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Synthesis, characterization and antimicrobial activities of some metal(ii) complexes of mixed ligands- dimethyl dithiocarbamic and para aminobenzoic acids

Aderoju A. Osowole[1,]*, Sherifat M. Wakil[2] and Esther Q. Okediran[1]

[1]Inorganic Chemistry unit, Department of Chemistry, University of Ibadan, Ibadan, Nigeria.

[2]Department of Microbiology, University of Ibadan, Ibadan, Nigeria.

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ABSTRACT

Some metal(II) complexes of mixed ligands-dimethydithiocarbamic and *p*-aminobenzoic acids were synthesized (M = Mn, Fe, Co, Ni, Cu and Zn) and characterized by solubility, percentage metal, conductivity, infrared and electronic spectra measurements. Infrared data showed that the dimethydithiocarbamic and *p*-aminobenzoic acids coordinated through the sulphur atoms, and the carboxylate oxygen atoms to the metal atoms respectively. Electronic spectra and room temperature magnetic moments corroborated equilibrium between high spin and low spin octahedral geometry (spin-crossover) for the Mn(II), Fe(II), Ni(II) and Co(II) complexes, while the Cu(II) and Zn(II) complexes were octahedral and mononuclear. The antimicrobial activities of the metal complexes against *Escherichia spp*, *Streptococcus spp*, *Proteus sp*, *Candida sp*, *Salmonella sp*, *Bacillus spp*, *Staphylococcus sp* and *Pseudomonas spp* showed that the Mn(II), Fe(II) and Zn(II) complexes had very good antimicrobial activities against these microbes with inhibitory zones range of 7.0-20.0, 7.0-20.0 and 9.0-27.0 mm respectively, just like Streptomycin (7.0-29.0 mm) proving their potentials as broad-spectrum antimicrobial agents *in-vitro*.

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Introduction

Organic dithiocarbamate have attracted a great deal of importance due to their interesting chemistry and wide uses such as antibacterial, antifungal, antioxidant and anticancer (Greene *et al.*, 1999; Villa *et al.*, 1996). Industrially, dithiocarbamate are used as catalyst in the sulfur vulcanization of rubber (Mayadunne *et al.*, 1999; Nieuwenhuizen *et al.*, 2001) detection and analysis of biological nitric oxide produced endogenously from nitric oxide synthases (Fujii *et al*, 2000).

P-aminobenzoic acid (Vitamin B_x) is an intermediate in the bacterial synthesis of folate. Humans lack the enzymes to convert Vitamin B_x to folate, and therefore require folate from dietary sources such as green leafy vegetables. It is best known as a sunscreen because it can block ultraviolet radiation to the skin being UV absorber (Ludwig, 1991; Zarafonetis *et al.*, 1988).

Thus, our aims are to synthesize and characterize novel metal(II) mixed ligands complexes of dimethyldithiocarbamic and *p*-aminobenzoic acids. Furthermore, the ligands will be investigated for their suitability in forming complexes with spin-crossover, while the metal(II) complexes potentials as broad-spectrum antimicrobial agents *in-vitro* will be verified. This is a continuation of the research activities of our group on metal-based chemotherapeutic agents (Ekennia *et al.*, 2014; Osowole *et al.*, 2014a; 2014b)

Experimental

Materials and reagents

Reagent grade dimethyldithiocarbamic acid sodium salt, p-aminobenzoic acid, Copper(II) chloride tetrahydrate, Nickel(II) chloride hexahydrate, Cobalt(II) chloride hexahydrate, Manganese(II) chloride tetrahydrate, Zinc(II) sulphate heptahydrate, and Iron(II) sulphate heptahydrate were obtained from Aldrich and BDH chemicals, and were used as received, and solvents were purified by distillation.

