

Synthesis and Spectroscopic Studies of Biologically Active Co(II), Cu(II) and Ni(II) Complexes of Hydrazine Derived Schiff-base Ligands

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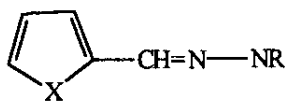
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Summary: Some new biologically active mixed ligand hydrazine derived Schiff-base ligands and their Co(II), Cu(II) and Ni(II) complexes have been synthesised and characterized on the basis of conductance and magnetic measurements, elemental analysis and ¹H-NMR, IR and electronic spectral data. The synthesised ligands and their complexes have been screened for their antibacterial activity. The activity data have shown the metal complexes to be more potential than the uncomplexed ligands against one or more bacterial species.

Introduction

Among the diamine ligands the hydrazines and substituted hydrazines are generally recognized as good donors towards metal ions [1-3] and usually behave as potentially unidentate [4,6], bidentate [7-9] or bridging ligands [10-12]. They also form polymeric complexes in some cases and hence are not amenable to absorption spectroscopic investigations. Available data [9,13] indicates that the chemical behaviour of these ligands however, is, practically comadent with that of other diamines.

Schiff-bases continue to occupy a significant position as ligands in metal coordination chemistry. As a part of our ongoing research programme concerning the synthesis and characterisation of metal complexes of Schiff-base ligand. It was therefore, considered of interest to prepare hydrazine derived Schiff-base ligands (L₁-L₆) (Fig. 1) and study their ligation properties towards Co(II), Cu(II) and Ni(II) metal ions and also their biological activity against pathogenic bacterial species.



- L₁ : X = NH R = Ph
 L₂ : X = NH R = H
 L₃ : X = O R = Ph
 L₄ : X = O R = H
 L₅ : X = S R = Ph
 L₆ : X = S R = H

(Fig. 1)

Results and Discussion

The Schiff-base ligands (L₁-L₆) were prepared by following the method as reported earlier [14-17]. The structural determination of these synthesised ligands was done with the help of IR, ¹H-NMR and their elemental analysis data.

The IR spectra of the free ligands (Table-1) show characteristic bands at 3110-3115, 2920, 2925, 1630, 1545 and 950-955 cm⁻¹ assigned, respectively, to ν(-NH₂), (-NH), (-C=N), (-C=C) and -N-N stretches. IR spectra of all the ligands showed the absence of a band at 1740 cm⁻¹ due to carbonyl (-C=O) stretching and appearance of a new strong band at 1630 cm⁻¹ due to azomethine (-C=N) linkage giving a definite clue for the formation of ligands (L₁-L₆). Also ¹H-NMR spectra (Table-1) of the title ligands showed the expected number of protons and CHN percentage, confirmed the molecular formulae of their respective structure (Fig. 1).

All the metal complexes (1-18) of the ligands were prepared by the stoichiometric reaction of the respective metals (II) as their chlorides and ligands in the molar ratio M:L = 1:2. All the synthesised complexes are found to be air and moisture stable solids and decompose without melting. They are soluble in DMSO, DMF and water and insoluble in other solvents. Conductance values (15-25 ohm⁻¹ cm² mol⁻¹) of the complexes in DMF showed that they are non-electrolyte [18,19]. Any possibility to show these compounds as polymeric compounds is ruled out because of their crystalline and solubility nature. Also, their

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Table-1: Physical, spectral and analytical data of ligands

