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Synthesis, Physicochemical and Biological Studies of Cobalt(II) and Copper(II) Complexes of Benzoylacetic Acid Hydrazide

FAO Adekunle^{1*}, JAO Woods² and OA Odunola¹

¹Department of Pure and Applied Chemistry, Ladoké Akintola University of Technology, Ogbomosho, Nigeria.

²Department of Chemistry, University of Ibadan, Ibadan, Nigeria

ABSTRACT

A new series of binary mononuclear complexes were prepared from the hydrazide ligand, benzoylacetic acid hydrazide (BENZA), with the metal ions, Co(II) and Cu(II). The complexes have been characterized by elemental analyses, and by IR, electronic reflectance spectra, room temperature magnetic susceptibility measurement and the biological activity of these complexes and ligand were determined. The ligand was found to react with the cobalt(II) complexes in a 1:3 mole ratio while 1:2 mole ratio was observed for the copper(II) complexes. The results from the infrared spectra of the benzoylacetic acid hydrazide revealed that the $\nu(\text{C}=\text{O})$, the carbonyl stretching frequency known as "amide I", the coupling between the in-plane bending $\delta(\text{N}-\text{H})$ and $\nu(\text{C}-\text{N})$ called "amide (II)" and the stretching frequency of the amino group $\nu(\text{NH}_2)$ experienced bathochromic shifts in the spectra of the complexes. These suggest the coordination to the metal(II) ions through these groups. The electronic transitions observed for the cobalt(II) complexes are consistent with a six coordinate octahedral geometry while for the copper(II) complexes the single broad bands assignable to ${}^2\text{T}_2 \rightarrow {}^2\text{E}$ transitions suggest a tetrahedral geometry. The compounds show no appreciable activity against some selected gram +ve and gram -ve bacteria except for the cobalt complex, $\text{Co}(\text{BENZA})_3(\text{NO}_3)_2$ which shows a high growth inhibition against one of the test organisms.

Keywords: Mononuclear, hydrazide, transitions, metal ions

**Corresponding author*

INTRODUCTION

Hydrazine derivatives have been investigated due to their coordination and biological activities as well as their use in analytical chemistry as metal - extracting agents [1]. Acid hydrazides $R-CO-NH-NH_2$ a class of Schiff base and their corresponding aroylhydrazones $R-CO-NH-N=CH-R'$ have remarkable biological activity and the dependence of their mode of chelation with transition metal ions present in living system have been of significant interest[2]. The development of the field of inorganic chemistry has increased the interest in Schiff base complexes, since it has been observed that many of these complexes may serve as models for biological important species and find applications in biometric catalytic reactions [3]. Schiff base metal complexes have been widely studied because they have industrial, antifungal, antibacterial, anticancer and herbicidal applications [2-5]. Hydrazides and their condensation products have also displayed a diverse range of properties such as anti-convulsant, anti-helmintic, anti-leprotic, anti-malarial, anti- HIV, anti-depressant, analgesic-anti-inflammatory, leishmanicidal and vasodilator activities [6-18].

Hydrazides based on $-CONHNH_2$ and their derivatives contain trigonal N- and O-donors making them potential chelating ligands[1]. These compounds with their derivatives have supramolecular interactions because they include hydrogen-bonding donors (amino groups) and acceptors (carbonyl), and thus hydrogen –bonding plays an important role in extending and stabilizing the structures of the resultant complexes [1]. The interest in ligands from the hydrazide family and their transition metals in coordination chemistry have been due to the different bonding modes shown by these ligands with both electron rich and electron poor metals [5].

In this paper, we are reporting the synthesis, Characterization and biological activities of the cobalt(II) and copper(II) complexes of the benzoylactic acid hydrazide(BENZAHA)[19].

The aim of this work is to synthesize the new metal(II)complexes of this ligand and to study the their coordination behavior , spectral and biological activities against some selected microorganisms.

