

Synthesis, Spectral and Pharmacological Study of Cu(II), Ni(II) and Co(II) Coordination Complexes

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Abstract

Complexes of Cu(II), Ni(II) and Co(II) with 2,5-Dihydroxy butyrophenone thiosemicarbazone(L_1) / 2,5-Dihydroxy benzophenone thiosemicarbazone(L_1') as primary ligand and 2,2'-bipyridyl(L_2) as a secondary ligand have been synthesized. Complexes were characterized by analytical data, molar conductance, magnetic measurement, electronic spectra, IR spectra and thermogravimetric analysis. The stereo-chemistry of the coordination complexes has been confirmed on the basis of electronic, spectral and magnetic moment studies. Racah's inter-electronic parameter(B), Cubic Ligand field splitting parameter ($10 Dq$) and Nephelauxetic ratio(β), g , λ , h have also been calculated and it has been found that the values are in accordance with the stereochemical structure of the coordination complexes. Elemental analysis and spectral studies suggest the octahedral stereochemistry for all the complexes. Ligands and their complexes with Cu(II), Ni(II) and Co(II) were also screened for their inhibitory effects against four organisms viz; *S.aureus*, *B.megaterium*, *B.cereus* and *E.coli* by cup-plate method. The results of the evaluation of antibacterial activity show that all the synthesized complexes exhibit considerable activities towards all the four pathogenic bacteria. The activity of the mixed complexes has been found to be greater than those of the metal salts and ligands. Moreover, it has also been noticed that the thiosemicarbazones show low activity towards *E. coli*.

Key words: 2,5 -Dihydroxy butyrophenone thiosemicarbazone (L_1), 2, 5-Dihydroxy benzophenone thiosemicarbazone (L_1'), 2, 2-bipyridyl(L_2), Cu(II), Ni(II) and Co(II) complexes.

Introduction

Metal thiosemicarbazone complexes are emerging as new class of experimental anticancer chemotherapeutic agents which exhibits inhibitory activities against cancer though inhibition of a crucial enzyme is obligatory for DNA-biosynthesis and cell division viz. ribonucleotide diphosphate reductase (RDR)¹. They have been used as drugs and are reported to possess a wide variety of biological activities against bacteria, fungi, and certain type of tumors and they are also a useful model for bioinorganic processes^{2,3}. Thiosemicarbazone complexes are having imine group ($-N=CH-$) which imparts the biological activity and chelating properties towards the central metal atom. These have been investigated for antiviral, anticancer, antimicrobial and anti-inflammatory activities⁴⁻⁷. From the literature survey up to date, it has been found that no considerable work seems to have been done on the mixed complexes of Cu(II), Ni(II) and Co(II) with 2,5-Dihydroxy butyrophenone thiosemicarbazone(L_1) / 2,5-Dihydroxy benzophenone thiosemicarbazone(L_1') as primary ligands and 2,2'-bipyridyl(L_2) as co-ligand. In this paper we have discussed the preparation of these mixed complexes which have been characterized on the basis of a number of physicochemical methods, viz. elemental analysis, molar conductance, magnetic moment measurements, IR and electronic reflectance, spectral studies for the determination of their compositions and structures. The structures of Cu(II), Ni(II) and Co(II) complexes have been further supported by thermogravimetric analysis. The antibacterial activity of these compounds has also been evaluated.

Material and Methods

All chemicals used were of A.R. grade. The complexes were analyzed using standard procedure⁸. Melting points of complexes were determined in open capillaries. The conductivity measurements were made on Systronic Conductometer. In visible region, the electronic spectra of the complexes in non-aqueous solution were recorded on Bausch and Lomb Spectronic-20 Spectrophotometer. For reflectance spectra, VSU-2p Spectrophotometer was used. MgO was used as a reference compound. All the magnetic susceptibility measurements on the powder form of chelates were carried at room temperature using Gouy's magnetic balance and Hg[Co(CNS)₄] as calibrant. All the pH measurements were carried out at room temperature on ELICO Digital pH meter. The IR spectra of the ligands and complexes were recorded in KBr in the range 4,000–700 cm^{-1} and 4,000–200 cm^{-1} on Beckmann IR 5A spectrophotometer in the Chemistry Department of CDRI, Lucknow. The analytical data, colour, conductivity, magnetic measurement and magnetic moment have been recorded in table - 1.

