



SYNTHESIS AND ANTIBACTERIAL STUDIES OF MALONIC ACID DERIVED SCHIFFBASE AND ITS COMPLEXES OF Co(II), Ni(II), Zn(II) AND Cd(II)

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ABSTRACT

The schiffbase 1,4,8,11-tetraazacyclotetradeca-4,7,11,14-tetraene-5,7,12,14-tetra-ol was synthesized in ethanolic media by the condensation of malonic acid and ethylene diamine in the presence of the corresponding metal salts. The ligand and its complexes were characterized using various characterization techniques. The complexes are formulated as $[M(L)]X_2$ due to their high conductivity values, where $M = \text{Co(II)}, \text{Ni(II)}, \text{Zn(II)}, \text{and Cd(II)}$ and $X = \text{Cl}$. The job method analysis revealed 1:1 metal-ligand ratio. The ligand and its complexes have been screened for in-vitro antimicrobial activity against *Staphylococcus aureus* (gram positive) and *Escherichia coli* (gram negative). Zinc complex showed highest activity against all the microbes tested while the Nickel complex showed the lowest activity.

INTRODUCTION

The design and study of metal-containing macrocycles is an interesting field of chemistry [1]. Several synthetic and natural macrocyclic compounds have been investigated due to their fascinating chemistry [2].

Transition metals complexes containing macrocycles are of considerable interest in terms of structural and coordination chemistry [3]. It is one of the most attractive and experimentally demanding frontiers in modern chemical sciences. It has grown in a half century from a readily defined and limited area into the most active research field of inorganic chemistry [4].

Macrocyclic compounds continue to attract considerable interest due to their countless possible applications arising from their ability to bind different kinds of substrates and their functional similarities with many bioligands[5].

The macrocyclic complexes showed a widespectrum of biological activities and appear

to be very promising for potential use as antifertile, antibacterial, antifungal, anti cancer [6]. A number of nitrogen donor macrocyclic derivatives have long been used for analytical, industrial and medical applications [7].

Motivated by these facts, this paper reported the synthesis, spectral and antibacterial studies of complexes of Co(II), Ni(II), Zn(II), and Cd(II) metal complexes derived from a schiff base formed by the condensation reaction of Malonic acid and ethylene diamine (Scheme 1).

EXPERIMENTAL

MATERIALS

All the chemicals and solvents(AR grade) were obtained from market and used as received. (Ethylene diamine, Malonic acid, Ethanol, Hydrochloric acid, Phosphorus pentoxide and Transition metal salts). The glass wares were washed, rinsed with ethanol and dried in oven before use.

PREPARATION OF THE LIGAND

A hot ethanolic solution (20 mL) of malonic acid (0.02 mol) and an ethanolic solution (20 mL) of ethylene-diamine (0.02 mol) were mixed with constant stirring. The mixture was refluxed at 80°C for 8 hrs in the presence of few drops of conc. HCl. The resulting solution was kept overnight at room temperature. Upon cooling a cream compound precipitate was formed. The precipitate was filtered, washed with cold Ethanol and dried in vacuum over P₄O₁₀.

SYNTHESIS OF METAL COMPLEXES

Hot ethanolic solution (20 mL) of the corresponding metal salts (0.001mol) and a hot ethanolic solution (20 ml) of the ligand (0.001mol) were mixed together with constant stirring. The reaction mixture was refluxed for 6 hrs at 75-80°C. On cooling a coloured compound was formed. The compound was filtered, washed with cold ethanol and dried in vacuum over P₄O₁₀.

SOLUBILITY TEST

The solubility test was carried out in various solvents by adding 0.1g of the samples in 3ml of the solvent and allowed to stand.

DETERMINATION OF MELTING/ DECOMPOSITION TEMPERATURE

10 mg of the ligand and/or complexes were placed in a dry capillary tube and mounted onto the Ag100 Barnstead/Electrothermal. The melting/decomposition temperature of each of the compound was read from the thermometer.

