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Synthesis, Characterization and Antibacterial Study of Co (II) and Cu (II) Complexes of Sulfamethoxazole

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Authors' contributions

This work was carried out in collaboration among all authors. Authors UAA, BM and ABM designed, supervised and reviewed all the drafts of the manuscript. Author NA carried out the research and author MMS wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Complexes of Co and Cu with SMZ were successfully synthesized (1:2 molar ratio) in good yield and characterized by using UV-vis, FTIR, melting point/decomposition temperature, electrical conductivity and solubility in different solvents of varying polarity and proticity. All the prepared complexes were coloured. From the IR results, 529, 631, 528 and 779 cm^{-1} bands were observed in the spectra of the complexes which were absent in the free ligand spectrum thus, showing the presence of metal-ligand bond (coordination) in the complexes. The electronic spectral data of the complexes suggest an octahedral and tetrahedral geometry for all the complexes. The ligand and the Co (II) complex were found to be soluble polar protic solvents at both room and elevated temperature while, Cu (II) complex was found to be insoluble in polar protic solvent (ethanol) at room temperature but soluble at elevated temperature. The metal complexes are insoluble in non-polar solvent at both temperatures. More so, the ligand was found to be soluble in non-polar solvent at both temperatures. The electrical conductivity measurements indicated that the synthesized complexes are non-electrolytes. The synthesized metal complexes showed improved broad-spectrum antimicrobial activity against *E. coli* and *S. aureus* as compared to the ligand. Thus, the complexes $[Co(C_{10}H_{11}N_3O_3S)]$ and $[Cu(C_{10}H_{11}N_3O_3S)]$ are good leads to be developed into antibiotics against the tested antimicrobial agents (*E. coli* and *S. aureus*).

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1. INTRODUCTION

Interest in coordination chemistry is increasing continuously with the preparation of organic ligands containing a variety of donour groups, and it has multiplied manifold when the ligands have biological importance [1]. The number and variety of nitrogen and sulfur chelating agents used to prepare new coordination and organometallic compounds have increased rapidly during the past few years [2]. Sulfur compounds and their metal complexes have antimicrobial activity and it showed a high dependence on the substituents [2]. Transition metal complexes are essential in catalysis, materials synthesis, photochemistry and biological systems. They display diverse chemical, optical and magnetic properties. Metal complex or coordination compound is a structure consisting of a central metal atom, bonded to a surrounding array of molecules or anions [3]. Antibiotics are substances which, even at low concentrations, inhibit the growth and reproduction of bacteria. Infectious disease treatment would have been inconceivable today without antibiotics [4]. Inspired by recent advances, we have tried in using sulfamethoxazole (a useful subclass of sulfur chelating agent) as ligand. Hence, sulfamethoxazole and complexes with earth-abundant, cheap and environmentally friendly metal such as Co and Cu were synthesized and characterized. Furthermore, as a continuation of our contributions, the synthesized ligand and the complexes were screened for their antibacterial activity.

2. MATERIALS AND METHODS

2.1 Materials

The chemicals $CoCl_2.6H_2O$, $CuCl_2.5H_2O$ and $C_{10}H_{11}N_3O_3S$ were purchased from LOBA Chemie. Glasswares were washed and oven dried at 110°C. The electrical conductivity of the ligand and the complexes was examined by EC/TDS/NaCl meter (HI9835 model, Hanna), and the FTIR transmission spectra were checked in the range of 4000 - 400 cm^{-1} using PerkinElmer version 10.03.09 using standard KBr techniques. The UV-spectra of the synthesized complexes with $C_{10}H_{11}N_3O_3S$ were acquired on a PerkinElmer 725 UV- vis spectrophotometer. The melting point/ decomposition temperature of the ligand and the complexes were obtained using Electro Thermal Melting Point (SMP10) apparatus. The bacterial strains *Staphylococcus aureus* (*S. aureus*) and *Escherichia coli* (*E. coli*) were obtained from the Specialist Hospital, Gombe, Nigeria.

2.2 Synthesis of the Metal Complexes

The complexes were synthesized with slight modification of Al-khoodir`s method [5]. A 5.06 g of sulfamethoxazole was dissolved in 25 cm^3 of ethanol and mixed with ethanolic solution of $CoCl_2.6H_2O$ (2.38 g) in a ratio of 2:1 (Co^{2+}: $C_{10}H_{11}N_3O_3S$). The mixture was refluxed for 2 hrs at 60°C, cooled, filtered, washed with ethanol and dried in a desiccator for 24 hrs. Similarly, copper complex sample was obtained by same procedure with copper (II) chloride pentahydrate (2.5 g).