Preparation and Isolation of the complexes: A solution containing primary ligand L_1 / L_1' (5.0 m mole) and a secondary ligand L_2 in 40 ml ethanol was added to a warm solution of metal salts (CuCl₂.2H₂O; NiCl₂.6H₂O; CoCl₂.6H₂O) in ethanol. After raising the P^H to 7.5 with alcoholic KOH solution, the mixture was refluxed on water bath for about two hrs. The precipitated solid was filtered, washed with distilled water ethanol (1:1) followed by ethanol and dried under vacuum.

Table-1
Analytical Data of Cu(II), Ni(II) and Co(II) Mixed Ligand Complexes

S. No.	Complex	% chemical analysis, found (calculated)					ΩM in DMSO ($\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$)	ΩM in PhNO_2 ($\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$)	MP ($^{\circ}\text{C}$)	Colour	MW Found (Calcd.)
		C	H	N	S	Metal					
1	$[\text{Cu}(\text{L}_1)(\text{L}_2)\text{H}_2\text{O}]$	51.50 (51.58)	4.60 (4.70)	14.20 (14.32)	6.43 (6.55)	12.89 (12.99)	10.40	8.6	247	Dark Green	475.0 (488.5)
2	$[\text{Cu}(\text{L}_1')(\text{L}_2)\text{H}_2\text{O}]$	55.00 (55.11)	3.95 (4.01)	13.26 (13.39)	6.40 (6.12)	12.03 (12.15)	11.12	10.10	240	Brown	512.5 (522.5)
3.	$[\text{Ni}(\text{L}_1)(\text{L}_2)\text{H}_2\text{O}]$	52.00 (52.09)	4.65 (4.75)	14.40 (14.47)	6.56 (6.61)	12.09 (12.13)	15.52	13.52	228	Light Yellow	475.30 (483.71)
4	$[\text{Ni}(\text{L}_1')(\text{L}_2)\text{H}_2\text{O}]$	55.57 (55.62)	3.97 (4.05)	13.48 (13.52)	6.10 (6.18)	11.25 (11.26)	14.12	10.30	245	Green	508.30 (517.71)
5	$[\text{Co}(\text{L}_1)(\text{L}_2)\text{H}_2\text{O}]$	51.98 (52.07)	4.70 (4.75)	14.40 (14.46)	6.58 (6.61)	12.10 (12.17)	13.10	9.12	220	Blue	475.0 (483.93)
6	$[\text{Co}(\text{L}_1')(\text{L}_2)\text{H}_2\text{O}]$	55.55 (55.60)	3.85 (4.05)	13.45 (13.51)	6.12 (6.17)	11.30 (11.37)	12.34	9.4	238	Pink	505.62 (517.93)

The complex was analyzed for metal, after acid decomposition, by complexometric titration with EDTA, using pyrocatechol violet as the indicator. N, C and H analysis were carried out micro analytically. Magnetic moments were determined at room temperature. Table-1 represents the analytical and magnetic data of the isolated solid complexes.

Results and Discussion

Analytical data reported in table-1 suggest 1:1:1 (M:L₁:L₂) (Where M=metal ion, L₁= thiosemicarbazone ligand and L₂=2,2'-bipyridyl) stoichiometry for the isolated complexes. They are insoluble in acetone, ethanol, benzene and chloroform, but their considerable solubility has been noticed in DMF and DMSO. The complexes are fairly stable at room temperature. They are non-hygroscopic and can be stored for a pretty length of period without decomposition. Conductivity data of 10⁻³ M solution of the complexes in DMSO and nitrobenzene correspond to very lower molar conductance value suggesting their non-electrolytic nature⁹. The molecular weight of the complexes determined by the Rast Camphor method corresponds with the weight of the formula, indicating their monomeric nature.

