

Synthesis, Spectral, Magnetic and *In-Vitro* Anticancer Properties of Some Metal (II) Complexes of 3-[2,4-dihydro-1H-inden-4- ylimino) methyl] naphthalene-2-ol

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Authors' contributions

Author OAA designed the study, wrote the protocol and performed the experiment, while authors OnAA and OK managed the interpretation of the cytotoxic data and author HAT managed the final manuscript. All authors read and approved the final manuscript.

Research Article

Received 26th March 2012
Accepted 13th October 2012
Published 4th December 2012

ABSTRACT

Novel Cu(II), Zn(II) and Pd(II) complexes of the Schiff base, 3-[2,4-dihydro-1H-inden-4-ylimino)methyl]naphthalen-2-ol, have been prepared and characterized by elemental analysis, ¹HNMR, molar conductance, room temperature magnetic moments, infrared and electronic spectral measurements. The purity of the ligands and the metal complexes are confirmed by microanalyses and ¹HNMR. The IR spectra shows that the Pd(II) exhibits geometric isomerism, being in the trans isomeric form, and the ligand is bidentate coordinating via the azomethine N and naphthalene O atoms. The Cu (II) and Pd (II) complexes assume a four-coordinate square planar geometry; while the Zn (II) complex is tetrahedral, as indicated by room temperature moment and electronic spectra measurements. The complexes are non-electrolytes in nitromethane. The in-vitro anticancer activities of the Schiff base and its Cu(II), Zn(II) and Pd(II) complexes against HT-29 (colon) carcinoma and MCF-7 (human breast) adenocarcinoma are evaluated.

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The results show that the HT-29 cells are generally more sensitive than the MCF-7 cells to the metal complexes; and the Zn (II) complex has the best broad-spectrum anticancer activity against both colon and breast carcinomas, with IC50 values of 20.15 and 22.50 μM respectively. The activity of the Zn (II) complex against colon carcinoma is about a third of Cis-platin activity in the same assay.

Keywords: Anticancer; broad-spectrum; *in-vitro*; non-electrolyte; Schiff base.

1. INTRODUCTION

Aminoindane based derivatives exhibit a range of bioactivities such as bronchodilators (Heinzelmann et al., 1948), anticancer, antimicrobial and anticonvulsant (Maruyama et al., 2001; Rao and Reddy, 1990; Rogers et al., 1989; Stewart et al., 1996) and as analgesics and protease inhibitors (Borenstein et al., 1984; Zon et al., 2005). Furthermore, Cr (III), Ru(III) and Ti(IV) complexes of various aminoindanyl Schiff bases are used as catalysts in Diels-Alder reactions of α,β -unsaturated aldehydes and ring opening of mesoaziridines, in the oxidation of benzyl alcohol and cyclohexanol to benzaldehyde and cyclohexanone; and in the oxidation of alkyl aryl sulfides to the corresponding sulfoxides (Bryliakov et al., 2007; Fernandez and Jacobsen., 1999; Gademann et al., 2002). In addition, VO (IV) complexes of some symmetric 2-hydroxy-1-naphthaldehyde Schiff bases have been found to be promising anti-diabetic agents (Nejo et al., 2009). In-depth literature search revealed that no information is available on the Schiff base, 3-[2,3-dihydro-1H-inden-4-ylimino)methyl] naphthalene-2-ol (derived from condensation of 2-hydroxy-1-naphthaldehyde and 4-aminoindane) and its Cu(II), Zn(II) and Pd(II) complexes (Abdullah and Badahdah, 2007; Blagus et al., 2010; Derebe et al., 2002; Kozlov and Gusak, 1999; Na et al., 1988; Nejo et al., 2010a, 2010b; Santos et al., 2000; Tuncel and Selahattin, 2005).

Therefore the aim of our study is primarily to synthesize and characterize the above named Schiff base and its metal (II) complexes, and evaluate their suitability as anticancer agents *in-vitro*. Secondly, the compounds with very good *in-vitro* anticancer activities will be used as treatments *in-vivo* in albino mice with various forms of cancer (this result will be presented in another paper). Thirdly, the *in-vitro* anticancer activities of these complexes will be compared with similar compounds earlier reported by us to investigate the effect of various substituents on their anticancer activities (Osowole et al., 2012a, 2012b). This study is a continuation of the research activities of our group in the search for lead compounds for drug development against various carcinomas (Osowole and Daramola, 2011; Osowole et al., 2010a, 2010b; Osowole, 2011; Osowole et al., 2012).

