Supramolecular coordination and antimicrobial activities of constructed mixed ligand complexes

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HIGHLIGHTS

► L_n behaves as bidentate ligand bonding through azomethine nitrogen and oxygen atoms.
► Substituents effect on reactivities depend mainly on the rate controlling step.
► The electron donating substituents increase the electron density at the metal.
► Antimicrobial activity of ligands depends on determined by the values of clear zone.

GRAPHICAL ABSTRACT

Substituents effect on reactivities depend mainly on the rate controlling step and the nature of the transient specie, while Hammett's relationship studies the reactivity trends in ligands and complexes with the stability.
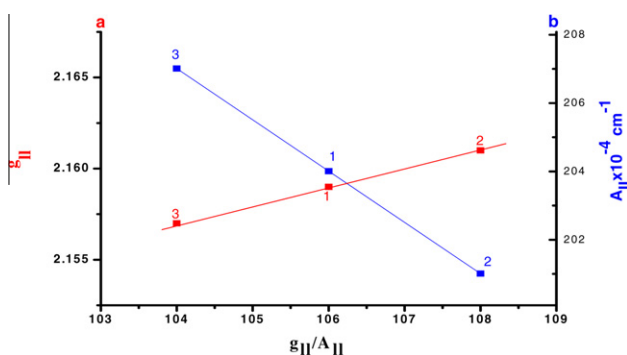
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ABSTRACT

A novel series of copper(II) and palladium(II) with 4-derivatives benzaldehyde pyrazolone (L_n) were synthesized. The mixed ligand complexes were prepared by using 1,10-phenanthroline (Phen) as second ligand. The structure of these complexes was identified and confirm by elemental analysis, molar conductivity, UV–Vis, IR and ^1H NMR spectroscopy and magnetic moment measurements as well as thermal analysis. The ligand behaves as a neutral bidentate ligand through ON donor sites. ESR spectra show the simultaneous presence of a planar *trans* and a nearly planar *cis* isomers in the 1:2 ratio for all N,O complexes $[Cu(L_n)_2]Cl_2 \cdot 2H_2O$. Schiff bases ($L_n$) were tested against bacterial species; namely two Gram positive bacteria (*Staphylococcus aureus* and *Bacillus cereus*) and two Gram negative bacteria (*Escherichia coli* and *Klebsiella pneumoniae*) and fungal species (*Aspergillus niger*, *Fusarium oxysporium*, *Penicillium italicum* and *Alternaria alternata*). The tested compounds have antibacterial activity against *S. aureus*, *B. cereus* and *K. pneumoniae*.

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Introduction

In the last few decades, mixed ligand complexes have been extensively studied in solution as well as in the solid state [1].

Ternary complexes are found to be more stable than binary complexes [2,3]. Steric effect and back donation have also been invoked to account for the preferred formation of mixed-ligand complexes [1].

Heterocyclic compounds such as pyridine (Py), 2,2′-bipyridine (bipy), 1,10-phenanthroline (Phen) and related molecules are good ligands due to the presence of at least one ring nitrogen atom with

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a localized pair of electrons. The successful application of heterocyclic compounds has led to the formation of series of novel compounds with a wide range of physical, chemical and biological properties, spanning a broad spectrum of reactivity and stability [2]. A large number of mixed-ligand complexes involving heterocyclic bases such as Py, bipy and Phen have been reported by many workers [1–12] due to their bioinorganic applications and thermal stability.

Our interest in this area is focused for a considerable time on the investigation of coordination chemistry of transition metal with using pyrazolone based ligand. To gain information about the structure and stereochemistry of such type of complexes. Therefore, in continuation of our earlier work on structural characterization of mixed ligand transition metal complexes containing rhodanine ligand [9–13], here we report the synthesis and characterization of mixed ligand Cu(II) complexes derived from the condensation of 4-aminoantipyrine (4-AAP) with p-derivatives benzaldehyde (L_n) as primary ligand and 1,10-phenanthroline as co-ligands. The complexes prepared were characterized by elemental analysis, conductance, magnetic measurements and spectral studies (IR, UV–Vis and ESR). Thermal stabilities of the complexes have also been discussed.

Antipyrine is an active moiety in pharmacological activity. Antipyrine is used as antinflammatory agents for the treatment of arthritis and analgesics [14–16]. Anticancer activity by antipyrine has also been reported [17]. Antipyrine is a marker in the study of transfer and biotransformations of drugs in the human body [18] and antipyrine metabolites are reported to show a positive correlation with plasma fibronectin level in monitoring patients with chronic liver illness (HBC, HCV and alcohol-related disease) [19].

Experimental

Materials

4-Aminoantipyrine, $CuCl_2 \cdot 2H_2O$, $PdCl_2$ and various aldehydes were purchased from Aldrich, and the other chemicals were of analytical grade quality.

Preparation of ligands (L_n)

Ethanolic solutions of 4-aminoantipyrine (0.1 mol) and 4-derivatives benzaldehyde (0.1 mol) were refluxed together for 4 h over a steam bath. The excess solvent was removed by evaporation and the concentrated solution was cooled in an ice bath with stirring. The Schiff base (L_n) which separated out as a colored powder and then recrystallized from ethanol. The purity of ligands was checked by TLC. Our synthetic route of Schiff base ligands is shown in Scheme 1. The color, yield %, M.P. °C and analytical data given in Table 1.

Preparation of copper(II) complexes

Preparation of $[Cu(L_n)_2]Cl_2 \cdot 2H_2O$ (1–4) (A)
Method A: To a solution of the ligand (L_n) (1.00 mmol) in 25 mL ethanol, an ethanolic (25 mL) solution of copper chloride (0.5 mmol) was added slowly with constant stirring over a period of 10 min in the molar ratio 2:1 (ligand:metal). The reaction mixture was heated to reflux for 3–4 h, concentrated to a small volume and allowed to cool. The formed solid product was removed by filteration washed several times with ethanol, and dried over $CaCl_2$. The purity of the formed compounds was monitored by TLC.

Preparation of $[Cu(L_n)(L)Cl_2]$ (5–8) (B)
Method B: A mixture of (5 mmol) (L_n) and (5 mmol) (Phen.) dissolved in 50 mL, ethanol was added to an solution of copper chloride (5 mmol). The reaction mixture was refluxed for 2–3 h with constant stirring to ensure the complete formation of the metal complexes. The precipitate was filtered and washed several times with 50% (v/v) ethanol–water to remove any traces of unreacted starting materials. Finally, the filtrate was dried in vacuum desiccators over anhydrous $CaCl_2$.

The obtain mixed ligand complexes are $[Cu(L_n)(L)Cl_2]$ (5–8) (B). Fig. 3II represents the proposed chemical structure of mixed ligand complexes.

L_n

X=OCH$_3$ (1), H (2), Cl (3), NO$_2$ (4)
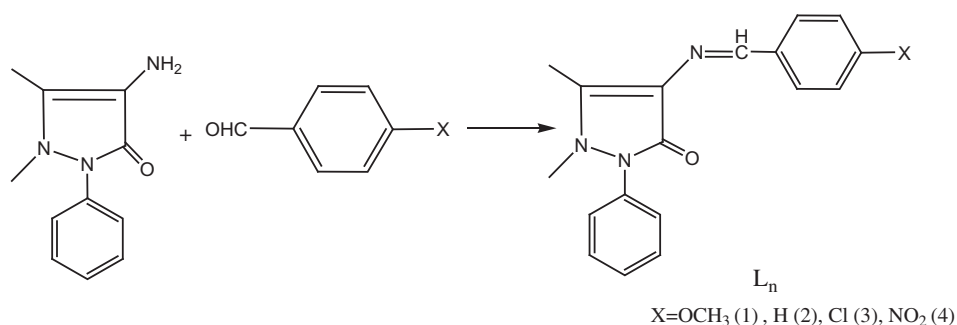
Scheme 1. Synthetic route of Schiff base ligands.

