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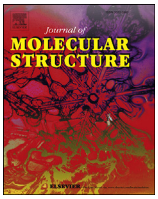

Coordination behavior of 3-amino-5,5′-dimethylhydantoin towards Ni(II) and Zn(II) ions: Synthesis, spectral characterization and DFT calculations

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ABSTRACT

The interaction of 3-amino-5,5′-dimethylhydantoin with nickel and zinc ions was investigated at different conditions by means of UV–Vis, FTIR spectroscopy and electrochemical methods as well as DFT quantum chemical calculations. Through calculated DFT frequencies and experimental FTIR spectra of the complexes the correlation analysis has been made. NBO analysis of the ligand and complexes provides the information about intramolecular resonance stabilization energy and charge transfer between ligand and metal ions. First derivative UV–Vis spectra were done in order to resolve the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ carbonyl electron transitions of the ligand and complexes. We have shown that complexes with 1:2 stoichiometry were formed at pH closed to physiological. The stability constant was determined for 3-amino-5,5′-dimethylhydantoin (***L***) and Ni(II) ions using differential pulse polarography data. The existence of one complex ($\bar{n} = 2$) is proved in the presence of high ligand concentration ($C_L = 2 \times 10^{-3} \div 6 \times 10^{-3}\ \mathrm{mol\ L^{-1}}$) and the values of the total constant is: $\lg\beta_{\mathrm{NI(II)-L}} = 9.5 \pm 0.4$ ($I = 0.1$). The UV–Vis spectroscopy and DFT calculations confirm the stoichiometry of the complexes. The results of the study are useful for incorporation with chemical equilibrium models for evaluation of the speciation and the reactions of metals with hydantoin derivatives in order to develop methods for determination of these metals in different milieu.

1. Introduction

Biometals as copper, zinc, iron, nickel and manganese are essential for the normal functioning of most plants and animals [1,2]. They are important for the function of many proteins present in living organisms, such as metalloproteins and enzymes that require metal ions as cofactors [2]. Processes including oxygen transport and DNA replication are carried out using enzymes such as DNA polymerase, which in humans requires magnesium and zinc to function properly [3]. It has been proved that nickel and cobalt play a direct role in nutritional phenomenon. When nickel is bound to ribonucleic acid plays an important role in skin pigmentation and has special affinity for bone and skin [4]. It has been reported that normal human plasma contains 0.012–0.085 $\mu g\ mL^{-1}$ of nickel (II) [5]. As can be seen, metal ions exhibit their biological activity after binding to a ligand. It has been established that the nature of the metal ion, the type of the ligand and the topology of the complex moiety are determinantal for the pharmacological efficacy and medicinal relevance of the metal complexes [6]. Such interaction and investigation of transition-metal ions with hydantoin derivatives is of immense biological importance [7]. It has been reported [8] that metal complexes of hydantoin derivatives Schiff bases with transition metals possess antitumor activity. For example, in contrast to free ligands silver complexes with hydantoins are strong cytotoxic agents [8].

Numerous applications have been found for hydantoin derivatives due to their antidepressant [9] and antiviral activities [10], the inhibition of HIV binding to lymphocytes [11], as well as their anti-convulsant and cardiac anti-arrhythmic effects [12]. Hydantoins are structural a fruitful area for investigation since they possess equal number of H-atom donors and acceptors and thus render rich variety of intermolecular bonding, as well as different

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modes for coordination to metal ions. Because complexes of the transition metal become more bacteriostatic and carcinostatic upon chelation of five-membered heterocyclic ligands containing two or more nitrogen, e.g. hydantoins, have sparked a great deal of interest. It is well established that the type of the substituents at 5th position in the hydantoin ring is of crucial importance for the pharmacological action of the corresponding compounds [8]. The structural characteristics of hydantoins and their metal complexes are attractive in view of the development of novel drugs [13] and for better understanding the structure-activity relationship. Great attention has been paid on synthesis, physicochemical properties and cytotoxic activity of Cu(II)-, Co(II)-, *cis*-Pt (II)- and Zn(II)-complex formation with hydantoin ligands. Quantum chemical and spectroscopic studies indicated a *cis*-square planar structure with a hydantoin ligand coordinated via the NH group [8,14–18].

Density Functional Theory (DFT) has become widely used to study the electronic structure and related properties of transition metal complexes. Calculation of metal complexes involving not only simple light elements but also several heavy atoms. Basically, there are two methods for obtaining highly accurate exchange-correlation functionals taking into account the occupation of orbitals: VSXC, containing 21 parameters, and the famous B3LYP. The first involve more parameters into the functionals and optimize the parameters referring to more experimental data, the second is to design more accurate forms of E_{xc} without catering to experimental data and fix their parameters by fitting more potential factors, exactly like PBE and TPSS [19,20]. Many works have used unrestricted open shell wavefunction using B3LYP exchange-correlation functionals (UB3LYP) with high accuracy [21–24]. S.F. Tayyari et al. have evaluated the capability of UB3LYP exchange-correlation functionals with different polarization and diffuse functions (6-31 + G, 6-31 + G* and 6-31 + G**) to study the several transition metal complexes. They have found that DFT calculations with these basis sets have good fit to the experimental data [21–24]. The increasing awareness of transition metal compounds by the developers of new exchange–correlation functionals should lead in the medium term to more accurate and more useful functionals.

