

Synthesis, Spectroscopic and Antimicrobial Studies of Transition Metal Complexes of N-Amino Quinolone Derivatives

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Abstract: In Iraq like most third world countries, attempts to discovered a new antibiotic drugs derived from coumarin and its metal complexes moreover develop the branch of applied in organic chemistry. Novel transition metal(II) complexes, $[M(L_1)_2Cl_2]$ and $[M(L_2)_2Cl_2]$, were synthesized from the reaction of $MCl_2 \cdot nH_2O$ ($M = Co, Ni, Cu$) with (Z)-1-(1-(1H-indol-3-yl)ethylideneamino)quinolin-2(1H)-one (L_1) or (E)-1-(2-hydroxybenzylideneamino)quinolin-2(1H)-one (L_2). The ligands were obtained from coumarin. N-amino quinoline-2-one (2) has been synthesized by the reflux of coumarin (1) with hydrazine hydrate in ethanol for 12 h. The azomethines (L_1, L_2) were prepared from the corresponding aryl carbonyls. The synthesized compounds were and characterized by element chemical analysis, molar conductance, magnetic susceptibility measurements, and spectral (electronic, and FT-IR) studies. The IR spectral data suggest the involvement of sulphur and azomethane nitrogen in coordination to the central metal ion. On the basis of spectral studies, an octahedral geometry has been assigned for all complexes. The free ligands and its metal complexes have been tested in vitro against a number of microorganisms in order to assess their antimicrobial properties.

Key words: Coumarin, quinoline, transition metal (II) complex

INTRODUCTION

Coumarins have stimulated extensive research in biology, organic chemistry and medicine, due to their antibiotic (Lewis *et al.*, 1996), anti-coagulant (Tai-Chi *et al.*, 1998; Ghulam *et al.*, 2007), anticancer (Manfredini *et al.*, 1997), anti-inflammatory (Borges *et al.*, 2005), and anti-HIV (Fuller *et al.*, 1994) properties. A number of natural or synthetic derivatives of coumarin have found pharmaceutical applications (Masche *et al.*, 1999). Coumarins are nowadays an important group of organic compounds that are used as additives to food and cosmetics, (O'Kennedy and Thornes, 1997) optical brightening agents (Zahradnik *et al.*, 1992) and dispersed uorescent and laser dyes. The derivatives of coumarin usually occur as secondary metabolites present in seeds, roots and leaves of many plant species. Their function is far from clear, though suggestions include waste products, plant growth regulators, fungi stats and bacterio stats. (Maeda, 1984; Murray *et al.*, 1982) It is there- fore of utmost importance that the synthesis of coumarin and its derivatives should be achieved by a simple and effective method. The synthesis of this heterocyclic nucleus is of current interest. Coumarins have been synthesized by several methods including Von Pechman, Knoevenagel, and Reformatsky reactions (Moradi *et al.*, 2008). 2-quinolone derivatives were found to be associated with various biological activities such as antitumor (Joseph *et al.*, 2002),

antimalarial (Xiao *et al.*, 2001), antiplatelet (Nishi *et al.*, 2000), antidepressant (Oshiro *et al.*, 2000), antiulcer (Banno *et al.*, 1988), plant virucides (Hung *et al.*, 1996; Dia *et al.*, 2004), antioxidant activity (Al-Omar *et al.*, 2006) and herbicides (Khan *et al.*, 2003). Many substituted quinoline-2-one derivatives have recently craned great interest in chemotherapy as ant tumor drugs (Jin *et al.*, 2005; Wissner *et al.*, 2000). Also a number of quinolones are excellent reservoir of bioactive substances (Al-Bayati *et al.*, 2004). 2-Quinolones are also valuable intermediates in organic synthesis, since they are easily converted into 2-chloro and 2-aminoquinoline derivatives (Godard *et al.*, 1994). Some Schiff bases bearing heterocyclic residues possess biological activities, such as analgesic, antiviral, antifungal and anticancer (Jarrahpour *et al.*, 2004). Transition metals have varying utility and interesting chemistry. Coordination compounds are important due to their role in biological and chemical systems in various ways. It has been observed that metal complexes with appropriate ligands are chemically more significant and specific than the metal ions and original (Al-Amiery *et al.*, 2010; Steinhardt and Beychok, 1964). This communication describes the synthesis, characterization and bioassay of some metal complexes with ligands (L_1 and L_2), derived from reaction of N-amino quinoline-2-one with 2-hydroxybenzaldehyde (for L_1) or of 1-(1H-indol-3-yl)ethanone (for L_2).

