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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF COPPER(II) SCHIFF BASE ADDUCTS OF SOME *p*-SUBSTITUTED ANILINE SCHIFF BASES

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ABSTRACT. The synthesis, characterization and antimicrobial activity of Cu(II) complexes of some *p*-substituted aniline Schiff base ligands have been carried out. The Schiff bases were obtained from salicylaldehyde and *o*-vanillin. The Cu(II) complexes have been characterized by elemental analysis, conductivity measurement, infrared and electronic spectral data. The complexes were obtained either as metal chelates $[Cu(L)_2]$ or Schiff base adducts $(CuCl_2.2LH).xH_2O$. The metal chelates were non-electrolytes while the Schiff base adducts exhibited 1:1 or 2:1 electrolytes in methanol. The Cu(II) complexes exhibited slight antimicrobial activity against *Escherichia coli* ATCC® 8739™*, *Staphylococcus aureus subsp. aureus* ATCC® 6538™*, *Bacillus subtilis subsp. spizizenii* ATCC® 6633™* and *Candida albicans* ATCC® 2091™*. The complexes exhibited significant antifungal activity.

KEY WORDS: Metal Chelates, Schiff bases, Adducts, Cu(II) complexes, Salicylaldimines

INTRODUCTION

Metal complexes have received overwhelming attention in main group and transition metal chemistry due to the ease of their preparation and structural variability. Schiff base metal complexes exist as metal chelates or as Schiff base adducts. Schiff base ligands especially salicylaldimines have been extensively reported to form metal chelates readily with metal ions [1-9]. In most cases, the *ortho*-hydroxyl Schiff base ligands coordinate as bidentate monobasic [5-8] via the imine nitrogen and the deprotonated phenolic oxygen, Figure 1.

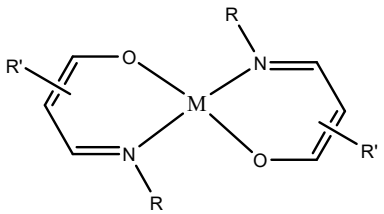

Figure 1. Schiff base metal chelate.

On the other hand, reaction of salicylaldimine (HSal) type ligands with metal salts could as well result in the formation of Schiff base adducts [10-14] containing the intact ligand moieties,

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MA_n.mLH. This is an uncommon occurrence and has been scarcely reported. The ability of the HSal ligand to retain the acidic hydrogen atoms when reacting with Lewis acids to form Schiff base adducts depends upon structural peculiarities, the nature of the coordinate bond and reaction conditions [14]. Specifically, compounds exhibiting strong intra-molecular hydrogen bonding, such as salicylaldimine type ligands, have high tendency to form adducts with Lewis acids. Also, most reported cases [10-14] of Schiff base adducts involve the use of metal chloride ($MCl_2.xH_2O$) salt. Bamfield [12] attributed the formation of Schiff base adducts to the interaction between the metal chloride salt and the keto-tautomer of the Schiff base ligands. A variety of diverse coordination modes, as shown in Figure 2, have been proposed for Schiff base adducts of salicylaldimine type ligand [14]. Although, the assignment of coordination mode for the Schiff base adducts could be somewhat ambiguous, the structure of an organotin Schiff base adduct, $Me_2SnCl_2.SalenH_2$, has been resolved by X-ray single crystal refinement [15]. The $SalenH_2$ ligand coordinates to the tin atom through the oxygen atom [11]. Therefore, formation of Schiff base adducts provides another structural variability to the chemistry of Schiff base metal complexes.

