SPECTROSCOPIC AND VOLTAMPEROMETRIC STUDIES OF Cu(II) COMPLEX WITH 3-AMINO-5,5-DIPHENYLHYDANTOIN

Stela Georgieva¹, Petar Todorov²

¹ Department of Analytical Chemistry
² Department of Organic Chemistry
University of Chemical Technology and Metallurgy
8 Kliment Ohridski, Sofia 1756, Bulgaria
E-mail: st.georgieva@uctm.edu

ABSTRACT

New copper(II)-aminohydrantoin complexes ([CuAPh₂Cl₂(OH)₂], [CuAPh₂(NH)₂(OH)₂], where APh is 3-amino-5,5-diphenylhydantoin), were synthesized and analyzed by means of elemental analysis, atomic absorption spectroscopy, UV-Vis spectroscopy and voltamperometric method. The complex forming processes in the Cu(II)-aminophenytoin (APh) system are studied by differential pulse polarography (DPP). The experiments are carried out at temperature of 20±1°C in ammonia buffer solution (pH = 8.2±0.1) at ionic strength I = 0.1. The reversibility of the reduction of the peak is proved and the equations of De Ford and Hume and these of Leden to DPP data are applied. The mean ligand number \( \bar{n} \) of the complexes formed is found from the slopes of the straight lines \( \Delta E'_p = f(\log C_{APh}) \) function. The existence of two complexes (\( \bar{n} = 1 \) and 2) is proved in the presence of high ligand concentration \( (C_{APh} = 2.10^{-4} - 3.10^{-3} \text{ mol l}^{-1}) \) and the values of its conditional and total stability constants are found. It was found that the values of the total constants are \( \lg \beta_{CuAPh} = 8.0 \), \( \lg \beta_{2CuAPh} = 10.9 \) (I = 0.1). A satisfactory good coincidence between the results obtained by the procedure proposed and the literature data is observed. The atomic absorption spectroscopy and elemental analysis confirm the compounds stoichiometry. The IR and UV/Vis spectra show that APh act as bidentate ligands with the coordination involving the carbonyl oxygen and the nitrogen atom of amino group.

Keywords: voltamperometry, hydantoin, Cu(II) complexes, UV-Vis spectroscopy, stability constants.

INTRODUCTION

The synthesis of new complexes of transit metal with organic ligands and estimation of stability (binding) constants of their complexes is of interest in many areas of chemistry. Quantitative data for acid-base, metal-ligand or enzyme-substrate equilibrium are invaluable for analytical chemistry, industrial chemistry, biochemistry, etc. Abbas Pezeshk et al., 1991, [1] reported that most of the labile copper in human plasma is loosely bound to albumin and the metal can bind to amino acids and possibly to other chelating agents. In recent last years Cu(II) hydantoin complexes have received much attention because of they proved to be useful as antitumor and anticonvulsant agents [2, 3]. The significant physiological activity (mainly hypnotic and anticonvulsant action) of different hydantoin derivatives is also well documented [4 - 12]. Hydantoin (1) contains several donor atoms and exhibits excellent coordination properties [13 - 15]. Great attention has been paid to cycloalkane-5-spirohydantoins after discovering their ability to inhibit aldose-reductase (the enzyme responsible for glucose conversion to sorbitol) and their application as therapeutic agents against diabetes [16]. It is also shown that the complexes of cyclopentane- and cyclohexane-5-spirohydantoins with cw-Pt(NH₃)₂Cl₂ are exhibiting cytostatic activity against leucemias L1210 and P388 [17 - 19]. Furthermore, the complexes as [Cu(H₂O)(Hyd)₂Cl] and [Co(H₂O)(Hyd)₃Cl₂NH₃₅H₂O (Hyd = 3-amino-5,5-dimethylhydantoin) have been demonstrated cytotoxic activity against human malignant cell lines [3]. The X-ray data proved unequivocally that...
the coordination to Cu(II) is realized via the endocyclic nitrogen atom [2, 17]. Taking into account all these data, in this paper synthesis of Cu(II) complexes with new biological active 3-amino-5,5-diphenylhydantoin (Fig. 1) and voltammetric and spectroscopic study on its structure were performed as far Cu(II) is very important biometal. The 3-amino-5,5-diphenylhydantoin was synthesized from benzyl followed by a benzilic acid rearrangement to 5,5-diphenylhydantoin. After that 5,5-diphenylhydantoin were transformed into 3-amino-5,5-diphenylhydantoin by means of NH₂NH₂.H₂O [20]. The new organic ligand has been fully characterized and the data proving the structure are given in [20].