CONDUCTIVITY MEASUREMENT

The molar conductance measurements of the ligand and its complexes were carried out in DMSO at room temperature and recorded using EC 215 conductivity meter.

JOB'S METHOD ANALYSIS

The ligand to metal ratio in the complexes was determined using "Job's method". A 0.001M solution of the ligand and 0.001M solution of the metal salt were prepared. Ten different solutions of variable volumes of the ligand to metal were prepared and their absorbances were separately determined at a fixed wavelength using T60 uv-vis spectrophotometer.

IN-VITRO ANTIBACTERIAL STUDIES

The antimicrobial activity of the ligand and its metal complexes were determined by agar well diffusion method against *Staphylococcus aureus* (gram positive) and *Escherichia coli* (gram negative). The bacterial cultures were maintained on the nutrient agar media by sub-culturing and incubation at approved temperature for 24hrs. The antibacterial activity was assessed by measuring the diameter of the inhibition zone. The test was conducted in triplicate and the mean of the diameter of inhibition was calculated. The activity of the ligand and complexes were compared with that of the standard drug.

TABLE1. Solubility Test

S/N	Compounds	Water	Met	Ethanol	DMSO	Benzene	Chloroform	Acetone	Diethyl ether
1.	C ₁₀ H ₁₆ N ₄ O ₄	S	SS	SS	S	IS	SS	IS	IS
2.	C ₁₀ H ₁₆ CoN ₄ O ₄ Cl ₂	S	S	SS	S	IS	SS	IS	IS
3.	C ₁₀ H ₁₆ NiN ₄ O ₄ Cl ₂	S	S	SS	S	IS	SS	IS	IS
4.	C ₁₀ H ₁₆ ZnN ₄ O ₄ Cl ₂	S	S	SS	S	IS	SS	IS	IS
5.	C ₁₀ H ₁₆ CdN ₄ O ₄ Cl ₂	S	S	SS	S	IS	SS	IS	IS

KEY: S=soluble SS=Sparingly Soluble IS=Insoluble, Met = methanol

TABLE2: Physical Data of the Synthesized Ligand and its Complexes

S/NO	MOLECULAR FORMULA	COMPOUNDS	YIELD (%)	MOL. WT.	M.P. (°C)	D.T (°C)	COLOUR
1.	C ₁₀ H ₁₆ N ₄ O ₄	(C ₁₀ H ₁₆ N ₄ O ₄)	72	256.12	154		Cream
2.	C ₁₀ H ₁₆ CoN ₄ O ₄ Cl ₂	[Co(C ₁₀ H ₁₆ N ₄ O ₄)]X ₂	72	386.10		264	Pink
3.	C ₁₀ H ₁₆ NiN ₄ O ₄ Cl ₂	[Ni(C ₁₀ H ₁₆ N ₄ O ₄)]X ₂	74	385.86		287	Green
4.	C ₁₀ H ₁₆ ZnN ₄ O ₄ Cl ₂	[Zn(C ₁₀ H ₁₆ N ₄ O ₄)]X ₂	68	392.54		211	Milk
5.	C ₁₀ H ₁₆ CdN ₄ O ₄ Cl ₂	[Cd(C ₁₀ H ₁₆ N ₄ O ₄)]X ₂	65	439.58		192	Off white

Where: X=Cl

TABLE 3: Elemental Analysis and Molar Conductance of the Synthesized Ligand and its Complexes

