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Spectroscopic, thermal characterization and cytotoxic activity of bi-, tri- and tetra-nuclear Pd(II) and Pt(II) complexes with diSchiff base ligands

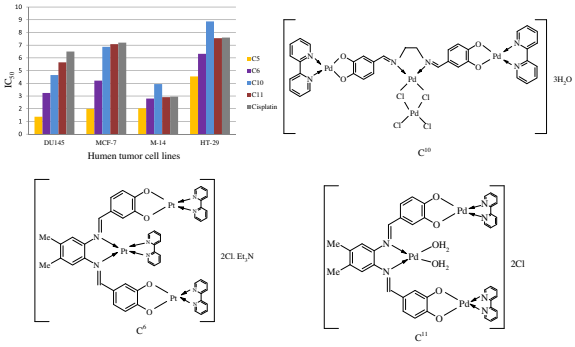
Wael Hussein Hegazy *

Department of Chemistry, Faculty of Science, Suez University, Suez 43533, Egypt

HIGHLIGHTS

- Poly-nuclear Pd(II) and Pt(II) complexes of diSchiff base ligands were synthesized.
- Structures are characterized by different spectroscopic techniques.
- Geometries of metal complexes are suggested using various methods.
- The cytotoxic results show promising chemotherapeutic antitumor activity.

GRAPHICAL ABSTRACT



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ABSTRACT

In this paper; new di-, tri-, and tetra-nuclear Pd(II) and Pt(II) complexes of N,N′-bis(3,4-dihydroxybenzylidene)ethan-1,2-diamine (EDH_4), N,N′-bis(3,4-dihydroxy-benzylidene)-benzene-1,2-diamine (PDH_4) and N,N′-bis-(3,4-dihydroxybenzylidene)-4,5-dimethyl-1,2-diamine ($MPDH_4$) ligands were synthesized by two different methods. The first method involve the synthesis of the three ligands from condensation reaction of 3,4-dihydroxybenzaldehyde ($L'H_2$) with ethylenediamine (en), o-phenylenediamine (o-PD), or 4,5-dimethyl-1,2-phenylendiamine (DMPD) in a mole ratio of 2:1 followed by the reaction of the resulting Schiff bases ligands with Pd(II) or Pt(II) ions in the presence of 2,2′-dipyridyl (L) to form the di- and tri-nuclear metal complexes. The second method involve the condensation of the Pd complex LPd(II)L′, (L = 2,2′-dipyridyl, L′ = 4-formylbenzene-1,2-bis(olate)) with en, o-PD, or DMPD in a mole ratio of 2:1, respectively, followed by reaction with $PdCl_2$ to form di-, tri-, and tetra-nuclear palladium(II) complexes, respectively. Structures of ligands and metal complexes are characterized by physical properties, FT-IR spectra and nuclear magnetic resonance. The geometries of metal complexes are suggested according to elemental analysis, electronic absorption spectra, thermal analysis, atomic absorption, magnetic susceptibility and molar conductance. Cytotoxic activity against lung large cell carcinoma (H460), prostate carcinoma (DU145), breast adenocarcinoma (MCF-7), amelanotic melanoma (M-14), colon adenocarcinoma (HT-29), and chronic myelogenous leukemia (K562) is also reported.

Introduction

Multinuclear transition metal complexes have become a central theme of current research because of their potential properties. Synthesis and characterization of polynuclear iron, cobalt, nickel,

* Tel.: +20 100 7777180; fax: +20 2 33033059.
E-mail address: whchemistry@hotmail.com

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copper and zinc complexes are reported by many researchers [1–7]. The wide range of coordination numbers and geometries, accessible redox states, thermodynamic and kinetic characteristics, and the intrinsic properties of the cationic metal ion and ligand itself offer the medicinal chemist a wide spectrum of reactivities that can be exploited. Biological evaluation of polynuclear complexes of different ligands with Fe(III), Co(II), Ni(II), Cu(II), Pd(II), Ag(I), Pt(II), Hg(II) and diorganotin(IV) are also reported in literature [4,7–16]. The aim of this work is to synthesize di- and tri-nuclear Pd(II) and Pt(II) complexes as synthetic models for multicenter active sites of biological systems by following two methods. The first method (method 1) involves the reaction of metal salts with each of the following three new di-Schiff base ligands: N,N′-bis(3,4-dihydroxybenzylidene)ethan-1,2-diamine (EDH_4) (Fig. 2), N,N′-bis(3,4-dihydroxybenzylidene)benzene-1,2-diamine (PDH_4) (Fig. 3), and N,N′-bis(3,4-dihydroxybenzylidene)-4,5-dimethyl-1,2-diamine ($MPDH_4$) (Fig. 4) prepared from the condensation reaction of 3,4-dihydroxybenzaldehyde with ethylenediamine (en), o-phenylenediamine (o-PD), or 4,5-dimethyl-1,2-phenylendiamine (DMPD), respectively. The second method (method 2) involves the condensation reaction of mononuclear Pd(II) mixed ligand complex of 3,4-dihydroxybenzaldehyde and 2,2′-dipyridyl (LPd(II)L′) (Fig. 1) (L = 2,2′-dipyridyl, L′ = 4-formylbenzene-1,2-bis(olate)) with (en), o-PD, or DMPD followed by further reaction with the metal salts to form the tri- and tetra-homonuclear metal complexes. The structures of the complexes were elucidated depending on elemental analysis, UV–Vis, ^{1}H NMR, and FT-IR spectra as well as, thermal analysis, atomic absorption, conductivity measurements, and magnetic susceptibility (see Table 1).