EXPERIMENTAL

General remarks

All reagents and solvents were analytical grade. The infrared (IR) spectra were recorded in KBr pellets with a Varian 660-IR Series FTIR instrument. Atomic absorption measurements were performed with an atomic absorption spectrometer (Perken Elmer 5000) at λ = 320 nm. Double-beam Spectrophotometer Cary (Varian) was used to record the UV-Vis spectra of the compounds using 1 cm path length quartz cells. The first derivative of the electronic spectra were performed by Savitsky-Golay with polynomials derivation of convolution coefficients 2. Elemental analyses (C, H, and N) were performed by standard micro-methods using the EuroEA Elemental Analyser.

Voltamperometric determination

Apparatus and solutions

The voltamperometric analyses were carried out with the 646 VA Processor and the 647 VA Stand from Metrohm (Switzerland). A static mercury drop as working electrode, Ag/AgCl reference electrode and a carbon auxiliary electrode were used. The potentiometric measurements were performed with pH-meter (Jenwey, England) using a glass pH electrode. The stock solutions of Cu(II) (0.01574 mol l⁻¹) were prepared by dissolution of Cu(NO₃)₂ in water. The stock water solution of aminophenytoin (0.04690 mol l⁻¹) was prepared from aminophenytoin. An ammonia buffer solution (0.1 mol l⁻¹; pH = 8.2 ± 0.1) was used as supporting electrolytes.

Procedure

10 ml of ammonia buffer solution (0.1 mol l⁻¹; pH = 8.2 ± 0.1) and 10 μl of copper working solution were introduced in the electrochemical cell. Oxygen was removed by bubbling of pure nitrogen through the solution for 10 minutes. The cathodic peak of Cu(II) was registered by DPP at an amplitude of 50 mV; a scan rate of the potential – 0.2 V s⁻¹ (U.Step = 6 mV, T.Step = 0.6 s) was chosen. The current and potential of the peak were measured. Volumes of 5 μl to 100 μl of the aminophenytoin solution were successfully introduced in the cell. After each aminophenytoin volume added the solution was purged with nitrogen for 5 minutes. The analytical signal was registered and the peak potential and the current were measured.

General procedures for the synthesis of the complexes

Synthesis of the complex 1 [CuL₂Cl₂(OH)₂]

The complex [CuL₂Cl₂(OH)₂] in methanol was prepared as follows: 0.5 mmol (0.08524 g) of CuCl₂.6H₂O (Merck, 99.5 %) dissolved in 10 ml methanol was added drop by drop to 1 mmol (0.2650 g) of the aminophenytoin dissolved in a mixture of 10 ml of the same solvent and 50 µl of methanol solution of NaOH (0.1 mol l⁻¹). The resulting solution (pH = 8.30) was placed in a vacuum desiccator over anhydrous CaCl₂ at room temperature. Within one week, green precipitate was formed from the solution. Yield: 61 %. Anal. calc. for [CuL₂Cl₂(OH)₂] (Mᵣ = 671.04 g/mol): 12.52 % (N); 53.70 % (C); 4.21% (H). Found: 11.43 % (N); 47.79 % (C); 4.11 % (H).

