



SYNTHESIS, SPECTROSCOPIC AND ANTIBACTERIAL STUDY OF ZINC, COPPER AND NICKEL COMPLEXES WITH A NEW DERIVATIVE OF L-ASCORBIC ACID

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The metal(II) ion complexes of a tetradentate ligand (**L**), namely bis[O,O-2,4-O,O-6,7-(thiocyanatecarboxylic methyldiene)]-L-ascorbic acid are synthesized and characterized by ^1H , ^{13}C -NMR, elemental analysis (CHN), mass spectroscopy, UV-visible and Fourier Transform infrared (FTIR) methods. This ligand is prepared from the reaction of the L-ascorbic acid and two moles of trichloroacetic acid in basic medium (compound **I**) with two moles of potassium thiocyanate. The reaction of (**L**) in ethanol with $\text{MCl}_2 \cdot x\text{H}_2\text{O}$ gave complexes with the general formula $[\text{M}(\text{L})\text{Cl}_2]$ (where $\text{M} = \text{Ni(II)}, \text{Cu(II)}$ and Zn(II) , respectively) characterized by FTIR, UV-Visible, molar conductance, atomic absorption, magnetic susceptibility. The analysis of IR, spectral data of all complexes indicated that (**L**) is bonded to metal(II) ions through the two nitrogen atoms of thiocyanate groups and two oxygen atoms of hydroxyl moieties. The synthesized complexes were proposed to be octahedral in geometry. Among these complexes, the Zn(II) complex demonstrated good antibacterial activity.

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Experimental

All of the solvents and chemicals were purchased from commercial vendors and were used without purification.

Introduction

L-Ascorbic acid (Vitamin C) is an essential nutritious substance for human body participating in many different biological processes. It is found extensively in various vegetables and fruits and is used clinically in the treatment and prevention of scurvy, drug poisoning, liver disease, allergic reaction, and atherosclerosis.¹

L-Ascorbic acid is an important antioxidant that protects the skin by scavenging and destroying free radicals and reactive oxygen-derived species.² L-Ascorbic acid is also used topically because of its ability to reduce wrinkles by promoting collagen synthesis³ and its skin-depigmenting activity.⁴ Because of these favorable effects, L-Ascorbic acid has long been used in pharmaceutical and cosmetic preparations.⁵

Thiocyanate-ion is known to be an important part in the biosynthesis of hypothiocyanite by a lactoperoxidase.⁶⁻⁸ Thus the complete absence of thiocyanate⁹ or reduced thiocyanate,¹⁰ in the human body, (e.g., cystic fibrosis) is damaging to the human host defense system.^{11,12}

Thiocyanate-ion shares its negative charge approximately equally between sulfur and nitrogen. As a consequence, thiocyanate can act as a nucleophile at either sulfur or nitrogen it is an ambidentate ligand. $[\text{SCN}]^-$ can also bridge two ($\text{M}-\text{SCN}-\text{M}$) or even three metals ($>\text{SCN}-$ or $-\text{SCN}<$).

Experimental evidence leads to the general conclusion that class A metals (hard acids) tend to form N-bonded thiocyanate complexes, whereas class B metals (soft acids) tend to form S-bonded thiocyanate complexes.¹³

Physical and spectral measurements

The melting points were uncorrected and measured on electrothermal Stuart apparatus, model SMP30. The metal content of the complexes was measured using atomic absorption technique by Perkin-Elmer 5000. Electrical conductivity measurements of the complexes were recorded at 25 °C for $10^{-3} \text{ mol L}^{-1}$ solutions in distilled water using Ltd 4071 digital conductivity meter. Magnetic susceptibility values were obtained at room temperature using the Gouy method, Johnson Matthey, model M₅B-MKs, were performed.

FT-IR spectra were recorded in KBr on Shimadzu-spectrophotometer in the range of 4000-400 cm^{-1} . Electronic spectra in distilled water were recorded using a spectrophotometer type Shimadzu in the range of 200-1100 nm with quartz cell of 1 cm path length. Mass spectrum for the ligand **L** was obtained by Agilent mass spectrometer, Eager 300 for EA1112. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker 300-MHz spectrometer in $\text{DMSO}-d_6$. Chemical shifts in ppm relative to internal TMS are reported. Elemental microanalyses were carried out by using Euro Vetro-3000A.