Magnetic Measurements: Cu(II) Complexes: The magnetic moment value of Cu(II) complexes generally falls in the range 1.75-2.20 B.M., irrespective of stereochemistry. The magnetic moment value at room temperature suggests the paramagnetic nature of Cu(II) complexes containing one unpaired electron. The higher value of the magnetic moment than the spin-only value (1.73 B.M) may be due to spin-orbit coupling. The observed magnetic moments (1.84-1.92 B.M.) for compounds $[\text{Cu}(\text{L}_1)(\text{L}_2)\text{H}_2\text{O}]$ and $[\text{Cu}(\text{L}_1')(\text{L}_2)\text{H}_2\text{O}]$ indicate distorted octahedral symmetry around Cu(II)¹⁰.

Ni(II) Complexes: Ni(II) possess a d⁸ electronic configuration with a possibility of two unpaired electrons having sp³d² hybrid orbitals and tendency to form the high spin octahedral complexes. In octahedral environment Ni(II) complexes have magnetic moment in the range 2.9-3.4 B.M.. Depending upon the magnitude of orbital contribution, tetrahedral complexes have magnetic moments in the range 3.5-4.2 B.M.¹¹. The complexes $[\text{Ni}(\text{L}_1)(\text{L}_2)\text{H}_2\text{O}]$; $[\text{Ni}(\text{L}_1')(\text{L}_2)\text{H}_2\text{O}]$ have magnetic moment value in the range 3.20 to 3.28 B.M. which confirms the octahedral stereochemistry of Ni(II) complexes¹².

Co(II) Complexes: The high spin octahedral complexes have the magnetic moment in the range 4.50-5.20 B.M. and the tetrahedral complexes have magnetic moment generally in the range 4.10-4.80 B.M. They may have higher magnetic moment than spin-only value due to higher orbital contribution. Magnetic moment values (4.96 and 5.02 B.M.) of the complexes $[\text{Co}(\text{L}_1)(\text{L}_2)\text{H}_2\text{O}]$; $[\text{Co}(\text{L}_1')(\text{L}_2)\text{H}_2\text{O}]$ show the presence of three unpaired electrons, and suggest a spin free octahedral configuration¹³.

Reflectance Spectral Studies: Cu(II) Complexes: The reflectance spectra of Cu(II) complexes $[\text{Cu}(\text{L}_1)(\text{L}_2)\text{H}_2\text{O}]$ and $[\text{Cu}(\text{L}_1')(\text{L}_2)\text{H}_2\text{O}]$ exhibits broad asymmetric band at 12,470-15,030 cm⁻¹. The two degenerate states, i.e. ²E_g and ²T_{2g} further split up into two components each. Thus three bands at 11,000-13,000, 14,000-16,000 and 16,000-18,000 cm⁻¹ correspond to transitions ²B_{1g}→²A_{1g}(v₁), ²B_{1g}→²B_{2g}(v₂) and ²B_{1g}→²E_g(v₃), respectively¹⁴. But due to small energy gap among these components, all the three bands envelop together, and a broad symmetrical band is observed. These values are in good agreement with the values reported for distorted octahedral complexes¹⁵.

Table- 2
Main IR Bands (cm⁻¹) observed in the Spectra of Cu (II), Ni (II) and Co (II) Mixed Ligand complexes

S. No.	Complexes	ν (C = N)	ν (C=N-N=C)	ν (C-S)	ν (N-N)	ν (M-N) Py/ Bipy	ν (M-N)	ν (M-O)	ν (M-S)
1	[Cu(L ₁)(L ₂)H ₂ O]	1645	1565	635	1050	270	460	510	300
2	[Cu(L ₁ ')(L ₂)H ₂ O]	1635	1560	640	1055	275	465	515	295
3	[Ni(L ₁)(L ₂)H ₂ O]	1620	1560	635	1050	265	470	510	310
4	[Ni(L ₁ ')(L ₂)H ₂ O]	1625	1565	640	1060	270	470	505	305
5	[Co(L ₁)(L ₂)H ₂ O]	1640	1570	635	1050	265	460	505	310
6	[Co(L ₁ ')(L ₂)H ₂ O]	1635	1570	645	1060	270	460	515	300

Electronic Spectra: Ni(II) Complexes: The electronic spectra of the solution of Ni(II) complexes in DMF [Ni(L₁)(L₂)H₂O]; [Ni(L₁')(L₂)H₂O] exhibits bands at 8,700-8,900, 13,950-14,500 and 24,600-25,000 cm⁻¹ which may be assigned to the following transitions: ³A_{2g}(F)→⁴T_{2g}(F)(v₁); ³A_{2g}(F)→⁴T_{1g}(F) (v₂) and ³A_{2g}(F)→⁴T_{1g}(p)(v₃)¹⁶. The appearance of these bands suggests octahedral stereochemistry for the complexes.