2. MATERIALS AND METHODS

2.1 Chemicals

Reagent grade 2-hydroxy-1-naphthaldehyde, 4-aminoindane, triethylamine, Copper (II) nitrate hexahydrate, Palladium (II) chloride dihydrate, and Zinc (II) nitrate heptahydrate were purchased from Aldrich chemicals and were used as received.

2.2 Syntheses

2.2.1 Preparation of 3-[2,4-dihydro-1H-inden-4-ylimino] methyl]naphthalene-2-ol

The ligand was prepared by refluxing for 3 h, a homogeneous solution of 1.94 g (1.13×10^{-2} moles) 2-hydroxy-1-naphthaldehyde and 1.5 g (1.13×10^{-2} moles) of 4-aminoindane in 60 mL of hot ethanol, to which 4 drops of acetic acid were added. The orange products [Fig. 1(A)] formed on cooling in ice were collected by suction, recrystallized from ethanol and dried over silica gel. The yield of the product was 2.59 g (80%).

Color (yellow); IR (KBr, cm^{-1}): ν_{OH} (3424s), $\nu_{\text{C}=\text{N}}$ (1620s 1580s 1540s); UV, kK_{Max} (): 24.74 (1×10^4), 31.25(1×10^5), 41.32(1×10^6); M.pt ($^{\circ}\text{C}$), 158-160; formula mass (287.36); CHN Anal. calcd(found) for $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}_3$: C, 83.60(83.63); H, 5.96(5.80); N, 4.87(4.65); $^1\text{Hnmr}$ (300 MHz, CDCl_3 , in ppm): 15.76 (s, OH), 9.4 (s, HCN), 7.30 - 8.14(m, 6H, C_{10}H_6); 7.0-7.27 (m, 3H, {C5' C6' C7' H₃}); 3.07-3.12(t, J = 7.52 Hz, 2H, C3'H₂); 2.98-3.05 (t, J = 7.46 Hz, 2H, C1'H₂); 2.10-2.22 (q, J = 7.44 Hz, 2H, C2'H₂).

2.2.2 Preparation of the metal complexes

The Cu (II) complex was prepared by refluxing for 3 h a homogeneous solution of 0.30 mmol (0.06 g) of Cu (II) nitrate hexahydrate and 0.60 mmol (0.17 g) of the Schiff base, to which 0.6 mmol (0.06 g) of triethylamine was added in 30 mL ethanol. The products precipitated as solids, which were filtered, washed with ethanol and dried over silica gel. The Pd (II) and the Zn (II) complexes were prepared from their chloride and nitrate salts using the same method. The analytical data were as follow:

$[\text{CuL}_2] \cdot \frac{3}{4}\text{H}_2\text{O}$: yield 0.12 g, 60%; Color(brown); IR(KBr, cm^{-1}): ν_{OH} (3500b), $\nu_{\text{C}=\text{N}}$ (1611s 1600s 1578s 1534m), $\nu_{\text{M}-\text{N}}$ (565s 521s) $\nu_{\text{M}-\text{O}}$ (498s 464s); VIS/UV, kK_{Max} (): 14.87(200), 23.61(500), 31.20(1×10^4), 38.0(1×10^5), 40.98(1×10^6); M.pt($^{\circ}\text{C}$), 208-210; formula mass (649.77); CHN Anal. calcd (found) for $\text{Cu}(\text{C}_{40}\text{H}_{33.5}\text{N}_2\text{O}_{2.75})$ C, 73.97(74.09); H, 5.20(4.77); N, 4.31(3.63); %Cu calcd (found)9.78(9.80); μ_{eff} , 1.93.

