



Synthesis, Characterization and antibacterial studies of tetraazamacrocyclic ligand and its Cd (II), Co (II), Cu (II), Ni (II), and Zn (II) complexes

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Abstract

Schiff base 6, 8, 15, 17-tetraphenyl-7, 16dihydrodibenzo[1,4,8,11]tetraazacyclotetradecine has been synthesized by the condensation of dibenzoylmethane and *o*-phenylenediamine. Its metal (II) complexes were prepared from the chloride salts of Cd(II), Co(II), Cu(II), Ni(II) and Zn(II). The ligand and its complexes were characterized by solubility, melting/decomposition temperature, FT-IR, molar conductance and magnetic susceptibility analyses. The ligand show band at 1696cm^{-1} due to azomethine which confirms the formation of the ligand, while this peak shifted towards the lower frequencies of 1618cm^{-1} , 1678cm^{-1} , 1596cm^{-1} , 1596cm^{-1} and 1596cm^{-1} in the spectra of Cd(II), Co(II), Cu(II), Ni(II), Zn(II) complexes respectively. This also indicates that the nitrogen of the azomethine have coordinated to the metal ions. An octahedral geometry has been proposed for the Cd(II), Co(II), Cu(II) and Zn(II) complexes whereas square planar geometry was proposed for the Ni(II) complex. 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 Cd(II) complex displayed an enhanced activity with the highest zone of inhibition (40mm) while Cu(II) complex showed least activity with 25mm zone of inhibition.

Keywords: Synthesis, characterization, ligand, complexes, antibacterial

INTRODUCTION

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



Macrocyclic compounds are synthetic or natural polydentate ligands, containing their donor atoms incorporated in a cyclic backbone or/and in substituents attached to it. They normally contain three donor atoms in a ring that have a minimum of nine atoms. The coordination chemistry of these compounds has now become a major subdivision of inorganic chemistry, while the active search for new types of macrocycles and the number of their applications has systematically increased since their discovery (Lindoy, 1989).

Several synthetic and natural macrocyclic compounds have been investigated, its chemistry has attracted the interest of both inorganic and bioinorganic chemists in recent years because of its 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 tetraazamacrocyclic ligand and their metal complexes have attracted growing interest among the coordination and bioinorganic chemist (Taset *et al.*, 2010). Macrocyclic Schiff base ligands have received special attention because of their mixed soft-hard donor character, versalite 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 metal macrocyclic complexes have received much attention as an active part of metalloenzymes (Canadaset *et al.*, 2000) as biomimic model compounds due to their resemblance with natural proteins like hemerythrin and enzymes (Chaudhary, 2002). The family of complexes with aza-macrocyclic ligands has remained a focus of scientific attention for many decades (Singh *et al.*, 2010).

This paper reports the synthesis of 6, 8, 15, 17-tetraphenyl-7, 16-dihydrodibenzo[1, 4, 8, 11]tetraazacyclotetradecine derived from Dibenzoyl methane and o-phenylenediamine, its complexes with cadmium (II), cobalt (II), copper (II), nickel (II) and zinc (II) and their antibacterial activities were studied.

MATERIALS AND METHODS

All the chemicals used were of analytical grade, procured from Zayo-Sigma 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 stumadzu FTIR spectrophotometer at the range of 4000-400 cm^{-1} . The magnetic susceptibility of the complexes was determined on MSB MKI at 25°C.

PREPARATION OF THE LIGAND

A hot ethanolic solution (20 ml) of dibenzoylmethane (4.49g, 0.02mol) and anethanolic solution (20 ml) of o-phenylenediamine (2.16g, 0.02mol) were mixed under constant stirring. The mixture was refluxed at 80-85°C for 8 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 P_4O_{10} in vacuum.



PREPARATION OF METAL COMPLEXES

An ethanolic solution (20 ml) of the corresponding metal salts (0.001mol) and a hot ethanolic solution (20 ml) 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.

