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SYNTHESIS, ANALYSIS AND BIOACTIVITY EVALUATION OF COPPER(II) TETRADENTATE SCHIFF BASE COMPLEX

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ABSTRACT

A tetradentate Schiff base ligand was prepared by a 2:1 molar condensation of 4 – (Benzeneazo) salicylaldehyde with o-phenylenediamine. The copper (II) chelate was synthesized by refluxing ethanolic solutions of the schiff base ligand and copper (II) chloride. The ligand and the copper (II) complex were characterized by melting point, decomposition temperature, molar conductance, infrared, elemental analysis, antibacterial, antifungal and potentiometry. The ligand is orange, has a melting point temperature of 193^oC, and percentage yield of 70%. The copper (II) complex is red, has decomposition temperature of 286^oC and percentage yields of 62%. The ligand and its copper (II) complex are not soluble in water and most common organic solvents except DMSO and DMF. The molar conductance of the complex determined is 7.9 ohm^{-1}cm^{2}mol^{-1}. The band at 1590cm^{-1} in the infrared spectral data of the ligand is assigned to v(C=N) stretching vibrations, which undergoes a shift to lower wave numbers at 1538cm^{-1} on coordination to the metal ions. The band at 586 and 511cm^{-1} are attributable to v(Cu-N) and v(Cu-O) vibration modes. The elemental analysis of the complex established 1:1 copper – ligand ratio. The antifungal and antibacterial tests carried out on the ligand and its copper (II) copper showed moderate activity. The dissociation constant of the ligand determined is 11.67, indicating a week acid. The ratio of metal to ligand determined potentiometrically suggested 1:1. The stability constant and the Gibb's free energy of copper (II) complex determined is 3.16X10^{11} and 4.15 KJmol^{-1}, respectively, establishing that the complex is very stable.

Keywords: 4 – (Benzeneazo) Salicylaldehyde, Potentiometry, Complex compound, Schiff base, Molar Conductance and Solubility.

INTRODUCTION

A Schiff base is a compound formed from the condensation of either an aldehyde or a ketone [1-3]. The carbonyl group of the aldehyde gives aldimines while that of ketone gives ketoimines. It has been known that different metal ions on interaction with Schiff bases yield chelates, for example Tsumaki [4] reported [Co(sal$_2$-en)] Complex which received a great attention owing to its ability to undergo reversible adduct formation with molecular oxygen. The oxygenation ability of the complex was first recognized by Hassan *et al* [5]. However, the mechanism for the oxygenation process was not well understood until recently with the advent of modern physical techniques. Xishi *et al* [6], reported the synthesis and characterization of a novel Schiff base ligand formed from the condensation of 2, 2-bis (P-methoxyphenylamine) and Salicylaldehyde and its Mn(II), Co(II) and Cu(II) complexes. Then Ben Saber *et al* [7], reported the synthesis and characterization of Cr(III), Fe(III), Co(II) and Ni(II) complexes with a Schiff base derived from 4-dimethylamino benzaldehyde and primary amines. The chemical analysis data showed the formation of (1:1) metal - ligand ratio and a square planar geometry was suggested for Co(II) and Ni(II) complex while an octahedral structure was suggested for Cr(III) and Fe(III) complexes. Ben Saber *et al* [7] reported the synthesis of a Schiff base derived from salicylaldeyde, and Histidine and its complex compounds with divalent transition metal ions. The complexes were investigated by elemental analysis and were found to be of 1:1 metal to ligand ratio.

Transition metal Schiff base complexes are used in various fields, such as medicine, agriculture, industries etc. For

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example, [Co (acac$_2$-en)] in dimethylformamide, pyridine and substituted pyridines proved to be involved in oxygen metabolism [8]. Transition metal complexes with 1, 10 – phenanthroline and 2, 2 – bipyridine are used in petroleum refining [9]. Schiff base formed by the condensation of 1-formyl-2-hydry-3- naphtholic arylamide with O-hydroxyl or O-methoxy aniline complexes of Co (II), Ni (II), Cu (II) and Zn (II) are useful as figments [10]. Oxovanadium Complexes have been found strongly active, against some type of Leukemia [11]. Transition metal complexes derived from a number of amino acids have been reported to have biological activity [12]. Morad *et al* [13] reported the antibacterial activity of Ni(II) with salicyaldehyde and 2-amino-benzoic acid complex. Popora and Berova [14] reported that copper is good for liver function, its level in blood and urine has influence in pregnancy disorders, nephritis hepatitis, leprosy, anemia and leukemia in children.

This paper reports the synthesis, analysis and bioactivity evaluation of N,N'-bis(4-enzeneazo salicylidene)-o-phenylenediiminatocopper(II) complex due to paucity of information.