Table 1
Elemental analysis (C, H, N)[a], color, yield (%) and melting point (°C) of ligands (L_n).

Compound	Color	Yield (%)	M.P. (°C)	Calc. (Exp.)%		
				C	H	N
L_1	Yellow	46.7	173	71.03 (71.17)	5.92 (5.99)	13.08 (13.37)
L_2	Pale yellow	52.2	195	74.23 (74.42)	5.84 (5.93)	14.43 (14.59)
L_3	Yellow	56.5	237	66.36 (66.45)	4.92 (5.13)	12.90 (13.21)
L_4	Pale yellow	67.0	261	64.29 (64.37)	4.76 (4.88)	16.67 (16.88)

[a] The excellent agreement between calculated and experimental data suggests the assignment suggested in the present work.

Preparation of $[Pd(L_n)_2]Cl_2$ (**9–12**) (**C**)

Method C: An ethanolic solution of 0.01 mol of $PdCl_2$ was mixed with the appropriate weight of the corresponding ligand (L_n) in ethanol (25–40 ml). The reaction mixture was boiled with stirring until the corresponding solid complex separated. On cooling the crystalline product formed was filtered off, washed several times with dry ethanol and dry diethyl ether and finally dried in a desiccator over fused $CaCl_2$.

Microbiological investigation

For this investigation the agar well diffusion method was applied [20,21]. The antibacterial activities of the investigated compounds were tested against two local Gram positive bacterial isolates (*Bacillus cereus* and *Staphylococcus aureus*) and two local Gram negative bacterial isolates (*Escherichia coli* and *Klebsiella pneumoniae*) on nutrient agar medium. Also, the activities were tested against four local fungal isolates (*Aspergillus niger*, *Alternaria alternata*, *Penicillium italicum* and *Fusarium oxysporium*) on DOX agar medium. The concentrations of each solution were 50 μg/ml, 100 μg/ml and 150 μg/ml. By using a sterile cork borer (10 mm diameter), wells were made in agar medium plates previously seeded with the test organism. 200 μl of each compound was applied in each well. The agar plates were kept at 4 °C for at least 30 min. to allow the diffusion of the compound to agar medium. The plates were then incubated at 37 °C or 30 °C for bacteria and fungi, respectively. The diameters of inhibition zone were determined after 24 h for bacteria and 7 day for fungi.

Measurements

Elemental microanalyses of the separated ligands and solid chelates for C, H, and N were performed in the Microanalytical Center, Cairo University, Egypt. The analyses were repeated twice to check the accuracy of the analyzed data. The metal content in the complexes was estimated by standard methods [22]. The ^1H NMR spectrum was obtained with a JEOL FX90 Fourier transform spectrometer with DMSO-d_6 as the solvent and TMS as an internal reference. Infrared spectra were recorded as KBr pellets using a Pye Unicam SP 2000 spectrophotometer. Ultraviolet–Visible (UV–Vis) spectra of the compounds were recorded in nuzol solution using a Unicom SP 8800 spectrophotometer. The magnetic moment of the prepared solid complexes was determined at room temperature using the Gouy's method. Mercury(II) (tetrathiocyanato)cobalt(II), $[Hg\{Co(SCN)_4\}]$, was used for the calibration of the Gouy tubes. Diamagnetic corrections were calculated from the values given by Selwood [23] and Pascal's constants. Magnetic moments were calculated using the equation, $\mu_{eff.} = 2.84[T\chi_M^{coor.}]^{1/2}$. TG measurements were made using a Du Pont 950 thermobalance. Ten milligram samples were heated at a rate of 10 °C/min in a dynamic nitrogen atmosphere (70 ml/min); the sample holder was boat-shaped, $10 \times 5 \times 2.5$ mm deep; the temperature measuring thermocouple was placed within 1 mm of the holder. The halogen content was determined by combustion of the solid complex (30 mg) in an oxygen flask in the presence of a KOH—H_2O_2 mixture. The halide content was then determined by titration with a standard $Hg(NO_3)_2$ solution using diphenylcarbazone indicator. ESR measurements of powdered samples were recorded at room temperature (Tanta university, Egypt) using an X-band spectrometer utilizing a 100 kHz magnetic field modulation with diphenyl picrylhydrazyle (DPPH) as a reference material. The conductance measurement was achieved using Sargent Welch scientific Co., Skokie, IL, USA. X-ray diffraction (XRD) is considered now as a powerful technique in the following subjects: phase identification, determination of crystal structure, phase diagram determination, quantitative phase analysis, precise parameter measurements, structure of polycrystalline aggregates, stress measurements, orientation of crystals.

Phase analysis of L_4 powder was performed at room temperature by a Philips X-ray diffractometer equipped with utilized monochromatic Cu Kα radiation ($\lambda = 1.5418$ Å). The X-ray tube voltage and current were 40 kV and 25 mA, respectively.

Results and discussion

Synthesis and characterization of ligand

The ligands (L_n) were prepared by stirring an appropriate amount of reactive *p*-derivatives benzaldehyde with the corresponding 4-aminoantipyrine in ethanol. Schiff base ligands (L_n) were light yellow in color and it is soluble in common organic solvents. The Schiff bases formed were characterized with respect to its composition by elemental and spectral analysis. Elemental analysis of the ligand (L_n) given in Table 1, IR spectra in Table 2 and ^1H NMR in Table 3. Elemental analysis of the ligand (L_n) show good agreement with theoretical data.

For the four compounds the yield %/M.P. °C of these compounds were found to be sensitive to the nature of the substituents, *X*, on the ligand. In case of L_4 with *X* = electron withdrawing NO_2, higher values (67/261) of the yield %/M.P. °C, respectively, are observed, whereas lower values (46.7/173) are observed for L_1 (*X* = OCH_3), reflects the electron donating nature of the substituent (Fig. 1).

Because of the high similarity of the X-ray diffraction, XRD, patterns for all ligands ($L_{1–4}$), we will suffice by mentioning the XRD patterns of L_4 as representative results for the rest of the ligands. The X-ray diffraction (XRD) pattern for the L_4 in powder form shows many peaks superimposed with a broad peak at $2\theta \simeq 8°$ (as shown in Fig. 2). This indicates the polycrystalline nature of the ligand under investigation in addition with some amorphous domains.

Table 2
Some selected bands of diagnostic importance from the IR spectra (cm^{-1}) of 4-AAP and ligands (L_n).

4-AAP	L_1	L_2	L_3	L_4	Assignment
3426	–	–	–	–	$\upsilon(NH_2)_{as}$
3315	–	–	–	–	$\upsilon(NH_2)_s$
3175	3085	3085	3086	3088	$\upsilon(CH)_{as}(Ar)$
3087	3036	3035	3037	3038	$\upsilon(CH)_s(Ar)$
2985	2935	2930	2928	2928	$\upsilon(CH)_{as}(CH_3)$
2918	2920	2022	2924	2925	$\upsilon(CH)_s(CH_3)$
1640	1644	1648	1650	1653	C=O
–	1590	1594	1596	1598	C=N
1405	1416	1418	1420	1423	N—CH_3
1310	1360	1370	1375	1380	C—N
1200	1179	1181	1183	1185	$\delta(CH_3)$
–	1017	1020	1022	1025	$\gamma(C=N)$
730	678	680	685	687	$\gamma(CH)ring$

Table 3
^1H NMR spectral data (δ ppm) of 4-AAP and ligands (L_n).

