

Synthesis, Characterization and Biological Activity of Mixed Ligands Complex of Co (II) Ions with Succinic Acid and Hexamethylenetetramine

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Abstract

Novel Co(II) complex with hexamethylenetetramine and succinic acid as ligands has been synthesized using slow evaporation method. The complex has been characterized by Fourier transform infrared, electronic spectra and elemental analyses. The nature of bonding and the stereochemistry of the complex have been deduced from infrared and electronic spectra measurements. Based on the study results a tetrahedral geometry has been proposed for this complex, in which the central metal ion is bonded to the ligands through hydrogen-bonding. The antibacterial activity has been evaluated by the disc diffusion method against five pathogenic bacteria (one gram positive and four gram negative). The biological activity data indicate that the metal complex showed enhanced inhibitory activity compared to the parent ligands. The present work relates to metal organic framework material which possesses anti-microbial properties to prevent or treat microbial infections, or provide surfaces which limit contamination by micro-organisms.

Keywords: Hexamethylenetetramine, succinic acid; biological activities; polymer

Introduction

In the development of antimicrobial drugs, metal complexes are playing an increasing role [1] and the metal chelates are found to have more antimicrobial activity than the chelating agents themselves [1,2]. Several metal chelates are known to possess antibacterial, antifungicidal, antiviral and anticancer activity. Transition metal complexes of multi- dentate nitrogen-donor ligands are reported to show enhanced thermodynamic and kinetic stability [3] in their application as anticancer, antitubercular, antibiotic, antimicrobial and antifungal agents [4]. Among the multi-dentate nitrogen-donor ligand, synthesis of some hexamethylenetetramine metal complexes [4, 5] and their antimicrobial activity have been reported [6]. In this present study, a novel cobalt (II) based metal-organic framework (MOF) was tested and shown to be highly effective at inactivating model micro organisms [1,7]; the Co serves as a central element and the ligands hexamethylenetetramine and succinic acid serve as bridging linkers.

Materials and Methods

All the chemicals and solvents used in this study comprising: Hexamethylenetetramine (HMTA, C₆H₁₂N₄), succinic acid (C₄H₆O₄), cobalt (II) chloride hexahydrate salts (COCl₂.6H₂O), ethanol, methanol, ammonia were all obtained from Sigma Aldrich and were of analytical grade. The solvents were used without further purification.

Melting point determination was carried out using a Thomas Hoover capillary melting point apparatus. Infrared spectra of the ligands and complex were recorded using pressed KBr discs in the range (4000-450 cm⁻¹) on Perkin-Elmer FT-IR spectrometer 1.00 versions (Wattman) and their Electronic spectra were measured in the range 200-800 nm at room temperature with Perkin Elmer spectrum Bk UV-Vis spectrophotometer.

Synthesis of the Cobalt (II) Complex

To a stirred solution of hexamethylenetetramine (5 mmol, 0.701g) in 10 ml methanol, 5 ml aqueous solution of COCl₂.6H₂O (5 mmol, 1.189g) was added dropwise with stirring at 20 °C for 10 minutes. Then a 5 ml methanol solution of succinic acid (5 mmol, 0.591g) was added dropwise with stirring to the mixture. The resulting mixture was stirred for three hours. The reddish- brown complex formed was filtered, washed with methanol and dried under vacuum. On the fifth day, violet crystals were observed to form from the precipitate.