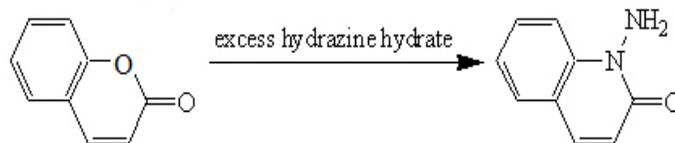


Fig. 1: Synthesis of N-amino quinoline-2-one (1)

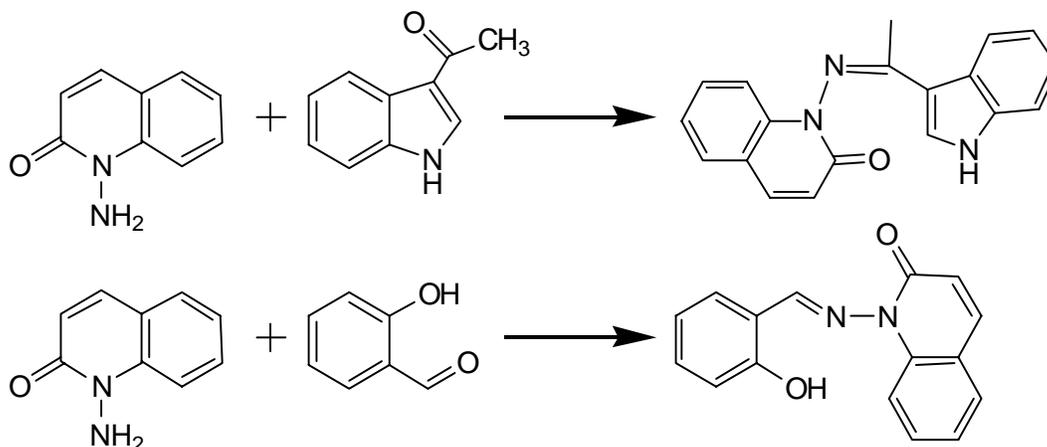


Fig. 2: Synthesis of the legends (L₁ and L₂)

MATERIALS AND METHODS

This study was done in the applied science department at the university of technology in Iraq. All chemical used were of reagent grade (supplied by either Merck or Fluka) and used as supplied. Melting points were determined on SMP40 melting point apparatus and were uncorrected. The IR spectra of the compounds were recorded on a shimadzu FT-IR-8300 spectrometer as KBr and CsI disks. The UV spectra were performed on Cintra-5-Gbes scientific equipment. Magnetic susceptibility measurement for complexes were obtained at room temperature using (Magnetic susceptibility Balance Model MSB-MKI). Flame atomic absorption of elemental analyzer, shimadzu AA-670 was used for metal determination. Elemental micro analysis, was carried out using C.H.N elemental analyzer model 5500-Carlo Erba instrument.

Synthesis of the Ligands (L₁ and L₂):

Synthesis of N-amino quinoline-2-one (1): Refluxing of coumarin (1.46 g, 0.01 mol) with excess hydrazine hydrate 99% (3.2g, 0.1 mol) in absolute ethanol 25 mL for 12 h, then cooled, the formed solid was collected and recrystallized from chloroform (Fig. 1).

Synthesis of Schiff bases: A mixture of compound 1 (0.8 g, 0.005 mol) and the (0.005 mol) 2-hydroxybenzaldehyde

(for L₁) or (0.0025 mol) of 1-(1H-indol-3-yl)ethanone (for L₂), was refluxed in absolute ethanol 25 ml for 6-8 h. The reaction mixture was cooled and the product obtained was recrystallized from ethanol, the melting points for L₁ and L₂ are 240 and 216°C, respectively (Fig. 2).