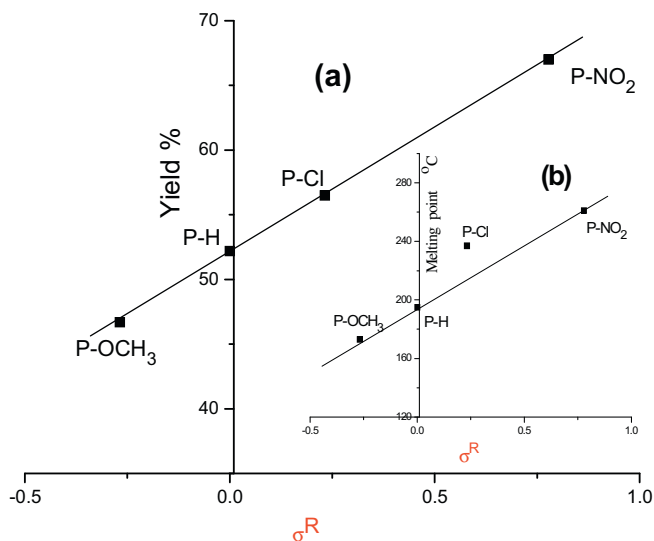| Assignment	Compound				
	L_1	L_2	L_3	L_4	(4-AAP)
C—CH_3	2.55	2.60	2.64	2.68	2.15
N—CH_3	3.09	3.15	3.22	3.27	2.84
NH_2	–	–	–	–	2.99
ArH	6.80–7.86	7.22–7.95	7.33–8.22	7.42–8.34	7.15–7.50
CH=N	9.71	9.48	9.40	9.36	–
OCH_3	3.27	–	–	–	–

Fig. 1. The relation between Hammett's substitution coefficient (σ^R) *vs.* (a) yield % and (b) melting point °C of ligand (L_n).
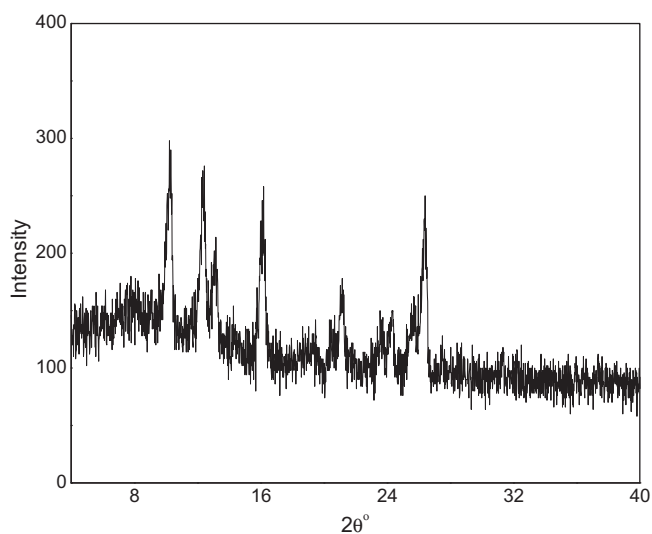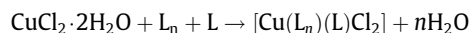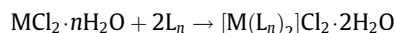

Fig. 2. X-ray diffraction patterns for ligands (L_4).

Synthesis and characterization of metal complexes

The complexes are stable in air and atmosphere. All the complexes are soluble in DMF and DMSO, but they are insoluble in some common organic solvents. The analytical data (Table 4) indicate that the metal to ligand ratio is 1:2 [M($L_n)_2$]Cl_2 (M:L_n) and 1:1:1[Cu(L_n)(L)Cl_2](L_n:M:co.ligand) molar ratios in mixed-ligand complexes as obtainable in the following reaction.

$$MCl_2 \cdot nH_2O + 2L_n \rightarrow [M(L_n)_2]Cl_2 \cdot 2H_2O$$

$$CuCl_2 \cdot 2H_2O + L_n + L \rightarrow [Cu(L_n)(L)Cl_2] + nH_2O$$

where L_n = primary ligands, L = co-ligand and M = Cu(II), n = 2 or Pd(II), n = nil.

All these complexes are colored, air stable and insoluble in common organic solvents except DMF and DMSO. The molar conductivity values of the compounds **1–4** and **9–12** in 10^{-3} M solution in DMF suggest that they are 1:2 electrolytes. But molar conductivity values of the compounds **5–8** shows that they are non-electrolyte indicating that the anions are coordinated to the central Cu(II) ion values of the compounds.

The ligand has two different bis-NO or N_3O cores (nitrogen of imine, keto O-atoms present in the pyrazolone ring and two azomethine nitrogen atoms in 1,10-phenanthroline to coordinate metal ions. There are variable binding possibilities to metal ions for ligand structural form (see Fig. 3). All binary complexes of Cu(II) and Pd(II) ions (**1–4** & **9–12**) have 1:2 metal-to-ligand stoichiometry, as shown in Fig. 3I. Moreover, the analytical data of metal chelates (Table 4) indicates that the metal ion in case of all mixed ligand complexes are coordinated to one mixed ligand molecule (1,10-phenanthroline) in addition to L_n molecule (Fig. 3II).

IR spectra

The spectra of the free ligands (L_{1-4}) display bands at 1645–1655 and 1590–1600 cm^{-1} due to $\upsilon(C{=}O)$ and $\upsilon(C{=}N)$, respectively. The spectra of complexes showed that these two bands of the free ligands were not observed at the same frequencies and the same intensities. They shift to lower frequencies and, at the same time, their intensities are lowered. They results indicate that the ligands act as neutral bidentate bonded to the metal through the azomethine-nitrogen and the keto-oxygen atoms. Further proof for the involvement of both azomethine-nitrogen and the keto-oxygen atoms in complexation is the appearance of weak bands in the far IR region of complexes at (400–450) and (475–

Table 4
Analytical data[a] of the complexes.[b]

Compound[c]	Method of preparation[d]	Calc. (Exp.)%				
		C	H	N	M	Cl
[Cu($L_1)_2$]Cl_2.$2H_2O$ (**1**)	A	56.12 (56.34)	4.68 (4.87)	10.34 (10.52)	7.82 (8.07)	8.74 (8.44)
[Cu($L_2)_2$]$Cl_2$$2H_2O$ (**2**)	A	57.25 (57.36)	4.77 (4.86)	11.13 (11.53)	8.42 (8.68)	9.41 (9.52)
[Cu($L_3)_2$]Cl_2.$2H_2O$ (**3**)	A	52.58 (52.42)	3.90 (4.02)	10.23 (10.44)	7.73 (7.82)	17.29 (17.32)
[Cu($L_4)_2$]Cl_2.$2H_2O$ (**4**)	A	51.13 (51.24)	3.80 (3.87)	13.29 (13.18)	7.54 (7.68)	8.43 (8.03)
[Cu(L_1)(L)Cl_2] (**5**)	B	58.53 (58.63)	4.25 (4.40)	11.01 (11.42)	10.00 (10.23)	11.17 (11.38)
[Cu(L_2)(L)Cl_2] (**6**)	B	59.45 (59.56)	4.13 (4.23)	11.56 (11.87)	10.49 (11.66)	11.25 (11.45)
[Cu(L_3)(L)Cl_2] (**7**)	B	56.25 (56.42)	3.75 (3.67)	10.94 (11.59)	9.93 (10.34)	16.64 (16.86)
Cu(L_4)(L)Cl_2] (**8**)	B	60.50 (60.65)	4.03 (4.21)	10.76 (10.87)	10.68 (10.78)	5.97 (6.09)
[Pd($L_1)_2$]Cl_2 (**9**)	C	55.65 (55.73)	4.64 (4.74)	10.25 (10.46)	12.99 (13.24)	8.67 (8.87)
[Pd($L_2)_2$]Cl_2 (**10**)	C	56.89 (56.98)	4.48 (4.57)	11.06 (11.25)	14.01 (14.42)	9.35 (9.55)
[Pd($L_3)_2$]Cl_2 (**11**)	C	52.15 (52.24)	3.81 (3.93)	10.14 (10.35)	12.85 (12.96)	17.14 (17.34)
[Pd($L_4)_2$]Cl_2 (**12**)	C	50.86 (50.94)	3.77 (3.88)	13.19 (13.35)	12.53 (12.65)	8.36 (8.55)

