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Synthesis, characterization and Antioxidant evaluation of Cu (II), Zinc (II) and Cd (II) complexes derived from 2-((2-(piperazine-1-yl)ethylimino)methyl)phenol

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ABSTRACT

The Schiff base ligand 2-((2-(piperazine-1-yl)ethylimino)methyl)phenol (L-OH) and its complexes of Cu (II), Zinc (II) and Cadmium (II) were synthesized and characterized by FTIR, ^{1}HNMR, UV-visible, elemental analysis, TGA and LC-MS. The structure of [$C_{13}H_{18}CdCl_2N_3O$] was confirmed by x-ray diffraction. The data obtained from the characterization shows that both complexes have composition of ML type. The thermal analysis results revealed high thermal stability for all the complexes and that the anions and the ligands are decomposed at first, and then followed by the decomposition of the whole complex at the subsequent steps. The resulting compounds were evaluated for antioxidant activity.

Keywords: Antioxidant, Characterization, Synthesis, X-ray.

Introduction

A large number of Schiff bases and their complexes have been investigated due to their ease of formation of complexes with transition metals. The Schiff base ligands derived from 1-(2-Aminoethyl)piperazine have attracted the interest of this study due to the heterocyclic nature of piperazine and its ability to hold primary, secondary and tertiary amine in one molecule. However, piperazine has many biological applications being used as a main ingredient of antihelmintis for the treatment of worm's infections, a moiety in psychoactive drugs (Alonso et al, 2005; Maria et al, 2005; Alireza et al, 2006). Nitrogen in piperazine ring plays an important role in biological research and pharmaceutical industries. Piperazine and its derivatives are important raw material for hardening of epoxy resins, corrosion inhibitors, insecticides, rubber accelerators, urethane catalysts and antioxidants (Can-Cheng et al, 2004; Chaudhary et al, 2006; Sadashiva et al, 2006). On the other hand, piperazine (ppz) and its derivatives are very interesting ligands because of their good bridging ability. They are usually employed as building blocks to form coordination polymers (Salvino *et al*., 2003; Bararjanian *et al*., 2010).

Recently, report has been made on pH dependent reversible translocation of Ni (II) ion from octahedral to square planar site in ditopic ligand system (Mukhopadhyay *et al*., 2003). Other report on the Ni (II) complexes on new flexidentate Schiff base ligands, where the piperazinyl arm can in principle have both boat and chair conformations that can force the molecule to display ambidentate ligation behavior (Mukhopadhyay *et al*., 2003).

Herein, we report the syntheses, characterization and antioxidant evaluations of the ligand and its complexes of Cu (II), Zn (II) and Cd (II).

Materials and Methods

Materials: 1-(2-Aminoethyl)piperazine, salicylaldehyde, $CuCl_2$, $ZnCl_2$, $CdCl_2$ salts and DMSO-d_6 were obtained from Aldrich. All solvent were of analytical grade and used without further purifications.

Synthesis:

The Schiff base ligand was prepared as follows:

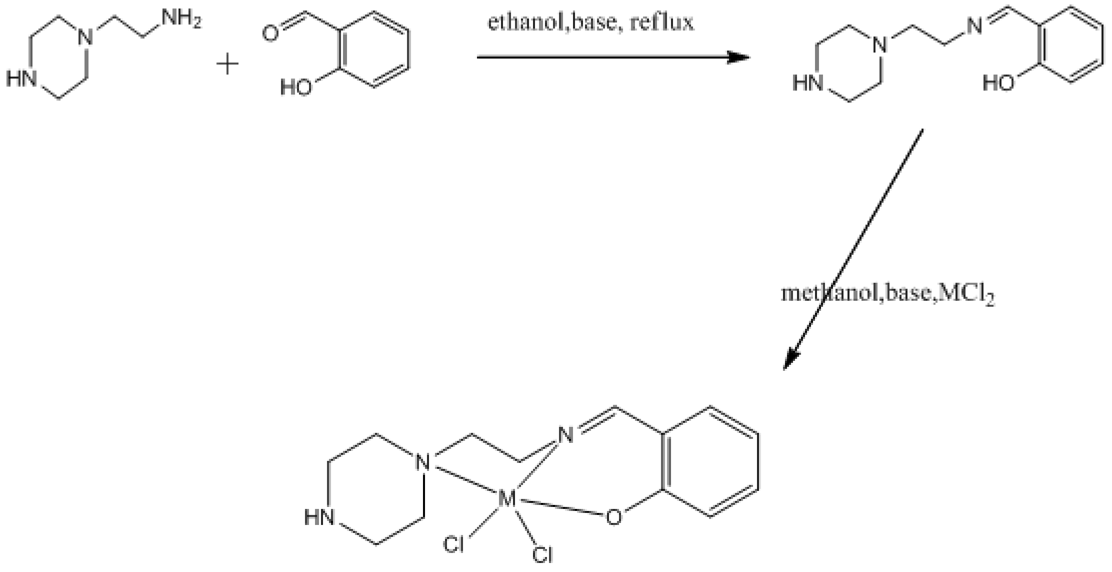
To a stirred solution of salicylaldehyde (2.44g, 20mmol) in absolute ethanol 20cm^3 was added dropwise an equimolar amount (2.58g) of 1-(2-Aminoethyl)piperazine and the resulting mixture was refluxed for one hour to obtained an orange solution. The solvent then removed by rotary evaporation to give red oil. After keeping the red oil for two days in vacuum, yellow needle-like crystals was produced which are not fit for x-ray diffraction analysis. Recrystallizations were carried out in methanol-chloroform mixture (70:30).