2.3 Antibacterial Assay of the Free Sulfamethoxazole and Its Complexes

Antibacterial susceptibility test was carried out using agar well diffusion technique. The surface of Muller Hilton's agar in a petri dish was inoculated uniformly with 0.3 cm^3 of 18 hrs old cultured bacteria. A 0.1, 0.05, 0.025, 0.0125 mg/cm^3 solution of each complex in DMSO was added to a 6 mm well bore hole into the agar. The plates were allowed to stand for 30 min after inoculation and then incubating at 37°C for 24 hrs. Zone of inhibition (ZI) of the complexes was recorded in diameter [6]. The experiments were conducted in duplicates.

3. RESULTS AND DISCUSSION

The temperature at which [Co($C_{10}H_{11}N_3O_3S$)] and [Cu($C_{10}H_{11}N_3O_3S$)] start to decomposed was 156 and 198°C respectively. While, the melting point of $C_{10}H_{11}N_3O_3S$ was 167°C as presented in Table 1 [7]. The differences in melting points can be the result of their different structural arrangements and bond strengths within the compounds. The cobalt complex was observed to be pink while, the copper complex was green. This could be due to d-d transition and charge transfer in cobalt and copper complexes respectively. The cobalt complex has the highest percentage yields of 90.46% and the copper complex has 88.58% yields. The electrical conductivity of the ligand and the

complexes was measured in dimethyl sulfoxide (DMSO) and were obtained to be in the range of 525-2930 μScm^{-1} (Table 1). Thus, indicating that the ligand and the complexes are non-electrolytes [7-9]. More so, this shows that there is no chloride ion outside the coordination sphere in all the complexes.

The results of the solubility test of the compounds in different solvents of various polarity and proticity are presented in Table 2. The ligand and the complexes are all soluble in water, methanol and ethanol at both room temperature and elevated temperature except that copper complex is insoluble in ethanol at room temperature. The metal complexes are insoluble in both ether and n-hexane at room and elevated temperatures while, the ligand ($C_{10}H_{11}N_3O_3S$) was soluble in ether and n-hexane at both room temperature and elevated temperatures [7,10,11].

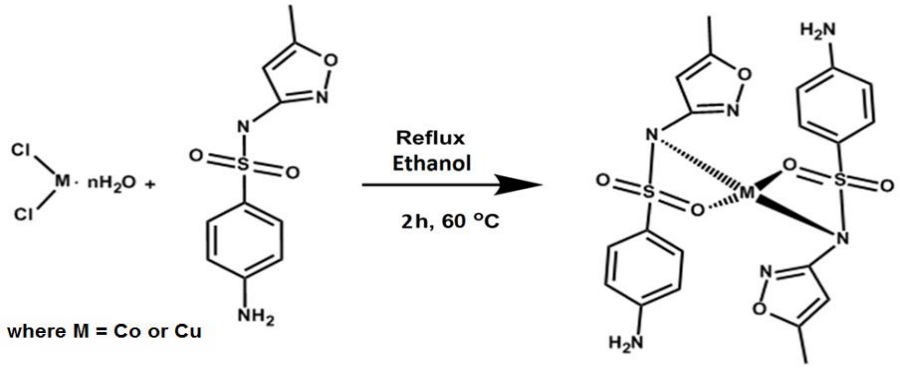
3.1 Infra-Red (IR) and Electronic Spectral Analysis

The IR spectral results of the ligand and the complexes results are shown in Table 3. The ligand behaves as a bidentate ligand and coordinates to the metal ion with different point of chelation group. Two strong absorptions at 3470 and 3015 cm^{-1} (for the ligand), 3554 and 3407 cm^{-1} (for cobalt complex) and 3471 cm^{-1} and 3342 cm^{-1} (for copper complex) indicated the presence of N-H and C-H respectively [9]. The IR bands at 1624 and 1389 cm^{-1} assignable to C=C and C=N respectively in the spectrum of the ligand were observed around 1672 and 1532 cm^{-1} in the case of cobalt complex and around 1637 and 1423 cm^{-1} for copper complex. The IR band around 1129 cm^{-1} due to S=O in the spectrum of the ligand are observed around 1198 cm^{-1} and 1127 cm^{-1} in cobalt and copper complexes respectively. New bands around 529, 631, 528 and 779 cm^{-1} in the spectrum of the complexes indicated the presence of M-O and M-N bonds [12,13].

The complexes of Co and Cu with $C_{10}H_{11}N_3O_3S$ exhibited absorption properties in the UV (400 - 460 nm) region when dissolved in DMF. The assignments have been done by comparing the observed values with previous similar work. The UV spectrum of $C_{10}H_{11}N_3O_3S$ exhibit absorption maxima at 420 nm. The electronic spectra of the metal complexes ([Co-$C_{10}H_{11}N_3O_3S$) and (Cu-$C_{10}H_{11}N_3O_3S$) showed broad bands at 440 and 460 nm respectively and are assigned to octahedral (A_1g-T_2g) and tetrahedral (d-d) geometry [14,15].