$[\text{ZnL}_2] \cdot 7\text{H}_2\text{O}$: yield 0.09 g, 40%; Color(Red); IR(KBr, cm^{-1}): ν_{OH} (3500b), $\nu_{\text{C}=\text{N}}$ (1618s 1582s 1542s), $\nu_{\text{M}-\text{N}}$ (514s 502s) $\nu_{\text{M}-\text{O}}$ (498s 472s); VIS/UV, kK_{Max} (): 21.10(3×10^3), 31.20(1×10^4), 41.32(1×10^6); D.t($^{\circ}\text{C}$), 230; formula mass (764.23); CHN Anal. calcd (found) for $\text{Zn}(\text{C}_{40}\text{H}_{46}\text{N}_2\text{O}_9)$ C, 62.87(62.80); H, 6.07(4.58); N, 3.67(3.49); %Zn calcd (found) 8.51(8.48); μ_{eff} , 3.60; D; $^1\text{Hnmr}$ (300 MHz, CDCl_3 , in ppm): 9.3 (s, HCN), 7.25-8.07 (m, 6H, C_{10}H_6); 7.02-7.24 (m, 3H, {C5' C6' C7' H₃}); 3.10-3.15(t, J = 7.44 Hz, 2H, C3'H₂); 2.99-3.06 (t, J = 7.50 Hz, 2H, C1'H₂); 2.13-2.23(q, J = 7.48 Hz, 2H, C2'H₂).

$[\text{PdL}_2] \cdot 2\text{H}_2\text{O}$: yield 0.15 g, 70%; Color(Green); IR(KBr, cm^{-1}): ν_{OH} (3500b), $\nu_{\text{C}=\text{N}}$ (1607s 1579s), $\nu_{\text{M}-\text{N}}$ (576s 501s) $\nu_{\text{M}-\text{O}}$ (474s 428s); VIS/UV, kK_{Max} (): 16.0(200), 23.41(3×10^3), 30.48(1×10^4), 36.76(1×10^6), 40.0(1×10^6); D.t($^{\circ}\text{C}$), 280; formula mass (715.14); CHN Anal. calcd(found) for $\text{Pd}(\text{C}_{40}\text{H}_{36}\text{N}_2\text{O}_4)$ C, 67.18(67.19); H, 5.07(4.46); N, 3.92(3.62); %Pd calcd(found)14.88(14.88); μ_{eff} , 29.0; D; $^1\text{Hnmr}$ (300 MHz, CDCl_3 , in ppm): 8.58 (s, HCN), 7.27-8.04 (m, 6H, C_{10}H_6); 7.1-7.26 (m, 3H, {C5' C6' C7' H₃}); 3.17-3.23(t, J = 7.26 Hz, 2H, C3'H₂); 3.01-3.06 (t, J = 7.36 Hz, 2H, C1'H₂); 2.01-2.09 (q, J = 7.42 Hz, 2H, C2'H₂).

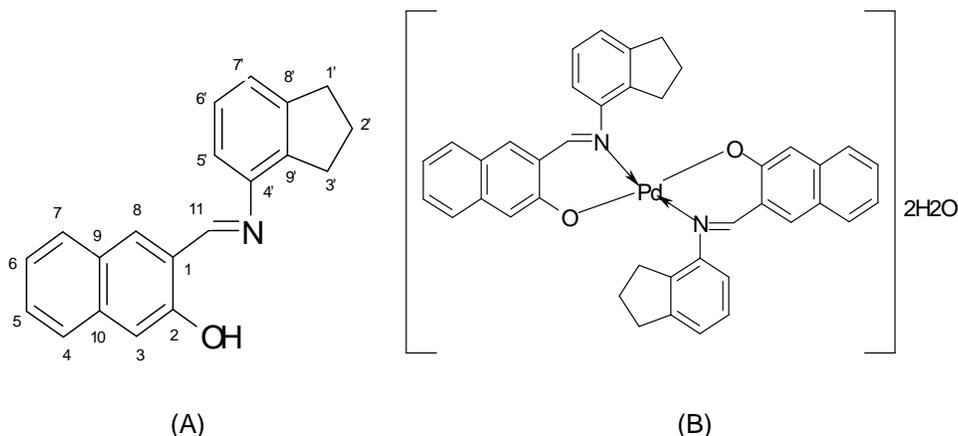


Fig. 1. The proposed structure for the ligand (A) and its Pd (II) complex (B).

2.3 Physical Measurements

The electronic and infrared spectra were recorded on a Perkin-Elmer 25 and a Thermo Nicolet FTIR 200 spectrophotometer respectively. The ¹H nmr spectrum was recorded on a 300 MHz Bruker DRX-400 NMR instrument in CDCl₃ at 295K; and ¹H chemical shifts were referenced to the residual signals of the protons of CDCl₃ and were quoted in ppm. The elemental analyses for C, H and N were recorded on a Thermo Quest CE Instruments flash EA1112 analyser, while percentage copper, palladium and zinc were determined titrimetrically (Bassett et al., 1978). Magnetic susceptibilities were measured on a Johnson Matthey magnetic balance at room temperature of 26°C, while diamagnetic corrections are calculated using Pascal's constants (Earnshaw, 1980). Electrolytic conductivities in nitromethane and melting points (uncorrected) were determined using a HANNA HI 991300 conductivity meter and Mel-Temp electro thermal machine respectively.

