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Synthesis, physicochemical and *in-vitro* antibacterial properties of some novel metal (II) complexes of 3-{[(6-methoxypyridin-3-yl)imino]methyl}-5-nitrophenol

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ABSTRACT

The Schiff base, 3-{[(6-methoxypyridin-3-yl)imino]methyl}-5-nitrophenol, formed by condensation of 5-amino-2-methoxypyridine and 2-hydroxy-5-nitrophenol; and its metal(II) complexes{where M = Mn, Co, Ni, Cu, Zn, Pd} have been synthesized and characterized by %metal, melting points, IR and electronic spectroscopies. The complexes analyse as [ML(NO3)] with the exception of the Ni(II), Cu(II) and Pd(II) complexes which analyse as [MLCl(H2O)] respectively. The IR data confirm that the Schiff base coordinates via the imine nitrogen and phenol oxygen atoms; while the electronic data support a 4-coordinate tetrahedral/squareplanar geometry for the metal complexes. The metal complexes are air-stable solids, which melt/decompose on heating in the temperature range 228-390 ^{o}C; while the metal–free Schiff base melts at 208-210 oC. The in-vitro antibacterial studies reveal that the Schiff base, its Co(II) and Zn(II) complexes have a broad-spectrum antibacterial activity against Bacillus cereus, Pseudomona aeuriginosa, Staphylococcus aureus and Proteus mirabilis with inhibitory zones range of 14.0-22.0mm.

Introduction

Schiff bases have received great attention from scientists worldwide, including our research group due to their uses as models for studying complex bioinorganic molecules, precursors in metal-organic chemical vapor depositions (MOCVD), catalysts in various organic reactions and anti-corrosion agents [1-6]. Furthermore, (chloropyridinyl)thiazolidine Schiff bases have potent antifungal activities against *Candida albicans,* which are comparable with the renowned drug greseofulvin [7], while various (methoxyphenyl)-3-chloroazetidin-2-one have good antihelmintic activity against the earthworm *Perituma posthuma* [8]. Moreover, the Schiff base (N,N-dimethyl-N'(2-pyridyl)ethylenediame picrate is a histamine antagonist [9], while (pyridinyl)methylthio-4H-triazole Schiff base induced apoptosis in human heptocarcinoma cell SMMC-7721 [10]. Detailed literature search shows that the Schiff base, 3-{[(6-methoxypyridin-3-yl)imino]methyl}-5- nitrophenol derived from the condensation of 2-hydroxy-5-nitrobenzaldehyde and 5-amino-2-methoxypyridine; and its metal chelates have not yet been reported [1-15]. Thus, the aim of this work is to synthesize, characterize and investigate the electronic and antibacterial properties of the Mn(II), Co(II), Ni(II), Cu(II), Zn(II) and Pd(II) complexes of the Schiff base, 3-{[(6-methoxypyridin-3-yl)imino]methyl}-5- nitrophenol for a better understanding of their geometries and potentials as broad-spectrum antibacterial agents. These metal complexes and its ligand are new, being reported here for the first time, and is a continuation of similar studies in our research group on some metal(II) complexes of the Schiff base 3-{[(6-methoxypyridin-3-yl)imino]methyl}naphthalen-2-ol [16].

Experimental details

Materials and Physical Measurements

Reagent grade 2-hydroxy-5-nitrobenzaldehyde, 5-amino-2-methoxypyridine, manganese(II) nitrate hexahydrate, cobalt(II) nitrate hexahydrate, nickel(II) chloride hexahydrate, copper(II) nitrate trihydrate, zinc(II) nitrate hexahydrate and palladium(II) chloride were purchased from BDH and Aldrich chemicals and were used as received. Solvents were distilled and dried before use according to standard procedures.

Melting points (uncorrected) were determined using the Stuart scientific melting point SMP1 machine, while electronic spectra (chloroform) and infrared spectra (KBr discs) were recorded on a Perkin-Elmer λ20 and a Perkin-Elmer FTIR paragon 1000 spectrophotometer respectively. The percentage manganese, cobalt, nickel, copper, zinc and palladium were determined titrimetrically [17].