MATERIALS AND METHODS

All the glass wares used were washed with detergent, rinsed with distilled water and dried in an oven. All the reagents and solvents used were of analytical grade (AnalaR or BDH) and were used without further purification. Molar conductance measurements were carried out using Cyber Scan 500 model. Electric metler balance model AB 54 was used for weighing. Infrared spectral analysis data were recorded using Fourier Transform IR Genesis series model Nujol, within 400 – 4000cm^{-1}. The pH measurements were carried out using Jenway pH meter model 3320. The molar conductance measurements were carried out on a cyber scan 500 model and the melting/decomposition temperatures were carried out using Gallenkamp melting point apparatus.

Preparation of the Schiff base ligand

0.01mol (1.814g) of o-phenylenediamine was added slowly into a solution of 0.02mol (4.5245g) 4-(Benzeneazo) salicylaldehyde (an intermediate) in 20cm^3 ethanol. After refluxing the reaction mixture for 2 hours, the precipitate that formed was separated, washed several times using ethanol, followed by recrystallisation in ethanol and drying at 50^{0}C in an oven overnight [15].

Preparation of copper (II) Schiff base complex

The complex was prepared by refluxing a mixture of aqueous solution of $CuCl_2.2H_2O$ (1.0mmol; 0.1705g) and hot ethanolic solution of the prepared Schiff base (0.524g) for 2 hours. The reaction mixture was allowed to cool in an ice bath and the greenish yellow precipitate obtained was separated, washed with ethanol and diethyl ether, followed by drying at 50^{0}C overnight [15].

Determination of dissociation Constant (pKa) of the tetradentate Schiff base

The dissociation constant of the Schiff base ligand was determined by introducing a standardized pH meter electrode into a 400cm^3 beaker containing magnetic stirrer bar, 90cm^3 water, 100cm^3 of 0.2mol dm^{-3} KNO_3 and 10cm^3 of 0.4mol dm^{-3} Schiff base ligand solution. To this mixture, 10cm^3 of standardized 0.5mol dm^{-3} aqueous solution of NaOH was added gradually and the corresponding pH value recorded after each addition [16].

Determination of number of coordinated Schiff base in the complex

To a 400cm^3 beaker containing 100cm^3 of 0.2 mol dm^{-3} KNO_3, 10cm^3 0.1 mol dm^{-3} HNO_3 90cm^3 of water and 1mmole of copper (II) chloride were added. Now 10cm^3 of 0.4 mol dm^{-3} sodium salt which was prepared by neutralizing a weighed solid ligand with calculated amount of standardized 0.5 mol dm^{-3} NaOH solution. After each 0.2cm^3 aliquote addition the corresponding pH was recorded. From the knowledge of the pH recorded, the average number of coordinated Schiff base per copper (II) ion was calculated as reported by Robert [16] and Angelici [17].

RESULT AND DISCUSSION

The N,N'–bis (4- Benzeneazo salicylidene)-o-phenylenediimine ligand was prepared by a 2:1 molar condensation of o-phenylenediimine with a reaction intermediate, 4–(Benzeneazo) salicylaldehyde. The copper (II) chelate was synthesized by refluxing ethanolic solutions of the schiff base ligand and copper (II) chloride [15]. The Schiff base ligand is orange, has a melting point of 193^{o}C and percentage yield of 70%. The complex is red, has decomposition temperature of 286^{o}C and percentage yield of 62%. The results are presented in Table 1. The solubility tests of the Schiff base ligand and its copper (II) complex in water and common organic solvents carried out revealed that the ligand is soluble in methanol, ethanol, DMSO and DMF, however, the complex is slightly soluble in most organic solvents but readily soluble insoluble in water, slightly soluble in most organic solvents, readily soluble in DMSO and DMF, but insoluble in water (Table 2). The molar conductance of 10^{-3}M complex in DMSO solution is 7.9 ohm^{-1}cm^{2}mol^{-1}, which is very low, suggesting that the complex is non electrolyte [18]. The result is in Table 3. The infrared spectral analysis of the free Schiff base ligand showed a band at 1590cm^{-1} assigned to *v*(C=N) stretching vibration, which undergoes a shift to lower wave numbers at 1538cm^{-1} on coordination to the metal ions. The band at 586 and 511cm^{-1} are attributable to *v*(Cu-N) and *v*(Cu-O) vibration modes, indicating that the ligand is coordinated to the copper (II) ion [19,20]. The result is contained in Table 4. The antibacterial test carried out on the free Schiff base ligand revealed only minimal activity on *E.*

coli spp with a diameter of inhibition zone of 11mm per 3000µg concentration. The copper (II) complex on the other hand showed higher activity against the bacterial isolates particularly at 3000µg concentration and is also found to be more active on *E. coli spp* with a diameter of inhibition zone of 22mm (Table 5). The results of the antifungal activities of the free Schiff base and its copper (II) complex are similar to that of antibacterial and that the copper (II) Schiff base complex exhibits higher activity against the bacterial and fungal isolates than the ligand (Table 6). The dissociation constant of the Schiff base ligand determined is 11.67, which revealed that it is highly basic. The result is presented on Table 7. The average number of Schiff base ligand coordinated to the copper (II) ion determined potentiometrically, is one, consistent with 1:1 metal – Schiff base (Table 8). The stability constant and the Gibb's free energy of the complex determined are 4.0X10^{13} and -75.8 KJmol^{-1}, indicating that the complex is very stable (Table 9).

