Biological Active Cobalt(II) and Nickel(II) Complexes of 12-Membered Hexaaza [N₆] Macrocyclic Ligand Synthetic and Spectroscopic Aspects

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Abstract: New cobalt(II) and nickel(II) complexes of 12-membered macrocyclic Schiff - base ligand containing thiosemicarbazone moiety as a part of ring have been prepared having general composition [MLX₂] where M = Co(II) or Ni(II), L=3,4,9,10-tetra-2-furanyl-1,2,5,6,8,11- hexaazacyclododeca-7,12- dithione - 2,4,8,10 – tetraene, X = Cl⁻, NO₃⁻, NCS⁻. The complexes have been characterized by elemental analysis, molar conductance, magnetic susceptibility measurements, spectral (IR, electronic, EPR) techniques and thermal analysis. Spectroscopic studies suggested a six coordinated octahedral geometry for all the complexes. The IR spectra of complexes suggest that ligand is coordinated to the metal ion through its four imines nitrogen. Conductivity measurements supported the non electrolytic nature of the complexes. The antifungal activities of complexes have been studied against a number of pathogenic fungi under laboratory conditions. The complexes showed good antifungal results. Thermal analysis of reported complexes suggests the absence of water molecule either in or outside the coordination sphere.

Keywords: Macrocyclic, Octahedral, Antifungal, Spectroscopic studies.

Introduction

Metal complexes with macrocyclic ligands have gained great research interest in recent years¹. The importance of macrocyclic complexes in coordination chemistry is because of various applications in biological processes such as photosynthesis and dioxygen transport².

Schiff base macrocyclic ligands derived from thiosemicarbazones are of significant interest not only for their wide biological properties as antibacterial, anti - cancer, antiviral, and antifungal agents^{3,4} but also for their capacity for chemical recognition of anions and metals of biochemical and environmental importance⁵⁻⁷. Macrocyclic complexes attract attention of chemist because of their resemblance with many natural systems like porphyrins and cobalamines⁸. The activity of such compounds is strongly dependent upon the nature of the heteroatomic ring and position of attachment to the ring as well as the form of the thiosemicarbazone moiety⁹⁻¹¹. In the light of above applications, it is proposed to synthesize some transition metal macrocyclic complexes from furil and thiosemicarbazide in order to study their stereochemistry and biological activities. The proposed structure of the complexes is given in scheme 1.

Experimental

All chemical used in this work were of A. R. grade and purchased from Sigma - Aldrich and used as such without further purification.

Instrumentation

The C and H were analyzed on Carlo - Erba 1106 elemental analyzer. The nitrogen content of the complexes was determined using Kjeldahl method. Molar conductance was measured on the ELICO (CM82T) conductivity bridge. Magnetic susceptibilities were measured at room temperature on Gouy balance using $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$. Electronic spectra were recorded in DMSO on Shimadzu UV mini - 1240 spectrophotometer. IR spectra (KBr) were recorded on FTIR spectrum BX-II spectrophotometer. EPR spectra of Co(II) complexes were recorded as polycrystalline sample at liquid nitrogen temperature on E₄-EPR spectrometer. Electronic impact mass spectrum was recorded on Jeol, JMS-DX-303 mass spectrometer. Thermal analysis of complexes was carried out TGA - DTA Shimatzu - 50 thermo analyzer.

Synthesis of complexes

A template reaction was carried out to synthesize the complexes. An EtOH solution (20 mL) of the respective divalent metal salt (10 mmol, 1.30 g) was mixed with a hot EtOH solution (20 mL) of thiosemicarbazide (20 mmol, 1.86 g). Then an EtOH solution (20 mL) of furil (3.5 g, 20 mmol) in the presence of a few drops of conc. HCl was added to the resultant solution. The solution was refluxed for about 5-7 hours as appropriate in each case. The coloured complexes precipitated out on cooling the reaction mixture overnight. The complexes were filtered, washed with ethanol and dried over P_4O_{10} . The general reaction for the formation of complexes is given below (scheme 1).