Preparation of 3-{[(6-methoxypyridin-3-yl)imino]methyl]5-nitrophenol}

A 20 mL solution of 1.2 x 10^{-2} mol (1.44 g) 5-amino-2-methoxypyridine in absolute ethanol was added drop wise to a stirring solution of 1.2 x 10^{-2} mol (2.0 g) of 2-hydroxy-5-nitrobenzaldehyde in 40 mL of absolute ethanol. The resulting yellow-colored solution was refluxed for 4 h after the addition of 4 drops of acetic acid. The yellow product formed on cooling to room temperature was filtered, and then recrystallized from ethanol. The yield of the title compound was 2.34 g (70%).

Preparation of the metal(II) complexes

The various complexes were prepared by gradual addition of 0.54 mmol $M(NO_3)_2.6H_2O$ {M = Mn, Co, Zn}/$ML_2.2H_2O$ {M = Ni, Cu, Pd}neat to a stirring 1.08 mmol (0.3 g) of the ligand in 30 mL of absolute ethanol. The resulting solutions were then buffered with 1.08 mmol (0.11 g) of triethylamine and refluxed

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for 6 h during which the products formed. The precipitated solids were filtered, washed with ethanol and dried over anhydrous calcium chloride.

Results and Discussion

The generalised equation for the formation of the complex is:

$M(NO_3)_2.6H_2O + HL \rightarrow [MLNO_3] + HNO_3 + 6H_2O$ ----------(1)
{where M = Mn(II),Co(II), Zn(II)}.

$MCl_2 . 2H_2O + HL \rightarrow [MLCl\ H_2O\ ] + HCl + H_2O$ ----------(2)
{where M = Ni(II), Cu(II), Pd(II)}.

The metal(II) nitrates/ chlorides complex with the ligand in the ratio 1M:1L, to form complexes of the type $[MLNO_3]$ and $[MLClH_2O]$ respectively. The formation of this ligand is confirmed by IR spectroscopy and its distinct melting point is in the range 208-210^{o}C. However, the metal complexes melt/decompose on heating in the temperature range 228-390 ^{o}C, confirming coordination. Furthermore the complexes all exhibit good solubility in methanol, ethanol, dimethyl sulphoxide and methylene chloride with the exception of the Zn(II) complex probably due to its polymeric nature.

Infrared spectra

The relevant infrared bands of the compounds are presented in Table 2. The broad band in the ligand at 3433 cm^{-1}, which disappears in the spectra of all the complexes is assigned as υ(OH), which indicates the involvement of the phenolic O in bonding to the metal ions. Similarly, the broad band at 3500cm^{-1} in the hydrated complexes is assigned as *ν*(OH) of coordinated water. The two sharp bands at 2912–2994 cm^{-1} in the ligand is indicative of a υ(C-H) stretching vibration [13]. This band is hypsochromic shifted to 2913–2999 cm^{-1} in the spectra of the complexes due to chelation. Furthermore, the uncoordinated C=N and C=C stretching vibrations occurred as coupled bands in the ligand around 1423.29 – 1657.94 cm^{-1}. Moreover, they are bathochromic and hypsochromic shifted to 1422.66 – 1656.94 cm^{-1} and 1423.50 – 1658.25 cm^{-1}, respectively in the metal complexes, confirming the involvement of the imine N atom in coordination to metal(II) ion. The δ(C-H) of the ligand at 1040 cm^{-1} is bathochromic shifted to 951 – 952 cm^{-1} in the metal(II) complexes, due to pseudo-aromatic nature of the chelates[14-15]. Further evidence of coordination is the prescence of strong and medium bands at 376 – 377 cm^{-1} and 549 – 598 cm^{-1} in the spectra of the metal complexes attributed to υ(M-O) and υ(M-N) respectively, these bands are absent in the ligand [7].