Synthesis of complexes: The salts [CoCl₂.6H₂O, NiCl₂.6H₂O, and CuCl₂.2H₂O] were dissolved in ethanol, and added to an ethanolic solution of ligands (L₁ and L₂) in (2:1) mole ratio ligand to metal respectively, with stirring. The mixture was heated under reflux for three hours, during this period, the precipitation was completed from, and collected by filtration, then washed with ethanol, and dried under vacuum for 4 h. All these complexes were analyzed by using different available techniques, the physical proportion of the ligands and its metal complexes are listed in Table 1.

Study of complexes formation in solution: Complexes of ligands with metal ions were studied in solution using ethanol (or DMF) as solvents, in order to determine (M:L) ratio in the complex following molar ratio method (Sulekh *et al.*, 2007). A series of solution were prepared having a constant concentration 10⁻³ M of metal ion and ligands. The [M/L] ratio was determined from relationship between absorption of the absorbed light and mole ratio of [M/L]. The results of complexes formation in ethanol were listed in Table 1.

Table 1: Physico analytical data for the ligands and metal complexes

Compound	Mole ratio	Color	M.P.	CHN analysis		
				C (%)	H (%)	N (%)
[Co (L ₁) ₂ Cl ₂]	1:2	Light green	202	62.31(63.80)	4.13(5.56)	11.47(12.21)
[Ni(L ₁) ₂ Cl ₂]	1:2	Yellow	199	62.33(63.91)	4.13(5.34)	11.48(12.19)
[Cu(L ₁) ₂ Cl ₂]	1:2	Brown	195	61.92(63.63)	4.10(5.05)	11.40(12.39)
[Co (L ₂) ₂ Cl ₂]	1:2	Light green	193	58.55(56.75)	3.38(4.45)	8.54(10.00)
[Ni (L ₂) ₂ Cl ₂]	1:2	Light yellow	232	58.58(60.65)	3.38(4.33)	8.95(10.21)
[Cu(L ₂) ₂ Cl ₂]	1:2	Dark green	111	58.15(60.01)	3.35(4.34)	8.48(10.01)