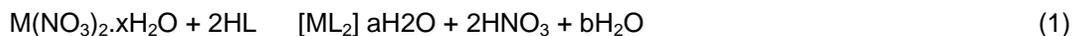
2.4 Anti-Cancer Studies

The MCF-7 (human breast adenocarcinoma) and HT-29 (colon carcinoma) cells were cultured and maintained in minimum essential medium (MEM) supplemented with 10% (V/V) of fetal calf serum (FCS) and 50 mg/L of gentamycin at the Institute of Medicinal and Pharmaceutical Chemistry, Technical University Braunschweig, Germany. A concentration of 100 mL of a cell suspension in a culture medium [7500 cells/mL (MCF-7) and 2500 cells/mL (HT-29)] were plated into each of 96 well plates and incubated for three days under culture conditions. After the addition of various concentrations of the test compounds, cells were incubated for another 96 h and 72 h respectively. The medium was then removed and the cells were fixed with 1% glutardialdehyde solution and stored under phosphate buffered saline (PBS) at 4°C. Cell biomass was determined by crystal violet staining, followed by the extraction of the bound dye with ethanol, and a photometric measurement at 590 nm. The test compounds were prepared fresh as stock solutions in DMF and diluted with the cell culture medium to the final assay concentrations (0.1% V/V DMF). Cis-platin was used as the reference drug. The IC₅₀ value was determined as the concentration causing 50% inhibition of cell proliferation and calculated as the mean of at least two independent experiments (Rubner et al., 2010).

3. RESULTS AND DISCUSSION

3.1 Analytical Data and Conductance Measurements

The reactions for the formation of the metal (II) Schiff base complexes are presented in equations 1 and 2 respectively. The compounds were formed in good yields of 60-70% with the exception of the Zn (II) complex, which had a yield of 40%.



{When M (II) = Cu, x = 6, a = 0.75, b = 5.25; Zn (II), x = 7, a = 7, b = 0}



The water molecules associated with the complex formation are outside the coordination sphere. This is because heating the hydrated complexes in a programmed oven in the temperature range 80-100°C for 1-3 hours leads to dehydration, with corresponding weight loss of 0.75, 2 and 7 water molecules respectively. It has been documented that the water of coordination is usually eliminated in the temperature range 120–250°C (Nejo et al., 2010; Refat et al., 2010). The structural formula of the ligand is provided in Fig. 1(A); and its formation is confirmed by microanalysis and ¹HNMR. The ligand melted in the range 158-160°C, while the complexes melted/decomposed in the range 208-280°C, confirming coordination. Single crystal of the complexes could not be isolated from any solution. Hence, analytical, magnetic and spectroscopic data have been used to propose possible structures, and the complexes are reported here for the first time.

The metal(II) complexes are non-electrolytes in nitromethane as shown by their molar conductivities (Λ_m) of 10.0-36.0 $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$, since a value of 60-118 $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$ is expected for 1:1 electrolyte (Geary, 1971).

3.2 Electronic Spectra and Magnetic Moments

The ultraviolet spectra of the compounds in chloroform are characterized by three peaks between 30.48-31.25, 36.76-39.00 and 40.82- 42.00 kK with molar absorptivities of $10^4 - 10^6 \text{ M}^{-1} \text{ cm}^{-1}$, assigned to $\pi \rightarrow \pi^*$ and charge transfer transitions (of various origins), respectively (Nejo et al., 2009; Nejo et al., 2010b). The molar absorptivities of the complexes in the visible region are in the range 10^2 - $10^3 \text{ M}^{-1}\text{cm}^{-1}$ ruling out octahedral geometry, since octahedral complexes have molar absorptivities in the range 1-50 $\text{M}^{-1}\text{cm}^{-1}$ (Nejo et al., 2010a).