Ligand No. Moi.formula	M.P. (°C)	IR (cm ⁻¹)	¹ H-NMR	Calcd.(Found)%		
				C	H	N
L ₁ C ₁₁ H ₁₁ N ₃	182	3214,3112,2925, 2020,1675, 1630, 1545,1115,955,782	6.8(2H, dd, C-3,4), 7.2(1H, d, C-5), 7.9(1H, d, C-8), 8.3(1H, s, NH), 7.4 (5H, m, -Ph)	71.36 (71.72)	5.94 (5.68)	22.68 (22.61)
L ₂ C ₃ H ₇ N ₃	135	3210, 3115, 2925, 2025,1675, 1630, 1545, 1375, 1115, 955, 785	6.85 (2H, dd, C-3,4), 7.2(1H, d, C-5), 7.9(1H, d, C-8), 8.3 (1H,s,NH), 9.5 (2H, s, NH ₂)	55.06 (55.17)	6.41 (6.88)	38.51 (38.37)
L ₃ C ₁₁ H ₁₀ N ₂ O	166	3215, 2925, 2025, 1670, 1630, 1545, 1110, 950, 785	6.8(2H, dd, C-3,4), 7.25 (1H, d, C-5), 7.9 (1H, d, C-8), 7.5 (5H, m, -Ph)	70.98 (71.08)	5.37 (5.46)	15.04 (15.21)
L ₄ C ₃ H ₆ N ₂ O	128	3210, 3115, 2025, 1670, 1630, 1545, 1110, 955, 785	6.8(2H, dd, C-3,4), 7.2(1H, d, C-5), 7.8 (1H, d, C-8), 9.5 (2H, s,NH ₂)	54.56 (54.61)	5.45 (5.89)	25.44 (25.09)
L ₅ C ₁₁ H ₁₀ N ₂ S	173	3210, 2920, 2022, 1670, 1630, 1545, 1115, 950, 780	6.85 (2H, dd, C-3,4), 7.2 (1H, d, C-5), 7.9 (1H, d, C-8), 7.45 (5H, m, -Ph)	65.34 (65.70)	4.94 (4.68)	13.84 (13.56)
L ₆ C ₃ H ₆ N ₂ S	142	3215, 3110, 2025, 1890, 1695, 1630, 1545, 1115, 955, 785	6.8(2H, dd, C-3,4), 7.2 (1H, d, C-5), 7.8 (1H, d, C-8), 9.5 (2H, s, NH ₂)	47.61 (47.55)	4.75 (4.82)	22.20 (22.04)

molecular weight and spectroscopic studies do not give such clue.



Magnetic susceptibility

The room temperature magnetic susceptibility measurements (Table-2) for the solid complexes are indicative of three unpaired electrons per Co(II) ion ($\mu_{\text{eff}} = 3.96 - 4.28$ B.M), one unpaired electron per Cu(II) ion ($\mu_{\text{eff}} = 1.88 - 2.16$ B.M) and two unpaired electrons per Ni(II) ion ($\mu_{\text{eff}} = 2.92 - 3.12$ B.M) suggesting [20-23] octahedral geometry for all the Co(II) and Ni(II) complexes and distorted octahedral geometry for the Cu(II) complexes having a d⁹ system.

Infrared spectra

The scrutiny of the infrared spectra of the ligands and their metal complexes indicated that the ligands are coordinated to the metal atom in possible three ways thus representing the ligands to act as tridentates. The following conclusions in this regard can be drawn.

a) The spectra of the ligands exhibit bands at 3110-3115 cm⁻¹ and 2920-2925 cm⁻¹ attributed to (-NH₂) and (-NH) vibrations which are changed and shifted to lower frequency indicating that the ligands are attached to the metal atom through these groups.

b) The IR spectra of the complexes indicate that the bands in the spectra of all ligands at 1630 cm⁻¹ due to azomethine (-C=N) linkage are shifted towards lower frequency by 5-10 cm⁻¹, respectively suggesting that the ligands are coordinated to the metal ion through the azomethine nitrogen.

c) The conclusive evidence, due to the new bands appearing in the spectra of metal complexes and not observed in the spectra of the ligands appearing at 515-520 cm⁻¹, 440-445 cm⁻¹ and 360-365 cm⁻¹ assigned [24-26] to M - N, M - O and M - S modes respectively, indicate that the X group (Fig. 1) heteroatoms are also coordinated to the metal (II) ion.

The above observations thus indicate that coordination between the metal (II) ions and the ligands can possibly take place involving the amine (-NH₂) in ligands L₂, L₄ and L₆ and the amide (-NH) in ligands L₁, L₃ and L₅, azomethine nitrogen (-C=N) and X heteroatoms (N, O or S).