MATERIALS AND METHOD

Reagents

Reagent grade ethylbenzoylacetate , hydrazine hydrate, cobalt(II) acetate tetrahydrate, cobalt(II) chloride hexahydrate, cobalt(II) sulphate heptahydrate, cobalt(II) nitrate hexahydrate and copper(II)acetate monohydrate, copper(II)chloride dihydrate, copper(II) sulphate pentahydrate, and copper(II) nitrate pentahydrate were purchased from the British Drug House Chemicals Ltd (BDH) and Aldrich Chemicals Co., and were used without further purification.

Preparation of the ligand

The ligand, benzoylacetic acid hydrazide was prepared according to our earlier report on the compound [19].

Preparation of the compounds

Preparation of $\text{Co}(\text{BENZA}\text{H})_3\text{SO}_4$

$\text{CoSO}_4 \cdot 7\text{H}_2\text{O}$ (2.40 g, 8.4 mmole) dissolved in 45mL 40% methanol was stirred while 3.00 g (16.9 mmole) was added dropwisely. Precipitation was observed after pH was raised to 9. Stirring continued for additional 1hr after which the pink coloured precipitates formed were filtered, washed with 40% methanol and deionised water and was dried over calcium chloride in a dessicator. (Yield 4.6 g, 77%). $\text{Co}(\text{BENZA}\text{H})_3\text{Cl}_2$ was similarly prepared. The same procedure was used in the preparation of the other cobalt(II)complexes except that precipitation were observed immediately without raising the pH to 9.

Preparation of $\text{Cu}(\text{BENZA}\text{H})_2(\text{OAc})_2$

1.68 g (8.4mmole) $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ was dissolved in 50mL 40% methanol and stirred in a 250mL beaker while benzoylacetic acid hydrazide (3.0 g, 16.9 mmole) dissolved in 10mL methanol was added dropwisely. Green precipitates were observed immediately, and the mixture was stirred for 1hr before it was filtered by suction, washed with 40% methanol, deionised water and dried over calcium chloride (3.15 g, 70%). Similar procedure was employed in the preparation of all the copper(II)benzoic acid hydrazide complexes.

Physical measurements

Elemental analyses were performed using a Perkin-Elmer 240C elemental analyser. The percentage metal was determined by the employment of complexometric titration using EDTA [20]. The infrared spectra were recorded on a Nicolet Avater 330FT- IR spectrophotometer using KBr discs. Genesys 10 scanning spectrophotometer (Thermo Electron Corporation) was used to record the electronic reflectance spectra of the ligand and complexes. Magnetic susceptibilities of the complexes were measured by Faraday method on an instrument by Sherwood Scientific, Cambridge.

Biological assay

The microorganisms employed for the screening are *Escherichia coli*, *Pseudomonas aeruginosa*, *Micrococcus acidophilus*, *Bacillus cereus*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas putrifaciens(A₁)*, *Streptococcus bovis*, *Proteus sp.*, *Salmonella typhi*, *Pseudomonas putrifaciens(Q)*, *Serratia marcescens*.

The media was prepared by dissolving 28 g of the nutrient agar in 1000 mL deionised water. The solution was sterilized at 121°C for 15 mins in an autoclave.

Concentrations of 10 µg/mL, 100 µg/mL and 1000 µg/mL of each of the complexes were dissolved in dimethylsulphoxide (DMSO). The dimethylsulphoxide was used as the negative control while gentamycine solution in DMSO was used as the positive control.

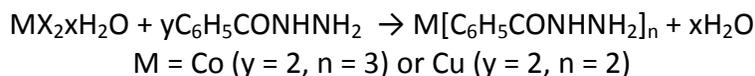
The twelve bacteria isolates were tested for sensitivity to some of the compounds by means of disc diffusion method [21 - 22].

RESULTS AND DISCUSSION

Preparation of the compounds

The benzoylactic acid hydrazide was prepared from the ethyl ester according literature procedure [19].