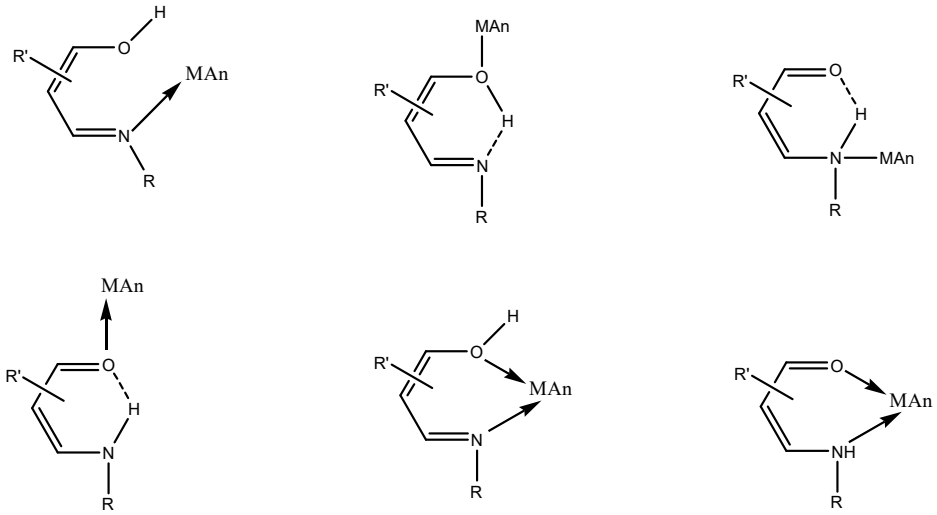


Figure 2. Structural types of salicylaldimine Schiff base adducts.

This study presents the synthesis and characterization of some Cu(II) metal chelates and Schiff base adducts. The Schiff base ligands were prepared from salicylaldehyde or *o*-vanillin and *p*-substituted aniline. The Schiff base ligands and the Cu(II) complexes have been evaluated for their antimicrobial activity.

EXPERIMENTAL

All the chemicals and reagents were of reagent grade and used without further purification. The ^{1}H- and ^{13}C-NMR spectra for the Schiff base ligands were recorded on Bruker Avance NMR equipment operating at 400 MHz using deuterated chloroform with TMS as internal standard. The FT-IR absorption spectra and the electronic spectra for the compounds were recorded on Perkin Elmer Spectrum 100 FT-IR and Perkin Elmer Lambda 25 spectrophotometer, respectively. The FT-IR spectrometer was equipped with a universal attenuated total reflectance (ATR) accessory. The elemental analysis, CHN, was done on Vario MICRO V1.6.2 elemental

analysen system GmbH, while the melting points (uncorrected) of the compounds were determined using the Galenkemp melting point apparatus. All the micro-organisms used for the antimicrobial study were obtained from Microbiologics, Cape Town.

Table 1. ^{1}H-NMR and ^{13}C-NMR Spectral data for the Schiff base ligands.