Preparation of $[M(L)(HL^1)X(H_2O)]$

To a stirring 20 mL of (70%) ethanolic solution of 0.8 g (4.46×10^{-3}moles) of dimethydithiocarbamic acid sodium salt, 0.61 g (4.46×10^{-3}) of p-aminobenzoic acid was added neatly in bits to give a clear solution, to which 0.88 g-1.23 g (4.463×10^{-3}moles) of the hydrated metal(II) chlorides (M =Mn, Co, Cu and Ni) and sulphates (M = Fe and Zn) were added in bits while stirring. The resulting colored homogeneous solutions were refluxed for 3 h and the coloured precipitates formed were filtered, washed with ethanol and dried over silica gel .

Physical measurements

The solid reflectance spectra of the complexes were recorded on a PC scanning spectrophotometer UVD-2960 machine in the range 190-900 nm and infrared spectra were recorded as KBr disc on a Perkin-Elmer FT-IR spectrum BX spectrometer in the range 4000-400 cm^{-1}. The room temperature magnetic susceptibilities at 298K were measured on Sherwood Susceptibility Balance MSB Mark 1, while melting points were determined with Mel-Temp electrothermal machine, and molar conductivity measurements of 1×10^{-3} M solutions in DMSO respectively were obtained using with electrochemical analyzer consort C933.

Antibacterial assay

Antimicrobial susceptibility tests were carried out using agar diffusion technique. The surface of Muller Hinton's agar in a Petri dish was inoculated uniformly with 0.3 mL of 18 h old test bacteria cultures. 10 mg/mL solution of each complex in DMSO was added to a 9 mm well bore hole into the agar. The

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Tele:

E-mail addresses: aderoju30@gmail.com

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plates were allowed to stand on the bench for 30 minutes after inoculation before incubating at 37°C for 24 h. Inhibitory zones diameter were taken as a measure of antibacterial activities of the complexes. The experiments were conducted in duplicates and Streptomycin was used as a reference drugs.

Results And Discussion

The reaction of the dimethydithiocarbamic acid sodium salt (NaL), p-aminobenzoic acid (HL^1) with the metal(II) chlorides (Mn, Ni, Cu and Co), $FeSO_4.7H_2O$ and $ZnSO_4.7H_2O$ gave coloured complexes in moderate to good yields according to generalized equations below:

$MCl_2.aH_2O + HL^1 + NaL \rightarrow [M(L)(HL^1)(Cl)(H_2O)] + NaCl + bH_2O$……………………………………………..(1)

(when M = Mn; a = 4, b = 3; M = Co, Ni; a = 6, b =5;M = Cu; a = 4, b =2)

$MSO_4.aH_2O+HL^1+NaL\rightarrow[M(L)(HL^1)(_{1/2}SO_4)] +Na(_{1/2}SO_4)+bH_2O$……………………………….(2)

(when M = Fe, a = 7, x = 0, b =7; M = Zn, a = 7, x = 1, b = 7)

The formation of the metal complexes was confirmed by % metal, distinct decomposition temperatures, IR and electronic spectroscopies. The ligands, dimethydithiocarbamic acid sodium salt (NaL) and p-aminobenzoic acid (HL^1) melted at 120°C and 187°C respectively, whereas their metal complexes decomposed in the range 232-271°C, confirming coordination. The analytical data, colors, % metal, melting points, molar conductivity and room temperature magnetic moments (μ_{eff}) for the complexes are presented in Table 1.

Molar Conductivity

The molar conductance values of the complexes in DMSO were within $9.70\text{-}22.20\Omega^{-1}cm^2mol^{-1}$ proving their non-electrolytic nature (Singh *et al*., 2002).

Electronic Spectra and Magnetic Moment

The Mn(II) complexes showed two absorption bands at 14.99 kK and 16.45 kK assigned to $^6A_{1g} \rightarrow {}^4E_{1g}$ and $^2T_{2g} \rightarrow {}^2A_{1g}$ transitions, typical of a high spin and low spin octahedral geometry. The effective magnetic moment of high spin Mn(II) complexes are expected to be close to the spin-only value of 5.90 B.M. since the ground term is $^6A_{1g}$ and thus, there is no orbital contribution, whereas low spin octahedral Mn(II) have moments of about 2.0 B.M. Consequently, an observed moment of 2.80 B.M was indicative of spin equilibrium *(spin-cross over)* between the high spin and low spin octahedral geometry (Conplate and Kaya, 2004).