Complexes:

To the stirred solution of the ligand (0.23g, 1mmol) in methanol 20cm^3, was added a solution of $CdCl_2$ (0.18g, 1mmol) also in 20cm^3 methanol at room temperature and stirred vigorously before allowed to settle. A milk color precipitate was formed which was filtered and the filtrate concentrated by rotary evaporation. After keeping the filtrate for two weeks, an orange crystalline solid was formed which was collected by filtration, wash with ethanol and dried in a vacuum. Recrystallizations were performed in methanol-chloroform mixture. Same procedure was adopted for the preparation of Cu (II) and Zn (II) complexes. The scheme of the reaction is shown in Fig. 1.

Crystallography

Diffraction data were measured using Bruker SMART Apex II CCD area-detector diffractometer (graphite-monochromated Mo-*K*α radiation, λ = 0.71073 Å). The orientation matrix, unit-cell refinement, and data reduction were all handled by the Apex2 software (SAINT integration, SADABS absorption correction (Bruker APEX2 2007)). The structure was solved using direct method in the program SHELXS-97 and was refined by the full matrix least-squares method on *F2* with SHELXL-97 (Sheldrick 2008). All the non-hydrogen atoms were refined anisotropically. The C–bound H atoms were placed at calculated positions and were treated as riding on their parent C atoms. The N– and O–bound H atoms were located in difference Fourier maps, and refined with distance restraints of O—H = 0.84 (2) Å and N—H = 0.91 (2) Å. Drawing of the molecules were produced with XSEED (Barbour, 2001). Crystal data and refinement are summarized in Table 5 and the structure of the complex shown in figure 2. CCDC 1600-5368 contains the supplementary crystallographic data for the crystal (www.ccdc.cam.ac.uk/conts/retrieving.html). The crystals obtained for the copper and zinc complex were not qualitative enough for x-ray diffraction analysis hence their proposed structure were expected to be similar with that of cadmium crystal structure which is in conformity with the structure proposed in Fig. 1.



where M = Cu (II), Zn (II) and Cd (II)

Fig. 1: Scheme of the Reaction

Results and Discussion

Microanalytical data of the samples were recorded (Table 1). ^{1}HNMR spectra of the samples were recorded in DMSO-d$_6$ using TMS as internal standard, FTIR spectra of the samples were recorded on Parkin Elmer 783 spectrophotometer in the wavelength range 4000cm-^{1} – 400cm-^{1} using KBr pellet. The UV-visible spectra were recorded on Shimadzu UV-1650 PC spectrophotometer using DMSO as solvent. Elemental analyses were carried out on Parkin Elmer 2400II elemental analyzer. Thermogravimetric analyses were conducted on Shimadzu TGA-3000H thermal analyzer in a dynamic nitrogen atmosphere with a heating rate of 10^{0}C min-^{1}

Table 1: Physical Measurements of the Compounds

Compounds	Colour	%yeild	MP/DT(^{0}C)	Formula	Calculated (found) C (%)	H (%)	N (%)
L-OH	red	60	30	$C_{13}H_{19}N_3O$	66.9(65.8)	8.2(7.9)	18.0(17.8)
Cu-L	green	58	296	$C_{13}H_{18}Cl_2CuN_3O$	47.6(45.2)	4.9(4.5)	11.5(10.9)
Zn-L	yellow	64	310	$C_{13}H_{18}Cl_2ZnN_3O$	42.4(41.7)	4.9(4.6)	11.4(10.6)
Cd-L	milk	62	318	$C_{13}H_{18}Cl_2CdN_3O$	37.6(35.3)	4.4(4.2)	10.1(9.8)

Mass Spectra

Mass spectra of the synthesized Schiff base ligand confirm the proposed formula by detecting the following peaks. The observed peak at m/z 130 can be assign to the decomposition of 1-(2-Aminoethyl)piperazine while the peak at m/z 233 can be attributable to the base ion. Other peaks observed at m/z 234, 235 and 236 can be ascribed to the decomposition of the whole compound (Ahmed and El-Sherif, 2011).