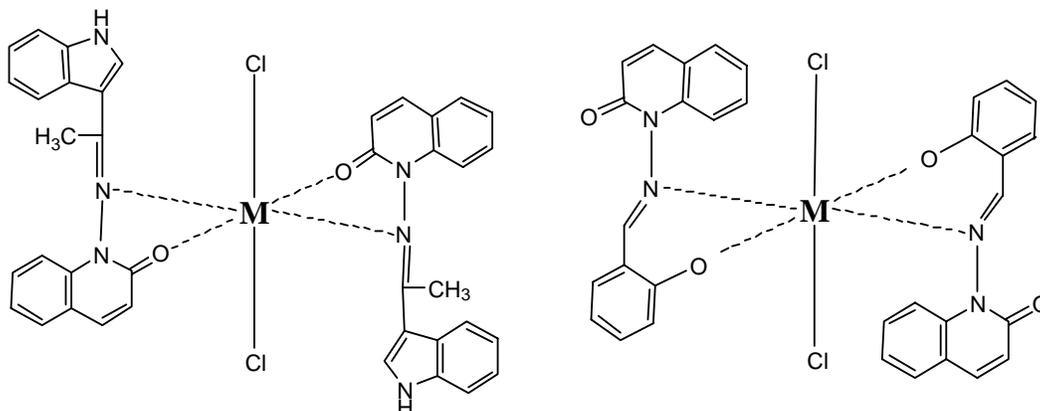


Fig. 3: The octahedral geometry of the complexes

Antibacterial activity: The antibacterial activity was estimated against *Staphylococcus aureus*, as gram positive and *E. coli* and *Pseudomonas aeruginosa* as gram negative, and evaluated by using of agar disc diffusion method on the basis of the size of inhibition zone formed around the paper discs. For each concentration, the mean diameter (mm) of inhibition zone developed was calculated. The test compounds in measured quantities were dissolved in DMF to get concentrations of 200 and 100 ppm of compounds. Twenty five millileter nutrient agar media was poured in each Petri plates. After solidification, 0.1 mL of test bacteria spread over the medium using a spreader. The discs of Whatmann no. 1 filter paper having the diameter 5.00 mm, were placed at four equidistant places at a distance of 2 cm from the center in the inoculated Petri plates. Filter paper disc treated with DMF served as control and Amoxicillin used as a standard drug. These Petri plates were kept in refrigerator for 24 h for pre diffusion. Finally, Petri plates were incubated for 24 h 30°C. The zone of inhibition was calculated in millimeters carefully.

RESULTS AND DISCUSSION

Schiff bases characterization: The Schiff bases, L₁ and L₂ are subjected to elemental analyses. The results of elemental analyses (C, H, N and S) with molecular formulae and melting points are presented in Table 1. The results obtained are in good agreement with those

calculated for the suggested formulae. The structures of the Schiff bases under study are given below in Fig. 1. The structures of these Schiff bases are also confirmed by IR spectra, which will be discussed later with metal complexes.

Compositions and structure of the schiff base complexes: The isolated complexes of Co(II), Ni(II) and Cu(II), ions with the Schiff base ligand L₁ and those of Co(II), Ni(II) and Cu(II), with the Schiff base ligand L₂ were subjected to elemental analyses (C, H, N and metal content), IR, magnetic studies, molar conductance to elucidate their molecular structures. Elemental analysis of the ligands and its metal complexes are reported in Table 1. The elemental analysis data agreed well with the proposed formulae for the ligands and metal complexes. The solubility of the complexes of ligands was studied in various solvents. The complexes are soluble in DMSO and DMF while insoluble in common solvents such as ether, chloroform, and carbon tetrachloride.

Characterization of the ligands and their complexes:

FT-IR: The FTIR spectrum (Table 2) of (Z)-1-(1-(1H-indol-3-yl)ethylideneamino)quinolin-2(1H)-one (L₁) and (E)-1-(2-(2-hydroxybenzylideneamino)quinolin-2(1H)-one (L₂). The spectrum of ligand (L₁) exhibited weak band at 3060 per cm, this could be attributed to $\nu(\text{C-H})$ aromatic. A strong band at 1683 per cm which belongs to carbonyl and the other strong bands belong to the $\nu(\text{C=N})$, $\nu(\text{C=C})$

Table 2: The FT-IR spectral data for the ligands and metal complexes

Compound	FT-IR spectral data							
	$\nu\text{C}=\text{O}$	$\nu\text{C}=\text{C}$	$\nu\text{C-Har}$	$\nu\text{C}=\text{N}$	C-N	C-Hali	N-H	Others
L_1	1683	1572 1523 1438	3060	1585	1244	2950	3394	C-Hvinyl=3132
$[\text{Co}(L_1)_2\text{Cl}_2]$	1668	1570	3055	1577	1222	2920	3401	M-N = 521, M-O = 453
$[\text{Ni}(L_1)_2\text{Cl}_2]$	1670	1570	3060	1569	1243	2950	3389	M-N = 532, M-O = 423
$[\text{Cu}(L_1)_2\text{Cl}_2]$	1670	1565	3064	1576	1240	2945	3390	M-N = 471, M-O = 443
L_2	1681	1573 1487	3046	1621	1271	-	-	O-H = 3200
$[\text{Co}(L_2)_2\text{Cl}_2]$	1677	1571	3050	1601	1266	-	-	M-N = 501, M-O = 465,
$[\text{Ni}(L_2)_2\text{Cl}_2]$	1679	1574	3043	1610	1267	-	-	M-N = 489, M-O = 461
$[\text{Cu}(L_2)_2\text{Cl}_2]$	1675	1570	3056	1611	1245	-	-	M-N = 535, M-O = 459