[a] Microanalytical data as well as metal estimations are in good agreement with the stoichiometry of the proposed complexes.
[b] The excellent agreement between calculated and experimental data supports the assignment suggested in the present work.
[c] L_n are the ligand as given in Scheme 1; air-stable; no-hygroscopic; insoluble in water; soluble in coordinating solvents such as DMF and DMSO.
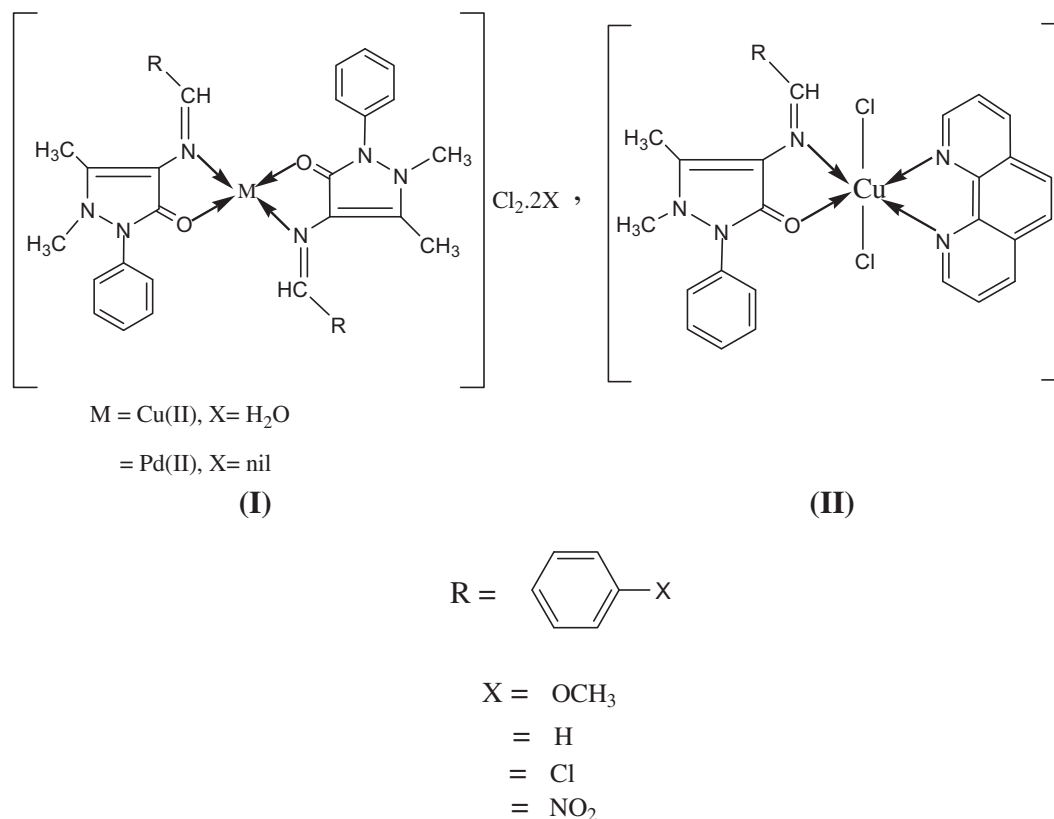[d] See text.

M = Cu(II), X= H_2O

= Pd(II), X= nil

(I)

(II)

R = (phenyl)—X

X = OCH_3

= H

= Cl

= NO_2

Fig. 3. Proposed structure of complexes.

505) cm^{-1} due to υ(M—N) and υ(M—O) respectively [9–13] which are absent in the free ligands. In the spectra of mixed 1,10-phenanthroline (L) complexes (**5–8**), the bands of L free ligand at 740 cm^{-1} are shifted to higher frequencies ~775 cm^{-1}. The OH stretching frequency appears in the spectra of complexes around 3400 cm^{-1} is attributed to the presence of water of hydration. Also, according to Stefov et al. [24], coordinated water should exhibit frequencies ~830, 570 and 448 cm^{-1}. The absence of spectral bands in these regions in the spectra of complexes indicates that the water molecules in these complexes are not coordinated but are present as lattice water. From the above mentioned, the ligands, act as neutral bidentate chelating agents coordinated to the Cu(II) *via* the azomethine-nitrogen and keto-oxygen atoms forming the more stable six-membered chelate rings.

^{1}H NMR spectra

The ^{1}H NMR spectra of the antipyrine Schiff bases (Table 3) display two sharp signals at 2.33–2.48 and 3.09–3.16 ppm with an integration equivalent to three hydrogens corresponding to the N—CH$_3$ and C—CH$_3$ groups. The aromatic rings give a group of multi signals at 6.80–7.86 ppm. The CH=N hydrogen for L$_n$ resonates at 9.46–9.81 ppm as a sharp singlet. The Pd(II) complexes shows a slight downfield shift of 0.3–0.6 ppm in the resonance peaks corresponding to the phenyl ring and the azomethine proton, which may be attributed to the coordination of the ligand to the Pd(II) ion. ^{13}C NMR of L$_{1-4}$ exhibited signals at 188–188.8 and 161–161.9 ppm corresponding to the carbon of C—O and C—N groups. Methyl groups were observed between 18.4 and 19.8 ppm. Also, the spectra showed peaks at 19–131 ppm corresponding to carbons of the phenyl ring.

Electronic spectra and magnetic moments of copper(II) complexes (**1–4**)

Elemental analysis, IR and molar conductivity data were used to prove the stoichiometry and formulation of the complexes. A square planar geometry was assumed for all the complexes based on their magnetic data and spectral studies.

Electronic spectra of ligand and its mononuclear copper(II) complexes were recorded in DMF solution. In the electronic spectra of the ligand and its mononuclear metal complexes, the wide range bands were observed due to either the π–π^* and $n \rightarrow \pi^*$ of C=N chromophore or charge-transfer transition arising from π electron interactions between the metal and ligand, which involved either a metal-to-ligand or ligand-to-metal electron transfer [25]. The electronic spectra of the free ligand in DMF showed strong absorption bands in the ultraviolet region (23,530–37,460 cm^{-1}), that could be attributed to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions in the benzene ring or azomethine (—C=N) groups for free ligand. The absorption bands between 37,460 and 23,530 cm^{-1} in free ligand changed a bit in intensity and remained slightly changed for metal complexes. The absorption shift and intensity change in the spectra of the metal complexes most likely originated from the metallation, increased the conjugation and delocalization of the whole electronic system and resulted in the energy change of the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions of the conjugated chromophore [26]. The electronic spectra of copper(II) complexes shows absorption band in the ranges 14,000–15,800 and 18,900–20,230 cm^{-1}, assignable respectively, to transitions $^2B_{1g} \rightarrow {}^2B_{2g}$ and $^2B_{1g} \rightarrow {}^2E_g$ of a square planar structure [27]. The copper(II) complexes paramagnetic and the room temperature magnetic moments values (1.80–2.10 B.M.) are indicative of one unpaired electron per Cu(II) ion. These values are closer to or slightly higher than the spin-only

Table 5
ESR spectral assignments for Cu(II) complexes.

