Singh, R. V. (2002): synthesis and biological studies of 16-26 membered tetraazamacrocyclic complex of tin(II). *Journal of Indian Chemical Society*, 79, 371
- Comba, P., Kerscher, M., Lampeka, Y. D., Lotzbeyer, L. L., Prizkow, H., and Tsybal, L. V. (2003): structural properties of cyclopentanone-bridged bis-macrocyclic ligand dicopper(II) complexes in the solid and in solution. *Inorganic Chemistry*, 42, 3387
- El-Hendawy A. M., Alkubasi, A. H., El-Ghany, A., El-Kourashym, K., and Sharab, M. N. (2001): *Polyhedron*. 20, 975
- Lindoy L. F. (1989): *The Chemistry of Macrocyclic Ligand Complexes*, Cambridge University Press, Cambridge
- Morad, F. M., Ei-ajaily, M. M., Gweirif, S. (2007): Preparation, physical characterization and antibacterial activity of Ni(II) Schiff Base complex. *Journal of Science and its Application*, 1, 72-75
- Puhilbhai, G., Vasudhevan, S., Kutti-Rani, S., and Rajago, G. (2009): *Spectrochimica Acta A*, 72, 687.
- Prabhakaran, B., Santhi, N., and Emayavaramban, M. (2013): Synthesis and spectral studies of Ru (II) carbonyl Schiff base complexes. *International letters of Chemistry, Physics and Astronomy*. 3, 53-66
- Sani U. and Baba M. A. (2016): synthesis, characterization, antimicrobial and antioxidant studies of 2-[(2-hydroxyphenyl) methylidene] hydrazine-1-carboxamide and its metal (II) complexes. *Bayero Journal of pure and applied sciences*. Volume 9 (1), 206-212
- Sengupta, P., Dinda, R., Ghosh, S., and Sheldrick, W. S. (2003): synthesis and characterization of some biologically active ruthenium(II) complexes of thiosemicarbazones of pyridine 2-aldehyde and thiophene 2-aldehyde involving some ring substituted 4-phenylthiosemicarbazides and 4-cyclohexylthiosemicarbazide. *Polyhedron*, 22, 477-453
- Singh D. P., Grover V., Kumar K., and Jain K. (2010): Metal ion prompted macrocyclic complexes derived from indole-2,3-dione (isatin) and O-phenylenediamine with their spectroscopic and antibacterial studies. *Acta Chimica Slovenica*. 57, 775-780
- Tas, E., Kilic, A., Durgun, M., Kupecik, L., Yilmaz, I., and Asslam, S. (2010): tetraaza macrocyclic complexes: synthesis, elucidation, antibacterial and antifungal studies. *Spectrochimica Acta A*, 75, 811
- Tyagi, M., Chandra, S., and Choudhary, S. K. (2001): Tetraaza macrocyclic complexes: Synthesis, spectral and antifungal studies. *Journal of chemical and pharmaceutical research*. 3 (1): 56-63.