On the basis of the spectral data and other analytical results of the Schiff base and its copper (II) complex, the following molecular structure of the complex is proposed.

Table 1. Physical properties of the Schiff base ligand and its copper (II) complex

Compound	Colour	Melting point (^{o}C)	Decomp. temp (^{o}C)	Percentage (%)
Schiff base	Orange yellow	193	-	70
[CuL]	Red	-	286	62

Table 2. Solubility of the Schiff base and its copper (II) complex

Compound	H_2O	Ethanol	Benzene	Acetone	Methanol	DMSO	DMF
Schiff base	IS	S	SS	SS	S	S	S
[CuL]	IS	SS	SS	IS	SS	S	S

Key S – Soluble SS – Slightly SolubleIS – Insoluble

Table 3. Conductivity measurement of the copper (II) Schiff base complex

Schiff base complex	Concentration moldm^{-3}	Electrical Conductivity Ohm^{-1} cm^{-1} x 10^{-6}	Molar Conductivity Ohm^{-1} cm^{2}mol^{-1}
[CuL]	1x10^{-3}	7.9	7.9

Table 4. Infrared spectral data of the Schiff base and its copper (II) complex

Compound	*v* (C = N)	*v* (phenolic C - O)	*v*(M - N)	*v* (M - O)
Schiff base (L)	1590	1340	-	-
[CuL]	1538	1304	586	511

Table 5. Antibacterial activity of Schiff base and its copper (II) complex

Compound	Clinical isolate	Diameter /Concentration			
	E. coli spp *Staph spp*	3000µg	2000µg	1000µg	Control
Schiff base (L)	√ √	11mm 00	00 00	00 00	00 00
[CuL]	√ √	22mm 18mm	13mm 9mm	00 00	00 00

Table 6. Antifungal activity of Schiff base and its copper (II) complex

Compound	Clinical isolate	Diameter /Concentration			
	A niger *C. albican*	3000µg	2000µg	1000µg	**Control**
Schiff base (L)	√ √	13mm 15mm	00 10mm	00 00	00 00
[CuL]	√ √	20mm 26mm	13mm 00mm	00 00	00 00

Table 7. Dissociation constant (pKa) of the tetradentate Schiff base

S/No		Vol. of NaOH (cm^3)	pH	[H$^+$]	[OH$^-$]	[Na$^+$]	A$_{total}$	pKa
1	200.5	0.5	9.56	1.80E-10	8.80E-05	1.20E-03	0.01995	10.9645
2	201.0	1.0	9.91	8.20E-11	2.00E-04	2.39E-03	0.0199	10.9919
3	201.5	1.5	10.22	4.00E-11	4.00E-04	3.57E-03	0.019851	11.1152
4	202.0	2.0	10.51	2.10E-11	7.80E-04	4.75E-03	0.019802	11.2851
5	202.5	2.5	10.74	1.20E-11	1.33E-03	5.93E-03	0.019753	11.4323
6	203.0	3.0	10.93	7.90E-12	2.05E-03	7.09E-03	0.019704	11.5684
7	203.5	3.5	11.07	5.70E-12	2.84E-03	8.26E-03	0.019656	11.6639
8	204.0	4.0	11.18	4.40E-12	3.65E-03	9.41E-03	0.019608	11.7356
9	204.5	4.5	11.27	3.60E-12	4.49E-03	1.06E-02	0.01956	11.7916
10	205.0	5.0	11.34	3.10E-12	5.28E-03	1.17E-02	0.019512	11.8233
11	205.5	5.5	11.41	2.60E-12	6.20E-03	1.28E-02	0.019465	11.8702
12	206.0	6.0	11.46	2.30E-12	6.96E-03	1.40E-02	0.019417	11.8816
13	206.5	6.5	11.51	2.10E-12	7.81E-03	1.51E-02	0.01937	11.9031
14	207.0	7.0	11.55	1.90E-12	8.56E-03	1.62E-02	0.019324	11.9064
15	207.5	7.5	11.58	1.80E-12	9.18E-03	1.73E-02	0.019277	11.8877
16	208.0	8.0	11.63	1.60E-12	1.03E-02	1.85E-02	0.019231	11.9365
17	208.5	8.5	11.66	1.50E-12	1.10E-02	1.96E-02	0.019185	11.9306
18	209.0	9.0	11.69	1.40E-12	1.18E-02	2.07E-02	0.019139	11.9301
19	209.5	9.5	11.72	1.30E-12	1.27E-02	2.18E-02	0.019093	11.9353
20	210.0	10.0	11.74	1.20E-12	1.33E-02	2.29E-02	0.019048	11.9082