Complex[a]	g_{II}	$g_\perp$	g_I	A_{II}[b]	g_{II}/A_{II}
1	2.157	2.064	2.095	207	104
2	2.159	2.063	2.095	204	106
3	2.161	2.066	2.098	201	108

[a] Numbers as given in Table 4.
[b] Expressed in units of cm^{-1} multiplied by a factor of 10^{-4}.

value, indicates absence of any magnetic exchange interactions between copper(II) ions.

ESR spectra of copper(II) complexes (1–4)

ESR spectra of copper(II) complexes recorded in polycrystalline state at room temperature also provides information about the square planar geometry of the copper(II) complexes. The spectra are typical for axial type complexes, from which g_{II}, $g_\perp$, g and A_{II} have be calculated (Table 5). The ordering of g values $g_{II} > g_\perp > 2.0023$ observed for copper(II) complexes indicates that the unpaired electron most likely resides in their d_{x2-y2} orbital [28] and $^2B_{1g}$ ground state [29]. g_{II} is a moderately sensitive function for indicating covalency and $g_{II} > 2.3$ and $g_{II} < 2.3$ is characteristic of anionic and covalent environments, respectively, in metal–ligand bonding. The fact that the g_{II} values are less than 2.3 is an indication of significant covalent bonding in copper(II) complexes [29].

In axial symmetry $G = g_{II} - 2/g_\perp - 2$ is a measure of the exchange interaction between Cu(II) centers in polycrystalline state. The value of $G > 4$ indicates negligible exchange interaction in solid complexes [30]. The G value in copper(II) complexes are less than 4 suggesting d_{x2-y2} ground state with a small exchange coupling [31]. The g_{II} and $|A_{II}|$ values indicate square planar coordination geometry for the CuN_2O_2 moiety. A_{II} the spectra are almost superimposable. Whatever the electron withdrawing or donor power and the *para* position of the substituent on the aromatic ring. In fact, the ESR parameters which relate to electron density in CuN_2-O_2 plan are relatively in sensitive to the substitution in these ligands aryl groups. Moreover the ratio g_{II}/A_{II} is an indication of the stereochemistry of the copper(II) complexes. Sagakachi and Addison [32] have suggested that this ratio may be an empirical indication of the tetrahedral distortion of a square planar geometry. The values lower than 135 cm^{-1} are observed for square planar structures and those higher than 150 cm^{-1} for tetrahedrally distorted complexes.

The lowest values of the ratio g_{II}/A_{II} for the *trans* species are indicative of a planar *trans* arrangement whereas the slightly higher values of the ratio g_{II}/A_{II} for the *cis* compounds indicate only a nearly planar *cis* arrangement.

Thermal gravimetric analyses of copper(II) complexes (1–4)

Thermal gravimetric analyses for $[Cu(L_n)_2]Cl_2 \cdot 2H_2O$ (1–4) complexes were obtained to give information concerning the thermal stability of the complexes and decide whether the water and sol-

vent molecules are in the inner or outer coordination sphere of the central metal ion. The results of thermal analyses show good agreement with the theoretical formula as suggested from the elemental analyses. The thermograms of the complexes (1–4) can be subdivided into three stages. The first stage extends up to 180 °C and corresponds to the weight loss of the hydrated water molecules during one exothermic process. The second stage extends up to 345 °C and corresponds to the weight loss of the two HCl molecules. The third stage above 345 °C with the formation of the corresponding metal oxides.

Electronic spectra and magnetic moment of copper(II) mixed ligand complexes (5–8)

Electronic spectra of six-coordinate Cu(II) complexes (5–8) arise from the electronic transition within a molecular or ion from a lower to a higher electronic energy level. The transition metal ions generally show a number of d-d transition bands depending on their electronic configuration from d^1 to d^9 in UV–Vis regions. The copper(II) complexes generally show a broad band in the 13,000–18,000 cm^{-1} region assigned to the envelop of $^2B_{1g} \rightarrow$ $^2E_g + {}^2B_{2g} + {}^2A_{1g}$ transitions [33]. These bands are only slightly shifted in DMSO solution and observed in the 15,200–15,400 cm^{-1}, suggesting a distorted octahedral geometry for all the complexes.

The magnetic moment of all the copper(II) complexes at room temperature lie in the range of 1.90–2.20 B.M., corresponding to one unpaired electron. This indicates that spin–spin coupling between unpaired electrons belonging to different copper ions is absent.

ESR spectra of copper(II) mixed ligand complexes (5–8)

To obtain further information about the stereochemistry and the site of the metal ligand bonding and to determine the magnetic interaction in the metal complexes, the ESR spectra of all Cu(II) complexes have been recorded. The spectra of the complexes show typical axial behavior with slightly different g_{II} and g values. The geometric parameter G, which is measure of exchange coupling interaction between two copper center explained by Hathaway [34] expression $G = (g_{II} - 2)/(g_\perp - 2)$. Accordingly, if the value of G is greater than four, the exchange interaction is negligible interaction, whereas when the value of G is less four a considerable interaction is indicated in solid complex. The trend $g_{II} > g_\perp > g_e$ (2.0023) observed for these complexes shows that the unpaired electron is localized in d_{x2-y2} orbital of the Cu(II) ions and the spectral features are characteristics of axial symmetry. For a Cu(II) complex, g_{II} is a parameter sensitive enough to indicate covalent. The g_{II} values for all the Cu(II) complexes (Table 6) are less than 2.3 is an indication of significant covalent bonding in these complexes. The complex under study may have six- coordinate tetragonal geometry.

Molecular orbital coefficients, α^2 (a measure of the covalency of the in-plane σ-bonding between a copper 3d orbital and the ligand

Table 6
ESR spectral assignments for Cu(II) mixed ligand complexes.

Complex[a]	g_{II}	$g_\perp$	g_e	G	α^2	β^2	A_{II}[b]	K_{II}^2	K_l^2	g_{II}/A_{II}
5	2.221	2.047	2.105	4.9	0.48	1.054	72.77	0.506	0.414	305
6	2.224	2.096	2.138	2.4	0.63	0.813	118.13	0.512	0.866	188
7	2.239	2.060	2.119	4.1	0.54	1.011	85.89	0.546	0.533	260

[a] Numbers as given in Table 4.
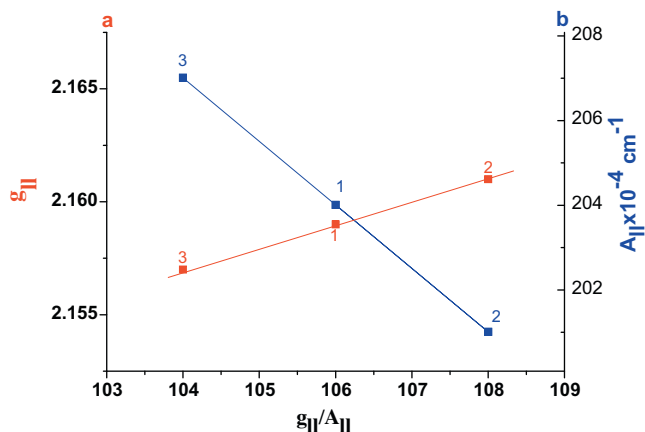[b] Expressed in units of cm^{-1} multiplied by a factor of 10^{-4}.