Infra Red Spectra

The IR spectra of the ligand showed a strong broad band at 3522cm^{-1} that can be assigned to intermolecular hydrogen bonding of O-H and amine. The appearance of this peak at a lower wavelength range of 3145-3321cm^{-1} in the spectra of Cu, Zn and Cd complexes indicates that the terminal secondary amine is free from complexation as confirmed in the x-ray structure of the cadmium complex (Fig. 2). The spectrum of the ligand also showed absorptions at 2829cm-^{1} and 762cm-^{1} which can be attributed to C-H aliphatic and aromatic bonds respectively. Another absorption at 1636cm^{-1} can be assigned to azomethine –C=N-, this peak shift to a lower frequencies of 1636cm^{-1}, 1629cm^{-1} and 1630cm^{-1} for Cu(II), Zn(II) and Cd(II) complexes respectively. This clearly indicates the involvement of the nitrogen of azomethine in complexation with the metal ions in their respective spectra (Alanso *et al.*, 2005 and Baraajanian *et al.*, 2010). Accordingly, the ligand act as tridentate chelating agent bonded to the metal ion via tertiary nitrogen (C-N) of piperazine moiety observed at the band regions 1201cm^{-1}, 1152cm^{-1} and 1154cm^{-1} in the spectra of Cu (II), Zn (II) and Cd (II) respectively. Absorptions at 633cm^{-1} and 551cm^{-1} in the spectra of Cu(II) can be assigned to M-O and M-N bonds respectively, similar bands were noticed at 573cm^{-1} and 530cm^{-1} in the spectra of Zn (II) and at 522cm^{-1} and 456cm^{-1} in the spectra of Cd(II), which are all due to M-O and M-N bonds respectively as shown in the Table 2 below.

Table 2: IR spectra for the L-OH and its complexes

Compound	ν (N-H)(OH)	ν(C-H) aliphatic	ν(C=N)	ν(C-C) aromatic	ν(C-N)	ν(O-H)	ν(C-H) aromatic	ν(M-O)	ν(M-N)
L($C_{13}H_{19}N_3O$)	3522	2829	1636	1278	1152	3442	762	-	-
Cu($C_{13}H_{19}N_3O$)	3145	2946	1600	1448	1201	-	753	633	551
Zn($C_{13}H_{19}N_3O$)	3237	2822	1554	1446	1154	-	768	573	530
Cd($C_{13}H_{19}N_3O$)	3321	2378	1594	1443	1156	-	780	522	456

^{1}HNMR spectra

The ^{1}HNMR spectra of the complexes were recorded in DMSO-d6. The spectra of Zinc manifested a signal at the chemical shifts δ 1.07 and δ 2.5 which can be assignable to piperazine secondary amine (N-H) and the methylene (CH_2) group respectively. The chemical shifts at δ 7.22 and δ 8.21 can be attributed to the azomethine group M-N. At a relatively low frequency of δ 6.16, a benzene ring of the salicylaldehyde is presumably appeared. However, the spectra of cadmium complex indicated signals at the chemical shift of δ 1.91 and δ 2.52 similar to that of Zn spectra which were assigned to the N-H and methylene (CH_2) groups respectively. This further proves the non involvement of the secondary amine of piperazine moiety in the complexation with metal ion as notice in the infra red spectra. The signal due to azomethine appeared at lower frequency of δ 7.02 while that of aromatic ring was shown at δ 6.46 akin to what was observed in the spectra of zinc due to structural similarity. The ^{1}HNMR spectra of the copper was unclear, this may be attributed to the paramagnetic nature of copper as shown in Table 3 below.