S/N	Ligands	^{1}H-NMR (δ) ppm	^{13}C-NMR (δ) ppm
1	L1	13.26 (1H, s,-OH); 8.66 (1H, s, HC=N); 7.44 (3H, m); 7.32 (3H, m); 7.07 (1H, d, J = 8.10); 6.98 (1H, t, J = 7.96).	163.08 (Ar-OH); 161.60 (HC=N); 149.00 (Ar-C=N); 133.53, 132.66, 122.98, 127.27, 121.56, 119.66, 119.44, 117.68 (Ar-C).
2	L2	13.01 (1H, s, -OH); 8.63 (1H, s, HC=N); 7.40 (4H, m); 7.30 (2H, d, J = 8.59); 7.10 (1H, d, J= 8.57); 7.00 (1H, t, J = 7.48).	163.39 (Ar-OH); 161.56 (HC=N); 147.53 (Ar-N=C); 133.83 (Ar-Cl); 132.93, 132.78, 129.94, 122.83, 119.58, 117.74 (Ar-C).
3	L3	12.97 (1H, s, -OH); 8.63 (1H, s, HC=N); 7.58 (2H, d, J = 8.64); 7.43 (2H, m); 7.19 (2H, d, J = 8.64); 7.06 (1H, d, J = 8.59), 6.98 (1H, t, J = 7.47).	163.45 (Ar-OH); 161.57 (HC=N); 148.03 (Ar-N=C); 133.88, 132.91, 132.80, 123.20, 120.78, 119.59, 117.75 (Ar-C).
4	L4	13.37 (1H, s, -OH); 8.66 (1H, s, HC=N); 7.40 (2H, m); 7.22 (2H, d); 7.20 (2H, d); 7.10 (1H, d, J = 8.16); 7.0 (1H, m); 2.48 (3H, s, -CH_3).	162.11 (Ar-OH); 161.56 (HC=N); 146.37 (Ar-N=C); 137.29 (Ar-CH_3); 133.29, 132.50, 130.40, 121.39, 119.71, 117.63 (Ar-C); 21.42 (-CH_3).
5	L5	13.41 (1H, s, -OH); 8.64 (1H, s, HC=N); 7.39 (2H, m); 7.32 (1H, t); 7.30 (1H, q); 7.05 (1H, m); 7.0 (1H, t); 6.98 (1H, t); 6.95 (1H, dd); 3.88 (3H, s, -OCH_3).	161.44 (Ar-OH); 160.88 (HC=N); 159.30 (Ar-OCH_3); 141.81 (Ar-N=C); 133.07, 132.34, 122.68, 119.82, 119.36, 117.57, 115.07 (Ar-C), 55.95 (-OCH_3).
6	L6	12.54 (1H, s, -OH); 8.63 (1H, s, HC=N); 8.30 (2H, d, J = 8.91); 7.5 (2H, m); 7.4 (2H, d, J = 8.91); 7.10 (1H, d, J = 8.15); 7.0 (1H, t, J = 7.49).	165.84 (Ar-OH); 161.74 (HC=N); 154.64 (Ar-N=C); 146.50 (Ar-NO_2); 134.96, 133.45, 125.69, 122.35, 120.02, 119.14, 117.98 (Ar-C).
7	L7	13.68 (1H, s, -OH); 8.67 (1H, s, HC=N); 7.46 (2H, t, J = 7.75); 7.31 (3H, m); 7.06 (2H, m); 6.94 (1H, t, J = 7.88Hz); 3.98 (3H, s, -OCH_3).	163.02 (HC=N); 151.99 (Ar-N=C); 148.97 (Ar-OCH_3); 148.66 (Ar-OH); 129.82, 127.37, 121.56, 118.92, 115.38, (Ar-C); 56.63 (-OCH_3).
8	L8	13.36 (1H, s, -OH); 8.64 (1H, s, HC=N); 6.93 (1H, t, J = 7.88); 7.10 (2H, m); 7.19 (2H, d, J = 8.69); 7.57 (2H, d, J = 8.69); 3.97 (3H,s,-OCH_3).	163.44 (HC=N); 151.85 (Ar-OCH_3); 148.96 (Ar-N=C); 147.73 (Ar-OH); 132.93 (Ar-Cl), 123.21, 120.88, 119.44, 119.13, 115.67 (Ar-C); 56.68 (-OCH_3).
9	L9	13.39 (1H, s, -OH); 8.63 (1H, s, HC=N); 7.10 (2H, dd, J = 7.22); 7.30 (2H, d, J = 8.51); 7.40 (2H, d, J = 8.54) ; 6.90 (1H, t, J = 7.86); 3.97 (3H, s, -OCH_3).	163.38 (HC=N); 151.84 (Ar-OCH_3); 148.95 (Ar-N=C); 147.23 (Ar-OH); 133.01 (Ar-Br); 129.95, 122.85, 119.11, 115.63, (Ar-C), 56.68 (-OCH_3).
10	L10	13.82 (1H, s, -OH); 8.66 (1H, s, HC=N); 7.04 (2H, m); 7.25 (4H, m); 6.91 (1H, t, J = 7.87); 3.97 (3H, s, -OCH_3) and 2.42 (3H, s,-CH_3).	162.03 (HC=N); 151.99 (Ar-OCH_3); 148.96 (Ar-OH); 146.01 (Ar-N=C); 137.40 (Ar-CH_3); 130.42, 121.39, 119.66, 118.82, 115.19 (Ar-C); 56.66 (-OCH_3); 21.42 (-CH_3).
11	L11	12.86 (1H, s, -OH); 8.68 (1H, s, HC=N); 8.30 (2H, d, J = 8.98); 7.40 (2H, d, J = 8.98); 7.10 (2H, d, J = 8.16); 7.0 (1H, m); 3.98 (3H, s,-OCH_3).	165.80 (HC=N); 154.43 (Ar-N=C); 152.04 (Ar-OCH_3); 149.04 (Ar-OH); 146.64 (Ar-NO_2); 125.62, 124.73, 122.29, 119.54, 119.16, 116.47 (Ar-C); 56.74 (-OCH_3).
12	L12	13.58 (1H, s, -OH); 9.62 (1H, s, -OH); 8.88 (1H, s, HC=N); 7.31 (2H, d); 7.18 (1H, d); 7.08 (1H, d); 6.89 (1H, d); 6.85 (2H, d) and 3.82 (3H, s, -OCH_3).	161.15 (HC=N); 157.83 (Ar-OH); 151.32 (Ar-OH); 148.74 (ArC=N); 139.90, 124.56, 123.47, 120.23, 119.29, 116.87, 116.03 (Ar-C), 56.78 (-OCH_3).