Synthesis of the complex 2 [CuL₂(NH)₂(OH)₂]

Cu(II) complex of 3-amino-5,5-diphenylhydantoin at pH 8.2 was obtained from solution of the ligand (1.0998 g) in ammonia buffer solution (0.1 mol l⁻¹) and corresponding metal chloride (0.5499 g) mixed in metal-to-ligand ratio
1:2. The blue complex was obtained as crystal precipitate, which was further filtrated, repeatedly washed with methanol and dried over CaCl₂ for two weeks. The crystals are stable at room temperature and soluble in alcohol and water. All chemicals were analytical grade reagents. Yield: 73%. Anal. calc. for [CuL₂(NO₃)₂(OH₂)]₂ (M_r = 634.20 g/mol): 17.67 % (N); 56.82 % (C); 5.40 % (H). Found: 16.32 % (N); 54.12 % (C); 5.29 % (H).

RESULTS AND DISCUSSION

The ligand 3-amino-5,5-diphenylhydantoin was prepared as described previously [20]. This ligand was used for preparation of two complexes. Deprotonation of the ligand is facilitated by the appropriate pH of reaction medium as a result of the presence of solutions of NaOH and ammonia buffer solution. Conditions for the synthesis of complex compounds are found by carrying out of pre-voltamperometric and spectrometric analyses in solution. Isolated in pure form complexes using the procedures given in 2.3 are characterized by IR spectrometry, elemental analysis and atomic absorption spectroscopy.

Voltammetric study

The experiments were carried out at 20°C in an ammonia buffer solution (pH = 8.2 ± 0.1) and an ionic strength I = 0.1. The copper concentration in the cell was 1.574.10⁻⁵ mol l⁻¹ and the aminophenytoin concentration was varied from 2.10⁻⁴ to 3.10⁻³ mol l⁻¹. In all ligand concentrations studied a single cathodic copper peak is observed. Its symmetrical form, the half-width W₁/₂ and the current i_p in the absence of ligand, do not change when ligand is added to the solution. The potential E_p is changed, only. The aminophenytoin concentration shifts E_p of the single copper peak to more negative potentials and the system Cu(II) - APh is classified by us as fully labile on the d. p. polarographic time scale [21].

The peak is symmetrical and the width of its left half at ½ of the peak highness is about 60 mV (Fig. 2). This value is very close to the theoretical one [22] and the reduction of Cu (II) is reversible (E_p = E'_p). The shape of the copper peak, its width and the peak current values do not change significantly in the presence of APh. Only a shift of the peak potential in a negative direction with an increase of the ligand concentration was observed. The lability of the chemical reactions and the reversibility of the electrode reaction give us the reason to apply the equations of De Ford and Hume, as well as these of Leden, to calculate formation constants. The semilogarithmic function of ΔE_p^r from lgC_APh is given in Fig. 3. Approximately two linear sections are observed, that indicates the formation of at least two complexes. The mean ligand number 〈n〉 of obtained complexes and the formal constants are found from the
slopes and intercept of the straight lines [22] and their values are given in Table 1.

The two sections were investigated by Leden’s functions and the results of the regression analysis are presented in Table 2 and Fig. 4. Reliable results for the formation constant of the CuAPh complex are obtained in the lower concentration range of the ligand, where the complex CuAPh predominated. By the same reason, the constant of CuAPh₂ complex is calculated from the F₀ function, applied at the higher ligand concentrations. The same results for β₁ and β₂ were obtained by the regression analysis of the F₁-function: \(F₁ = β₁ + β₂C_{HA}\). The ligand (3-amino-5,5-diphenylhydantoin (APh)) and copper(II) ions participate in side reactions with the ions of the solution. The copper(II) ions form a complex with NH₃ ions (lgβ₁ = 3.99; lgβ₂ = 7.33 [23]); APh is a weak base and it is protonated. According to the data given in the literature the values of pKa constants of structurally related species like phenytoin, thymine, 5-benzylideneimidazolidine-2,4-dione and 5-(4-methoxy benzylidene)imidazolidine-2,4-dion are pKa = 8.31, pKa = 9.9, pKa = 9.7 and pKa = 10.1, respectively [24, 25]. The total constants βᵢ of the obtained complexes (j = 1; 2) are calculated by the