Table 3: ^{1}H NMR spectra for the L-OH and its complexes

Compounds	Chemical Shifts in ppm				
	M-N	N-H	CH_2	Aromatic	C=N
L-OH	-	1.92	2.21	6.78	7.97
CuL-OH	No clear spectra				
ZnL-OH	8.21	1.07	2.50	6.16	7.22
CdL-OH	8.18	1.91	2.52	6.46	7.02

UV-visible spectra

The UV-visible spectra of the ligand showed two absorption band maxima. The intense band at 319nm emanate from n-π* electronic transition. The intensity of this band increases and shifted to a lower wavelength of 302nm. This can be due to the effect of isolated chromophores of azomethine (-CH=N-) and the two nitrogen group present at different positions in the piperazine ring. This high intensity then dropped at 406nm band. The bands at 243nm and 275nm can be assign to π-π* electronic transition associated with the aminoethyl group. The bathochromic shift of 339nm observed in the ligand spectra was also noticeable at a high frequency of 372nm in the spectra of Cu (II) complex which correspond to the ligand- metal charge transfer. The band region at 654nm can be attributed to d-d electronic transition in the copper. However, in the spectra of zinc complex a comparable band appeared at 379nm that is analogous to the bands at 339nm and 372nm found in the ligand and copper complex. This could also have same interpretation of ligand-metal charge transfer. This absorption then shifted to a lower wavelength of 279nm due to π-π* electronic transition. Similarly, the cadmium complex also showed a band shift at 362nm due to ligand-metal charge transfer. However, the band at 276nm can be assign to π-π* electronic transition of the chelate ring as shown in the Table 4 below.

Table 4: UV-visible spectra of L-OH and its complexes

Compound	Wavelength	Absorption	Description
L7	302	3.263	n-π*
	339	3.175	n-π*
	406	1.290	n-π*
	243	0.350	π-π*
Cu-L	275	3.524	π-π*
	372	1.669	L-MCT
	654	0.157	d-d
Zn-L	351	2.799	L-MCT
	279	2.636	π-π*
	369	2.613	L-MCT
Cd-L	362	2.659	L-MCT
	276	2.613	π-π*

Thermogravimetric Analyses

The thermogravimetric analyses were carried out in a dynamic nitrogen atmosphere for the complexes prepared. The spectra of the copper complex manifested a weight loss of 7.738% and 32.185% at a temperature of 120 - 150^{0}C and 290 - 320^{0}C which can presumably be assigned to the removal of anions from the complex. Another weight loss of 51.125% observed at 720^{0}C can be ascribed to the decomposition of the whole ligand leaving behind the metal oxide as residue. On the other hand, the zinc complex demonstrated a weight loss of 32.78% at the temperature range 200 - 400^{0}C due to decomposition of anions. At high temperature range of 570 - 750^{0}C, a significant weight loss of 25.23% was discerned which is attributable to the removal of ligand from the chelate leaving behind the metal oxide as residue. Moreover, the spectra of the cadmium complex showed a weight loss of 21.99% at the temperature range of 200 - 310^{0}C which is close to the value obtained for the decomposition of anions in Cu and Zn spectra. The second derivative of weight loss at 73.96% and temperature range of 400 - 630^{0}C can be due to the removal of ligand from the chelate.

Generally, all the complexes exhibit high thermal stability due their ability to undergo more than one step of decomposition. This is a very good requirement for biological evaluations.

Crystallographic Analysis

In the complex $[CdCl_2(C_{13}H_{19}N_3O)]$, the Cd^{2+} ion is penta-coordinated with the N,N,O-tridentate Schiff base 2-{[2-(piperazin-4-ium-1-yl)ethyl]iminomethyl}phenolate ligand and two Cl atoms in a highly distorted square-pyramidal geometry; the piperazine ring adopts a chair conformation. In the crystal structure, adjacent molecules are linked together via N—H….O and N—H….Cl hydrogen bonds, forming infinite layers parallel to the ab plane. The layers are further connected through C—H….Cl interactions into a three dimensional network.

Table 5: Crystal data and refinement parameters for the Cd(II) complex

	Cadmium Complex
Empirical formula	$[CdCl_2(C_{13}H_{19}N_3O)]$
Formula weight	416.61
Temperature (K)	100
Crystal system , Space group	Orthorhombic, *Pbca*
Unit cell dimensions	7.06570(10)
a (Å)	14.7512 (16) Å
b (Å)	13.1406 (15) Å
c (Å)	
α (°)	95.7700(10)
β (°)	
γ (°)	1765.01(4)
Volume (Å^3)	3221.4 (6) Å^3
Z, Density (calculated) (g cm^{-3})	8
Absorption coefficient (mm^{-1})	
F(000)	1664
Crystal size (mm^3)	0.45 × 0.39 × 0.18 mm
θ range for data collection (°)	θ = 2.4–31.3°

Index ranges	14604 /3455 [R_{int} = 0.0267]
Reflections collected / unique	To θ = 26.00° : 99.8%
Completeness	0.8211 and 0.6552
Max. and min. transmission	3455 / 2 / 225
Data / restraints / parameters	1.064
Goodness-of-fit on F^2	R_1 = 0.0343, wR_2 = 0.0883
Final *R* indices [$I>2\sigma$ (I)]	R_1 = 0.0397, wR_2 = 0.0923
R indices (all data)	1.112 and -0.520