The cobalt(II) and copper(II) complexes prepared in good yield by reacting the respective metal(II) salts with the benzoylactic acid hydrazide ligand gave a composition of 1:3 mole ratio for the cobalt(II) complexes while 1:2 mole ratio was observed in the copper(II) complexes as shown below:



The complexes were characterized by elemental analysis, IR and UV-Vis spectra. The complexes are stable in air and light and are soluble in acetone, DMSO, ethanol and methanol, sparingly soluble in the inorganic solvent CHCl_3 and CH_3NO_3 and insoluble in water. The colour of the complexes ranges from pink to lilac for the cobalt complexes while grey, brown and green colours were observed in the copper complexes. The results of the analytical data are summarized in Table 1.

Infrared Spectra

The IR spectra of the ligand and complexes are presented in Table 2. In the coordination of ligands to metal in the spectra of hydrazides complexes, three major vibrations that have been used to infer coordination include the $\nu(\text{C}=\text{O})$, the carbonyl stretching mode called "amide I", the coupling between the in-plane bending $\delta(\text{N}-\text{H})$ and $\nu(\text{C}-\text{N})$ called "amide (II)" and the stretching frequency of the amino group $\nu(\text{NH}_2)$ [23]. An exhaustive comparison of the IR spectra of the ligand and complexes gave information about the mode of bonding of the ligand in the metal complexes. The characteristic IR bands of the Co(II) and Cu(II) complexes are between 1612 – 1600 cm^{-1} in the cobalt(II) for the $\nu(\text{C}=\text{O})$ carbonyl ("amide I") and νNH_2 ranges from 3100 - 3412 cm^{-1} while for the copper complexes the $\nu(\text{C}=\text{O})$ carbonyl are observed from 1606 - 1622 cm^{-1} and νNH_2 between 3120 - 3363 cm^{-1} . The spectrum of the ligand have been observed for the $\nu(\text{C}=\text{O})$ and νNH_2 at 1626 cm^{-1} and 3452 cm^{-1} respectively. The shift to

lower frequency in the amino group bands in all the complexes suggest that this group takes part in coordination. The coordination of the nitrogen to the metal atom would be expected to reduce the electron density of the amino group link and thus cause a shift in the N-H band [3, 5,19,21,22]. Moreover, in the spectra of the complexes a considerable negative shift in $\nu(\text{C}=\text{O})$, "amide 1" are observed indicating a decrease in the stretching force constant of C-O as a consequence of coordination through the carbonyl - oxygen atom of the free ligand [5,19,21,22]. The small shift to lower frequency in "amide 11" band can be taken as additional evidence of the participation of the $\nu(\text{C}=\text{O})$ group in the bonding [5]. The ligand from the information obtained from the IR data acts as a neutral bidentate Lewis base through the $\nu(\text{C}=\text{O})$ carbonyl and the amino groups [2-5, 19, 21,22].