S/N	MOLECULAR FORMULA	COMPOUNDS	MOLAR CONDUCTANCE (ohm ⁻¹ cm ² mole ⁻¹)
1	C ₁₀ H ₁₆ N ₄ O ₄	(C ₁₀ H ₁₆ N ₄ O ₄)	-
2	C ₁₀ H ₁₆ CoN ₄ O ₄ Cl ₂	[Co(C ₁₀ H ₁₆ N ₄ O ₄)]X ₂	147
3	C ₁₀ H ₁₆ NiN ₄ O ₄ Cl ₂	[Ni(C ₁₀ H ₁₆ N ₄ O ₄)] X ₂	141
4	C ₁₀ H ₁₆ ZnN ₄ O ₄ Cl ₂	[Zn(C ₁₀ H ₁₆ N ₄ O ₄)] X ₂	222
5	C ₁₀ H ₁₆ CdN ₄ O ₄ Cl ₂	[Cd(C ₁₀ H ₁₆ N ₄ O ₄)] X ₂	329

Where: X=Cl

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

S/N	MOLECULAR FORMULA	COMPOUNDS	Assignments		
			v (C=N)	v(O-H)	v(M-N)
1	C ₁₀ H ₁₆ N ₄ O ₄	(C ₁₀ H ₁₆ N ₄ O ₄)	1655	2935	-
2	C ₁₀ H ₁₆ CoN ₄ O ₄ Cl ₂	[Co(C ₁₀ H ₁₆ N ₄ O ₄)]X ₂	1596	2997	419
3	C ₁₀ H ₁₆ NiN ₄ O ₄ Cl ₂	[Ni(C ₁₀ H ₁₆ N ₄ O ₄)] X ₂	1600	2902	418
4	C ₁₀ H ₁₆ ZnN ₄ O ₄ Cl ₂	[Zn(C ₁₀ H ₁₆ N ₄ O ₄)] X ₂	1600	2902	418
5	C ₁₀ H ₁₆ CdN ₄ O ₄ Cl ₂	[Cd(C ₁₀ H ₁₆ N ₄ O ₄)] X ₂	1628	2980	426

Where: X=Cl

TABLE 5: Job's method analysis

mole fraction, x (total volume = 10ml)	Absorbance at different wavelength, (λnm)			
	Co(II)	Ni(II)	Zn(II)	Cd(II)
0.1	0.13	0.20	0.13	0.11
0.2	0.19	0.31	0.19	0.19
0.3	0.40	0.48	0.38	0.21
0.4	0.40	0.53	0.40	0.32
0.5	0.45	0.72	0.53	0.47
0.6	0.33	0.47	0.32	0.21
0.7	0.22	0.36	0.21	0.16
0.8	0.07	0.14	0.14	0.10
0.9	0.04	0.08	0.11	0.12

TABLE 6: Anti bacterial Screening Data of the Ligand and its Metal Complexes

Compounds	Anti-bacterial					
	Staphylococcus			Escherichia coli		
	10 ⁻¹	10 ⁻²	10 ⁻³	10 ⁻¹	10 ⁻²	10 ⁻³
(C ₁₀ H ₁₆ N ₄ O ₄)	6mm	6mm	6mm	6mm	6mm	6mm
[Co(C ₁₀ H ₁₆ N ₄ O ₄)]X ₂	30mm	14mm	07mm	26mm	18mm	12mm
[Ni(C ₁₀ H ₁₆ N ₄ O ₄)] X ₂	15mm	16mm	06mm	24mm	16mm	07mm
[Zn(C ₁₀ H ₁₆ N ₄ O ₄)] X ₂	31mm	25mm	10mm	30mm	20mm	14mm
[Cd(C ₁₀ H ₁₆ N ₄ O ₄)] X ₂	25mm	22mm	12mm	21mm	18mm	18mm
Ciproflaxacin (+)	43mm	38	32	57mm	43	36
Distilled water (-)	6mm	6mm	6mm	6mm	6mm	6mm