Materials and methods

All chemicals and solvents (AR) were obtained from Merck except absolute ethanol was (Sigma–Aldrich). ^{1}H and ^{13}C NMR was recorded on Perkin Elmer 283B and 300 MHz Varian XL-300 instruments. IR spectra were recorded on a Perkin Elmer (Spectrum 1000) Fourier-transform infrared (FTIR) spectrometer, using KBr pellets. Elemental analyses were determined at the micro-analytical center, Cairo University, and the results are in agreement with calculated values. Melting points (uncorrected) were determined on Gallenkamp melting point apparatus. Electronic absorptions were recorded in DMF on a Shimadzu UV-1800 automatic spectrophotometer. Thermal analysis were measured under a nitrogen flow rate of 30 cm^3 min^{-1} using a Shimadzu TGA-60H thermo balance from room temperature up to 1000 °C. The metal contents of the complexes were determined by atomic absorption technique using Varian-AA 775 atomic absorption spectrophotometer. Molar conductance A_m, (Ω^{-1} cm^2 mol^{-1}), at 25 °C of freshly prepared (0.001 mol dm^{-3}) metal chelates in DMF was determined using a YSI-32 model conductometer. The magnetic susceptibilities were measured using a Sherwood Scientific Ltd. Magnetic susceptibility balance (England).

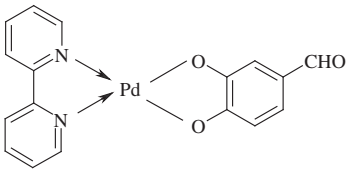

Fig. 1. LPd(II)L′, (L = 2,2′-dipyridyl, L′ = 4-formylbenzene-1,2-bis(olate)).

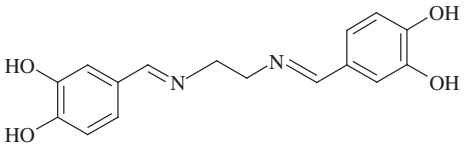

Fig. 2. N,N′-bis(3,4-dihydroxybenzylidene)ethan-1,2-diamine (EDH_4).

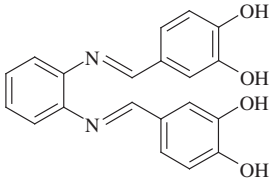

Fig. 3. N,N′-bis(3,4-dihydroxybenzylidene)benzene-1,2-diamine (PDH_4).

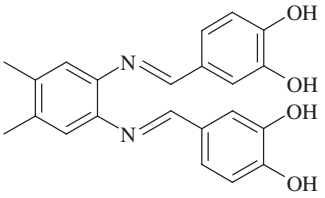

Fig. 4. N,N′-bis(3,4-dihydroxybenzylidene)-4,5-dimethyl-1,2-diamine ($MPDH_4$).

Preparation methods

Method 1

Synthesis of Schiff bases EDH_4, PDH_4, and $MPDH_4$, General Procedure: to a solution of 0.362 mmol diamine in a minimum amount of absolute ethanol (en, o-PD) or methanol (DMPD) containing 2 drops of piperidine, an ethanolic solution of 0.724 mmol 3,4-dihydroxybenzaldehyde was added. Precipitation took place immediately giving yellow, brown, and orange-yellow products, respectively. The mixtures were heated under reflux with continuous stirring for 1.5 h to allow for complete precipitation. The products were filtered, washed with ethanol, methanol, ether, and vacuum dried.

Synthesis of bi-nuclear (C^1, C^2) and tetra-nuclear (C^3) palladium bis(dipyridyl) Schiff base complexes. Di-nuclear palladium complexes C^1 and C^2 were prepared as follows: to a stirred ethanolic solution of Schiff bases (0.166 mmol EDH_4 and 0.143 mmol PDH_4) Pd(II) chloride (59%-Merck) (0.333 and 0.286 mmol, respectively), 2,2′-dipyridyl (0.333 and 0.287 mmol, respectively), and triethylamine (Et_3N) (0.665 and 0.574 mmol, respectively) were added in a minimum amount of ethanol. Precipitation took place immediately. Reflux was continued for 6 h with continuous stirring. The products were filtered off, washed with ethanol, and vacuum dried. C^3 was prepared by treating an ethanolic solution of 0.132 mmol $MPDH_4$ with a solution mixture of excess 0.586 mmol Pd(II) chloride (59%-Merck), 0.265 mmol 2,2′-dipyridyl, and 0.531 mmol Et_3N in ethanol. The mixture was heated under reflux for 6 h. A brown precipitate was formed. The product was filtered off, washed several times with hot ethanol, and vacuum dried.

Synthesis of a tri- nuclear palladium bis(dipyridyl) Schiff base complex (C^4). To an ethanol solution of 0.06 mmol C^1, 0.06 mmol Pd(II) chloride (59%-Merck) dissolved in a minimum amount of ethanol was added with continuous stirring for 2.5 h during which the color of solution changed to dark brown. The mixture was heated