Sensitivity Test

All the species used for this test were derived from stock cultures obtained from Applied Microbiology Laboratory of Veritas University, Abuja. Five species of bacteria namely: *Staphylococcus aureus* (Gram-Positive bacteria), *Escherichia coli*, *Salmonella typhi*, *Pseudomonas Aeruginosa* and *Klebsiella pneumonia* (Gram-

negative bacteria) were used for this study. The microbial isolates were maintained on an agar slant at 4 °C in the laboratory. The strains were sub-cultured on fresh agar plate, 24 hours prior to any antibacterial test [2]. The ligands, cobalt (II) chloride and cobalt (II) complex were diluted in sterilized distilled water at 100mg/mL. The sterilized paper discs were impregnated with 1mg of the solution of the test compound using a sterile pipette and allowed to dry prior to testing

Diffusion test

In vitro antibacterial activity of the ligands, metal salt and complex were evaluated using disc-diffusion method. Nutrient Agar was employed as microbial growth medium. The antibacterial diffusion tests were carried out by using Kirby Bauer Method, a Disc diffusion method. Hexamethylenetetramine, succinic acid, metal salt, Gentamycin solutions and DMF are used as controls. 100µg antimicrobial agents (prepared complexes) were loaded on the discs by soaking in test solution and discs were placed on the surface of the sterile nutrient agar medium with aid of sterile forceps and the plates were incubated at 37°C for 24hrs. Antimicrobial activity was evaluated by measuring the diameter of growth inhibition zone (IZ) in mm around the discs. Compounds were considered active when the IZ was greater than 6mm.

Results and Discussion

The physical properties of the complex as presented in Table 1 shows that the Co (II) complex was isolated as red crystals. The cobalt (II) complex decomposed on melting from violet to blue and finally to black at 320 °C. The variation in the color with increasing temperature could be due to changes in the crystal structure. The Co (II) complex is air stable and insoluble in water, ethanol and methanol. The complex and its ligands were generally soluble in ammonia. The results obtained from solubility tests showed that the complex is soluble in coordinating solvents. These observations are in agreement with tetrahedral Co(II) complexes reported in the literature [8]. The micrograph of Co (II) complex using x4 and x10 magnifications as presented in Fig. 1 and 2 show the size and shape of the complex to be tetrahedral.

Table 1: Physical properties of ligands and Co (II) complex

	Colour	Physical state	yield (%)	Melting point (°C)
(CH ₂) ₆ N ₄	white	crystalline	-	200
C ₄ H ₆ O ₄	white	crystalline	-	186
COCl ₂ .6H ₂ O	red	crystalline	-	86
Co(II) complex	violet	crystalline	60.3	320

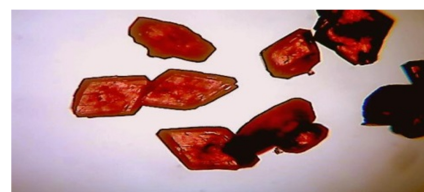


FIGURE 1: Micrograph of cobalt (II) complex using x4 magnification

Table 2: Solubility of the ligands and Co(II) in some solvents

Compound	Solvents			
	Water	Ethanol	Methanol	Ammonia
(CH ₂) ₆ N ₄	Soluble	Insoluble	Insoluble	Soluble
C ₄ H ₆ O ₄	Insoluble	Soluble	Soluble	Soluble
COCl ₂ .6H ₂ O	Soluble	Soluble	Soluble	Soluble
Co complex	Insoluble	Insoluble	Insoluble	soluble



FIGURE 2: Micrograph of cobalt(II) complex using x10 magnification

The infrared spectrum of the complex was compared with that of the free ligands and qualitative differences between the spectra have been used in diagnosing the different coordination mode of the metal and ligands in the complex. The infrared spectrum of the complex is as presented in Fig. 3. The infrared absorption spectra of Co (II) complex shows three bands at 1452, 1360, and 1230 cm⁻¹ assigned to ν_{as}(CH₂), ν_s(CH₂) and ν(C-N), respectively. Similar vibrational frequencies are recorded in the literature for similar compounds [9, 10].