Average pKa = 11.67308

Table 8. Determination of average number of coordinated Schiff base to copper (II) ion

S/NO	Vol(cm^3)	pH	[H$^+$]	[OH$^-$]	M$_{total}$	Log[A^{2-}]	$\bar{n}$
1	0	2.29	0.003432	4.70652E-12			
2	0.2	2.33	0.00313	5.1606E-12	0.004995	-11.83	0.51
3	04	2.37	0.002854	5.65848E-12	0.00499	-11.86	0.54
4	0.6	2.43	0.002486	6.49681E-12	0.004985	-11.89	0.54
5	0.8	2.48	0.002216	7.28954E-12	0.00498	-11.93	0.57
6	1	2.55	0.001886	8.56446E-12	0.004975	-12	0.58
7	1.2	2.63	0.001569	1.02967E-11	0.00497	-12.11	0.59
8	1.4	2.73	0.001246	1.29628E-11	0.004965	-12.38	0.61
9	1.6	2.84	0.000967	1.66994E-11	0.00496	-13.14	0.64
10	1.8	3.99	0.000685	2.35885E-11	0.004955	-12.01	0.66
11	2	3.18	0.000442	3.65342E-11	0.00495	-11.57	0.69
12	2.2	3.51	0.000207	7.81088E-11	0.004946	-11.09	0.72
13	2.4	4.03	6.24E-05	2.58643E-10	0.004941	-10.49	0.78
14	2.6	4.86	9.24E-06	1.74864E-09	0.004936	-9.64	0.84
15	2.8	5.39	2.73E-06	5.92516E-09	0.004931	-9.11	0.92
16	3	5.59	1.72E-06	9.39074E-09	0.004921	-8.91	0.99
17	3.2	5.72	1.27E-06	1.26678E-08	0.004916	-8.78	1.08
18	3.4	5.79	1.09E-06	1.48833E-08	0.004912	-8.71	1.16
19	3.6	5.84	9.67E-07	1.66994E-08	0.004907	-8.66	1.24
20	3.8	5.87	9.03E-07	1.78937E-08	0.004902	-8.63	1.32
21	4	5.89	8.62E-07	1.8737E-08	0.004897	-8.61	1.39
22	4.2	5.92	8.04E-07	2.00771E-08	0.004892	-8.58	1.48
23	4.4	5.95	7.51E-07	2.1513E-08	0.004888	-8.55	1.56
24	4.6	5.97	7.17E-07	2.25268E-08	0.004883	-8.53	1.64
25	4.8	6	6.69E-07	2.41379E-08	0.004878	-8.49	1.72
26	5	6.02	6.39E-07	2.52755E-08	0.004873	-8.48	1.79
27	5.2	6.06	5.83E-07	2.77141E-08	0.004869	-8.44	1.88

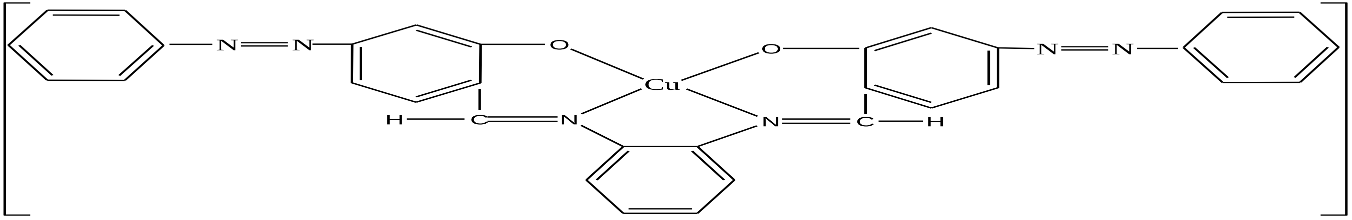
28	5.4	6.1	5.31E-07	3.03879E-08	0.004864	8.39	1.96
29	5.6	6.14	4.85E-07	3.33196E-08	0.004864	-8.36	2.04
30	5.8	6.19	4.32E-07	3.73852E-08	0.004859	-8.31	2.12
31	6	6.27	3.59E-07	4.49469E-08	0.004854	-8.23	2.19

Average n value = 1.156

Table 9. Stability constant and the Gibb's free energy of the complex

Compound	Stability constant (K)	Gibb's Free Energy (kJmol^{-1})
[CuL]	4.0X10^{13}	-75.8

Figure 1. proposed molecular structure of the copper (II) Schiff base complex



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