3.2 Antibacterial Screening of the Complexes

The ZI of the $C_{10}H_{11}N_3O_3S$ (SMZ) and the complexes are presented in Table 4. The SMZ displayed a moderate activity against *E. coli* (10-16 mm) and *S. aureus* (6-8 mm). The activity of Co (II) and Cu (II) complexes against *E. coli* and *S. aureus* significantly improved relative to the SMZ with ZI > 16 mm for both microorganisms. Increased activity of the complexes is due to chelation, which reduced the polarity of the metal atom and subsequently increased lipophilic character, favoring its permeation through lipid layers of the bacterial membrane. [16-20]. Therefore, [Co($C_{10}H_{11}N_3O_3S$)] and [Cu($C_{10}H_{11}N_3O_3S$)] could be considered as lead compounds to be developed into antibiotics against the two tested bacterial strains (*E. coli* and *S. aureus*).



Scheme. 1. Synthesis of Co and Cu complexes with SMZ

Table 1. Physical properties and electrical conductivity of the ligand and of their metal (II) complexes

	Compound	M.P/D.T (°C)	E. conductivity (µS/cm)	Colour	Yield (%)
1	$C_{10}H_{11}N_3O_3S$	167	525	White	-
2	$[Co(C_{10}H_{11}N_3O_3S)]$	198	2930	Pink	90.46
3	$[Cu(C_{10}H_{11}N_3O_3S)]$	156	978	Green	88.58

** M.P/D.T = melting point/decomposition temperature*

Table 2. Result of solubility tests of the ligands and of their metal (II) complexes in some solvents

S/N	Compound	Ethanol		Water		Methanol		Ether		n-Hexane	
		RT	ET	RT	ET	RT	ET	RT	ET	RT	ET
1	$C_{10}H_{11}N_3O_3S$	S	S	S	S	S	S	SS	SS	S	S
2	$[Co(C_{10}H_{11}N_3O_3S)]$	SS	S	S	S	SS	SS	IS	IS	IS	IS
3	$[Cu(C_{10}H_{11}N_3O_3S)]$	IS	S	S	S	SS	S	IS	IS	IS	IS

**RT = Room Temperature, ET = Elevated Temperature, S = Soluble SS = Slightly Soluble, IS = Insoluble*

Table 3. Major IR spectra of the complexes with SMZ ($C_{10}H_{11}N_3O_3S$) in cm^{-1}

Compound	N-H	C-H	C=C	C=N	S=O	N-O	C-O	M-O	M-N
$C_{10}H_{11}N_3O_3S$	3470	3015	1622	1389	1129	1322	1672	-	-
$[Co(C_{10}H_{11}N_3O_3S)]$	3554	3407	1672	1532	1198	1438	1130	529	631
$[Cu(C_{10}H_{11}N_3O_3S)]$	3471	3342	1637	1423	1127	1334	1056	528	779

Table 4. Zone of inhibition (ZI) of $C_{10}H_{11}N_3O_3S$, $[Co(C_{10}H_{11}N_3O_3S)]$ and $[Cu(C_{10}H_{11}N_3O_3S)]$ (ZI in mm) in various concentrations of 0.0125, 0.025, 0.05 and 0.1 mL

Compound	Microorganism							
	E. coli				*S. aureus*			
	0.0125	0.025	0.05	0.1	0.0125	0.025	0.05	0.1
SMZ	8	18	24	28	8	12	20	22
[Co-SMZ]	21	26	29	36	14	21	24	27
[Cu-SMZ]	14	20	28	35	12	14	22	26

Key: < 9: weak, 9 - 16: moderate and >16: significant

4. CONCLUSION

In the present study, complexes of Co and Cu with $C_{10}H_{11}N_3O_3S$ were successfully synthesized (1:2) in good yield and characterized with FTIR, melting points/decomposition temperature, solubility and electrical conductivity. The electronic spectral data of the complexes suggest an octahedral and tetrahedral geometry for all the complexes. The electrical conductivity indicate that the synthesized complexes are non-electrolytes. The synthesized metal complexes showed improved broad-spectrum antimicrobial activity against *E. coli* and *S. aureus* as compared to the ligand. Thus, the complexes $[Co(C_{10}H_{11}N_3O_3S)]$ and $[Cu(C_{10}H_{11}N_3O_3S)]$ are good leads to be developed into antibiotics against the tested antimicrobial agents (*E. coli* and *S. aureus*).

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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