Similarly, the Fe(II) complex had two absorption bands at 16.10 kK and 18.80 kK, which were assigned to $^5T_{2g} \rightarrow {}^5E_g$ and $^1A_{1g} \rightarrow {}^1T_{2g}$ transitions of 6-coordinate, high spin and low spin octahedral geometry. A moment of 5.0-5.5 B.M is usually expected for high spin octahedral Fe(II) complexes while low spin, octahedral complexes are expected to be diamagnetic. In this study, a moment of 4.22 B.M was observed, which was indicative of spin equilibrium *(spin-crossover)* between the high spin and low spin octahedral geometry (Salmon *et al*., 2009).

The Co(II) complex, had three absorption bands at 14.95 kK, 17.86kK and 21.05kK consistent with high and low spin octahedral geometry. The first two bands were assigned to $^4T_{1g}(t_{2g}^5e_g^{\ 2}) \rightarrow {}^4T_{2g}(t_{2g}^4e_g^3)$ and $^2E_g(t_{2g}^6e^1_g) \rightarrow {}^2T_{1g}(t_{2g}^5\ eg^{\ 2})$ transitions while the third band was assigned to M→L CT respectively. Moments in the range 4.7- 5.2 B. M and 2.0-2.2 B.M. are expected for high spin and low spin octahedral complexes respectively. However, a magnetic moment of 2.50 B.M was observed for this complex, collaborative of spin equilibrium *(spin-crossover)* between the high spin and low spin octahedral geometry(Manhas *et al*., 1995).

Similarly the Ni(II) complex showed two absorption bands at 13.26 kK and 16.92 kK typical of six coordinate high spin and low spin octahedral geometry, and were assigned to $^3A_{2g} \rightarrow {}^3T_{1g}$, and $^1B_{1g} \rightarrow {}^1A_{1g}$ transitions. Room temperature magnetic moments in the range 2.8-3.3 B.M were reported for high spin octahedral Ni(II) while low spin octahedral Ni(II) complexes were diamagnetic. Thus, an observed moment of 2.11 B.M corroborated spin equilibrium *(spin-crossover)* between the high spin and low spin octahedral geometry(Ma *et al*., 2011).

The Cu(II) complex exhibited two absorption bands at 14.90 kK and 16.31 kK typical of a 6-coordinate, trigonal (octahedral) geometry, and were assigned to $^2B_{1g} \rightarrow {}^2B_{2g}$ and $^2B_{1g} \rightarrow {}^2E_g$ transitions. A moment in the range 1.9–2.2 B.M. is usually observed for mononuclear copper(II) complexes, regardless of stereochemistry, expectedly higher than the spin only moment due to orbital contribution and spin-orbit coupling. This Cu(II) complex had a moment of 2.16 B.M, complimentary of octahedral geometry (Soenmez and Haciyusufoglu, 2006) . The Zn(II) complex was expectedly diamagnetic with M→L CT transition at 20.39 kK (Rao and Reddy, 1990). Thus, the ligands, p-aminobenzoic benzoic acid and sodium dimethydithio carbamic acid, were suitable in forming complexes with spin-crossover.

Infrared spectra

The IR spectra data of ligands and their complexes are presented in Table 2. The infrared spectra of *p*-aminobenzoic acid showed absorption bands due to $v$asy(NH_2) and $v$sy (NH_2) at 3461 cm^{-1} and 3382 cm^{-1} respectively. These bands are not significantly shifted with respect to those of the complexes, though it overlapped with vOH bands in the metal complexes. The little shift was due to hydrogen bonding as previously reported (Demartzi-Kovala and Tsangaris, 1986) not as a result of coordination. The vOH band in *p*-aminobenzoic acid was observed at 3364 cm^{-1}, and it shifted to 3468-3437 cm^{-1} in the complexes due to coordination of the hydroxy oxygen atom without deprotonation. The v(C=O) band was observed at 1666-1573 cm^{-1} in p-aminobenzoic acid. However, it shifted to 1630-1525 cm^{-1} in the metal(II) complexes due to coordination of the carbonyl oxygen atom to the metal atom. The v(C=S) at 1240-1117 cm^{-1} in dimethydithiocarbamic acid sodium salt shifted to 1052-970 cm^{-1} in the metal(II) complexes due to coordination of both S-donor atoms to the metal atom (Onwudiwe and Ajibade, 2011). Furthermore, bands due to M-O, M-S and M-Cl were absent in the ligands, dimethyldithio carbamic acid sodium salt and p-aminobenzoic acid. However, these bands were observed at 586-508 cm^{-1}, 465-365 cm^{-1} and 387-352 cm^{-1}respectively in the metal complexes confirming coordination (Obaleye *et al*, 2008).