Table 3: Selected IR Absorption Bands (cm^{-1}) of the Complexes

complex	$\nu_{\text{as}}(\text{CH}_2)$	$\nu_{\text{s}}(\text{CH}_2)$	$\nu(\text{C-N})$
Co (II) complex	1452	1360	1230

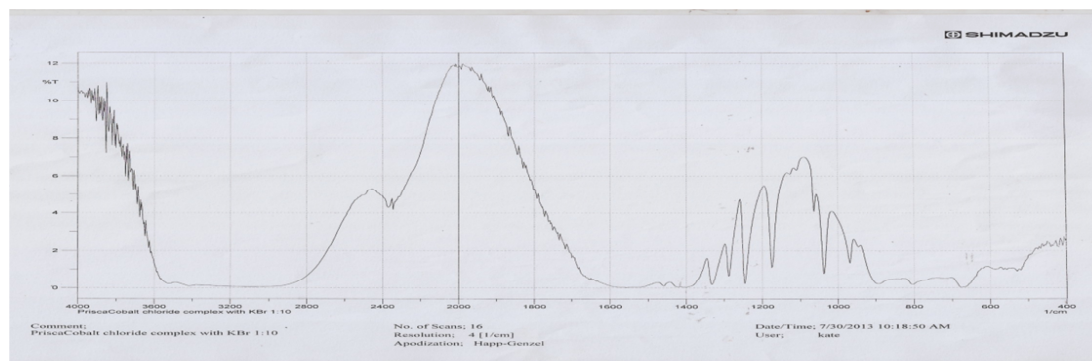


FIGURE 3: IR spectrum of Co (II) complex

The electronic spectral data of the complex recorded in dimethylsulfoxide is presented in Table 4. The electronic absorption spectra of the cobalt (II) complex reveals three bands at 265, 285 and 326 cm^{-1} assigned to ${}^4\text{T}_{1\text{g}}(\text{F})$, ${}^4\text{T}_{1\text{g}}(\text{P})$ and ${}^4\text{T}_{1\text{g}}(\text{F})$ ${}^4\text{A}_{2\text{g}}$ transitions [11, 12].

Table 4: Band Positions and proposed transitions for Co(II) Complex

Complex	Band position(nm)	Assignment
Co (II) complex	265	${}^4\text{T}_{1\text{g}}(\text{F})$
	285	${}^4\text{T}_{1\text{g}}(\text{P})$
	326	${}^4\text{T}_{1\text{g}}(\text{F}), {}^4\text{A}_{2\text{g}}$

From the antimicrobial profile presented in Table 5; Cobalt (II) complex displays a significant inhibitory effect on the growth of tested bacterial species. The hexamethylenetetramine ligand (HMTA), was found to be active against only one (*S. typhi*) of the 5 tested bacterial strains; whereas the succinic acid has relatively low antibacterial activity.

Table 5: Inhibition zone (mm) of the ligands, complex and reference antibiotic against tested bacterial strain

Tested compound	<i>Staphylococcus aureus</i> (G+)	<i>Escherichia coli</i> (G-)	<i>Salmonella typhi</i> (G-)	<i>Pseudoms Aeroginoa</i> (G-)	<i>Klebsiella pneumoniae</i> (G-)
1	0.0	0.0	7.0	0.0	0.0
2	0.0	3	3	0.0	2
3	45	15	21	45	45
4	16	20	23	23	24

Key: G+ = gram positive bacteria, G- = gram negative bacteria

1= $(\text{CH}_2)_6\text{N}_4$, 2 = $\text{C}_4\text{H}_6\text{O}_4$, 3 = Co(II) complex, 4 = Gentamycin

Conclusion

Novel Co(II) complex with hexamethylenetetramine and succinic acid as ligands has been synthesized and characterized by Fourier transform infrared, electronic spectra and elemental analyses. A tetrahedral structure has been proposed for this complex based on its infrared and electronic spectra measurements. The antibacterial activity evaluated by the disc diffusion method against five pathogenic bacteria (one gram positive and four gram negative) showed enhanced inhibitory activity of the Co(II) complex compared to the parent ligands. The bioactivity of this compound may be further studied on metal complex acting as drugs in various diseases.

Author Information

The authors declare no competing financial interest.

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