Co(II) Complexes: Electronic spectra of the complexes under study exhibits bands at 8,250-8,340(v₁), 17,500-17,650(v₂) and 20,000-20,100cm⁻¹(v₃) which corresponds to transitions ⁴T_{1g}(F)→⁴T_{2g}(F)(v₁); ⁴T_{1g}(F)→⁴T_{2g}(F)(v₂) and ⁴T_{1g}(F)→⁴T_{1g}(p)(v₃). The appearance of these bands suggests octahedral geometry around Co(II)¹⁷. The v₃ band is seen quite sharp while v₂ band is very weak. The octahedral geometry of these complexes is further supported by the value of v₂ / v₁ which comes out to be 2.12 and 2.11, respectively. The values of β obtained in the case of both the complexes are less than unity which clearly show the considerable amount of covalency in the metal ligand bond.

IR Studies: IR spectral data of Cu(II), Ni(II) and Co(II) are recorded in table-2. On comparing the infrared absorption spectra of free ligands and their complexes, active coordination sites bonding the metals are located. The spectra of the mixed ligand complexes shows change in the frequency of (N-C-N), (C=S) and (NH-C=S). The disappearance in the -NH-C=S absorption frequency with the formation of new band for azine (C=N-N=C) at 1550-1570 cm⁻¹ suggests coordination of the metal ion through the azine N and thiol S of the enolic form of thiosemicarbazones¹⁸. The stretching and deformation frequencies expected for the NH₂ group and the usual C=O stretch of the ketone are found to be absent and in their place is present a strong band at 1570cm⁻¹ assignable to the stretching mode of the coordinated and conjugated C=N group¹⁹. The (N-N) stretching band seen at 1030-1040cm⁻¹ in the spectra of thiosemicarbazones shows a positive shift of 20-25 cm⁻¹ in the spectra of the mixed complexes. Such

a positive shift of the ν(N-N) band on complexation also indicates the bonding of the metal ion with the azomethine nitrogen of the ligand²⁰. The bands observed at 3420 and 3210 cm⁻¹ assigned to ν_{as}NH₂ and ν_sNH₂ in the thiosemicarbazones, which remain unchanged, indicate the non-participation of the -NH₂ group in complexation.

The coordination of 2,2'-bipyridyl is indicated by the positive shift of (C=C), (C=N) ring stretching frequencies and the presence of their deformation modes at 1170 and 1980 cm⁻¹. The position of the bands found in the spectrum of 2,2'-bipyridyl has been completely changed in the spectra of the complexes where it is used as co-ligand, and new bands appeared at ~1590 and 1560 cm⁻¹ confirming the coordination nature of bipyridyl ligand. The 400 cm⁻¹ band of bipyridyl (C-C out of plane bending) shifts to higher frequency and splits into two components in the complexes, which again confirms the coordination of bipyridyl through two nitrogen²¹. Some new non-ligand bands appearing in the far IR region around 310-295 cm⁻¹ and have been noticed in the spectra of metal complexes, are assigned to ν(M-N), ν(M-O) and ν(M-S), respectively. An additional band at ~260 cm⁻¹ has also been observed in all the complexes indicating bipyridyl - nitrogen coordination with the metal ion²².

The IR-spectra of complexes (MLL'H₂O) exhibits bands in the regions 3390-3410 and 880-900 cm⁻¹ assignable to stretching and rocking modes of coordinated water²³. From the IR spectral data, it has been inferred that both the thiosemicarbazone ligands act as tridentate with C=O, -CH=N-, -SH as coordinating sites, while secondary ligand 2, 2'-bipyridyl acts as bidentate.

Thermogravimetric Studies The mode of coordination of ligands in the mixed complexes has been further supported by their thermogravimetric studies.