Regular tetrahedral compounds of copper(II) usually have a single broad band of 10^2 molar intensity below 10.0 kK, while regular octahedral complexes have a single broad band above 10.0 kK, and square-planar complexes usually have two bands between 10.0-20.0 kK with molar absorptivities of 10^2 - $10^3 \text{ M}^{-1} \text{ cm}^{-1}$ (Tuncel and Selahattin, 2005). The Cu (II) complex studied, displays two absorption bands at 14.87 and 23.61 kK, and is consequently square planar with bands assigned to the ${}^2\text{B}_{1g}$, ${}^2\text{A}_{1g}$ and ${}^2\text{B}_{1g}$, ${}^2\text{E}_{1g}$ transitions. An observed moment of 1.93 B.M indicates that it is monomeric and complimentary of square-planar geometry (Nejo et al., 2010b).

The Pd (II) complex exhibits two absorption bands at 16.00 and 23.41 kK, typical of square planar geometry and are assigned to the ${}^1\text{A}_{1g}$, ${}^1\text{B}_{1g}$ and ${}^1\text{A}_{1g}$, ${}^1\text{E}_{2g}$ transitions. It is expectedly diamagnetic (Osowole and Daramola, 2011; Osowole, 2011). As expected, the

Zn (II) complex has no d-d band but a M L CT band at 21.10 kK, and its diamagnetism is corroborative of a 4-coordinate tetrahedral geometry (Rao and Reddy, 1990).

3.3 Infrared and ¹Hnmr Spectra

The assignments of the infrared bands were made by comparing the spectra of the compounds with reported literature on similar systems (Abdullah and Badahdah, 2007; Blagus et al., 2010). The uncoordinated C=N stretching vibrations occur as three bands expectedly at 1620-1540 cm⁻¹ in the ligand (Derebe et al., 2002; Na et al., 1988). Furthermore, they are bathochromic shifted to 1618-1534 cm⁻¹ on coordination to the metal ions as three to four bands, except for the Pd(II) complex which has two bands, indicative of the involvement of the N donor atom of C=N in coordination. The possession of two $\nu(\text{C}=\text{N})$ bands by the Pd (II) complex indicates that it exhibits geometric isomerism, and it is in the trans isomeric-isomeric {Fig. 1(B)} form (Nejo et al., 2010a). The strong band at 3424 cm⁻¹ in the ligand is assigned as νOH stretching frequency, and it is conspicuously absent in the spectra of the complexes, indicative of the deprotonation and the involvement of the naphthalenol O in chelation. The new broad band at 3500 cm⁻¹, in the complexes is assigned to $\nu(\text{OH})$ crystallization water. The presence of bands due to $\nu(\text{M}-\text{O})$ and $\nu(\text{M}-\text{N})$ at 498-428 and 576-501 cm⁻¹ respectively is further evidence of coordination. These bands are absent in the ligand (Blagus et al., 2010; Derebe et al., 2002; Tuncel and Selahattin, 2005).

The naphthalenol proton in HL is observed at 15.76 ppm, while the imine proton is seen as a singlet at 9.40 ppm. The naphthalene protons resonate as a multiplet at 7.30-8.14 ppm while the protons at C5', C6' and C7' in the indane ring are observed as a multiplet at 7.0-7.27 ppm. The 2H at C1', C2' and C3' resonate as a triplet, a quintet and a triplet at 2.98-3.05 ppm, 2.10-2.22 ppm and 3.07-3.12 ppm respectively. Furthermore, the [ZnL₂] and [PdL₂] spectra show the absence of the naphthalenol proton and this confirms coordination through the naphthalene O atom. The imine protons are seen as singlets down field at 9.30 and 8.53 ppm respectively. Similarly, the naphthalene protons and indane protons on C5', C6' and C7' resonate as multiplets down field at 7.24-8.07 and 7.02-7.26 ppm respectively. The 2H on C1', C2' and C3' in indane ring are seen mostly up field as triplets, quintets and triplets at 2.99-3.06 ppm, 2.01-2.23 ppm and 3.10-3.23 ppm respectively. These shifts indicate coordination through the imine N atom (Osowole et al., 2010b).