Synthesis of ligand (**L**)

Firstly, compound **I** was prepared according to literature.¹⁴ Then KSCN (0.20 g, 2 mmol) was added to a solution of compound **I** (0.36 g, 1 mmol). The reaction mixture was stirred for three hours at the room temperature. The solid product was filtered off and washed with EtOH, then recrystallized from MeOH:H₂O mixture (3:1). M. p. 198 °C, yield 80 %.

Table 1. Physical properties and analytical data for the synthesized ligand (**L**) and its complexes.

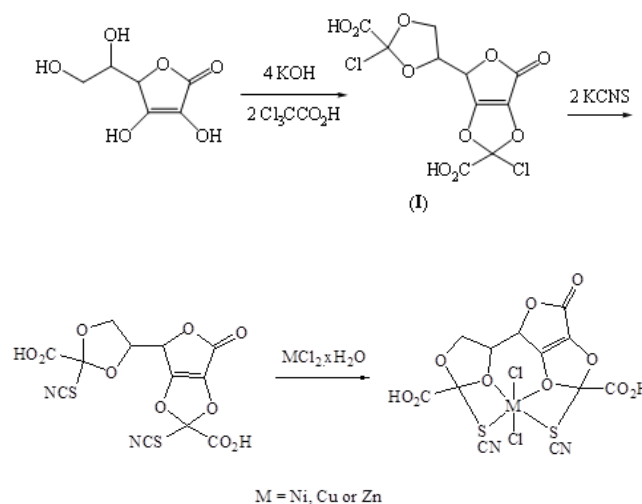
Empirical formula	Color	M.p. ^o C	Yield, %	Found(Calc.) (%)				
				C	H	N	S	M(II)
Ligand (L) C ₁₂ H ₆ N ₂ O ₁₀ S ₂	Yellow	198	80	35.57 (35.82)	1.57 (1.50)	6.25 (6.96)	15.34 (15.94)	—
[Cu(L)Cl ₂]	Green	238	79	26.25 (26.85)	1.33 (1.13)	4.98 (5.22)	11.71 (11.95)	11.66 (11.84)
[Ni(L)Cl ₂]	Olive	251	81	27.77 (27.10)	1.19 (1.14)	5.66 (5.27)	12.35 (12.06)	11.62 (11.03)
[Zn(L)Cl ₂]	White	248	87	26.17 (26.76)	1.18 (1.12)	5.46 (5.20)	11.78 (11.91)	12.36 (12.14)

Table 2. Magnetic moments and electronic spectral bands (cm⁻¹) of the complexes.

Complex	μ_{eff} , B.M.	Band position, cm ⁻¹	Assignments	B-complex	β	10Dq (ν_1) theoretical, cm ⁻¹
Ligand (L)	—	40000	$\pi \rightarrow \pi^*$	—	—	—
L -Ni(II)	3.18	25773 ν_3 14556 ν_2 9174 ν_1	3A _{2g} → 3T _{1g} (P) 3A _{2g} → 3T _{1g} (F) 3A _{2g} → 3T _{2g}	773.38	0.75	13920
L -Cu(II)	2.02	12422	2E _g → 2T _{2g}	—	—	—
L -Zn(II)	Diamagnetic	40983	ILCT	—	—	—

Synthesis of complexes

The ligand (**L**) (0.40 g, 1 mmol) was dissolved in a mixture of 15 mL methanol + 5 mL water. A solution of NiCl₂·6H₂O (475 mg, 2 mmol) in (20 mL) methanol was then gradually added to the solution of (**L**) with stirring to obtain a precipitation accompanied by a visible color change. The mixture was then refluxed for a further 3 h on a hot plate to ensure the completion of the reaction. The yellow precipitate was then filtered off, washed with methanol. The same procedure was used for the synthesis of the Cu(II) and Zn(II) complexes. The isolated complexes are colored solids, stable in air and insoluble in common organic solvents but completely soluble in water, DMSO and DMF. Some physical properties of synthesized ligand (**L**) and its complexes are shown in Table 1.

**Scheme 1.** Preparation of the ligand (**L**) and its complexes.

RESULTS AND DISCUSSION

Bis[O,O-2,4:O,O-6,7(thiocyanatecarboxylic methylidene)] L-ascorbic acid (**L**), was obtained in a good yield by the reaction of the compound (**I**) with potassium thiocyanate, in the ratio of 1:2. Then the metal complexes were obtained from the reaction of ligand (**L**) with MCl₂·xH₂O in EtOH, having the general formula [M(**L**)Cl₂] (where M = Ni(II), Cu(II) and Zn(II), respectively; Scheme 1).