Electronic spectra

The electronic spectra of Co(II) complexes exhibit well resolved three bands at 19115-20520 cm⁻¹, 16190-17225 cm⁻¹ and 9500-9555 cm⁻¹ assigned to transition ⁴T_{1g}(F) → ⁴T_{2g}(P) (V₁), ⁴T_{1g}(F) → ⁴T_{2g}(F) (V₂) and ⁴T_{1g}(F) → ⁴T_{2g}(F) (V₃) in an octahedral environment [27,28]. The Cu(II) complexes, similarly, showed three bands in the region 31120-31270 cm⁻¹, 22480-22585 cm⁻¹ and 14515-15155 cm⁻¹. The lower energy band may be assigned as the 10 Dq band for a distorted octahedral configuration corresponding [29] to the transition ²E_g → ²T_{2g}. The band in the region 22480-

Table-2: Physical, analytical and spectral data of metal complexes

Complex No.	M.P.(°C) Mol. Formula (Decomp)	B.M (μeff)	IR (cm^{-1})	λ_{max} (cm^{-1})	Calcd (Found) %			
					C	H	N	
1.	[Co(L ₁) ₂ Cl ₂]	215-217	4.28	3214, 2925, 2020, 1790, 1675, 1625, 1540, 1115, 955, 782, 520.	9555, 16220, 20520.	52.83 (52.31)	4.39 (4.97)	16.79 (16.46)
2.	[Co(L ₂) ₂ Cl ₂]	208-210	4.26	3215, 2920, 2022, 1795, 1675, 1625, 1545, 1115, 950, 780, 515.	9500, 16190, 20250.	34.60 (34.18)	3.74 (3.83)	24.2 (23.88)
3.	[Co(L ₃) ₂ Cl ₂]	212-214	4.25	3210, 2925, 2020, 1795, 1670, 1625, 1545, 1115, 950, 780, 520, 445	9555, 17215, 19115.	52.62 (51.92)	3.98 (4.06)	11.15 (11.59)
4.	[Co(L ₄) ₂ Cl ₂]	218-220	4.18	3215, 3112, 2020, 1795, 1670, 1625, 1540, 1115, 955, 785, 515, 440	9515, 17210, 19150.	34.32 (34.84)	3.42 (4.02)	16.00 (15.77)
5.	[Co(L ₅) ₂ Cl ₂]	210-212	3.88	3210, 2920, 2020, 1795, 1670, 1620, 1540, 1115, 950, 780, 515, 360.	9555, 17225, 19115.	49.46 (49.66)	3.74 (3.28)	10.48 (11.10)
6.	[Co(L ₆) ₂ Cl ₂]	206-208	3.96	3215, 3115, 2022, 1790, 1675, 1620, 1545, 1115, 950, 780, 515, 365.	9500, 17220, 20100.	31.43 (32.18)	3.14 (2.98)	14.65 (14.78)
7.	[Cu(L ₁) ₂ Cl ₂]	220-222	2.12	3215, 2925, 2020, 1790, 1675, 1625, 1540, 1115, 955, 780, 520.	14750, 22515, 31200.	52.45 (52.81)	4.16 (4.57)	16.67 (16.51)
8.	[Cu(L ₂) ₂ Cl ₂]	218-220	2.16	3210, 2920, 2022, 1795, 1670, 1625, 1545, 1115, 950, 785, 515	14755, 22585, 31270.	34.45 (34.59)	3.72 (4.18)	24.08 (24.24)
9.	[Cu(L ₃) ₂ Cl ₂]	208-210	2.12	3210, 2925, 2020, 1795, 1670, 1625, 1545, 1115, 950, 780, 520, 445	15150, 22515, 31120.	52.14 (51.76)	3.94 (4.23)	11.05 (10.82)
10.	[Cu(L ₄) ₂ Cl ₂]	222-224	2.14	3215, 3112, 2020, 1795, 1670, 1625, 1540, 1115, 955, 785, 515, 445.	15555, 22480, 31180.	33.87 (34.36)	3.38 (3.49)	15.79 (15.99)
11.	[Cu(L ₅) ₂ Cl ₂]	215-217	1.88	3210, 2920, 2020, 1795, 1670, 1620, 1540, 1115, 950, 780, 515, 360	14580, 22515, 31270.	49.04 (49.66)	3.71 (3.89)	10.39 (11.01)
12.	[Cu(L ₆) ₂ Cl ₂]	204-2-6	1.92	3215, 3115, 2020, 1795, 1670, 1620, 1545, 1115, 950, 785, 515, 365	14515, 22510, 31200.	31.43 (31.88)	3.14 (3.79)	14.64 (14.54)
13.	[Ni(L ₁) ₂ Cl ₂]	203-204	3.03	3215, 2925, 2020, 1795, 1675, 1625, 1540, 1115, 955, 780, 525	9555, 16222, 25500.	52.92 (52.36)	4.40 (5.11)	16.80 (16.92)
14.	[Ni(L ₂) ₂ Cl ₂]	198-200	3.11	3210, 2920, 2020, 1795, 1670, 1625, 1540, 1115, 950, 785, 510.	10200, 16222, 25210.	34.64 (34.85)	3.74 (4.22)	24.22 (24.58)
15.	[Ni(L ₃) ₂ Cl ₂]	212-214	3.12	3210, 2925, 2020, 1795, 1670, 1625, 1545, 1115, 950, 785, 525, 440.	9885, 16220, 25550.	52.65 (52.77)	3.98 (2.58)	11.15 (11.36)
16.	[Ni(L ₄) ₂ Cl ₂]	206-208	3.08	3215, 3112, 2020, 1795, 1670, 1625, 1540, 1115, 950, 785, 515, 445	10115, 16180, 25580.	34.34 (34.81)	3.43 (3.56)	16.01 (15.84)
17.	[Ni(L ₅) ₂ Cl ₂]	196-198	2.96	3210, 2925, 2022, 1770, 1695, 1620, 1545, 1115, 955, 780, 515, 360.	10110, 16200, 25500.	49.48 (49.72)	3.74 (4.11)	10.48 (10.63)
18.	[Ni(L ₆) ₂ Cl ₂]	192-194	2.92	3215, 3117, 2020, 1795, 1670, 1620, 1545, 1115, 955, 785, 515, 365.	10190, 16215, 25310.	31.45 (31.66)	3.14 (3.80)	14.66 (14.28)