Electronic spectra

The ultraviolet spectra of the compounds in chloroform are characterized by three peaks between 27.24-28.99, 36.10-39.22 and 42.92 kK with molar absorptivities of 10^4 - 10^6 M^{-1} cm^{-1}(Table 2). These bands are assigned to π-π* and charge transfer transitions (of various origins). The molar absorptivities of the complexes in the visible region are in the range 10^2-10^3 $M^{-1}cm^{-1}$ ruling out octahedral geometry, since octahedral complexes have molar absorptivities in the range 1-50 $M^{-1}cm^{-1}$ [1]. The Mn(II) and Co(II) complexes have lone band each at 22.52 and 22.67 kK respectively, assigned to $^6A_1 \rightarrow {}^4E_1$ (G) and $^4A_2 \rightarrow {}^4T_1$ (P) transitions, of a four coordinate tetrahedral geometry [18]. On the contrary, the Ni(II) complex has two bands at 11.76 and 23.20 kK typical of four coordinate tetrahedral geometry and are assigned to $^3T_1(F) \rightarrow {}^3T_2$, ($\nu_2$) and $^3T_1(F) \rightarrow {}^3A_2$, ($\nu_3$) transitions [19]. The Cu(II) complex studied displays an absorption band at 22.15 kKwhich is assigned to $^2B_{1g} \rightarrow {}^2E_{1g}$ transition, typical of a four coordinate square planar geometry, since tetrahedral Cu(II) complexes have a single absorption band below 10.00 kK [20]. The Zn(II) complex shows only the metal to ligand charge transfer transition at 22.52 kK, since no d-d transition is expected. Thus, the geometry is tetrahedral [21]. The electronic spectrum of Pd(II) complex exhibits an absorption band at 22.72 kK, assigned to $^1A_{1g} \rightarrow {}^1E_{2g}$ transition, of a four coordinate square planar geometry [22]. However, in the absence of room temperature magnetic moment measurements and suitable crystals for single X-ray structural determination, the assignment of geometry is tentative (Figure 1).

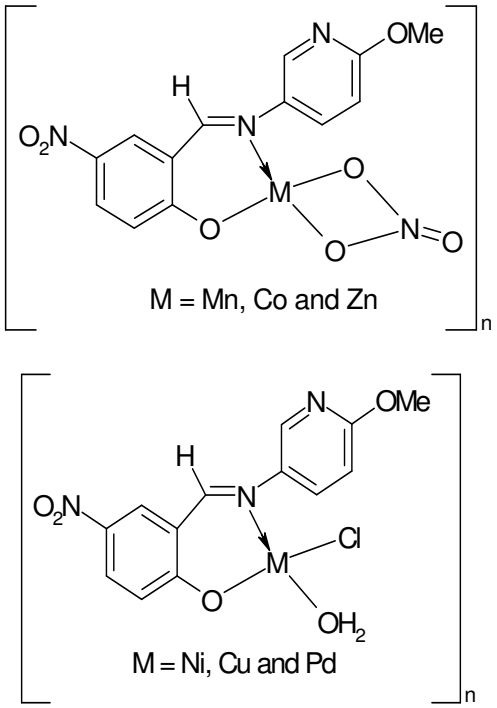

Figure 1: Proposed structures for the metal complexes (n =1).

Antibacterial activities

The antibacterial activities are shown in Figure 2. The ligand and its complexes are inactive against *E. coli* and *K. oxytoca,* but are active against *B. cereus,* and *Proteus mirabilis* with inhibitory zone range of 16.0-22.0 mm and 15.0-21.0 mm respectively, exception for the Cu(II) complex. The inactivity of the ligand and its complexes against *E. coli* and *K. oxytoca* may be attributed to the former being in the spore stage, while the latter has extended-spectrum beta-lactamase, which inactivates the compounds [23-24]. The ligand, Mn(II), Co(II) and Zn(II) complexes are active against *P. aureginosa* with inhibitory zone range of 14.0-19.0 mm, while Mn(II), Ni(II) and Cu(II) complexes are inactive against *S. aureus* due to their probable lipophobic nature [21]. The increased activities of some of the metal complexes are attributed to chelation . This increases the lipophilic character of the chelate, favouring its permeation into the bacterial membrane, thus causing the death of the organism [25]. Furthermore, the ligand, Co(II), and Zn(II) complexes have broad-spectrum activity against *B. cereus, P. aureginosa, S. aureus and P. mirabilis* with inhibitory zone range of 14.0-22.0 mm, thus proving their potential usefulness as broad-spectrum antibacterial agents. However, their activity was much lower than that of streptomycin with inhibitory zone range of 27.0 – 37.0 mm.