Table 1 The analytical data for the compounds

Compound (Empirical formula)	FW	Colour	% yield	μ_{eff} B.M	Mpt($^{\circ}\text{C}$)	% Observed (Calculated)			
						Metal	C	H	N
BENZA $\text{C}_9\text{H}_{10}\text{N}_2\text{O}_2$	178.19	White	70		156 – 158	-	60.44 (60.66)	5.62 (5.66)	15.66 (15.72)
$\text{Co}(\text{BENZA})_3(\text{OAc})_2$ $\text{C}_{31}\text{H}_{36}\text{N}_6\text{O}_{10}\text{Co}$	711.60	Pink	64	2.04	160	8.08 (8.28)	52.12 (52.32)	5.24 (5.10)	11.80 (11.81)
$\text{Co}(\text{BENZA})_3\text{Cl}_2$ $\text{C}_{27}\text{H}_{30}\text{N}_6\text{O}_6\text{Cl}_2\text{Co}$	664.51	Lilac	76	3.16	150	8.59 (8.87)	49.02 (48.80)	4.62 (4.55)	12.44 (12.65)
$\text{Co}(\text{BENZA})_3\text{SO}_4$ $\text{C}_{27}\text{H}_{30}\text{N}_6\text{O}_{10}\text{SCo}$	689.58	Pink	77	4.07	160	8.13 (8.55)	47.06 (47.03)	4.52 (4.39)	12.20 (12.19)
$\text{Co}(\text{BENZA})_3(\text{NO}_3)_2$ $\text{C}_{27}\text{H}_{30}\text{N}_8\text{O}_{12}\text{Co}$	717.52	Lilac	67	3.37	160	8.23 (8.21)	45.41 (45.20)	4.62 (4.21)	15.77 (15.62)
$\text{Cu}(\text{BENZA})_2(\text{OAc})_2$ $\text{C}_{22}\text{H}_{26}\text{N}_4\text{O}_8\text{Cu}$	538.02	Green	70	0.89	130	11.61 (11.81)	49.48 (49.11)	5.11 (4.87)	10.12 (10.41)
$\text{Cu}(\text{BENZA})_2\text{Cl}_2$ $\text{C}_{18}\text{H}_{20}\text{N}_4\text{O}_4\text{Cl}_2\text{Cu}$	490.93	Brown	54	0.94	102	12.62 (12.94)	44.01 (44.04)	3.86 (4.11)	11.22 (11.41)
$\text{Cu}(\text{BENZA})_2\text{SO}_4$ $\text{C}_{18}\text{H}_{20}\text{N}_4\text{O}_8\text{SCu}$	516.00	Dirty-green	60	-	154 – 156	(12.20) (12.31)	41.82 (41.90)	4.13 (3.91)	10.66 (10.86)
$\text{Cu}(\text{BENZA})_2(\text{NO}_3)_2$ $\text{C}_{18}\text{H}_{20}\text{N}_6\text{O}_{10}\text{Cu}$	543.94	Grey	50	-	120	11.55 (11.68)	40.06 (39.75)	3.66 (3.71)	15.22 (15.45)

Electronic Spectra

The solid reflectance spectra of the ligand and complexes studied are presented in Table 2. The assignment of bands done by comparing the observed values with previous work done [19,23,24]. The absorption spectra of BENZA in the uv region revealed bands at 49.75×10^3 and $38.61 \times 10^3 \text{cm}^{-1}$ assigned to $\pi \rightarrow \pi^*$ and $\pi \rightarrow n$ transitions respectively of the carbonyl group within the ligand. A shift was observed in these bands in the spectra of the complexes. The $n \rightarrow \pi^*$ transitions in the complexes was only in the $\text{Cu}(\text{BENZA})_2(\text{NO}_3)_2$ complex observed at $30.68 \times 10^3 \text{cm}^{-1}$.

In the visible region, the experimentally observed transitions for cobalt(II) have been reported as ${}^4T_{1g} \rightarrow {}^4T_{2g}$, ${}^4T_{1g} \rightarrow {}^4A_{2g}$, and ${}^4T_{1g} \rightarrow {}^4T_{1g}(P)$, denoted as ν_1 , ν_2 and ν_3 transitions respectively[23]. $\text{Co}(\text{BENZAHA})_3\text{Cl}_2$ displayed all the three transitions at $9.22 \times 10^3 \text{cm}^{-1}$, $16.23 \times 10^3 \text{cm}^{-1}$ and $20.41 \times 10^3 \text{cm}^{-1}$ assigned to the transitions ${}^4T_{1g} \rightarrow {}^4T_{2g}$, ${}^4T_{1g} \rightarrow {}^4A_{2g}$, and ${}^4T_{1g} \rightarrow {}^4T_{1g}(P)$ respectively. The other complexes exhibited only the ${}^4T_{1g} \rightarrow {}^4T_{1g}(P)$ transition each at $20.28 \times 10^3 \text{cm}^{-1}$, $20.49 \times 10^3 \text{cm}^{-1}$ and $18.80 \times 10^3 \text{cm}^{-1}$ respectively for $\text{Co}(\text{BENZAHA})_3(\text{OAc})_2$, $\text{Co}(\text{BENZAHA})_3\text{SO}_4$ and $\text{Co}(\text{BENZAHA})_3(\text{NO}_3)_2$. These transitions are suggestive of a high spin octahedral geometry.