The molar conductance of all complexes was obtained to be 16, 21 and 19 Ω⁻¹ cm² mol⁻¹, respectively. This indicates that all of the three complexes are non-electrolyte.¹⁵ So based on elemental analysis and molar conductance data, all complexes have [M(**L**)Cl₂] formula in which two chloride ions are placed on coordination sphere.

A single sharp band was observed at 2056 cm⁻¹ in IR spectrum of (**L**) that can be assigned to -SCN group, although its position was found to be lower by 25–35 cm⁻¹ in its complexes. This behavior suggests that nitrogen atom of the thiocyanate coordinated to the metal(II) ions.

New bands appeared at around 470 and 455 cm⁻¹ in all complexes, which were attributed to the ν(M–O) and ν(M–N) stretching vibrations, respectively.¹⁶ The two strong bands at 1722 and 1670 cm⁻¹ due to asymmetric and symmetric frequencies of ν(C=O) in (**L**), were observed to shift to 1717–1729 and 1675–1680 cm⁻¹ in the spectra of all complexes.¹⁷ Since no considerable change was observed for ν(C=O) of (**L**) and its complexes, it was concluded that the oxygen atoms of the carbonyl in the carboxylic group are not involved in the coordination to the metal ions.

The ¹H-NMR spectrum of (**L**) displayed several signals at 4.54 ppm is attributed to CH-6, while CH-5 of lactone ring appears at 6.34 ppm. The proton signal of CH₂-7 appeared at 3.36 ppm, the signal at 8.30 ppm can be assigned to OH of carboxylic acid.

¹³C-NMR spectrum showed a weak signal at 179 ppm which belongs to the carboxylic acid, while the C=O carbon signal appears at 162 ppm. The two peaks at 129 and 138

ppm are attributed to C-2 and C-4 carbons, respectively. This may be due to the conjugated double bond from C-1 to C-4 causing upfield shift of C-4 carbon signal. The C-N carbon signal of thiocyanate appears at 111 ppm, the signals at 79, 70 and 62 ppm assigned to C-5, C-6 and C-7 carbon atoms, respectively.

The mass spectra of the ligand (**L**) exhibit fragmentation patterns as expected. Therefore the results of mass spectroscopy showed good agreement with the molecular weight 402 as expected. The peak for $[M+H]^+$ was observed at m/z 403.

The electronic spectra of (**L**) and its complexes show an absorption band in the region 250–260 nm that can be attributed to intra-ligand transfer $\pi \rightarrow \pi^*$ transition.¹⁸ The electronic absorption bands, as well as the magnetic moment values of ligand **L** and its complexes, are summarized in table 2. Spectrum of Ni(II) complex exhibited three bands in the visible region at 25773 cm^{-1} ($^3A_{2g} \rightarrow ^3T_{1g(P)}$) (ν_3), 14556 cm^{-1} ($^3A_{2g} \rightarrow ^3T_{1g(F)}$) (ν_2) and the last one is at 9174 cm^{-1} can be attributed to $^3A_{2g} \rightarrow ^3T_{2g}$ (ν_1). The ratio of ν_2/ν_1 (1.59) was applied on Tanabe-Sugano diagram for d^8 octahedral complexes,^{19,20} B_{complex} and β , $10Dq(\nu_1)$ were calculated theoretically. The spectrum of Cu(II) complex showed a broad band at 12422 cm^{-1} assigned to $^2E_g \rightarrow ^2T_{2g}$ transition which refers to Jahn-Teller distortion of octahedral geometry.²¹ The Zn-complex is diamagnetic. As it is expected due to the d^{10} electronic configuration of Zn(II) ion, its electronic spectra did not show any d-d transition, only band assigned to charge transfer transition at 40983 cm^{-1} .

Table 3. Antimicrobial activity of ligand **L** and its complexes; diameter of growth of inhibition zone, mm.

Compounds	<i>S. aureus</i>	<i>E. coli</i>
Ligand (L)	0	0
Ni-complex	14	18
Cu-complex	17	21
Zn-complex	20	24

The ligand (**L**) and its complexes have been screened for antibacterial activities. The results of the microbial screening of (**L**) and its complexes are given in table 3. The antibacterial monitoring data showed that ligand (**L**) does not exhibit any activity. While its complexes demonstrated antibacterial activity towards Gram negative bacteria (*E. coli*), and Gram positive bacteria (*S. aureus*). The increased activity of the metal complexes can be described based on chelating theory.

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