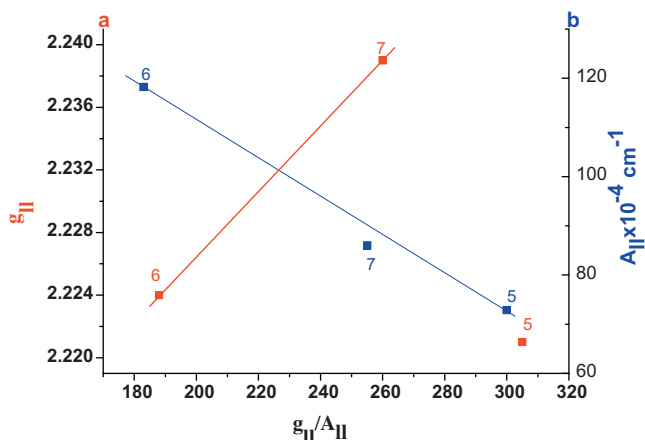**Fig. 4.** The relation between g_{ll}/A_{ll} vs. (a) g_{ll} and (b) $A_{ll} \times 10^{-4}$ cm^{-1}.

Fig. 5. Plot of (a) g_{ll} and (b) $A_{ll} \times 10^{-4}$ cm^{-1} vs. g_{ll}/A_{ll}.

orbitals) and β^2 (covalent in-plane π-bonding), were calculated by using the following equations:

$$\alpha^2 = (A_{ll}/P) + (g_{ll} - 2.0023) + 3/7(g_\perp - 2.0023) + 0.04$$

$$\beta^2 = (g_{ll} - 2.0023)E/ - 8\lambda\alpha^2$$

The observed values of α^2 and β^2 parameters indicate that the complexes have covalent character and there is interaction in the out-of-plane π-bonding. The lower values of α^2 compared to β^2 indicate that the in-plane σ-bonding is more covalent than the in-plan π-bonding. According to Hathaway [35], $K_{ll} \approx K_\perp \approx 0.77$ for pure in-plane σ-bonding and $K_{ll} < K_\perp$ for in-plane π-bonding, while for out of plane π-bonding $K_{ll} > K_\perp$. In all the Cu(II) complexes, it is observed that $K_{ll} < K_\perp$ which indicates the presence of significant in-plane π-bonding. Based on these observations, a distorted octahedral geometry is proposed for Cu(II) complexes. The ESR study of the Cu(II) complexes has provided supportive evidence to the conclusion obtained on the basis of electronic spectrum and magnetic moment value.

The plot of g_{ll} and $A_{ll} \times 10^{-4}$ cm^{-1} vs. of f gives straight line with increase the value of f decrease g_{ll} and increase the $A_{ll} \times 10^{-4}$ cm^{-1} (Figs. 4 and 5). It seems that the electron withdrawing p-substituent increase the positive charge on the metal ion leading to a increase in f and $A_{ll} \times 10^{-4}$ cm^{-1} and subsequently a decrease in g_{ll}.

Thermal gravimetric analyses of copper(II) mixed ligand complexes (5–8)

The thermal decomposition process of mixed ligand complexes (**5–8**) involves three decomposition steps. The complexes show no mass lose up to 280 °C, respectively, revealing the absence of either water or solvent molecules in these complexes. The first decomposition step takes place in the temperature range 430–450 °C, corresponding to the decomposition of half of the molecule (L_n). The second take place in the 500–600 °C range may be attributed to the decomposition of the remaining half of the molecule (L_n). The third of decomposition which starts at 655 °C is a continuous one. The steady mass loss observed in this step may be due to the decomposition of 1,10-phenanthroline molecule (L) and leaving anhydrous CuO.

Electronic spectra and magnetic moments of palladium(II) complexes (9–12)

The complexes (**9–12**) exhibit three spin allowed d-d transitions from lower lying d-levels to the empty d_{x2-y2} orbital. Although other two electronic transitions are also observed but their intensities are very weak and are neglected. The complexes show the absorptions bands at 18,422–20,645 ($^1A_{1g} \rightarrow A_{2g}$), 27,290–27,890 ($^1A_{1g} \rightarrow {}^1B_{1g}$) and 31,120 ($^1A_{1g} \rightarrow {}^1E_g$) cm^{-1} d–d transitions [36]. Moreover in the complexes, the high intensity charge transfer absorption bands are also observed at 44,980 ($^1A_{1g} \rightarrow {}^1A_{2u}$) and 36,670–37,140 ($^1A_{1g} \rightarrow {}^1E_u$) cm^{-1} transitions. These absorption bands suggest that the complexes possess D_{4h} symmetry and square planar geometry. The magnetic moment studies show that all the complexes of Pd(II) are diamagnetic with spin-paired d^8 system.

Structural interpretation

From all of the above observation and according to the data reported in this paper based on the IR, molar conductivity, spectral and magnetic susceptibility, the structure of these complexes is given as shown in Fig. 3. The structure proposed for Cu(II) and Pd(II) complexes (**1–4** and **9–12**) is square planar while for copper(II) mixed ligand for complexes (**5–8**) is octahedral. This indicates that, the ligand behaves as bidentate chelating ligand and both azomethine-nitrogen and keto-oxygen are the two sites of coordination.

Microbiological investigation

The C=N linkage in azomethine derivatives is an essential structural requirement for biological activity [37]. Several Schiff bases have been reported to possess remarkable antibacterial, antifungal, anticancer and diuretic activities [38–41]. The antibacterial action of Schiff base ligand may be significantly enhanced by the presence of azomethine groups which have chelating properties. These properties may be used in metal transport across the bacterial membranes or to attach to the bacterial cells at a specific site from which it can interfere with their growth [42].

The antimicrobial activity of L_1, L_2, L_3 and L_4 ligand was tested against bacteria and fungi. More than one test organism used tested to increase the chance of detection of their antimicrobial activities. The used organisms in the present investigations included two Gram positive bacteria (*B. cereus* and *S. aureus*) and two Gram negative bacteria (*E. coli* and *K. pneumoniae*) in addition to different kinds of fungi (*A. niger*, *A. alternata*, *P. italicum* and *F. oxysporium*).

The results of the antibacterial activities of the synthesized compounds were recorded in Table 7. Some of the used ligands were found to have antibacterial activity against Gram positive

Table 7
Antibacterial activities of some *p*-derivatives 4-aminoantipyrine against *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli* and *Klebsiella pneumoniae*. Inhibition zone was recorded as mm.

Compound	Concentration (µg/ml)	Gram positive bacteria		Gram negative bacteria	
		Bacillus cereus	*Staphylococcus aureus*	*Escherichia coli*	*Klebsiella pneumoniae*
L₁	50	−ve	3 mm	−ve	−ve
	100	−ve	3 mm	−ve	−ve
	150	1 mm	5 mm	−ve	1 mm
L₂	50	−ve	−ve	−ve	2 mm
	100	−ve	1 mm	−ve	7 mm
	150	−ve	3 mm	−ve	7 mm
L₃	50	−ve	−ve	−ve	2 mm
	100	−ve	−ve	−ve	2 mm
	150	−ve	−ve	−ve	4 mm
L₄	50	7 mm	3 mm	−ve	−ve
	100	11 mm	3 mm	−ve	−ve
	150	11 mm	1 mm	−ve	8 mm

Table 8
Antifungal activities of some *p*-derivatives 4-aminoantipyrine against *Aspergillus niger*, *Fusarium oxysporium*, *Penicillium italicum* and *Alternaria alternata*. Inhibition zone was recorded as mm.