The copper(II) complexes showed one broad band at $15.34 \times 10^3 \text{cm}^{-1}$, $15.46 \times 10^3 \text{cm}^{-1}$, $16.29 \times 10^3 \text{cm}^{-1}$ and $16.16 \times 10^3 \text{cm}^{-1}$ respectively for $\text{Cu}(\text{BENZAHA})_2(\text{OAc})_2$, $\text{Cu}(\text{BENZAHA})_2\text{Cl}_2$, $\text{Cu}(\text{BENZAHA})_2\text{SO}_4$ and $\text{Cu}(\text{BENZAHA})_2(\text{NO}_3)_2$. These bands are assigned to ${}^2T_2 \rightarrow {}^2E$ transition. The observed spectra conform with tetrahedral geometry as there were no splitting of bands as a result of Jahn- Teller distortion found in octahedral geometry arising from the unequal occupation of the e_g pair of orbitals.

Table 2 Key infrared frequencies and electronic spectra transitions (cm^{-1})

COMPOUND	AMIDE(I)	AMIDE(II)	νNH_2	$\nu(\text{C}-\text{H})$	Electronic bands($\times 10^3$)
BENZAHA	1626(m)	1600(s)	3452(w)	3120(m)	49.75, 38.61
$\text{Co}(\text{BENZAHA})_3(\text{OAc})_2$	1600(m)	1553(m)	3120(s)	3022(w)	36.90, 20.28
$\text{Co}(\text{BENZAHA})_3\text{Cl}_2$	1612(m)	1592(m)	3399(s)	3029(w)	36.90, 20.41, 16.23, 9.22
$\text{Co}(\text{BENZAHA})_3\text{SO}_4$	1600(m)	1592(m)	3412(s)	3023(m)	37.31, 20.49
$\text{Co}(\text{BENZAHA})_3(\text{NO}_3)_2$	1600(w)	1558(w)	3100(w)	-	45.46, 36.90, 18.80
$\text{Cu}(\text{BENZAHA})_2(\text{OAc})_2$	1618(m)	1579(m)	3363(m)	3016(m)	44.84, 37.31, 15.34
$\text{Cu}(\text{BENZAHA})_2\text{Cl}_2$	1618(m)	1594(s)	3247(m)	3010(m)	46.08, 37.31, 15.46
$\text{Cu}(\text{BENZAHA})_2\text{SO}_4$	1622(m)	1566(w)	3120(m)	3047(m)	37.31, 16.29
$\text{Cu}(\text{BENZAHA})_2(\text{NO}_3)_2$	1606(s)	1566(m)	3333(m)	3065(w)	30.68, 16.16

Antibacterial activities

The result of the antibacterial activity of ligand and complexes studied against *Escherichia coli*, *Pseudomonas aeruginosa*, *Micrococcus acidophilus*, *Bacillus cereus*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas putrifaciens(A₁)*, *Streptococcus bovis*, *Proteus sp.*, *Salmonella typhi*, *Pseudomonas putrifaciens(Q)*, *Serratia marcescens* showed no zone of inhibition for most of the complexes and the ligand. The cobalt complex, $\text{Co}(\text{BENZAHA})_3(\text{NO}_3)_2$ only showed high growth inhibition[25] of 19 mm at 1000 $\mu\text{g}/\text{mL}$ against *Pseudomonas putrifaciens(A₁)*.

CONCLUSION

This study reports the successful synthesis of the title compounds in good yield and from the elemental analysis, UV-Visible and IR spectra data it was possible to determine the type of coordination of the ligand to the metal complexes. In the complexes, it is concluded that the ligand acts as a neutral bidentate through the nitrogen atom of the amino and the

oxygen atom of the carbonyl groups. The greater stability of the tris-complexes of the cobalt(II) is demonstrated by the fact that this ligand yield only the tris complexes regardless of the metal – ligand ratio used in the preparation. All the compounds except one do not have microbicidal activity.

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