22585 cm^{-1} can be attributed to intra-ligand charge transfer. In some cases this band emerges with the high intensity ligand band. Also, the highest energy band observed around 31120-31270 cm^{-1} is assigned to charge transfer transitions.

The electronic spectra of the Ni(II) complexes showed three bands at 25210-25580 cm^{-1} , 16180-16222 cm^{-1} and 9555-10110 cm^{-1} assignable, respectively, to the transitions ${}^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$ (V_2), ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ (V_2) and ${}^3A_{2g}(F) \rightarrow {}^3T_{2g}(V_3)$ consistent with an octahedral geometry [30,31].

On the basis of these observations it is proposed that all the complexes show an octahedral geometry in which the two ligands acting as tridentates, possibly accommodate themselves

around the metal atom in such a way that a stable configuration of a metal chelate is attained.

Experimental

Material and Methods

All the chemicals used in the present study were of Analar grade, Cobalt(II), copper(II) and nickel(II) were used as their chloride salts. Conductance and magnetic measurements were made on a YSI model - 32 conductivity bridge and a Gouy balance, respectively. Infrared spectra were recorded in Nujol mulls on a R10 Hitachi spectrophotometer. ${}^1\text{H-NMR}$ spectra of the ligands in DMSO- d_6 were obtained on a R10-Perkin Elmer spectrometer. Electronic spectra in DMF were studied on a Hitachi double-beam U-2000 model spectrophotometer using glass cells of 1 cm