RESULTS

Table 1: Physical data of the synthesized ligand and its complexes

S/N	COMPOUND	COLOUR	YIELD (%)	M.P/D .T (°C)	MOL. WT.
1	(C ₄₂ H ₃₂ N ₄)	Dark brown	82.53	75	592.26
2	[Cd(L ₁)Cl ₂]	Brown	79.73	150	706.17
3	[Co(L ₁)Cl ₂]	Black	60.24	124	651.20
4	[Cu(L ₁)Cl ₂]	Dark brown	61.45	205	655.19
5	[Ni(L ₁)Cl ₂]	Black	65.79	320	650.20
6	[Zn(L ₁)Cl ₂]	Dark brown	85.06	114	656.19

Table 2: Solubility test of the ligand and its metal (II) complexes in some common solvents

S/N	Compound	Acetone	Aceto-nitrile	Chloroform	Diethylether	Distilled water	Ethanol	Ethyl Acetate	DMSO	Methanol	n-hexane	xylene
1	(C ₄₂ H ₃₂ N ₄)	S	S	S	SS	IS	S	S	S	S	IS	IS
2	[Cd(L)Cl ₂]	SS	SS	IS	SS	IS	S	SS	S	S	IS	IS
3	[Co(L)Cl ₂]	S	SS	IS	IS	IS	SS	IS	S	S	IS	IS
4	[Cu(L)Cl ₂]	SS	IS	IS	IS	IS	SS	IS	S	SS	IS	IS
5	[Ni(L)Cl ₂]	SS	IS	IS	IS	IS	S	SS	S	S	IS	IS
6	[Zn(L)Cl ₂]	S	S	SS	SS	IS	S	IS	S	S	IS	IS

Where L= C₄₂H₃₂N₄

Table 3: Magnetic moments and molar conductance of the synthesized complexes

S/N	COMPOUND	MOLECULAR FORMULA	μ _{eff} (B.M)	MOLAR CONDUCTANCE (Ω ⁻¹ cm ² mole ⁻¹)
1	[Cd(L)Cl ₂]	C ₄₂ H ₃₂ CdN ₄ Cl ₂	diamagnetic	59
2	[Co(L)Cl ₂]	C ₄₂ H ₃₂ CoN ₄ Cl ₂	3.87	113
3	[Cu(L)Cl ₂]	C ₄₂ H ₃₂ CuN ₄ Cl ₂	1.73	55
4	[Ni(L)Cl ₂]	C ₄₂ H ₃₂ NiN ₄ Cl ₂	2.83	240
5	[Zn(L)Cl ₂]	C ₄₂ H ₃₂ ZnN ₄ Cl ₂	diamagnetic	53



Table 4: 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]	0.29	0.84	1.77	2.97	3.92	3.97	3.88	2.32	1.36	0.01
2	[Co(L)Cl ₂]	0.34	0.74	1.59	2.54	3.51	3.61	3.23	2.12	1.15	0.02
3	[Cu(L)Cl ₂]	0.38	0.79	1.83	3.08	3.92	4.07	3.36	2.43	1.26	0.01
4	[Ni(L)Cl ₂]	0.35	0.81	1.70	2.78	3.81	3.89	3.35	2.18	1.17	0.02
5	[Zn(L)Cl ₂]	0.36	0.80	1.88	2.72	3.43	3.79	3.30	2.07	1.31	0.01

Table 5: Infrared Absorption Frequencies (cm⁻¹) of the Ligand and its Metal Complexes