<table>
<thead>
<tr>
<th>Studied system</th>
<th>Data from linear sections</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total concentration of APh, mol l⁻¹</td>
</tr>
<tr>
<td>Cu(II)-APh</td>
<td>2.10⁻⁴÷ 8.10⁻⁴</td>
</tr>
<tr>
<td></td>
<td>8.10⁻⁴÷ 3.10⁻³</td>
</tr>
</tbody>
</table>

Table 1. The means ligand number and values of formal stability constant calculated by De Ford and Hume function ( = f (-lgCAPh)).
equation:
\[ \lg \beta_j = \lg \beta_j^0 + \alpha \log \alpha_{Cu(NH_3)} + j \log \alpha_{APh(H)} \]
where \( \alpha \) denote the side reaction coefficients:
\[ \alpha_{APh(H)} = 1 + 10^{6.1} C_{NH_3}^{2} \]
and \( \alpha_{Cu(NH_3)} = 3.6 \) [26]. The values of \( \alpha \)-coefficients calculated and \( \beta_j \)-values, determined
by us, as well as the literature data about \( \beta \), are given in Table 3. A good coincidence between obtained results and these for copper(II) complex with similar organic structure compounds (3-amino-5,5-dimethylphenytoin) given in the literature is observed.

**Table 2. Results from the regression analysis of the \( F_0 \) and \( F_1 \)-function:**

<table>
<thead>
<tr>
<th>Studied system</th>
<th>Total concentration of APh ( \text{mol L}^{-1} )</th>
<th>Number of experiments</th>
<th>Correlation coefficient</th>
<th>Regression equation</th>
<th>Formal formation constants</th>
</tr>
</thead>
<tbody>
<tr>
<td>( Cu(II)-APh )</td>
<td>( 2.10^{4} \div 3.10^{3} )</td>
<td>8</td>
<td>0.971</td>
<td>( F_0 = 0.8 + 9.3 \times 10^4 C_{APh} + 1.2 \times 10^7 C_{APh}^2 )</td>
<td>( \lg \beta_j^0 = 4.0 \pm 0.2 )</td>
</tr>
<tr>
<td></td>
<td>( 8.10^{4} \div 3.10^{3} )</td>
<td>5</td>
<td>0.911</td>
<td>( F_1 = 1.5 \times 10^4 + 1.1 \times 10^7 C_{APh} )</td>
<td>( \lg \beta_j = 7.0 \pm 0.3 )</td>
</tr>
</tbody>
</table>

**Table 3.** The values of \( \alpha \)-coefficients calculated and stability constants found at \( I = 0.1 \).

<table>
<thead>
<tr>
<th>Complex</th>
<th>( \alpha )-coefficients calculated</th>
<th>Formation constants</th>
<th>Literature data for ( Cu \ (II) – 5,5 )-dimethylhydantoin [25]</th>
</tr>
</thead>
<tbody>
<tr>
<td>( CuAPh )</td>
<td>0.359</td>
<td>3.6 [26]</td>
<td>( F_0 = 1 \div 10^{4} \times 10^4 C_{APh} + 3 \times 10^6 C_{APh}^2 )</td>
</tr>
<tr>
<td>( CuAPh_2 )</td>
<td>0.359</td>
<td>3.6 [26]</td>
<td>( F_1 = 10^4 + 1.1 \times 10^7 C_{APh} )</td>
</tr>
</tbody>
</table>

**Fig. 4.** Regression analysis of the \( F_0 \) and \( F_1 \)-function: \( F_0 = 1 + \beta_j C_L + \beta_j^0 C_{L}^2 \); \( F_1 = \beta_j^1 + \beta_j^2 C_{HA} \).
The UV-Vis spectra of the Cu(II)-APh and of the free ligand in ammonia buffer solution (pH = 8.2±0.1) were recorded in the range from 200 to 900 nm (Fig. 5). The absorption spectra in the UV domain contain a wide band, centered at 220 nm for the complex and 257 nm for free ligand. As can be seen (Fig. 5), the two-absorption spectra are overlapped. For this reason, the differential spectrum has been dropped, with several peaks standing out (Fig. 6). The shift of n-π* characteristic band in the UV spectra, attributed to the C=O bond (262 nm for Cu(II)-APh, 277 nm for APh) is due to the involving of the non-bonding electron pairs of the oxygen in the metal-ligand bond formation. Furthermore, the spectra of the complex solutions in methanol and water are not differ.