Scheme 1. Template condensation between thiosemicarbazide and furil in presence of divalent metal salt

Results and Discussion

The general composition for the complexes is MLX_2 (where $M = Co(II)$ or $Ni(II)$ and $X = Cl^-$, NO_3^- , NCS^-). All the complexes provide proper C, H and N results (Table 1). The complexes are insoluble in common organic solvents but soluble in DMSO and DMF.

Molar conductance measurements

The low value of molar conductance ($12 - 18 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$), which was carried out in DNF at the concentration of 10^{-3} M , indicates (Table 1) the non electrolytic nature of complexes¹². Therefore, these complexes may be formulated as $[MLX_2]$. The low molar conductance may be due to large size of anionic coordination sphere¹³.

Table1. Physical properties and analytical data of complexes

Complexes	Color	M.P. °C	Molar Conductance $\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$	Yield %	Elemental analysis found (calculated), %			
					M	C	H	N
[CoLCl ₂]	Brown	248	12	62	9.72	42.82	2.19	13.64
CoC ₂₂ H ₁₄ N ₆ O ₄ S ₂ Cl ₂					(9.51)	(42.58)	(2.25)	(13.54)
[Co L(NO ₃) ₂]	Light pink	260	15	65	8.92	39.15	2.19	16.76
CoC ₂₂ H ₁₄ N ₈ O ₁₀ S ₂					(8.76)	(39.22)	(2.08)	(16.64)
[Co L(NCS) ₂]	Brown	256	18	68	8.92	43.25	2.19	16.72
CoC ₂₄ H ₁₄ N ₈ O ₄ S ₄					(8.87)	(43.30)	(2.10)	(16.84)
[NiLCl ₂]	Dark brown	252	15	64	9.45	42.75	2.15	13.64
NiC ₂₂ H ₁₄ N ₆ O ₄ S ₂ Cl ₂					(9.36)	(42.64)	(2.26)	(13.57)
[Ni L(NO ₃) ₂]	Light green	245	14	60	8.72	39.35	2.15	16.78
NiC ₂₂ H ₁₄ N ₈ O ₁₀ S ₂					(8.63)	(39.28)	(2.08)	(16.66)
[Ni L(NCS) ₂]	Green	255	12	64	8.86	43.45	2.17	16.95
NiC ₂₄ H ₁₄ N ₈ O ₄ S ₄					(8.73)	(43.37)	(2.10)	(16.86)

Magnetic moment

Magnetic moment measurements for the complexes were made at room temperature. The cobalt(II) complexes show magnetic moment in the range 4.62 - 4.90 BM (Table 2), a value in accordance with a high spin configuration showing the presence of octahedral¹⁴ environment around the cobalt(II) ion in the complexes. The experimental values are higher than spin only value due to orbital angular momentum contribution in d^7 system. On the other hand the nickel(II) complexes show magnetic moment in the range 2.89 - 3.02 BM, consistent with the octahedral¹⁵ stereochemistry for the complexes with a $^3A_{2g}$ ground state.

Table 2. Electronic, EPR spectral and magnetic moment data of cobalt(II) and nickel(II) complexes

Complexes	ν_1, cm^{-1}	ν_2, cm^{-1}	ν_3, cm^{-1}	$\mu_{\text{eff}}, \text{B.M.}$	g
[Co LCl ₂]	9680	14204	20680	4.90	2.02
[Co L(NO ₃) ₂]	9950	15015	20680	4.62	2.15
[Co L(NCS) ₂]	9875	14870	22883	4.84	2.13
[Ni LCl ₂]	11650	17350	27140	2.89	-
[Ni L(NO ₃) ₂]	11600	17560	27700	2.92	-
[Ni L(NCS) ₂]	11794	6949	27027	3.02	-