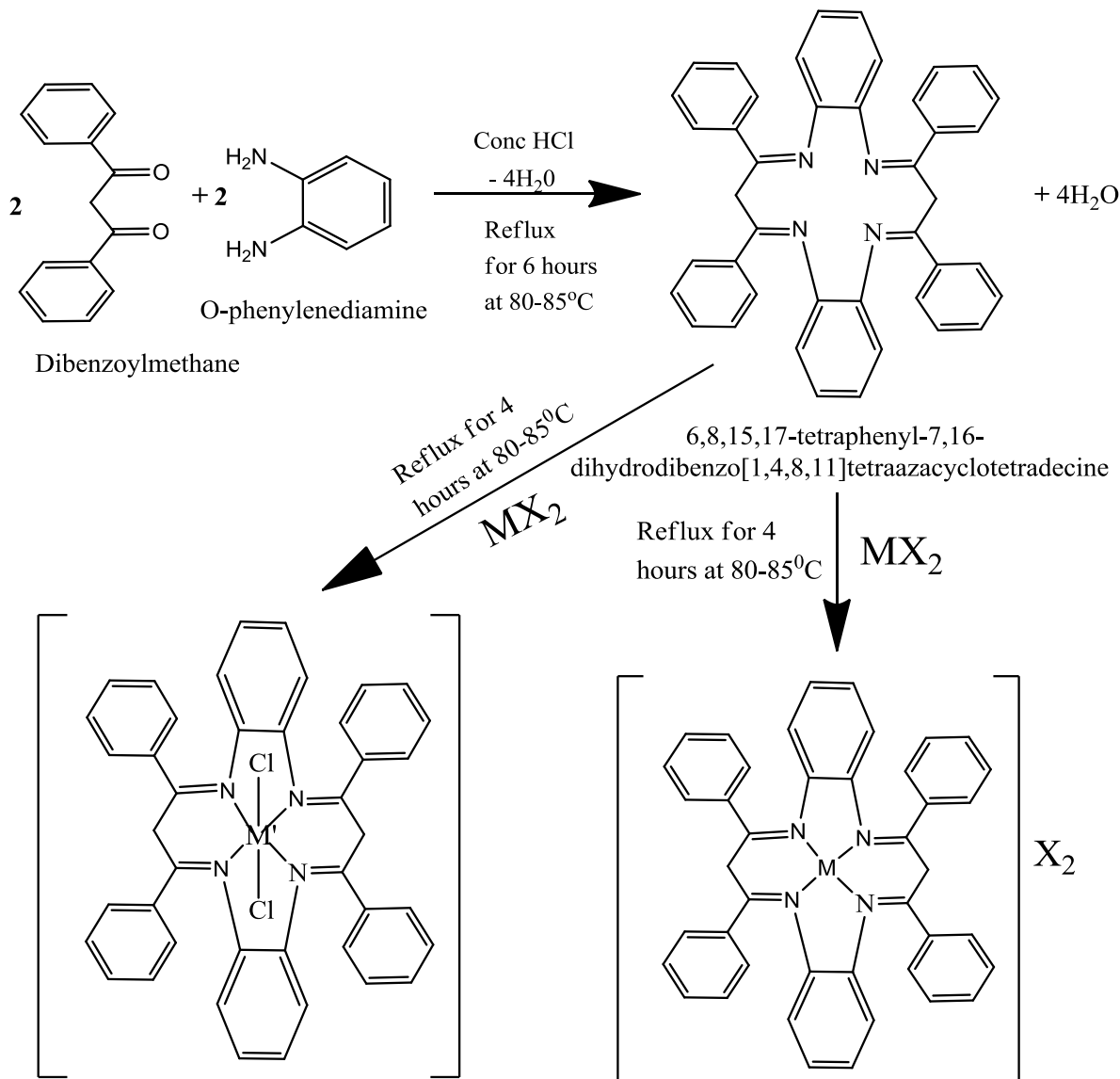
S/N	COMPOUND	MOLECULAR FORMULA	ASSIGNMENTS	
			ν (C=N)	ν (M-N)
1	L	(C ₄₂ H ₃₂ N ₄)	1696	-
2	[Cd(L)Cl ₂]	C ₄₂ H ₃₂ CdN ₄ Cl ₂	1618	413
3	[Co(L)Cl ₂]	C ₄₂ H ₃₂ CoN ₄ Cl ₂	1678	407
4	[Cu(L)Cl ₂]	C ₄₂ H ₃₂ CuN ₄ Cl ₂	1596	427
5	[Ni(L)Cl ₂]	C ₄₂ H ₃₂ NiN ₄ Cl ₂	1596	416
6	[Zn(L)Cl ₂]	C ₄₂ H ₃₂ ZnN ₄ Cl ₂	1596	409

Table 6: Antibacterial screening of the ligand and its complexes

S/N	Compounds	Concentrations and zone of Inhibition					
		50,000µg/ml		5,000µg/ml		500µg/ml	
		<i>S. Aureus</i>	<i>E. Coli</i>	<i>S. Aureus</i>	<i>E. Coli</i>	<i>S. Aureus</i>	<i>E. Coli</i>
1	L	29mm	28mm	22mm	25mm	10mm	19mm
2	[Cd(L)Cl ₂]	34mm	40mm	22mm	31mm	16mm	25mm
3	[Co(L)Cl ₂]	27mm	35mm	19mm	23mm	16mm	17mm
4	[Cu(L)Cl ₂]	25mm	32mm	23mm	28mm	16mm	22mm
5	[Ni(L)Cl ₂]	34mm	35mm	23mm	20mm	15mm	10mm
6	[Zn(L)Cl ₂]	32mm	32mm	23mm	24mm	14mm	20mm