Cu(II)Complexes: The complexes [Cu(L₁)(L₂)H₂O]; [Cu(L₁')(L₂)H₂O] having observed loss in weight (3.70 and 3.52%) in 140-180°C temperature range, coincides with the removal of one molecule of water²⁴. TG curves of these

complexes reveal that they remain unchanged up to 230-240°C. These complexes show a gradual decomposition up to 280°C, but above this temperature, the rate of decomposition is found increased, and practically at 340°C to 350°C, the weight loss (35.73 and 33.50%) has been observed which is consistent with the removal of 2,2'-bipyridyl molecule from the above complexes. Further, a slow decomposition has continued and rapid mass loss takes place at ~700°C which is evident from the TG curve of the complexes. At this temperature, the weight of the remaining residues coincides with the weight of CuO (calculated 16.28 and 15.22%).

Ni(II) Complexes: The complexes $[\text{Ni}(\text{L}_1)(\text{L}_2)\text{H}_2\text{O}]$; $[\text{Ni}(\text{L}_1')(\text{L}_2)\text{H}_2\text{O}]$ have revealed the behaviour similar to Cu(II) complexes on heating at 80-120°C which clearly indicates that these complexes contain water held in the same fashion as in Cu(II) complexes²⁵. The elimination of the 2,2'-bipyridyl molecule takes place at ~340°C. At about 670°C to 680°C the organic entity is completely eliminated and a residue is left behind, which remains unchanged on further heating in the case of all the complexes²⁶.

Co(II) Complexes: The complexes $[\text{Co}(\text{L}_1)(\text{L}_2)\text{H}_2\text{O}]$; $[\text{Co}(\text{L}_1')(\text{L}_2)\text{H}_2\text{O}]$ show decomposition at ~150°C and the loss in weight is consistent with the elimination of one molecule of water which clearly indicates that the water molecule is present in the coordination sphere. These complexes show decomposition at ~300°C, and 2, 2'-bipyridyl molecule seems to be eliminated. Both the complexes show further decomposition from 330°C to 340°C, and practically at 630°C to 650°C the thiosemicarbazone molecule is eliminated leaving behind CoO ²⁷.

Evaluation of Antibacterial Activity: Cu(II), Ni(II) and Co(II) mixed ligand complexes have been screened for their inhibitory effects against four organism viz S.aureus, B.megaterium, B.cereus (gram positive) and E.coli (gram negative) by cup plate method²⁸. The zones of inhibition have been measured and the activity results regarding the ligands and their complexes have been recorded.

Conclusion

Elemental analysis and spectral studies suggested the octahedral stereochemistry for all the complexes. The results of the evaluation of antibacterial activity showed that all the synthesized complexes exhibit considerable activities towards all the four pathogenic bacteria. The activity of the mixed complexes was found to be greater than those of the metal salts and ligands^{29,30}. Moreover, it has been noticed that the thiosemicarbazones showed less activity towards E.coli. The increased activity of the mixed ligand complexes might be due to the combined activity effect of both the ligands present in the metal complexes. The proposed octahedral structure of Cu(II), Ni(II) and Co(II) complexes with 2,5-Dihydroxy butyrophenone thiosemicarbazone / 2,5- Dihydroxy benzophenone

thiosemicarbazone and 2,2'- bipyridyl where M = Cu(II), Ni(II) and Co(II), has been shown in figure-1.

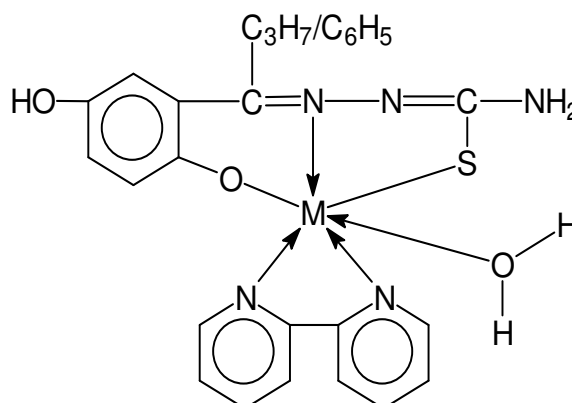


Figure-1

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