IR spectra

IR spectral bands of the complexes give valuable information regarding the coordination behavior of ligand to metal ions in complexes. The relevant IR spectral bands of complexes are presented in Table 3. The IR spectra of the complexes show the absence of absorption $\text{ca. } 3400 \text{ cm}^{-1}$, it clearly indicates the absence of free amino group. A medium intensity band at $\text{ca. } 1580 - 1620 \text{ cm}^{-1}$ characteristic to the imines $\nu(\text{C}=\text{N})$ stretching frequency¹⁶ appeared at lower frequencies, suggesting that coordination takes place through the azomethine nitrogen atoms. The appearance of a band at $410 - 450 \text{ cm}^{-1}$ $\nu(\text{M}-\text{N})$ also indicates that metal is bonded with imines nitrogen. The band assigned to thioamide¹⁷ at $\text{ca. } 825 \text{ cm}^{-1}$ $\nu(\text{C}=\text{S})$ was present in the spectrum of free thiosemicarbazide remains almost at the same position in the complexes, it suggest that this group was not involved in coordination. Thus it may be concluded that ligand acts in tetra dentate fashion and coordinated to metal ion through its four imines nitrogen atoms.

Table 3. IR spectral data (cm^{-1}) of Co(II) and Ni(II) complexes

Complexes	$\nu(\text{NH})$	$\nu(\text{C}=\text{N})$	$\nu(\text{C}=\text{S})$	$\nu(\text{M}-\text{N})$
[Co L Cl ₂]	3216 b	1565 s	827 m	420 m
[Co L (NO ₃) ₂]	3220 b	1550 s	820 m	425 m
[Co L(NCS) ₂]	3280 b	1545 s	825 m	410 m
[Ni LCl ₂]	3260 b	1562 s	827 m	445 m
[Ni L(NO ₃) ₂]	3250 b	1560 s	822 m	430 m
[Ni L(NCS) ₂]	3280 b	1558 s	820 m	450 m

Bands due to anions

The IR spectral bands at $\text{ca. } 1450 - 1400$, $1320 - 1290$ and $1070 - 1020 \text{ cm}^{-1}$, in the spectra of nitrate complexes suggest that both nitrate groups are coordinated to the central metal ion in unidentate fashion¹⁸. Thiocyanate anion may coordinate in different ways. It can shows linkage isomerism. The complexes are under study show a single sharp band at $\text{ca. } 2050 - 2080 \text{ cm}^{-1}$ (Figure 1), indicating both thiocyanate groups are N bonded¹⁹.

Figure 1. IR spectrum of Ni(II) thiocyanato complex*Electronic spectra*

The electronic spectra of reported complexes were recorded in DMSO. The Co(II) complexes show electronic spectral bands at $\text{ca. } 9680 - 9990$, $14204 - 15015$ and $20680 - 22883 \text{ cm}^{-1}$

(Table 2). These transition may be assign to ${}^4T_{1g} \rightarrow {}^4T_{2g}(F)$, ${}^4T_{1g} \rightarrow {}^4A_{2g}(F)$ and ${}^4T_{1g} \rightarrow {}^4T_{1g}(P)$ respectively. The positions of bands indicate that Co(II) complexes have an overall octahedral geometry²⁰ (Figure 2). Ni(II) complexes display three well defined absorption bands (Table 2) in the range ca. 11650 - 11794 , 16949 - 17670 cm^{-1} and 27027- 27700, these spectral bands may be assigned to ${}^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$ (ν_1), ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ (ν_2) and ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ transitions. These spectral bands indicate an octahedral environment around Ni(II) ion²¹ (Figure 3).