Note: L^1 = Sal-H; L^2 = Sal-Cl; L^3 = Sal-Br; L^4 = Sal-Me; L^5 = Sal-OMe; L^6 = Sal-NO_2; L^7 = Ovan-H, L^8 = Ovan-Cl, L^9 = Ovan-Br, L^{10} = Ovan-Me, L^{11} = Ovan-NO_2, L^{12} = Ovan-OH.

Synthesis of the Cu(II) complexes

The Cu(II) complexes were prepared by reacting a series of *p*-substituted aniline derived Schiff bases with Cu(II) chloride dihydrate, $CuCl_2.2H_2O$ in hot ethanolic solution under stirring condition. The Schiff bases, L^1–L^{12} were obtained from salicylaldehdye, *o*-vanillin and *p*-substituted aniline (X = H, Cl, Br, Me, OMe, NO_2 and OH). The ^{1}H- and ^{13}C-NMR spectral data for the Schiff base ligands are presented in Table 1.

Hot ethanolic solution of $CuCl_2.2H_2O$ was gradually added to a hot ethanolic solution of the ligand in a ratio 1:2. The resulting solution was stirred for 30 min with slight heating to obtain the Cu(II) complexes. Diethyl ether was used to induce precipitation in cases where the precipitate did not form on stirring. The precipitate was filtered under suction, washed with ethanol and dried in a vacuum desiccator over silica gel. The analytical and the spectroscopic data are presented in Tables 2 and 3, respectively.

Table 2. Physical and analytical data for the complexes.

Complex	Colour	%Yield	M.P.	Molar mass	% Found (calculated)				$*\Lambda_M$
			(℃)	(g/mol)	C	H	N	Cu	
$Cu(L^1)_2Cl_2.\ 2\frac{1}{2}H_2O$	Brown	69	128 -130	572.05	54.59 (54.69)	4.41 (4.26)	4.90 (5.91)	11.11 (11.62)	183.00 (2:1)
$Cu(L^2)_2Cl_2.\ 2H_2O$	Brown	55	160-162	633.95	49.26 (49.61)	3.82 (3.33)	4.42 (4.72)	11.02 (10.15	138.00 (2:1)
$Cu(L^3)_2Cl_2.\ H_2O$	Brown	75	171-172	704.77	44.31 (44.56)	3.15 (2.82)	3.97 (4.07)	9.02 (8.72)	126.50 (2:1)
$Cu(L^4)_2Cl_2.\ H_2O$	Brown	57	156-158	575.01	58.49 (58.68)	4.91 (4.71)	4.85 (5.00)	11.79 (11.05)	83.00 (1:1)
$Cu(L^5)_2$	Red	77	170-172	516.07	65.08 (65.16)	4.92 (4.69)	5.34 (5.43)	11.98 (12.31)	1.60 (DMF)
$Cu(L^6)_2.\ \frac{1}{2}H_2O$	Orange	90	>250	555.03	56.60 (56.26)	3.48 (3.48)	10.13 (10.09)	11.12 (11.45)	6.39 (DMF)
$Cu(L^7)_2Cl_2.$ $H_2O.\ \frac{1}{2}EtOH$	Brown	88	124-126	629.42	55.34 (55.52)	4.97 (4.69)	4.45 (4.44)	10.10 (9.80)	134.2 (2:1)
$Cu(L^8)_2$	Green	84	194-196	584.85	57.30 (57.50)	4.05 (3.79)	4.76 (4.79)	11.01 (10.87)	1.57 (DMF)
$Cu(L^9)_2Cl_2.H_2O$	Brown	56	179-180	764.93	43.97 (43.47)	3.43 (3.16)	3.66 (3.61)	8.31 (7.72)	99.80 (1:1)
$Cu(L^{10})_2Cl_2.2\frac{1}{2}H_2O$	Brown	60	168-170	671.19	53.69 (54.41)	5.41 (5.33)	4.17 (4.23)	9.47 (9.60)	82.70 (1:1)
$Cu(L^{11})_2.2EtOH$	Brown	78	>250	698.09	55.17 (55.06)	4.91 (4.38)	8.03 (8.00)	9.10 (8.79)	6.61 (DMF)
$Cu(L^{12})_2Cl_2.H_2O$	Brown	67	178-180	637.09	52.79 (52.44)	4.11 (4.31)	4.40 (5.03)	9.98 (9.77)	131.00 (2:1)