The literature survey reveals that no systematic study of complexes of transition metal ions with biologically active aminohydantoin has been reported. There are several literature reports devoted to the preparation of aminohydantoin “complexes” with copper and cobalt [18,25–27]. Although the high biological and medical impact of Ni and Zn and hydantoin compounds as well as the intensive research on Ni(II) and Zn(II) compounds or on hydantoin complexes [28,29], quantitative data about Ni(II) and Zn(II) 3-amino-5,5′-dimethylhydantoin systems have not been published so far.

In this work, we have investigated the synthesis conditions, structure and spectral properties of the Zn(II) and Ni(II) 3-amino-5,5′-dimethylhydantoin complexes by voltamperometric, spectroscopic methods and DFT quantum chemical calculations using B3LYP exchange-correlation functionals (UB3LYP) combined with the 6-31 + G (d,p) polarization and diffuse functions. The calculated vibrational bands were compared to the experimental FTIR spectra in order to spectra-structure correlation analysis. First derivative UV–Vis spectra were used to resolve the $\pi\to\pi^*$ and $n\to\pi^*$ carbonyl electron transitions of the ligand and complexes. The method of continuous variations (MCV or the method of Job) to UV–Vis spectra were used in order to prove the complexes stoichiometry [30]. Application of electrochemical techniques was due to their advancement over other techniques in the field of investigation of complex formation owing to their possibility to identify type of complexes, their stoichiometry, specificity and easy and fast detection of the synthesis conditions. The voltammetric calculation of ligand number of the complex and it formation constant was done using the equations of De Ford and Hume, as well as these of Leden to DPP data. The proposed structure of cited complexes of Ni(II) and Zn(II) ions with aminohydantoin ligand could be essential in regard to the hidden pathways by which such compounds exert their biochemical properties.

2. Experimental

2.1. Used materials

All chemicals were of analytical-reagent grade, and deionized water was used throughout. The $NiCl_2\cdot6H_2O$ and $Zn(NO_3)_2\cdot6H_2O$ were obtained from Valerus Ltd (BG) and Merck. The solvents were supplied from local supplier Valerus Ltd and Sigma Aldrich. The starting aminohydantoin ligand ***L*** (3-amino-5,5′-dimethylimidazolidine-2,4-dione) was synthesized from 5,5′-dimetylhydantoin by means of $NH_2NH_2\cdot H_2O$ according to our previous work [31]. Melting points (Mp) were determined on Koffler microscope and were uncorrected (Mp of the ligand: 149–152 °C; Mp of the complexes > 300 °C). The Elemental analyses (C, H, and N) were performed by standard micro-methods using the EuroEA Elemental Analyser.

2.2. Synthesis of the complexes

2.2.1. Synthesis of the complex **1** $[NiL_2(NH_3)_2]\cdot2H_2O$

Ni(II) complex of 3-amino-5,5′-dimethylhydantoin at pH = 8.2 was obtained from solution of 1.00 mmol ligand (0.1430 g) in ammonia buffer solution (0.1 mol L^{-1}) and corresponding 0.5 mmol metal chloride ($NiCl_2\cdot6H_2O$; 0.1188 g) mixed in metal-to-ligand ratio = 1:2. The blue-green complex was obtained as precipitate, which was further filtrated, repeatedly washed with methanol and dried over $CaCl_2$ for two weeks. The compound is stable at room temperature and soluble in ethanol and water (1: 2). *Yield: 68%.* Anal. calc. for $[NiL_2(NH_3)_2]\cdot2H_2O$ (MW = 426.12 g mol^{-1}): 19.72% (N); 36.64% (C); 7.33% (H). Found: 18.92% (N); 36.12% (C); 6.89% (H).

2.2.2. Synthesis of the complex **2** $[ZnL_2].2H_2O$

The complex $[ZnL_2].2H_2O$ was prepared as follows: 0.5 mmol (0.1372 g) of $Zn(NO_3)_2\cdot6H_2O$ dissolved in 10 mL water solution of KNO_3 (0.1 mol L^{-1}) was added drop by drop to 1.00 mmol (0,14320 g) of the aminohydantoin dissolved in a mixture of 10 mL of the same solvent and 5 µL of solution of NaOH (0.01 mol L^{-1}). The resulting solution (pH = 8.30 ± 0.01) was placed in a vacuum desiccator over anhydrous $CaCl_2$ at room temperature. Within one week, white precipitate was formed from the solution. *Yield: 61%.* Anal. calc. for $[ZnL_2].2H_2O$ (MW = 401.24 g mol^{-1}): 20.42% (N); 32.08% (C); 6.22% (H). Found: 20.84% (N); 32.79% (C); 6.28% (H).

The synthesis of complexes are presented on Scheme 1.

2.3. Electrochemical measurement

2.3.1. Solutions

A 0.1 mol L^{-1} ammonia buffer solution (pH = 8.23 ± 0.01) and alkaline solution of 0.1 mol L^{-1} KNO_3 (pH = 8.30 ± 0.01) were used as supporting electrolytes. The stock solutions of Ni(II) (0.01704 mol L^{-1}), Zn(II) (0.01210 mol L^{-1}) and 3-amino-5,5′-dimethylhydantoin (0.1731 mol L^{-1}) were prepared by dissolution of $NiCl_2\cdot6H_2O$, $Zn(NO_3)_2\cdot6H_2O$ and the aminohydantoin in deionized water, respectively.

2.3.2. Procedure

Cyclic voltamperometry (CV): A 10 mL volume of supporting