Figure 2. Electronic spectrum of Co(II) chloro complex

Figure 3. Electronic spectrum of Ni(II) thiocyanato complex

EPR spectra

EPR spectra of the Co(II) complexes were recorded as polycrystalline samples. At room temperature no EPR signal was observed because the lattice spin relaxation of Co(II) broadens the lines at higher temperature. The complexes show a very broad isotropic signal at liquid nitrogen temperature. The observed g values are lie in the range 2.02 - 2.15 (Table 2). It is well known that the value of g is less than 2.003 for transition metal complexes containing d - shell less than half filled, whereas g is greater than 2.003 for complexes containing d - shells more than half filled. The observed g values suggest that d - shell is more than half filled in Co(II) complexes. The deviation of the g values from the free electron value (2.0023) may be due to interaction between the spin and orbital motion of the electron. This interaction prevents complete quenching of the orbital contribution.

FAB mass spectra

The electronic impact mass spectrum of the Co(II) complex show a molecular ion $[\text{CoC}_{22}\text{H}_{14}\text{N}_6\text{O}_4\text{S}_2\text{Cl}_2]^+$ peak at $m/z = 621$ amu (Figure 4). Since the calculated mass of this complex was 620 amu therefore the molecular ion peak may be corresponding to $M^+ + 1$ peak. It suggests the monomeric nature of the complex and confirms the proposed formula. It also shows a series of peaks correspond to various fragments. Their intensity gives the idea regarding the stabilities of the fragments.

Figure 4. EI Mass spectrum of $[\text{CoLCl}_2]$

Antifungal screening

The antifungal activities of reported macrocyclic complexes were tested against various fungi viz. *A. Niger*, *A. Alternata*, *F. Oxysporum* and *F. Odum* under laboratory conditions by food poison technique²² at 50 - 100 ppm concentrations. The experimental data (Table 4) suggest that complexes provided satisfactory antifungal strength. % Inhibition was calculated by using the formula²³, $\% I = 100(C-T)/C$, where C and T are the diameter (mm) of the fungus colony in the control and treatment respectively.

Table 4. Antifungal screening data of the Co(II) and Ni(II) complexes fungal inhibition % (conc. in ppm)

Complexes	<i>A. Niger</i>		<i>F. Odum</i>		<i>A. Alternata</i>		<i>F. Oxysporum</i>	
	100	50	100	50	100	50	100	50
$[\text{Co L Cl}_2]$	55	50	48	41	57	50	59	51
$[\text{Co L}(\text{NO}_3)_2]$	50	45	56	49	52	45	62	54
$[\text{Co L}(\text{NCS})_2]$	56	50	58	50	58	49	55	47
$[\text{Ni LCl}_2]$	55	49	55	48	51	44	58	51
$[\text{Ni L}(\text{NO}_3)_2]$	60	54	62	54	60	50	52	45
$[\text{Ni L}(\text{NCS})_2]$	58	52	56	51	58	48	60	52

Thermal analysis

Thermogravimetric and differential thermal analysis of some reported complexes have been carried out in the temperature range 50-700 °C. The TG curves of complexes clearly indicate the absence of water molecules inside or outside the coordination sphere as no significant mass loss observed up to 120-150 °C. The decomposition of organic part of complexes started around 250°C as indicated by major fall in the % weight loss. Finally around 650°C complexes converted into their metal oxides as end product. The conversion of complexes

into metal oxide has been found in accordance with the proposed formulae for the complexes. In DTA curve of Ni(II) chloro complex three exothermic peaks have been observed in the temperature range 250 - 540 °C. The TGA curve of Co(II) nitrato complex shows that the decomposition has been started nearly 390 °C. The general pattern of thermal degradation of the complexes may be given as follows

Figure 5. Antifungal screening data of the complexes

Conclusion

The synthesis of Co(II) and Ni(II) complexes has been achieved. The complexes have been characterized by various physicochemical techniques. These studies confirmed the expected structures for the complexes. IR spectra indicate that the macrocyclic Schiff - base ligand acts in tetradentate fashion by bonding to the central metal ion through the imines nitrogen. The mass spectra show the monomeric nature of the complexes. Antifungal results show that complexes exhibited good antifungal potential.

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