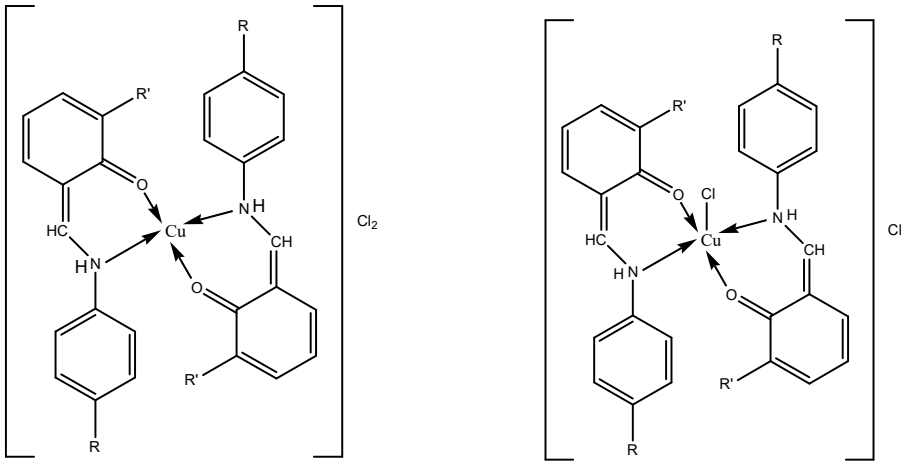
$*\Lambda_M$ ($\Omega^{-1}cm^2mol^{-1}$). Note: L^1 = Sal-H; L^2 = Sal-Cl; L^3 = Sal-Br; L^4 = Sal-Me; L^5 = Sal-OMe; L^6 = Sal-NO_2; L^7= Ovan-H, L^8 = Ovan-Cl, L^9 = Ovan-Br, L^{10} = Ovan-Me, L^{11} = Ovan-NO_2, L^{12} = Ovan-OH.

RESULTS AND DISCUSSION

Elemental analysis and conductivity measurement

The physical and the analytical data for the complexes are presented in Table 2. The Cu(II) complexes were obtained in high yield and the micro analytical data indicate the complexes are relatively pure. Analysis of the CHN results indicates the isolation of the Cu(II) complexes as inner chelates for ligands L^5, L^6, L^8 and L^{11} while ligands L^1–L^4, L^7, L^9, L^{10} and L^{12} complexes

were obtained as Schiff base adducts in 1:2 stoichiometric ratio comprising two molecules of the ligands, two atoms of chlorine and one of copper. The metal chelates were non-electrolytes with molar conductivity values of 6.61–1.57 $\Omega^{-1}cm^2mol^{-1}$ while the Schiff base adducts were either 1:1 (99.8–82.7 $\Omega^{-1}cm^2mol^{-1}$) or 2:1 (183–126.5 $\Omega^{-1}cm^2mol^{-1}$) electrolytes in methanol [16]. The complexes are, therefore, proposed to be of the forms $[CuL_2].xH_2O$ for the metal chelates and $[Cu(LH)_2Cl]Cl.xH_2O$ or $[Cu(LH)_2]Cl_2.xH_2O$ for the Schiff base adducts (Figure 3).



$[Cu(LH)_2]Cl_2$ $[Cu(LH)_2Cl]Cl$

R = H, Cl, Br, Me, OMe; R' = H or OMe

Figure 3. Proposed structures for the Schiff base adducts.