and $\nu(\text{C-N})$ were found at 1585, 1572 and 1244 per cm respectively, while the infrared spectra of the prepared complexes of (L_1) exhibited $\nu(\text{C=N})$ in the range of 1569-1577 per cm which shows a shifting to the lower frequencies, it is which indicated the coordination of (L_1) with metal ions through the nitrogen atoms in their structures. The spectra bands of complexes at 1668-1670 per cm were characterized for the carbonyl group which indicates that the oxygen atom of the carbonyl group was coordinated to the metal ion. The ligand (L_2) shows two moderately strong bands at 3200 and 1621 per cm assigned as ν O-H and ν C=N groups. On complexes formation the former band shifts to lower energy while the phenolic O-H group disappears in the prepared complexes, this supports the deprotonation and linkage of O atom to the central metal ion (Erich *et al.*, 1989). The stretching frequency at 1573 per cm can be attributed to C=C bond. A strong band appearing at 1681 per cm can be assigned to carbonyl group. A medium band at 1271 per cm may be assigned to C-N stretching vibrations. The absorption band in the range (471-535) and (423-465) per cm were assigned to (M-N) and (M-O) bands. The spectra bands of complexes at 1675-1679 per cm were characterized for the carbonyl group which did not suffer a shift. Thus, it is suggested that the oxygen atom of the carbonyl group is not coordinated to the metal ion.

Magnetic susceptibility and conductivity measurements: Co(II) complexes are in the range of 4.7-5.1 BM indicating that the Co(II) complexes are typically high spin complexes and having octahedral structure moreover the molar conductance of these complexes in DMF was 12.56, 14.12 oh/m cm^2/mol (L_1 and L_2 complexes respectively) which shows that the chloride ions are coordinated to the cobalt (II) ion. The Ni(II) complexes exhibit the magnetic moment values in the range 2.7-3.3 BM, indicating octahedral coordination

moreover the molar conductance of these complexes in DMF was 11.00, 11.87 oh/m cm^2/mol (L_1 and L_2 complexes, respectively) which shows that the chloride ions are coordinated to the nickel (II) ion. The Cu(II) complexes exhibit magnetic moment in the range of 1.4-1.9 BM indicating distorted octahedral nature for these complexes moreover the molar conductance of these complexes in DMF was 19.11, 17.32 oh/m cm^2/mol (L_1 and L_2 complexes, respectively) which shows that the chloride ions are coordinated to the copper (II) ion. Molar conductivity measurement in DMF solvent at 25°C showed that the complexes were non-electrolyte.

Electronic absorption spectrum: The UV-visible spectrum of ligands solution in absolute ethanol shows three distinct peak at 340 nm ($\epsilon_{\text{max}} \times 10^6 = 0.86$), 262 nm ($\epsilon_{\text{max}} \times 10^6 = 0.35$), 222 nm ($\epsilon_{\text{max}} \times 10^6 = 1.1$) for L_1 , and two distinct peaks 356 nm ($\epsilon_{\text{max}} \times 10^6 = 0.86$), 289 nm ($\epsilon_{\text{max}} \times 10^6 = 0.28$) for L_2 which were assignable to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions, respectively (Sreekanth *et al.*, 2003).

- The electronic spectra of light green Cobalt (II) complex (L_1) showed two spin allowed transitions at 17950 and 21610 per cm assignable to $T_{1g}(\text{F}) \rightarrow A_{2g}(\text{F})$ and ${}^4T_{1g}(\text{F}) \rightarrow {}^4T_{2g}(\text{P})$ transitions respectively, are in agreement with octahedral arrangements for Co(II) ion.
- The electronic spectra of light green cobalt (II) complex (L_2) showed three spin allowed transitions at 14520, 17000, and 22150 cm^{-1} assignable to ${}^4T_{2g}(\text{F}) \rightarrow {}^4A_{2g}$, $T_{1g}(\text{F}) \rightarrow A_{2g}(\text{F})$ and ${}^4T_{1g}(\text{F}) \rightarrow {}^4T_{2g}(\text{P})$ transitions respectively, are in agreement with octahedral arrangements for Co(II) ion.
- The electronic spectra of yellow Ni (II) complex (L_1) showed three spectral bands at 10500, 16120 and 19800 assignable to ${}^3A_{2g} \rightarrow {}^3T_{2g}(\text{F})$, ${}^3A_{2g}(\text{F}) \rightarrow {}^3T_{1g}(\text{F})$ and ${}^3A_{2g}(\text{F}) \rightarrow {}^3T_{1g}(\text{P})$ transition was in