3.4 Anticancer Activity

The anticancer activities are presented in Table 1. The HT-29 cells are generally more sensitive to the compounds than MCF-7 cells. The metal free ligand is more active against HT-29 cells than the Cu (II) and Pd (II) complexes, but is less active than the Zn (II) complex. The increasing order of activity is [CuL₂] < [PdL₂] < HL < [ZnL₂]. In contrast, coordination enhances the activity of the metal complexes against MCF-7 cells, and the increasing order of activity is HL < [PdL₂] < [CuL₂] < [ZnL₂]. In both cases, the Zn (II) complex has the best in-vitro anticancer activity against HT-29 and MCF-7 cells. Furthermore, the enhanced activity of [ZnL₂] (IC₅₀ value of 20.15 μM) which is about a third of Cis-platin activity (IC₅₀ value of 7.0 μM) in the same assay against HT-29 cells, is of interest in the development of tumor therapeutics.

Table 1. *In-vitro* anticancer activities of the ligand and its Cu (II), Zn (II) and Pd (II) Complexes

| Compound | IC ₅₀ [μM] Human breast adenocarcinoma (MCF-7) | IC ₅₀ [μM] Colon carcinoma (HT 29) |
|--|---|---|
| CDDP | 2.0 | 7.0 |
| HL | 52.50±0.06 | 26.28±0.01 |
| [CuL ₂] $\frac{3}{4}$ H ₂ O | 29.89±0.09 | 55.98±0.35 |
| [ZnL ₂]7H ₂ O | 22.50±0.05 | 20.15±0.01 |
| [PdL ₂] 2H ₂ O | 49.95±0.01 | 43.12±0.25 |

CDDP = *Cis-platin*

It is interesting to note that from our earlier studies that when the ligands are diphenol and 5-nitrophenol Schiff bases appended with aminoindane moiety, the HT -29 cells are not sensitive but in the present study where the phenolic ring is changed to naphthalen-2-ol, the HT-29 cells are sensitive with activity of about a quarter that of Cis-platin in the same assay. Thus, the presence of the naphthalene ring induces better anticancer activities in the ligand against colon cancer. On the contrary, the activity of the 5-nitrophenol ligand against MCF-7 cells is 33.3 μM while naphthalen-2-ol and diphenol ligands have about the same activity with IC₅₀ values ~ 52.1 μM against MCF-7 cells. The activity of the latter two is about 2/3rd that of the 5-nitrophenol ligand (Osowole et al., 2012a, 2012b). In addition, the Pd(II) and Cu(II) complexes of the diphenol Schiff base (Osowole et al., 2012b) have the best anticancer activities against both MCF-7 and HT-29 carcinomas with IC₅₀ values of 0.92, 1.67, 15.65 and 12.97 μM respectively (Osowole et al., 2012b). This is followed by the Zn(II) and Cu(II) complexes of the naphthalen-2-ol Schiff base (present study) with IC₅₀ values 22.50, 20.15, 29.89 and 55.98 μM while the Zn(II) complex of the nitrophenol Schiff base has the least activity with IC₅₀ values of 19.90 and 51.60 μM (Osowole et al., 2012a).

Therefore, we conclude that the presence of diphenol and naphthalen-2-ol groups appended to aminoindane increase the *in-vitro* anticancer activities against both MCF-7 and HT-29 carcinomas (Osowole et al., 2012a, 2012b).

4. CONCLUSION

The Schiff base, 3-[2, 4-dihydro-1H-inden-4-ylimino) methyl] naphthalen-2-ol, coordinates to the Cu (II), Zn(II) and Pd(II) ions using the azomethine N and naphthalenol O atoms. The complexes assume a 4-coordinate tetrahedral/square-planar geometry, as corroborated by room temperature magnetic moments, infrared and electronic spectral measurements. The Pd (II) complex exhibits geometric isomerism being in the trans isomeric form. The *in-vitro* anticancer activities of the Schiff base and its Cu (II), Zn (II) and Pd (II) complexes against HT-29 (colon) carcinoma and MCF-7 (human breast) adenocarcinoma show that the HT 29 cells are generally more sensitive than the MCF-7 cells to the metal complexes, with the Zn (II) complex having the best broad-spectrum anticancer activity against both colon and breast carcinomas with IC₅₀ values of 20.15 and 22.50 μM respectively.