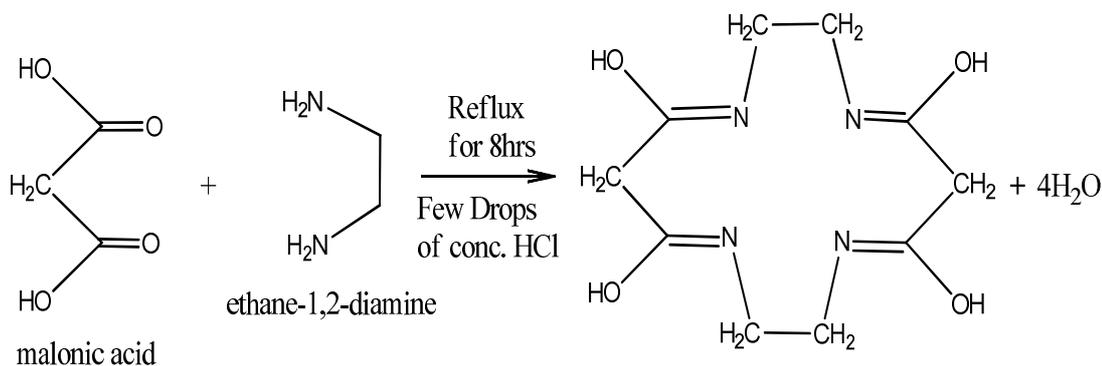
DISCUSSION

The prepared ligand and its metal complexes shows complete solubility in water and Dimethyl sulfoxide (DMSO) but slightly or completely insoluble in most of the organic solvents used as shown in table 1. This indicates that the synthesized compounds are more of inorganic than organic and hence can be considered as polar compounds because of their high solubility in polar solvents and insolubility or slightly soluble in non polar or partially polar solvent respectively.

The melting point/decomposition temperature of the ligand and its complexes ranges between 154°C – 287°C as shown in table 2. The high melting/decomposition temperature range values indicate high purity and thermal stability of the compounds. Moreover, the more obtained in a good yield. temperature of the complexes are higher than that of the free ligand which indicates incorporation of the various metal and can also be an evidence for the stability of the complexes.

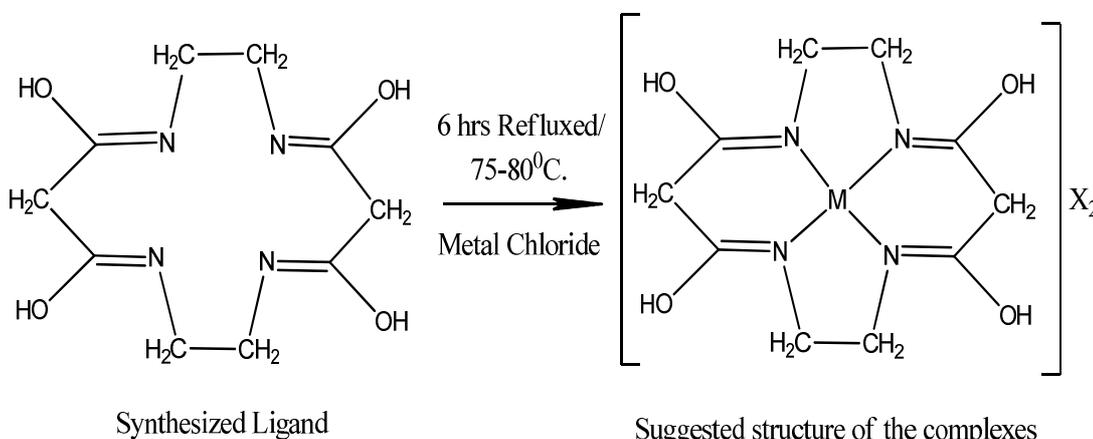
The complexes give molar conductance values of the range 141-329 ohm⁻¹cm²mole⁻¹ indicating the presence of counter ions [8-10]. Thus these complexes may be formulated as [M (L)] X₂ Where M=Co(II), Ni(II), Zn(II) and Cd(II) X= Cl.