Compound	Concentration (µg/ml)	*Fusarium oxysporium*	*Penicillium italicum*	*Aspergillus niger*	*Alternaria alternata*
L₁	50	1 mm	2 mm	−ve	−ve
	100	1 mm	2 mm	−ve	−ve
	150	1 mm	2 mm	−ve	−ve
L₂	50	−ve	−ve	−ve	−ve
	100	−ve	−ve	−ve	−ve
	150	−ve	−ve	−ve	−ve
L₃	50	−ve	−ve	−ve	−ve
	100	−ve	−ve	−ve	−ve
	150	−ve	−ve	−ve	−ve
L₄	50	−ve	−ve	−ve	−ve
	100	−ve	−ve	−ve	−ve
	150	1 mm	1 mm	−ve	−ve

bacteria namely; *B. cereus* (inhibition zone of L₄ = 7, 11 and 11 mm at conc. = 50, 100 and 150 µg/ml respectively) and *S. aureus* (inhibition zone of L₄ = 3 and 3 mm at conc. = 50 and 100 µg/ml respectively), (inhibition zone of L₂ = 1 and 3 mm at conc. = 100 and 150 µg/ml respectively) and (inhibition zone of L₁ = 3 and 5 mm at conc. = 50 and 150 µg/ml respectively). Also some of these compound have antibacterial activity against Gram negative bacterium (*K. pneumoniae*) (inhibition zone of L₂ = 2 and 7 mm at conc. = 50 and 150 µg/ml respectively) and inhibition zone of L₃ = 2, 2 and 4 mm at conc. = 50, 100 and 150 µg/ml respectively, but no effect was recorded against *E. coli*.

The results of the antifungal activities of the synthesized compounds were recorded in Table 8. Some the used ligands were found to have low antifungal activity against *P. italicum* and *F. oxysporium*, but no effect was observed against *A. niger* and *A. alternata*.

The screening data revealed that most of the tested compounds showed good antimicrobial activity (see Fig. 6). The compound L₄ exhibited good antibacterial activity, almost close to that of the standard. Similar to other investigations, most of our compounds moderately inhibited the growth of Gram positive bacteria [43]. The L₄ is more active than L₃, L₂ and L₁ against *B. cereus*, *S. aureus* and *K. pneumonia*e). Whereas the L₁ is more active than L₂, L₃ and L₄ against *P. italicum* and *F. oxysporium*.

The values of clear zone for ligands are related to the nature of the *p*-substituent as they increase according to the following order *p*-(OCH₃ < H < Cl < NO₂) [29,44]. This can be attributed to the fact that the effective charge experienced by the d-electrons increased due to the electron withdrawing *p*-substituent (L₃ and L₄) while it decreased by the electron donating character of L₁. This is in
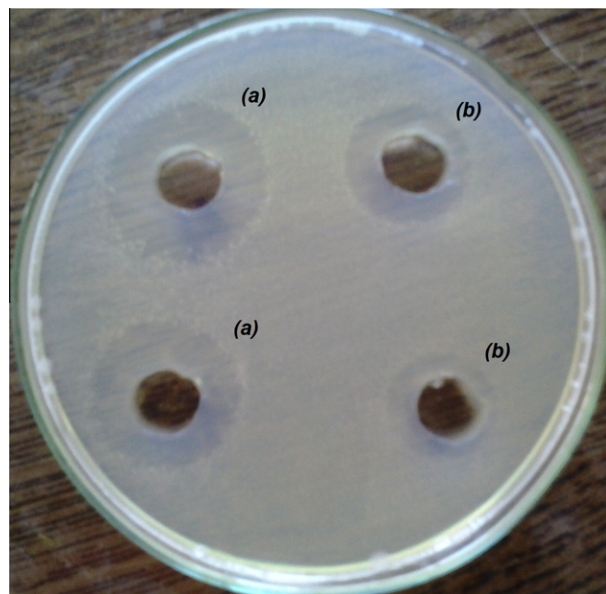

Fig. 6. Effect of L₂ and L₃ against *Klebsiella pneumoniae*. Inhibition zone was recorded as mm as a result of L₂ at conc. = 150 µg/ml (a) and L₃ at conc. = 150 µg/ml (b).

accordance with that expected from Hammett's constant σ^R as shown in Fig. 7 that correlates the values of inhibition zone (mm) with σ^R. It is clear that these values increase with increasing
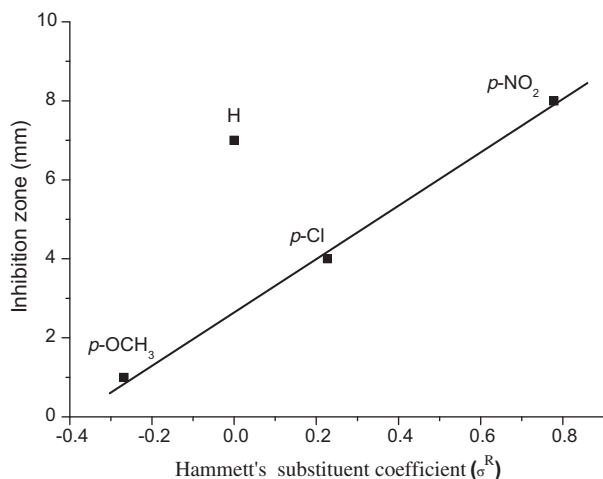
Fig. 7. The relation between Hammett's substitution coefficient (σ^R) vs. inhibition zone of ligand (L_n) against *Klebsiella pneumoniae* conc. = 150 µg/ml.

σ^R. It is important to note that the existence of methoxy group enhances the electron density on the coordination sites and simultaneously decreases the values of clear zone.

Conclusion

This study has suggested that L_n behaves as a chelating bidentate ligand, bonding through azomethine nitrogen and ketonic oxygen atoms. The IR data reveal that the anions are not binded to the metal ions and the metal ions do not occupy all the available sites in the metal chelate due to steric constraints.

The stoichiometric data of Cu(II), Pd(II) and Cu(II) mixed ligand complexes and their physico-chemical investigations indicate that the probable coordination number of copper(II) in these complexes is six-coordinate [octahedral structure; Fig. 3I] and four-coordinate [square planar structure; Fig. 3II].

Substituents effect on reactivities depend mainly on the rate controlling step and the nature of the transient specie, while Hammett's relationship studies the reactivity trends in ligands and complexes with the stability, *i.e.*, the lower the stability the higher the reactvities. Based on Hammett's relationship, electron withdrawing substituents enhance the stabilities of these complexes owing to the decrease of electron density at the metal atoms and thus the increase of the positive charge on the metal. Therefore, this effect results in decreasing reactivity. In contrast, the electron donating substituents increase the electron density at the metal, hence leading to decrease the stability of the metal chelates.

The study indicates the possibilities of significant variations of the structure and, therefore, properties of metal chelate complexes caused by diverse structural modifications of the Schiff base ligands. Studied in this respect is dominated by problems arising from the influence of strong electron-withdrawing and electron-releasing substituents in the aryl rings of the aromatic and heterocyclic Schiff base compounds, which is essential for defining basicity and ligating abilities of the nitrogen centers in the ligand. It is expected that the investigation into these problems may be promoted by further extended studies of the series containing relevant ligands.

The antimicrobial studies data reveal that the values of clear zone for ligands are related to the nature of the *p*-substituent.