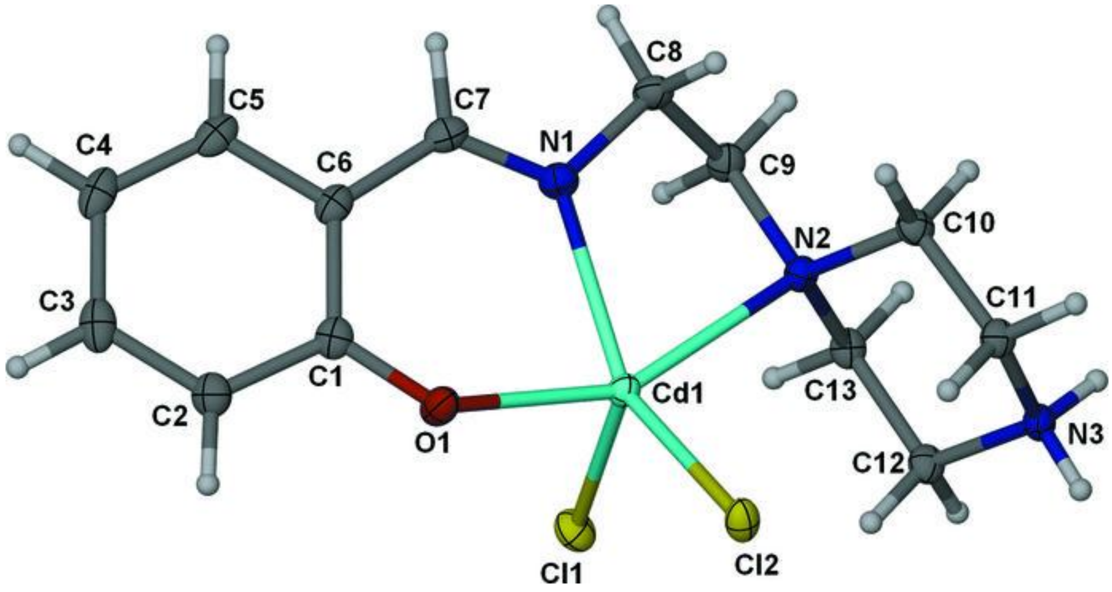


Figure 2: crystal structure for the complex [$CdCl_2(C_{13}H_{19}N_3O)$]

Biological Activity

The compounds synthesized were screened for antioxidant activities against hydroxyl radicals as a function of concentration from 0-0.8μM according the procedure (Alireza *et al.*, 2006). The result of these evaluations shows a continuous decrease in antioxidant activity from ligand to its complexes of Cu (II), Zn (II) and Cd (II). The ligand showed the highest frap-value of 103.3 when compared to the value of 57.6, 41.4 and 20.1 found for the Cu(II), Zn(II) and Cd(II) complexes respectively. Generally the compounds are not good potentials for antioxidant activity. The result is shown in Table 6 below.

Table 6: Antioxidant results for the L-OH and its complexes

Samples	Rep1	Rep2	Rep3	Mean	Avg-blnk	Frap value
Vit C 10x	1.064	1.088	1.1	1.084	1.002	1431.4
Q 10x	1.802	1.838	1.928	1.856	1.774	2534.3
GA 10x	1.987	2.014	1.989	1.997	1.915	2735.2
L-OH	0.944	1.138	1.139	1.140	1.072	903.30
CuL-OH	0.723	1.122	1.122	1.122	1.040	557.60
ZnL-OH	0.605	1.102	1.126	1.111	1.029	441.40
CdL-OH	0.230	1.340	1.250	1.320	1.200	350.00

Where Rep1,2 and 3 means Replicate 1,2 and 3 rspectively and Avg-Blnk means average blank absorption

Conclusion

Herein, we reported the synthesis of the Schiff bases obtained from the reaction of 1-(2-Aminoethyl)piperazine and salicylaldehyde using Cu (II), Zn (II) and Cd (II) chloride salts. The compounds were characterized by FTIR, ^{1}HNMR, UV-visible, LC-MS, TGA, CHN and crystal diffraction. Based on the analytical data obtained, square pyramidal structure has been suggested for the complexes. According to the TGA data obtained, the complexes revealed high thermal stability which is very crucial for biological evaluations on the compounds. However, this study did not recommend the use of piperazine compounds as antioxidants due to their low activity when compared to vitamin C or Gallic acid.

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