Infrared study

Some selected infrared spectral data for the Schiff base complexes are presented in Table 3. The phenolic hydroxyl stretching vibration for the free Schiff base ligands were observed as a broad and weak band at 3100–2200 cm^{-1} due to strong intramolecular hydrogen bonding which is characteristic of ortho-hydroxyl Schiff base ligands [17]. In addition, the vibrational absorption band for the azomethine group, C=N, appeared at 1616–1598 cm^{-1} [18-21]. The broad hydroxyl band of the OH group disappeared in the Cu(II) chelates of L^5, L^6, L^8& L^{11}, indicating coordination of the ligands via the deprotonated oxygen atom [22-23]. This was corroborated by the bathochromic shift in the phenolic C-O stretch of the free ligands at 1280–1270 cm^{-1} to 1330–1318 cm^{-1}. Also, the azomethine absorption band underwent negative shift in the spectra of the metal chelates by -20 cm^{-1} to -8 cm^{-1}, suggesting coordination via the imine nitrogen [2, 6, 17, 18]. A new strong band was, however, observed in the spectral of the Schiff base adducts at 1641–1628 cm^{-1}. This band was absent in the metal chelates and it indicates the presence of a quinoid system in the Schiff base adducts [12] as shown in Figure 3. In addition, the presence of the N-H group is indicated by the appearance of a weak to medium band at 3500–3100 cm^{-1} [6] in the spectra of the Schiff base adducts. The OH stretching vibration of the lattice water also absorbed in this region [6, 22]. The coordination mode of the Schiff base ligands was further substantiated by the assignment of metal-ligand vibration bands in the far-infrared spectra of the metal complexes. The bands corresponding to the ν_{Cu-N}, ν_{Cu-O} and ν_{Cu-Cl} bonds were observed at 592–534 cm^{-1}, 515–424 cm^{-1} and 387–346 cm^{-1}, respectively [20, 24].

Table 3. Selected infrared and electronic spectral data for the complexes.

S/N	Compound	ν_{NH}/ν_{OH}	$\nu_{C=N}$	ν_{CO}	ν_{Cu-N}	ν_{Cu-O}	ν_{Cu-Cl}	λ (nm)
1	$Cu(L^1)_2Cl_2.\ 2\frac{1}{2}H_2O$	3261, 3215	1606, 1634	1315	534, 564	497, 515	387	230, 280, 383, 713
2	$Cu(L^2)_2Cl_2.\ 2H_2O$	3322, 3241, 3205	1606, 1628	1309	589	426, 463	346	240, 282, 386, 810
3	$Cu(L^3)_2Cl_2.\ H_2O$	3119	1603, 1633	1309	586	442, 512	368	223, 240, 282, 385, 804
4	$Cu(L^4)_2Cl_2.\ H_2O$	3251, 3210	1606, 1638	1316	585	465, 503	364	282, 383, 750
5	$Cu(L^5)_2$	-	1600	1325	591	426, 496	-	230, 273, 299, 384, 501, 674
6	$Cu(L^6)_2.\ \frac{1}{2}H_2O$	-	1610	1320	587	491, 424	-	374, 423,
7	$Cu(L^7)_2Cl_2.$ $H_2O.\ \frac{1}{2}EtOH$	3494, 3438	1608, 1633	1309	540	464, 424	355	231, 287, 391, 748
8	$Cu(L^8)_2$	-	1598	1318	584, 562	492, 441	-	234, 293, 396, 405, 517
9	$Cu(L^9)_2Cl_2.H_2O$	3114	1613, 1637	1308	543, 528	492, 436	372	284, 394, 756, 819
10	$Cu(L^{10})_2Cl_2\ .2\frac{1}{2}H_2O$	3251, 3207	1611, 1641	1305	595, 537	495, 442	347	231, 288, 388, 794
11	$Cu(L^{11})_2.$ 2EtOH	3210	1603	1330	540, 573	466, 442	-	307, 412, 770
12	$Cu(L^{12})_2Cl_2.H_2O$	3448, 3180	1608, 1641	1311	592, 538	492, 448	387	280, 313, 389, 502

Note: L^1 = Sal-H; L^2 = Sal-Cl; L^3 = Sal-Br; L^4 = Sal-Me; L^5 = Sal-OMe; L^6 = Sal-NO_2; L^7 = Ovan-H; L^8 = Ovan-Cl; L^9 = Ovan-Br; L^{10} = Ovan-Me; L^{11} = Ovan-NO_2; L^{12} = Ovan-OH.