ACKNOWLEDGEMENTS

One of us, Aderoju Osowole thanks TWAS-COMSTECH for the research grant 09-137 RG/PHA/AF/AC_C-UNESCO FR: 3240231226; TWAS-DFG for a fellowship, The Abdus

Salam International Centre for Theoretical Physics (ICTP) Trieste, Italy for financial support and the University of Ibadan, Ibadan, Nigeria for Research Leave. Prof Ingo Ott of the Institute for Medicinal and Pharmaceutical Chemistry, Technical University, Braunschweig, Germany is acknowledged for his assistance with the elemental analyses and collaboration on the cell line studies.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

- Abdullah, M.A., Badahdah, K.O. (2007). Synthesis of some new anils: Part 1. Reaction of 2-hydroxy-benzaldehyde and 2-hydroxynaphthaldehyde with 2-amino pyridine and 2-Aminopyrazine. *Molecules*, 12, 1796-1804.
- Bassett, J., Denney, R.C., Jeffery, G.H., Mendham, J. (1978). *Vogel's Textbook of Quantitative Inorganic Analysis*, fourth ed. ELBS, London.
- Blagus, A., Činčarić, D., Frišić, T., Kaitner, B., Stilinović, V. (2010). Schiff bases derived from hydroxyaryl aldehydes: molecular and crystal structure, tautomerism, quinoid effect coordination compounds. *Macedonian Journal of Chemistry and Chemical Engineering*, 29(2), 117–138.
- Borenstein, M.R., Abou-Gharbi, M.A., Doukas, P.H. (1984). Synthesis of spiroimides of pharmacologic interest. *Heterocycles*, 22(11), 2433-2438.
- Bryliakov, K.P., Talsi, E., Boreskov, P. (2007). Asymmetric oxidation of sulfides with H₂O₂ catalyzed by titanium complexes with amino alcohol derived Schiff bases. *Journal of Molecular Catalysis A: Chemical*, 264(1-2), 280-287.
- Derebe, M.G., Raju, V.J.T., Retta, N. (2002). Synthesis and characterization of some metal complexes of a Schiff base derived from ninhydrin and L-alanine. *Bull. Chem. Soc. Ethio.*, 16(1), 53-64.
- Earnshaw, A. (1980). *The Introduction to Magnetochemistry*, third ed. Academic Press, London.
- Gademann, K., Chavez, D.E., Jacobsen, E.N. (2002). Highly enantioselective inverse-electron demand hetero-Diels-Alder reactions of α,β -unsaturated aldehydes. *Angewandte Chemie, International Edition*, 41(16), 3059-3061.
- Geary, W.J. (1971). The use of conductivity measurements in organic solvents for the characterization of coordination compounds. *Coordination Chemistry Review*, 7, 81-122.
- Heinzelmann, R.V., Kolloff, H.G., Hunter, J.H., Upjohn, C., Kalamazoo, M.I. (1948). Physiologically active indanamines. II. Compounds substituted in the aromatic ring. *Journal of the American Chemical Society*, 70, 1386-1390.
- Kozlov, N.G., Gusak, K.N. (1999). Cyclic α,β -diketones. *Russ. J. Org. Chem.*, 35(3), 402-414.
- Li, Z., Fernandez, M., Jacobsen, E.N. (1999). Enantioselective ring opening of meso aziridines catalyzed by Tridentate Schiff base chromium(III) complexes. *Organic letters*, 1(10), 1611-1613.
- Maruyama, W., Youdim, M.B.H., Naoi, M. (2001). Antiapoptotic properties of rasagiline, N-propargylamine-1(R)-aminoindan, and its optical (S)-isomer TV1022. *Annals of the New York Academy of Sciences (Neuroprotective Agents)*, 93(9), 320-329.
- Na, C., Zhao, G., Liu, G., Li, B. (1988). Preparation and characterization of some Schiff bases from o-vanillin and diamines. *Jilin Daxue Ziran Kexue Xuebao*, 2, 103-107.