Table 3: The Antibacterial activity of legands and metal complexes against the tested bacteria

Compound	Antibacterial activity of legands and metal complexes the zone of inhibition was measured in mm (Concentration in ppm)					
	Staphylococcus aureus zone mm		E. coli zone mm		Pseudomonas aersginosa zone mm	
	100	200	100	200	100	200
L ₁	6	13	7	12	5	12
[Co (L ₁) ₂ Cl ₂]	8	18	9	19	11	21
[Ni(L ₁) ₂ Cl ₂]	8	19	11	17	9	21
[Cu(L ₁) ₂ Cl ₂]	9	21	11	18	12	22
L ₂	8	17	9	14	5	11
[Co (L ₂) ₂ Cl ₂]	9	22	10	19	11	23
[Ni (L ₂) ₂ Cl ₂]	12	19	11	24	9	22
[Cu(L ₂) ₂ Cl ₂]	11	20	11	19	10	23
Amoxicillin	14	25	10	17	13	24

agreement with octahedral arrangements for Ni(II) ion.

- The electronic spectra of light yellow Ni (II) complex (L₂) showed spectral band at 408 nm assignable to ³T_{1g}(F)→³T_{2g}(F) transition was in agreement with octahedral arrangements for Ni(II) ion.
- The electronic spectra of brown copper (II) complex (L₁) showed one spin allowed transitions at electronic spectrum of the Cu(II) complex assigned to E_{2g}→²T_{2g} (Al-Sha'alan *et al.*, 2007) transition which is in conformity with octahedral geometry.
- The electronic spectra of dark green copper (II) complex (L₂) shows strong band at 287 nm which belongs to the charge transfer. The second band found in the visible region at 442 nm was attributed to the electronic transition E_{2g}→²T_{2g}.

Stereo suggested structures of complexes: According to the above mentioned data (spectra, molar conductance, molar ratio and magnetic properties), the proposed structures of completes were shown as below:

Antibacterial activity: The Schiff base ligand was found to be biologically active. It is known that chelation tends to make ligands act as more powerful and potent bactericidal agent. The values indicate that the metal complexes had a higher antibacterial activity than the free ligand. Such increased activity of the metal complexes can be explained on the basis of the overtone concept and chelation theory (Shraddha *et al.*, 2010; Nevin, 2004; Bhojya and Ramappa, 1999) According to the overtone concept of cell permeability, the lipid membrane that surrounds the cell favors the passage of only lipid soluble materials, due to which liposolubility is an important factor controlling the antimicrobial activity. On chelation, the polarity of the metal ion is reduced to a great extent due to the overlap of the ligand orbital and the partial sharing of the positive charge of the metal ion with donor groups. Furthermore, it increases the delocalization of electrons over the whole chelate ring and enhances the lipophilicity of the complex. This increased lipophilicity enhances the penetration of the complex into the lipid

membrane and blocks the metal binding sites on the enzymes of the microorganism.

Antibacterial activity (Table 3) was leads to the following conclusions:

- The metal complexes show more activity than the ligands against tested bacteria.
- Antibacterial activity of Cu (II) complexes has higher activity than the other complexes.

CONCLUSION

Based on the reported results, it may be concluded that ligands act as bidentate ligands, coordinating through one of the nitrogen atom and the oxygen. In the present investigations, all the complexes are found to be mononuclear, based on the FT-IR spectral data. The coordination number six is attained by coordination with the two bidentate ligand molecules and two chloride atoms. Based on the physicochemical and the spectral studies the tentative structures proposed for the complexes are shown in Fig. 1.

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