Electronic spectra study

The electronic spectral data for the Cu(II) complexes exhibited three different absorption bands due to transitions arising from the Schiff base ligands. The high energy bands at 234–223 nm and 293–273 nm correspond to the $\pi \rightarrow \pi^*$ transition of the benzene rings [25] and the azomethine group respectively [20, 26] while the third band at 412–341 nm was assigned to the $n \rightarrow \pi^*$ of the azomethine group, C=N [19]. In addition, a broad band corresponding to the d–d transition of the Cu(II) ion was observed at 674–423 nm and 819–713 nm in the spectra of the Cu(II) chelates and the Schiff base adducts, respectively [27].

Biological study

The Cu(II) complexes and the free ligands were evaluated for their antimicrobial activity against *Escherichia coli* ATCC® 8739™*, *Staphylococcus aureus subsp. aureus* ATCC® 6538™*, *Bacillus subtilis subsp. spizizenii* ATCC® 6633™*and *Candida albicans* ATCC® 2091™* using disc diffusion technique and two-fold serial dilution methods.

Disc diffusion technique

The qualitative antimicrobial susceptibility testing of the compounds was evaluated using the disc diffusion technique [28]. The micro-organisms were cultured on nutrient agar at 37 °C for 24 h to obtain the primary culture. About 10 mL bacterial suspension containing 10^6-10^8 CFUs was prepared from the primary culture using saline water. Sterile Mueller Hinton plates were then inoculated with 0.1 mL of the bacterial suspension and discs soaked with the test compounds were firmly placed on it. The plates were incubated at 37 °C for 16 h and the zone of inhibition was measured as millimetres diameter. Ampicillin and dimethylformamide (DMF)

were used as standard antibacterial drug and control solvent respectively. The test was repeated two more times for those compounds that showed activity of more than 6.5 mm and their activity was recorded as average zone of inhibition as presented in Figures 4 and 5. Similar procedure was repeated for the antifungal susceptibility testing of the compounds at 28 °C for 48 h using potato disc assay and ketoconazole in place of Mueller Hinton agar and penicillin, respectively.

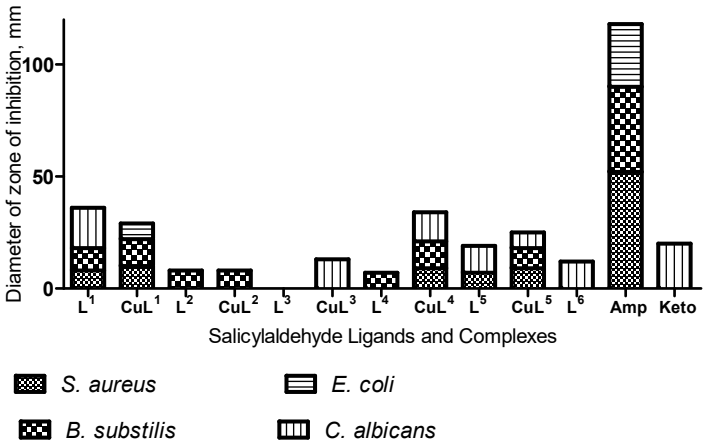


Figure 4. Disc diffusion result of the salicylaldehyde-based complexes.

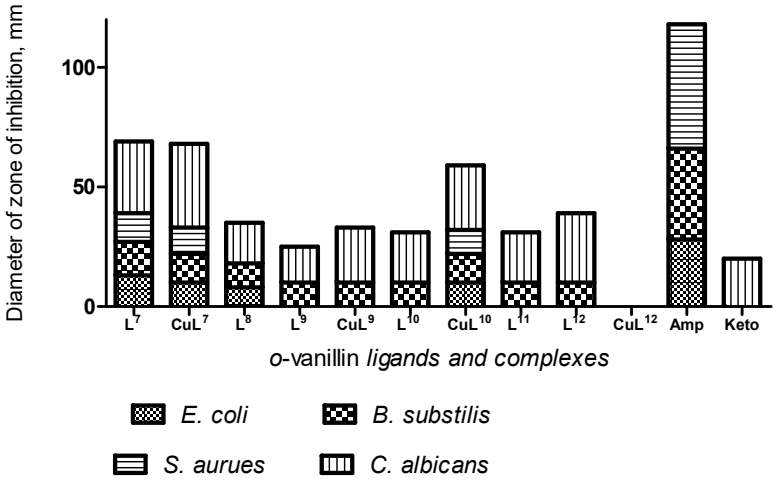


Figure 5. Disc diffusion result of the *o*-vanillin Schiff base complexes.