**Atomic absorption spectroscopy**

The copper complexes theoretical concentrations have similar values with those of the synthesized complex, which demonstrates that complete reaction has taken place (Table 4).

**Table 4. Copper concentrations obtained by means of atomic spectroscopy.**

<table>
<thead>
<tr>
<th>Complexes</th>
<th>Copper complex concentration, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Synthesized</td>
</tr>
<tr>
<td>[CuL2Cl2(OH2)2]</td>
<td>9.04</td>
</tr>
<tr>
<td>[CuL2(NH3)2(OH2)2]</td>
<td>11.92</td>
</tr>
</tbody>
</table>

**IR spectra**

IR spectroscopy confirms the structure of the above mentioned compounds (Fig. 6). The comparative analysis of the IR-spectra of the free hydantoin ligands and the Cu(II) complexes (complex 1 and complex 2) revealed that energy of ν(C=O) and ν(C=O) vibrations are changed upon coordination (Fig. 6). The absorption band related to the stretching vibrations ν(C=O) is observed at 1735, 1719 and 1725 cm⁻¹, for the two complexes Cu(II)-aminohydantoin. The shift of the bands generated by ν(C=O) mode upon complexing means that they are involved in a coordination. The ν(C=O) and ν(C=O) vibrations in aminohydantoins and other hydantoins cause the absorption observed in the range 1783 - 1779 cm⁻¹ and 1740 - 1720 cm⁻¹, respectively. The low intensities of these bands in Cu(II) complexes are probably caused by the hydrogen bonds between the carbonyl oxygen and the atoms of the water molecules coordinated to the metal ion. In the spectra of the complexes the broad absorption in the frequency range 3495 - 2980 cm⁻¹ with a multiple structure of the bands is assigned to ν of both the (N–H) and the (C–H) stretching vibration.

**Fig. 5.** UV-Vis spectra of Cu(II)-APh (1) and the free ligand (2) in ammonia buffer solution.
The complexes Cu(II)-aminophenytoin bands at 3357 cm\(^{-1}\) can be related to \(\nu(O-H)\) vibration of coordinated water molecules. Additionally, the \(\delta(H_2O)\) peak at \(\approx 1598\) cm\(^{-1}\) for the complex of Cu(II)-aminophenytoin suggests the presence of a coordinated water molecule inside the coordination sphere.

**CONCLUSIONS**

Two new copper complexes in aquatic and methanol solutions were synthesized ([CuL\(_2\)Cl\(_2\)(OH\(_2\))\(_2\)] and [CuL\(_2\)(NH\(_3\))\(_2\)(OH\(_2\))\(_2\)]) and analyzed by means of: elemental and voltamperometric analysis, atomic absorption, IR and UV/Vis spectroscopies. Voltammetric analysis allowed establishing the stoichiometry of compounds and calculated of formal stability constants that are: \(\lg \beta' = 4.0\) and \(\lg \beta'' = 7.0\) for CuAPh and CuAPh\(_2\), respectively. Elemental analysis and atomic absorption spectroscopy results revealed the formation of the two mixed copper complexes at studied pH. The IR-spectra show that aminophenytoin act as bidentate ligands with coordination involving the carbonyl oxygen and the nitrogen atom of amino group. The obtained data allow us to propose the formulas for the studied metal complexes as shown in Fig. 7.

**REFERENCES**

3. S. Georgieva, P. Todorov, D. Wesselinova, Synthesis, characterization and cytotoxic activity of novel Cu (II) and Co (II) complexes with 3-amino-5, 5-di-