Table-3: Antibacterial Activity Data of ligands/ Metal Complexes

Ligands/ Complexes	Microbiol species			
	a	b	c	d
L1	++	++	+	++
L2	+	++	++	+
L3	+	+	+	+
L4	+	++	+	++
L5	-	+	+	++
L6	+	+	++	++
1	+++	+++	++	+++
2	++	++	+++	++
3	++	+++	++	++
4	++	+++	++	+++
5	+	++	++	++
6	++	++	+++	+++
7	++++	+++	++	++++
8	++	+++	++	++
9	+	++	++	++
10	++	+++	+	++
11	+	++	+	+++
12	++	++	+++	++
13	+++	+++	+	+++
14	++	+++	++++	++
15	++	++	++	+
16	++	+++	++	+++
17	+	++	++	++
18	++	+++	++	+++

a = *Staphylococcus aureus*, b = *Pseudomonas aeruginosa*, c = *Klebsiella pneumoniae* d= *Proteus vulgaris*. Inhibition zone diameter (mm) +, 6-10, ++, 10-14, +++, 14-18, +++++, 18-22.

thickness. Elemental analysis of C,H, and N were determined on a Coleman automatic analyser. All melting point were taken on a Gallenkamp melting point apparatus and are uncorrected. Antibacterial studies were carried out with the help of the Microbiology Laboratory, Department of Pathology, Quaid-e-Azam Medical College, Bahawalpur. These studies were done on wild pathogenic bacterial species collected from urine and blood samples of infected patients admitted in local Bahawal Victoria Hospital, Bahawalpur.

Preparation of ligands

N-2-(pyrrolylmethylene)phenyl hydrazine (L1)

Pyrrol-2-aldehyde (0.82 mL, 0.01 M) in ethanol (15 mL) was added to an ethanolic solution (20 mL) of phenyl hydrazine (0.5 mL, 0.01 M). Then 2-3 drops of conc. H₂SO₄ were added and mixture refluxed for 1 h. The reaction mixture was cooled and the solid product thus obtained was filtered, washed with ether (2 x 10 mL) and dried. It was crystallized in aqueous ethanol to give L₁ (50%).

The same methodology was adopted using the same molar ratio of the respective reagents for the preparation of other ligands, L₂ (55%), L₃ (48%), L₄ (50%), L₅ (52 %) and L₆ (55%).

Preparation of metal complexes

An ethanolic solution (20 mL) of ligand (0.02 M) was added to a stirred aqueous solution (15 mL) of respective metal(II) chloride (0.01M). The mixture was refluxed for 2 h. The resulting mixture was cooled, filtered and reduced to nearly a half volume (15 mL) by an evaporator. This concentrated solution was left overnight at room temperature which resulted in the formation of a solid product. The product thus obtained was filtered, washed with ethanol (2 x 10 mL), then with ether (1 x 10 mL) and dried. Crystallization from hot aqueous ethanol (50%) gave 1 (50%), 2 (55%), 3 (48%), 4 (52%), 5 (50%), 6 (55%), 7 (52%), 8 (55%), 9 (45%), 10 (52%), 11 (52%), 12 (50%), 13 (52%), 14 (55%), 15 (45%), 16 (53%), 17 (52%) and 18 (52%).

Antibacterial studies

Preparation of disc

The ligand/metal complex (30 µg) in dimethylformamide (DMF) (0.01 L) was applied on a paper disc prepared from blotting paper (3 mm diameter) with the help of micropipette. The discs were left in an incubator for 48 h at 37°C and then applied on specific bacteria grown on agar plate.

Preparation of agar plate

For this purpose, minimal gar was used for the growth of specific bacterial species. For *Staphylococcus* species, a blood agar base with low pH was used. The blood agar base (40 g) was first suspended in cold distilled water (1L) and then heated to boiling. It was sterilised at 120°C for 15 min and later on allowed to cool at 50°C. Then 5% sterile defibrinated sheep blood was added to it and the mixture was poured into previously washed and sterilised petri dishes which were stored at 40°C for inoculation.

Procedure of inoculation

This was done by means of platinum wire loop which was first made red hot on a flame,

allowed to cool in air and then used for the application of bacterial strains. The preculture was first prepared in 2ml of nutrient broth by selecting a suitable colony of bacterial species, and later on transferred to a nutrient broth which was incubated for 2 h at 37°C. Then 500 µl of culture was spread on the agar plate which was incubated for 24 h at 37°C.

Application of disc.

A sterilised forcep was used for the application of paper disc on the already inoculated agar plates. When the disc was applied, it was incubated at 37°C for 24 h. Then the diameter of the zone of inhibition around the disc was measured.

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