The IR spectrum of the ligand exhibited complete absence of band that correspond to primary amine and/or carbonyl group. This suggests the condensation of the amino group with the carbonyl for the formation of azomethine, this is apparently shown at 1655 cm⁻¹ (C=N). However, this band has shifted to a lower frequency on complexation. The decrease in absorption bands indicates the participation of C=N group in coordination with the metal ion(s). Moreover, the noticeable bands at 2902-2997cm⁻¹ and 411- 426 cm⁻¹ can be assigned to various ν(O-H) and ν(M-N) groups respectively. Moreover, the job method analysis revealed 1:1 metal-ligand ratio as noticeable in Table 5 and Figure 1 - 4.



Scheme 1: Synthesis of the ligand

Suggested Structure of the Ligand



Synthesized Ligand

Suggested structure of the complexes

Scheme 2: Synthesis of the complexes
Where M= Co(II), Ni(II), Zn(II) and Cd(II) and X=Cl

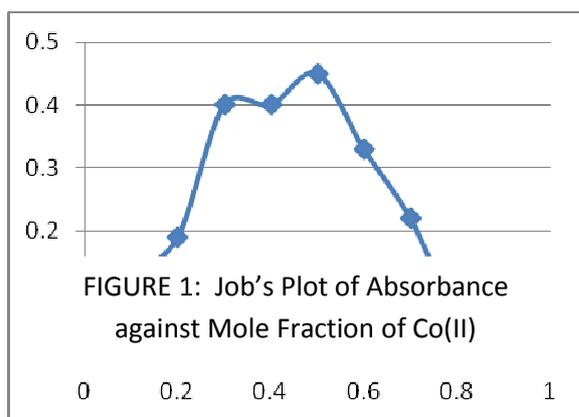


FIGURE 1: Job's Plot of Absorbance against Mole Fraction of Co(II)

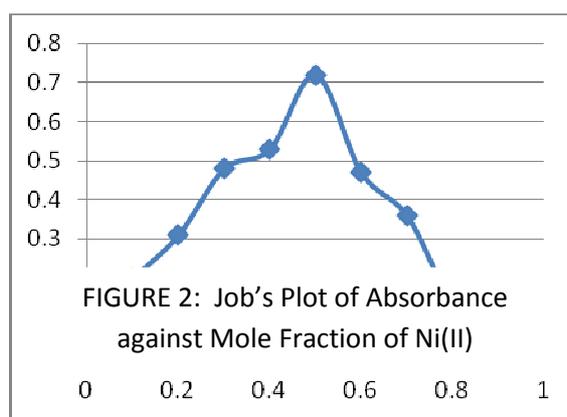


FIGURE 2: Job's Plot of Absorbance against Mole Fraction of Ni(II)

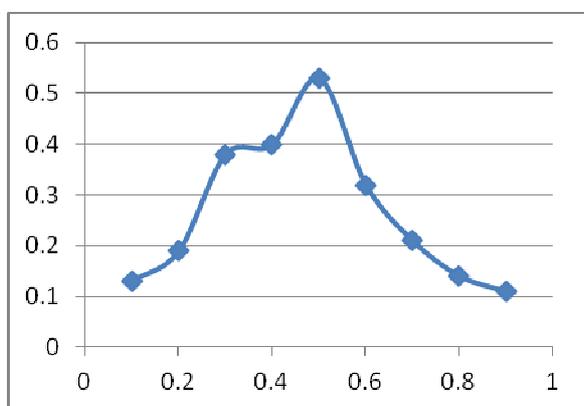


FIGURE 3: Job's Plot of Absorbance against Mole Fraction of Zn(II)

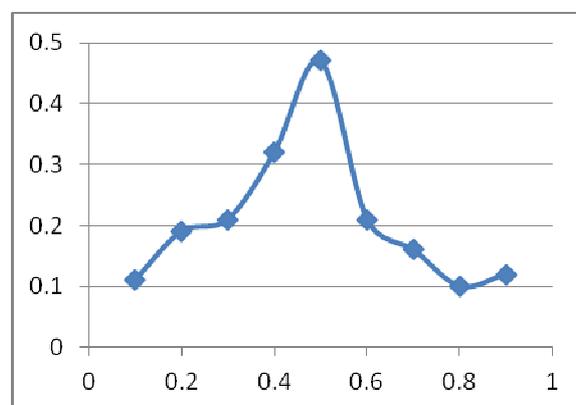


FIGURE 4: Job's Plot of Absorbance against Mole Fraction of Cd(II)