Where L= C₄₂H₃₂N₄

SCHEME OF THE REACTION



Where $M=\text{Ni(II)}$, $M'=\text{Cd(II)}$, Co(II) , Cu(II) , and Zn(II) and $X=\text{chloride ions}$

Scheme 1: Synthesis of ligand and its metal complexes

DISCUSSION

The condensation of dibenzoylmethane and O-phenylenediamine yields 6,8,15,17-tetraphenyl-7,16-dihydrodibenzo[1,4,8,11]tetraazacyclotetradecine ligand. The metal (II) complexes were obtained by refluxing the ligand and the metal chlorides as shown in the scheme of the reaction. The compounds were obtained in high yields as shown in table 1 which provide enough quantities for various characterization and antibacterial study.



The solubility test as shown in table 2 showed that the ligand and its metal complexes exhibit different behaviour in some common solvents. Most of the compounds were found to be soluble in methanol and ethanol with only few that were slightly soluble. The ligand and its metal complexes are completely soluble in dimethyl sulphoxide (DMSO) which may be due to the high dielectric constant of the solvent (Sani and Baba, 2016).

The ligand is dark brown in colour while the complexes appeared to have brown, black, dark brown, black and dark brown colours for Cd(II), Co(II), Cu(II), Ni(II) and Zn(II) complexes respectively. The colour of the ligands can be attributed to the presence of the chromophore (C=N) in its structure while that of the complexes is assignable to the charge transfer and various electron transitions.

The ligand melts at a temperature of 75°C, while its metal complexes decomposed at temperatures of 150°C, 124°C, 205°C, 320°C and 114°C for Cd(II), Co(II), Cu(II), Ni(II) and Zn(II) complexes respectively and it indicates possible coordination of the various metals used and high thermal stabilities of the compounds. The compounds were assigned the compositions shown in table 1. The molar conductance values of the Ni(II) complex in DMSO was 240Ω⁻¹cm²mole⁻¹ indicating 1:2 electrolytic nature. However, the molar conductance values for the rest of the complexes falls within the range 55-113Ω⁻¹cm²mole⁻¹ as shown in table 3. 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.

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 at maximum absorbance corresponding to the ligand mole fraction suggest 1:1 metal-ligand ratio in the complexes as shown in table 4. Thus these complexes may be formulated as [M(L)]X₂ and [M'(L)₂]X₂ where M=Ni(II) and M'= Cd(II), Co(II), Cu(II), Zn(II), L= ligand, while X=Cl.

At room temperature, the Co(II), Cu(II) and Ni(II) complexes showed magnetic moments of 3.87, 1.73 and 2.83 corresponding 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 important IR bands and their assignment in the ligand and its complexes are shown in table 5. 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 1696cm⁻¹ that is assignable to azomethine and confirms the formation of the ligand. On complexation, the peak shifted towards the lower frequencies 1618cm⁻¹, 1678cm⁻¹, 1596cm⁻¹, 1596cm⁻¹ and 1596cm⁻¹ for Cd(II), Co(II), Cu(II), Ni(II), Zn(II) complexes respectively which indicates that the nitrogen atoms of azomethine groups are coordinated to the metal ions. The absorption peaks at 413cm⁻¹, 407cm⁻¹, 427cm⁻¹, 416cm⁻¹ and 409cm⁻¹ can be assigned to ν(M-N) for Cd(II), Co(II), Cu(II), Ni(II), Zn(II) complexes respectively.

The synthesized compounds were also tested for their antibacterial activity against *Staphylococcus aureus* and *Echerichia coli* using agar cup-plate method at three different concentrations. The results are



listed in table 6 as determined by measuring the zone of inhibition (mm). The result showed that the Cd(II) complex has highest zone of inhibition(40mm)at the concentration of 50,000 μ g/ml against *Echericha coli*, while Cu(II) and Zn(II) complexesshowed the lowest zone of inhibitions(32mm)at the same concentration against *Echericha coli*. The ligand was also found to be active against both *Staphylococcus aureus* and *Echerichia 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 (Moradet *al.*, 2007).

CONCLUSION

6,8,15,17-tetraphenyl-7,16-dihydrodibenzo[1,4,8,11]tetraazacyclotetradecine has been synthesized by the condensation of dibenzoylmethane 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 *Echerichia coli* though most of its complexes displayed enhanced activity as complexation tends to make the ligands acts more powerful and effective bactericidal agents. The activity increased with increasing concentration of the complexes.



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