Table 1. Analytical data for the ligand and its complexes

Compounds	Formular mass	Colour	% yield	M. p (^{0}C)	% Metal (exp)
HL ($C_{13}H_{11}N_3O_4$)	273.24	Peach	80	208-210	-
$[MnLNO_3]$ ($MnC_{13}H_{10}N_4O_7$)	390.34	Orange	70	302-304	(14.06) 14.07
$[CoLNO_3]$ ($CoC_{13}H_{10}N_4O_7$)	394.33	Brown	70	246-248	(15.08) 14.94
$[NiL(Cl)H_2O]$ ($NiC_{13}H_{12}N_3O_5$)	385.58	Yellow	70	380*	(15.03) 15.23
$[CuL(Cl)H_2O]$ ($CuC_{13}H_{12}N_3O_5$)	390.41	Green	70	390*	(16.26) 16.28
$[ZnLNO_3]$ ($ZnC_{13}H_{10}N_4O_7$)	400.77	Yellow	70	228-230	(16.73) 16.31
$[PdL(Cl)H_2O]$ ($PdC_{13}H_{12}N_3O_5$)	433.27	Brown	70	346*	(24.86) 24.56

Key: * = decomposition temperature, Exp = experimental.

Table 2. Relevant infrared and electronic spectral data of the ligand and its complexes

Compound	νOH	ν(C=N) + ν(C=C)	ν(M—N)	ν(M—O)	Electronic transitions, kK (ε)
HL	3433s	1657.94s 1423.29s	-	-	27.24 (1.0 x 10^5), 28.99 (1.0 x 10^5), 42.92 (1.0 x 10^5)
$[MnLNO_3]$	-	1657.62s 1423.18s	598m	376s	22.52(200), 36.10 (1.0 x 10^4), 38.60 (1.0 x 10^5).
$[CoLNO_3]$	-	1657.58s 1423.16s	567m	376s	22.67(100), 38.91 (1.0 x 10^6), 39.68 (1.0 x 10^5).
$[NiL(Cl)H_2O]$	3500b	1657.74s 1423.19s	587m	377s	11.76(100), 23.20(100), 38.02(1.0 x 10^6).
$[CuL(Cl)H_2O]$	-	1658.16s 1423.76s	549m	376s	22.15(300), 37.45(1.0 x 10^5), 38.02 (1.0 x 10^6), 39.22 (1.0 x 10^5).
$[ZnLNO_3]$	-	1656.94s 1422.66s	581m	377s	22.52(200), 38.02(1.0 x 10^5), 36.76 (1.0 x 10^4).
$[PdL(Cl)H_2O]$	3500b	1658.25s 1423.50s	564m	376s	22.72(300), 38.02(1.0 x 10^5), 37.59 (1.0 x 10^5), 39.22 (1.0 x 10^5).

Key: b = broad, m = medium, s = strong, ε = molar absorptivity, 1kK = 1000cm^{-1}

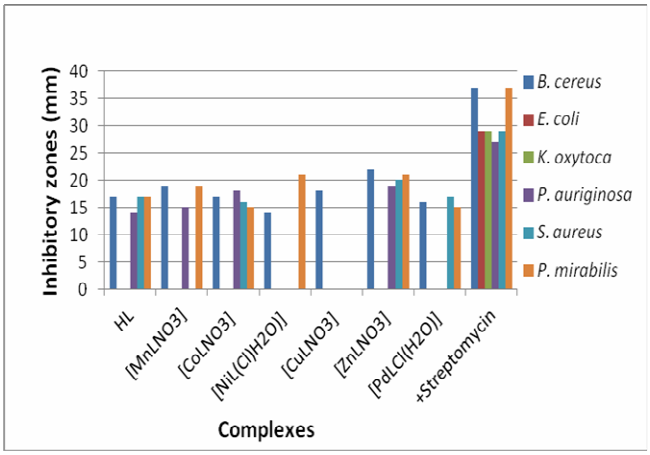

Figure 2: Histogram showing the comparative activities of the compounds

Conclusion

The tridentate Schiff-base ligand coordinates to the Mn(II), Ni(II), Co(II), Cu(II), Pd(II) and Zn(II) ions in a bidentate manner using the azomethine N and phenol O atoms. The assignment of a 4-coordinate tetrahedral/square-planar geometry to metal(II) complexes is corroborated by infrared and electronic spectral measurements. The antibacterial studies show that the ligand and its complexes have selective inactivity against *E. coli* and *K. oxytoca;* interestingly, the metal-free Schiff base, Co(II), and Zn(II) complexes have broad-spectrum activity against *B. cereus, P. aureginosa, S. aureus and P. mirabilis* with inhibitory zone range of 14.0-22.0 mm.

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