All the complexes tested are active against gram-positive (*Staphylococcus aureus*) and gram-negative (*Escherichia coli*) bacteria. The former being much susceptible to the compounds compared to the later bacterial isolates as shown in table 6. In addition, the complexes show high antibacterial activity than the free ligand which may be due to the presence of metal ion in the lattice of the ligand which makes it more active antibacterial.

The antibacterial results show inhibition on *Staphylococcus aureus* and *Escherichia coli* in the following order Ligand < Ni < Gd < Co < Cd < Zn and Ligand < Ni < Co < Cd < Gd < Zn respectively. From this order, Zinc complex was found to be

the most active against all the microbes tested while the Ni complex has the least activity.

CONCLUSION

The macrocyclic complexes synthesized and characterized were found to be scarcely investigated and their biological activities were less assessed. This paper therefore considers the use of macrocyclic compounds for various biological studies as pertinent due to their analogy with many bioligands such as porphyrin, this will provide an avenue for substituting and/or upgrading any bioligand malfunctioning. Therefore, a detail characterization need to be conducted to fully ascertain the structures of these compounds for their possible used as potential anti bacterial.

REFERENCES

1. Chandra, S., Gupta, L. K., and Agrawal, S. (2007). Modern spectroscopic and biological approach in the characterization of a novel 14-membered [N₄] macrocyclic ligand and its transition metal complexes. *Transition Metal Chemistry*, 32, 240–245.
2. Rakesh, L. S., Sabharwal, K. N., AND Paul, A.N. (2015). Synthesis and Characterization of [16]-Membered Dioxo Diaza Naphthaldehyde based Macrocyclic Ligands and its Complexes of Co(III), Ni(II) and Cu(II) Perchlorate ions. *International Journal of pharmaceutical sciences and research*, 6, 4895-4903.
3. Wang, Q., Tang, K. Z., Liu, W. S., Tang, Y., and Tan, M. Y. (2009). Lanthanide complexes derived from hexadentate macrocyclic ligand: Synthesis, spectroscopic and thermal investigation. *Journal of Solid State Chemistry*, 182, 31.
4. Chandra, S., & Kumar, R. (2009). Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. *Spectrochimica Acta Part A*, 66, 74.
5. Bozic, L. T., Marotta E. and Traldi P. (2007). Macrocyclic complexes: Synthesis and characterization. *Polyhedron*, 26, 1663.
6. Chaudhary, A., Bansal, N., Garraj, A., and Singh, R. V. (3003). Antifertility, antibacterial, antifungal and percent disease incidence aspects of macrocyclic complexes of manganese(II). *Journal of Inorganic Biochemistry*, 96, 393-400.
7. Singh, D. P., Kumar, R., Malik, V., and Tyagi, P. (2007). Template synthesis, spectroscopic studies and biological activities of macrocyclic complexes derived from thiocarbohydrazide and glyoxal. *Journal of Enzyme Inhibition Medicinal Chemistry*, 22, 177-182.
8. Monika, T., Sulekh C., and Sunil, Kumar. C. (2011). Tetraaza macrocyclic complexes: Synthesis, spectral and antifungal studies. *Journal of Chemical and Pharmaceutical Research* 3(1), 56-63.
9. Singh, D. P., Vidhi G., Krishan, K., and Kiran J. (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.
10. Sulekh, C., Monika T., and Swati A. (2010). Synthesis and characterization of a tetraaza macrocyclic ligand and its cobalt(II), nickel(II) and copper(II) complexes. *Journal of Serbian Chemical Society*, 75(7), 935–941.