Antibacterial Activities

The inhibitory zones of the activities of various compounds against the microbes used are presented in Table 3. *p*-aminobenzoic acid (HL^1) was moderately active against all the tested microbes with inhibitory zones range of 7.0-13.0 mm. However, dimethydithiocarbamic acid sodium salt (NaL) exhibited very good activities against all the tested microbes with the exception of Pseudomonas *sp* (clinical) with inhibitory zones range of 7.0-20.0 mm. The Mn(II), Fe(II) and Zn(II) complexes had very good antimicrobial activities against all the microbes used with inhibitory zones range of 7.0-20.0, 7.0-20.0 and 9.0-27.0 mm respectively, just like Streptomycin with inhibitory zones range of 7.0-29.0 mm, proving their potentials as broad-spectrum antimicrobial agents.

Table 1: Analytical data for the ligands and their metal(II) complexes

Complex	**Molar mass**	**Colour**	**% Yield**	**%Metal Exp (Theo)**	**M.p (^{o}C)**	**^m**	**μ_{eff} (B.M)**
NaL	144.22	White	-	-	120	-	D
HL^1	137.14	Off-white	-	-	187	-	D
[Mn(L)(HL^1) Cl(H$_2$O)]	367.82	Lt pink	30.0	15.19 (14.94)	271*	19.37	2.80
[Fe(L)(HL^1)($_{1/2}$SO$_4$)]	362.21	Brown	85.0	15.44 (15.42)	232*	10.51	4.22
[Co(L)(HL^1)Cl(H$_2$O)]	370.81	Green	30.0	16.31 (15.89)	250*	10.12	2.50
[Ni(L)(HL^1)Cl(H$_2$O)]	370.59	Lt Green	40.0	15.91 (15.84)	240*	9.98	2.13
[Cu(L)(HL^1)Cl($_{1/2}$H$_2$O)]	366.42	Green	70.0	17.57 (17.34)	241*	22.00	1.90
[Zn(L)(HL^1)($_{1/2}$SO$_4$)]	371.73	White	80.0	18.08 (17.59)	241*	9.70	D

NaL= dimethydithiocarbamic acid sodium salt; HL^1= *p*-aminobenzoic acid; Exp = experimental; Th = Theoretical; D = Diamagnetic; Lt = light; M.p = melting point;* = decomposing temperature; ^m = molar conductance(Ω^{-1}cm^{2}mol^{-1});

Table 2: Infra-red and electronic spectra data of the metal(II) complexes

Complex	*v*(OH)	*v*(NH$_2$)	*v*(C=O)	*v*(C=S)	*v*(M-O)	*v*(M-S)	*v*(M-Cl)	*Electronic spectra (kK)*
NaL	-	-	-	1240s 1117s	-	-	-	27.32, 29.24
HL^1	3364m	3461s 3382m	1666s 1573s	-	-	-	-	32.15
[Mn(L)(HL^1)Cl(H$_2$O)]	3448b	3448b 3344m	1606s 1532s	1040m 970s	563s 508s	423m 400s	370s 353s	14.99, 16.45, 29.67
[Fe(L)(HL^1)($_{1/2}$SO$_4$)]	3437b	3437b 3390b	1630s 1601sh	979m	572s	465s	385s 354s	16.10, 18.80, 28.45, 31.15
[Co(L)(HL^1)Cl(H$_2$O)]	3437b	3437b 3392b	1605m 1526s	1052m 985s	581s	442s	386s 354s	14.95, 17.86, 21.05, 29.76
[(Ni(L)(HL^1)Cl(H$_2$O)]	3449b	3449b 3366m	1605s 1547s	1015m 973s	586s 515s	443m 414s	387s 354s	13.26, 16.92, 29.41
[Cu(L)(HL^1)Cl(H$_2$O)]	3444b	3444b 3350m	1625s 1609s	972s	550s	446m 400m	386s 352m	14.90, 16.31, 29.67
[Zn(L)(HL^1)($_{1/2}$SO$_4$)(H$_2$O)]	3468b	3468b 3350m	1610s 1525s	991w 973s	565s 516s	446m	380s 354s	29.76, 30.96