- Nejo, A.A., Kolawole, G.A., Dumbley, M.C., Opoku, A.R. (2010a). Spectral, magnetic, biological, and thermal studies of metal (II) complexes of some unsymmetrical Schiff bases. *Journal of Coordination Chemistry*, 63(24), 4367–4379.
- Nejo, A.A., Kolawole, G.A., Nejo, A.O. (2010b). Synthesis, characterization, antibacterial, and thermal studies of unsymmetrical Schiff-base complexes of cobalt(II). *Journal of Coordination Chemistry*, 63(24), 4398–4410.
- Nejo, A.A., Kolawole, G.A., Opoku, A.R., Wolowska, J., O'Brien, P. (2009). Synthesis, characterization and preliminary insulin-enhancing studies of symmetrical tetradentate Schiff base complexes of oxovanadium (IV). *Inorganica Chimica Acta*, 362, 3993–4001.
- Oswole, A.A., Daramola, A.O. (2011). Synthesis, physicochemical and Biological activities of some metal (II) complexes of (methylsulfanyl)-2,4-benzenediol Schiff base. *Elixir Appl. Chem.*, 39, 4876-4879.
- Oswole, A.A., Kempe, R., Schobert, R., Balogun, S.A. (2010a). Synthesis, characterization and in-vitro biological activities of some metal (II) complexes of 3-(-1-(4-methyl-6-chloro)-2-pyrimidinylimino) methyl-2-naphthol. *Canadian Journal of Pure and Applied Science*, 4(2), 1169-1178.
- Oswole, A.A., Kempe, R., Schobert, R., Effenberger, K. (2010b). Synthesis, spectroscopic, thermal and in-vitro anticancer properties of some M (II) complexes of 3-(-1-(4, 6-dimethyl-2-pyrimidinylimino) methyl-2-naphthol. *Synth. React. Inorg. Met. Org. Chem and Nano-Met.Chem.*, 41(7), 825-833.
- Oswole, A.A., Ott, I. (2012a). Synthesis, characterization, *in-vitro* anticancer and antimicrobial properties of some metal (II) complexes of 4-[(2,3-dihydro-1*H*-inden-4-ylimino) methyl] benzene-2,4-diol. *International Research Journal of Pure and Applied Chemistry* (In press).
- Oswole, A.A., Ott, I., Ogunlana, O.M. (2012b). Synthesis, spectroscopic, anticancer and antimicrobial properties of some metal (ii) complexes of 2-[(2,3- dihydro-1*H*-inden-4-ylimino)methyl]-5-nitrophenol. *International Journal of Inorganic Chemistry*, doi:10.1155/2012/206417.
- Oswole, A.A. (2011). Synthesis, characterization, in-vitro antibacterial and Anti-cancer studies on some metal (II) complexes of (methylsulfanyl) chromenol Schiff base. *Elixir Appl. Chem.*, 39, 4827-4831.
- Rao, N.S.R., Reddy, M.G.R. (1990). Studies on the synthesis, characterization and antimicrobial activity of new Co (II), Ni(II) and Zn(II) complexes of Schiff base derived from ninhydrin and glycine. *Biometal*, 3, 19–23.
- Refat, M.S., Alghool, S., De Farias, R.F. (2010). Synthesis, Spectral, and Thermal Studies of Cu(II), Ni(II), Fe(III), and Sn(II) Complexes with Captopril Drug. *Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry*, 40 (9), 585 - 591.
- Rogers, G.A., Parsons, S.M., Anderson, D.C., Nilsson, L.M., Bahr, B.A., Kornreich, W.D., Kaufman, R., Jacobs, R.S., Kirtman, B. (1989). Synthesis, in-vitro acetylcholine-storage-blocking activities, and biological properties of derivatives and analogs of trans- 2-(4- phenylpiperidino) cyclohexanol (vesamicol). *Journal of Medicinal Chemistry*, 32(6), 1217-1230.
- Rubner, G., Bendorf, K., Wellner, A., Bergemann, S., Ott, I., Gust, R. (2010). [Cyclopentadienyl] metal carbonyl complexes of acetylsalicylic acid as neo-anticancer agents. *European J. Med. Chem.*, 45, 5157-5163.
- Santos, I.C., Vilas-Boas, M., Piedade, M.F.M., Freire, C., Duarte, M.T., De Castro, B. (2000). Electrochemical and X-ray studies of nickel (II) Schiff base complexes derived from salicylaldehyde. Structural effects of bridge substituents on the stabilisation of the +3 oxidation state. *Polyhedron*, 19, 655–664.

- Stewart, J.M., Lajos, G., Whalley, E.T. (1996). Bradykinin antagonist peptides containing indane -substituted amino acids for use in the treatment of inflammatory responses. *PCT Int. Appl.*, 61.
- Tuncel, M., Selahattin, S. (2005). Synthesis and characterization of copper(II), nickel(II) and cobalt(II) complexes with azo-linked Schiff base ligands. *Synth. React. Inorg. Met.-Org. Chem. Nano-Met. Chem.*, 35(3), 203-212.

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