A series of studies in our laboratories, have been published highlighting the chemistry, structural models and the chemical equilibria of compounds and their complexes. The presentations and discussions of these published papers explored many impor-

tant points and still many questions remain. Further studies with the title ligands, using different metal ions, are in progress and will be published in due course.

References

[1] D. Banerjea, Mixed-Ligand Complexes in Coordination Chemistry, Tata McGraw-Hill Publishing Company Limited, New Delhi, 1993. p. 323.
[2] (a) B.V. Agarawala, S. Hingorani, Synth. React. Inorg. Met.-Org. Chem. 20 (1990) 123;
(b) M.N. Patel, M.M. Patel, P.E. Cassidy, J.W. Fitch, Inorg. Chim. Acta 118 (1986) 33.
[3] R.A. Lai, S. Adhikari, A. Kamar, J. Chakraborty, Synth. React. Inorg. Met.-Org. Chem. 31 (2001) 65.
[4] B. Peng, G. Liu, L. Liu, D. Jia, K. Yu, J. Mol. Struct. 692 (2004) 217.
[5] F. Caruso, C. Pettinari, F. Marchetti, M. Rossil, C. Opazo, S. Kumar, S. Balwani, B. Gohash, Bioorg. Med. Chem. 17 (2009) 5716.
[6] A. Kimata, H. Nakagawa, R. Ohyama, T. Fukuuchi, S. Ohta, T. Suzuki, N. Miyata, J. Med. Chem. 50 (2007) 5053.
[7] M.P. Clark, S.K. Laughlin, M.J. Laufersweile, R.G. Bookland, T.A. Brugel, A. Golebiowski, M.P. Stbat, J.A. Townes, J.C. Vanrens, J.F. Djung, M.G. Natchus, L.C. Hsieh, S.C. Xu, R.L. Walter, M.J. Mekel, S.A. Heitmeyer, K.K. Brown, K. Juergens, Y.O. Taiwo, M.J. Janusz, J. Med. Chem. 47 (2004) 2724.
[8] H. Zhang, C.S. Liu, X.H. Bu, M. Yang, J. Inorg. Biochem. 99 (2005) 1119.
[9] A.Z. El-Sonbati, A.A. El-Bindary, M.A. Diab, Spectrochim. Acta A 59 (2003) 443.
[10] A.Z. El-Sonbati, A.S. Al-Shihri, A.A. El-Bindary, Inorg. Organomet. Polym. 14 (2004) 53.
[11] A.Z. El-Sonbati, A.S. Al-Shihri, A.A. El-Bindary, Inorg. Organomet. Polym. 13 (2003) 99.
[12] A.Z. El-Sonbati, M.A. Diab, A.A.M. Belal, Sh.M. Morgan, J. Mol. Struct. 1027 (2012) 92.
[13] A.Z. El-Sonbati, M.A. Diab, A.A. El-Bindary, M.K. Abd El-Kader, Spectrochim. Acta A 99 (2012) 211.
[14] S.M. Sondi, V.K. Sharma, R.P. Verma, N. Singhal, R. Shukla, R. Raghubir, M.P. Dubey, Synthesis 878 (1999) 878.
[15] A.P. Mishra, J. Indian Chem. Soc. 76 (1999) 35.
[16] V.C. Filho, R. Correa, Z. Vaz, J.B. Calixto, R.J. Nunes, T.R. Pinheiro, A.D. Andricopulo, R.A. Yunes, Farmaco 53 (1998) 55.
[17] R. Rose, D.S.R. Murty, G. Chakrapani, J. Radioanal. Nucl. Chem. 265 (2005) 115.
[18] A. Pastrakuljic, R.N. Patel, S. Kumar, K.B. Pandeya, J. Inorg. Biochem. 89 (2002) 61.
[19] A. Grieco, A. Matera, P. Di-Rocco, S. Marcoccia, A. Giancaterini, B. Alfei, G. Addolorato, F. Varlese, G. Gasbarrini, Hepato-Gastroenterology 45 (1998) 1731.
[20] M.B. Coyle, Manual of Antimicrobial Testing, American Society for Microbiology, Washington, 2005.
[21] R. Gupta, R.K. Saxena, P. Chaturvedi, J.S.J. Virdi, J. Appl. Bact. 78 (1995) 378.
[22] A.I. Vogel, Text Book of Quantitative Chemical Analysis, Sixth ed., Person Education, India, 2004.
[23] P.W. Selwood, Magnetic Chemistry, Interscience Pub. Inc., New York, 1956.
[24] V. Stefov, V.M. Petrusevski, B. Soptrajanov, J. Mol. Struct. 293 (1993) 97.
[25] M. Odabasoglu, F. Arslan, H. Olmez, O. Buyukgungor, Dyes Pigments 75 (2007) 507.
[26] Z. Chen, Y. Wu, D. Gu, F. Gan, Spectrochim. Acta A 68 (2007) 918.
[27] A.B.P. Lever, Inorganic Electronic Spectroscopy, Elsevier, New York, 1968.
[28] O.I. Singh, M. Damayanti, N.R. Singh, R.K.H. Singh, M. Mohapatra, R.M. Kadam, Polyherdon 24 (2005) 909.
[29] A.Z. El-Sonbati, M.A. Diab, A.A. El-Bindary, S.G. Nozha, Spectrochim. Acta A 83 (2011) 490.
[30] M.A. Diab, A.A. El-Bindary, A.Z. El-Sonbati, O.L. Salem, J. Mol. Struct. 1018 (2012) 176.
[31] M.A. Diab, A.Z. El-Sonbati, R.H. Mohamed, Spectrochim. Acta A 77 (2010) 795.
[32] U. Sagakuchi, A.W. Addison, J. Chem. Soc. Dalton Trans. 75 (1979) 600.
[33] A.B.P. Lever, Inorg. Electron. Spectrosc., Second ed., Elsevier, New York, 1984.
[34] B.J. Hathaway, in: J.N. Bradly, R.D. Gillard (Eds.), Essays in Chemistry, Academic Press, New York, 1971, p. 61.
[35] B.J. Hathaway, Structure and Bonding, Springer Verlag, Heidelberg, 1973. p. 60.
[36] A.B.P. Lever, Inorganic Electronic Spectroscopy, First ed., Elsevier, Amsterdam, 1968.
[37] A. Iqbal, H.L. Siddiqui, C.M. Ashraf, M. Ahmad, G.W. Weaver, Molecules 12 (2007) 245.
[38] S.V. More, D.V. Dongarkhadekar, R.N. Chavan, W.N. Jadhav, S.R. Bhusare, R.P. Pawar, J. Indian Chem. Soc. 79 (2002) 768.
[39] H.M. Safwat, F.A. Ragab, N.M. Eid, M. Abdel-Gawad, Egypt. J. Pharm. Sci. 29 (1988) 99.
[40] K.P. Sharma, V.S. Jolly, P. Phatak, Ultra Sci. Phys. Sci. 10 (1998) 263.
[41] M. Barboiu, C. Luca, E. Pop, M.E. Brewster, A. Dinculescu, Eur. J. Med. Chem. 31 (1996) 597.
[42] N. Raman, S. Sobha, A. Thamaraichelvan, Spectrochim. Acta A 78 (2011) 888.
[43] A.L. El-Ansary, H.M. Abdel-Fattah, N.S. Abdel-Kader, Spectrochim. Acta A 79 (2011) 522.
[44] N.A. El-Ghamaz, M.A. Diab, A.Z. El-Sonbati, O.L. Salem, Spectrochim. Acta A 83 (2011) 61.