b = broad; m = medium; s = strong; w = weak; NaL= dimethyldithiocarbamic acid sodium salt; HL^1 = p-aminobenzoic acid ;1kK=1000 cm^{-1}

Table 3: Antibacterial activities of the ligands and their metal(II) complexes

Microorganism /Complexes		[(Mn(L)(HL^1)Cl(H$_2$O)]	[Fe(L)(HL^1)($_{1/2}$SO$_4$)]	[Co(L)(HL^1)Cl(H$_2$O)]	[(Ni(L)(HL^1)Cl(H$_2$O)]	[Cu(L)(HL^1)Cl (H$_2$O)]	[Zn(L)(HL^1)($_{1/2}$SO$_4$)]	NaL	HL^1	Streptomycin
E. coli ^{Ec}		20±0	18±0	7±0	R	11±0	20±0	9±0	9±0	7±0
S. pyogenes		20±0	20±0	R	R	R	10±0	11±0	10±0	8±0
Proteus sp		17±0	15±0	R	9±0	11±0	17±0	13±0	10±0	25±0
Candida sp		15±0	15±0	8±0	9±0	19±0	11±0	11±0	13±0	7±0
Salmonella sp		19±0	15±0	R	10±0	11±0	17±0	11±0	11±0	5±0
Streptococcus sp		11±0	9±0	R	10±0	9±0	15±0	10±0	7±0	11±0
Bacillus sp ^{F}		15±0	11±0	7±0	7±0	7±0	15±0	12±0	9±0	6±0
Staphylococcus sp		30±0	31±0	R	13±0	20±0	27±0	20±0	13±0	29±0
Pseudomonas sp ^{C}		13±0	11±0	R	15±0	11±0	9±0	R	9±0	11±0
Pseudomonas sp ^{E}		7±0	9±0	R	9±0	6±0	13±0	7±0	7±0	19±0
Bacillus sp		15±0	15±0	7±0	9±0	11±0	16±0	11±0	11±0	29±0
E. c oli		19±0	7±0	7±0	9±0	9±0	18±0	9±0	9±0	20±0

R = Resistance; NaL = NaL= dimethyldithiocarbamic acid sodium salt; HL^1 = p-aminobenzoic acid; F= Food; Ec = Ec27(*E. coli)*; C= Clinical; E = Environment.

The Cu(II) complex was active against all the microbes used with the exception of *S. pyogenes* with inhibitory zones range of 6.0-20.0 mm, while the Ni(II) complex had no activity against *E.coli (Ec27)* and *S. pyogenes* but was active against the remaining microbes with inhibitory zones range of 7.0-15.0 mm. The Co(II) complex had the least activity being active against *Escherichia spp, Candida albicans* and *Bacillus spp* with inhibitory zones range of 7.0-8.0 mm respectively, due to its probable lipophobic nature (Rao and Reddy, 1990). Expectedly, the metal complexes were generally more active than the ligands 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 (Singh *et al*., 2002).

Conclusion

Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) complexes of the mixed ligands, dimethyl dithiocarbamic and *p*-aminobenzoic acids, were found to be covalent in DMSO. Electronic spectra and room temperature magnetic moment data corroborated octahedral geometry for all the metal complexes. Furthermore, the in-*vitro* antimicrobial studies of the complexes against some microbes were generally good with the exception of the Co(II) complex.

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