Minimum inhibitory concentration (MIC)

The quantitative antimicrobial activity of the test compounds was evaluated using micro dilution broth method according to Clinical and Laboratory Standard Institute (formally NCCLS) [28]. Two-fold serial dilutions of the compounds were prepared in 96 micro wells plates using sterile nutrient broth as diluent. The plates were inoculated with 5 μL bacterial suspensions containing

10^6–10^8 CFUs and incubated at 37 °C for 16–18 h. The MIC value was defined as the lowest concentration of the compounds giving complete inhibition of visible growth. The MIC values for the compounds varied from 3.125 mg/mL to 0.0122 mg/mL and the result is presented in Table 4.

Nearly all the compounds exhibited significant antifungal activity against *Candida albicans* and were more potent than the standard antifungal agent, ketoconazole (Keto). They were, however, not as effective as ampicillin (Amp). The *Bacillus substilis* and *Escherichia coli* strains exhibited the most and least antimicrobial susceptibility respectively. *E. coli* is a gram negative bacterium with a thick peptidoglycan cell wall which reduces the permeation of the test compounds into the microorganisms. Furthermore, the *o*-vanillin derived compounds possess higher activity than the salicylaldehyde analogues. The presence of the *ortho*-methoxy group could be responsible for the enhancement of the antimicrobial activity of the Schiff base ligands in the *o*-vanillin derived compounds. The biological activity of Schiff base compounds is often associated [20] with the presence of the of the azomethine functional group, HC=N, and the basicity of the nitrogen atom in this group depends on the nature of the substituents on either or both of the aldehyde and amine moiety of the Schiff base compounds. The inductive effect of the methoxyl group at the *ortho* position reduces the basicity of the azomrthine nitrogen and may thus be responsible for the enhanced antimicrobial activity of the *o*-vanillin based compounds over the salicylaldimine analogues. Similarly, the aniline based compounds exhibited higher antimicrobial activity than the *p*-substituted analogues.

Lastly, the antimicrobial activity of the Cu(II) complexes did not follow any regular pattern. It varied from positive to no effect and even slight reduction in the antimicrobial activity of the free ligands. The complexes of ligands L1, L4, L5, L7, L11 and L10 exhibited higher activity than the free ligands while the ligand L12 complex showed lower potency than the free ligand. The antimicrobial activity of the remaining complexes did not differ significantly from the free Schiff base ligands.

Table 4. MIC values for the Cu(II) complexes (1 x 10^{-1} mg/mL).

Compounds	Gram-positive		Gram-negative
	S. aureus	*B. substilis*	*E.coli*
L^1	-	7.8125	-
CuL^1	3.9062	3.9062	7.8125
L^2	-	3.9062	-
CuL^2	-	3.9062	-
L^4	-	7.8125	-
CuL^4	0.9766	7.8125	-
CuL^5	31.25	7.8125	-
L^7	3.9062	3.9062	7.8125
CuL^7	0.2441	1.9531	0.3125
L^8	7.8125	7.8125	-
CuL^8	*ns	*ns	*ns
L^9	-	31.25	-
CuL^9	-	31.25	-
L^{10}	-	3.9062	-
CuL^{10}	0.1220	7.812	31.250
L^{11}	-	3.9062	-
L^{11}	15.625	3.9062	3.9062
L^{12}	0.4883	0.9766	3.9062
CuL^{12}	7.8125	0.9766	1.9531

*ns: Not soluble.

CONCLUSION

The reaction of Cu(II) chloride salt, $CuCl_2.2HO$, with a series of *p*-substituted salicylaldimine Schiff bases yielded both the prevalent inner metal chelates $[CuL_2]$ and the partially resolved Cu(II) Schiff base adducts $(LH)_2.CuCl_2$. The metal chelates were non-electrolytes while the Schiff base adducts were either 1:1 or 2:1 electrolytes in dimethylformamide. The Cu(II) complexes exhibited significant antifungal activity against *Candida albicans*.

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