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Synthesis and DNA Binding Studies of a Tetraazamacrocyclotetradecane Co(II) Complex

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A tetraazamacrocyclotetradecane cobalt(II) complex, CoL·$(ClO_4)_2$ (L = 5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazamacrocyclotetradecane) was synthesized and characterized by IR spectra and elemental analysis. The interaction of the CoL·$(ClO_4)_2$ with DNA were studied by cyclic voltammetry. In the presence of DNA, the reduction peak of CoL·$(ClO_4)_2$ shifted to more positive values and the peak current decreased significantly. The experimental results indicate that the complex could interact with DNA by intercalation binding.

Key Words: Tetraazamacrocycle, Cobalt(II) complex, Synthesis, DNA, Cyclic voltammetry, Intercalation.

INTRODUCTION

The nucleic acid is the important composition of the organisms. It plays an important role in biological growth, development and reproduction and other activity[1]. Study of the structure activity relationship and interaction mechanism between small molecules and biological macromolecules DNA have the important significance to the molecular recognition and the information transmission of biological systems at the molecular level[2-4]. Recently, design and synthesis of macrocyclic complexes and study of the interaction with DNA are one of the major subjects of coordination chemistry[5-8].

In this paper, the tetraazamacrocyclotetradecane transition metal complex, CoL·$(ClO_4)_2$ (L = 5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazamacrocyclotetradecane) was synthesized and characterized by IR spectra and elemental analysis. The interaction of the CoL·$(ClO_4)_2$ with Calf thymus DNA (CT-DNA) have been investigated by cyclic voltammetry.

EXPERIMENTAL

All reagents were of AR grade and used without further purification. IR spectra was record on a Nexus-870 spectrophotometer. Elemental analyses for C, H and N were performed on a Elementar Vario EL-III analyzer. Calf thymus DNA obtained

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from Huamei Chemical (China). Cyclic voltammetric measurements of CoL·$(ClO_4)_2$ was accomplished with LK2005 (Electro-chemical analyzer, Tianjin Lanlike Instrument Company, China). The three-electrode system was composed of a glassy carbon electrode(GCE) as working electrode, an electrode Ag/AgCl as the reference electrode and a platinum electrodes auxiliary electrode. All electrochemistry experiments were carried out at 25 ºC. Water was double distilled. All solutions were deoxygenated *via* purging with N_2 for 10 min prior to measurement.

Synthesis: The 5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazamacrocyclotetradecane (L)·$(ClO_4)_2$ was synthesized according to the literature[9]. To 20 mL methanol solution of L (1 mmol) were respectively added 20 mL H_2O solution of $Co(ClO_4)_2·6H_2O$ (1 mmol), then refluxed for 6 h and standing at room temperature for 0.5 h. The brownish yellow powdery solids was obtained separately. IR spectrum (KBr, cm^{-1}): 3470, 3260 ν(O-H, N-H); 2971, 1383 ν(C-H); 1274 ν(C-N); 1085, 623 ν(ClO_4^-). Elemental analysis (%): Calcd. (Found); C, 35.44 (35.36); H, 6.69 (6.54); N, 10.33 (10.26).

Electrochemical studies of the interaction between CoL·$(ClO_4)_2$ and CT-DNA: Different quantities of complex CoL·$(ClO_4)_2$ and the differential pulse voltammetry and cyclic voltammetry curves were recorded on a LK2005 electrochemical analyzer with the three-electrode system described above in water solution. Then different quantities of CT-DNA were added to the solution followed by recording the CV curves. The potential scanning range is from -2.25 to 2.0 V. The scanning rate is 0.3 V s^{-1}. The sample interval is 0.001 V and the quiet time is 2 s.

RESULTS AND DISCUSSION

Determination of the electrochemical analysis conditions

Effect of the complex concentration: Different concentrations of complex (0.005, 0.01, 0.02, 0.04 and 0.08 mmol/L) were used. Among them, scanning results show that 0.04 mmol/L is best choice for CoL·$(ClO_4)_2$ in cyclic voltammetric analysis.

Effect of pH: The relationship between the pH value and the variation of the peaks current (ΔI_{pa}) of $[CoL]^{2+}$ before and after adding DNA were studied in phosphate buffer(pH = 5-8). Consequently, about pH 7 was chosen for $[CoL]^{2+}$ as the best pH values of the reactions.

Effect of scanning rate: The relationship between I_{pa} and scanning rate was studied. I_{pa} of $[CoL]^{2+}$ was directly proportional to the square root of the scanning rate in the rang from 0.10 to 0.90 V s^{-1}, which indicates that the electrode process of the complex are controlled by the diffusion of $[CoL]^{2+}$ on the electrode surface. Therefore 0.3 V s^{-1} is suitable scanning rate for the electrode reactions of the $[CoL]^{2+}$.

Effect of supporting electrolyte: Before supporting electrolyte adding to the solution of $[CoL]^{2+}$, there were no any redox peak currents observed. After addition of three different supporting electrolyte, KCl, NH_4Cl and KNO_3 to the solution, respectively, clear redox peak currents appeared. According to the experiment results, better redox peak currents would achieved when use KNO_3 as the supporting electrolyte for the solution of $[CoL]^{2+}$ and the solution of $[CoL]^{2+}$ with DNA.

Electrochemical studies of the interaction between the complex and DNA: Typical cyclic-voltammetric behaviour of $[CoL]^{2+}$ for a solution without CT-DNA and in the presence of CT-DNA are shown in Figs. 1 and 2, respectively.

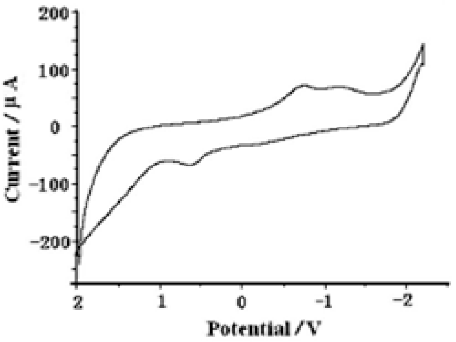

Fig. 1. CV of $CoL\cdot(ClO_4)_2$ in optimal condition

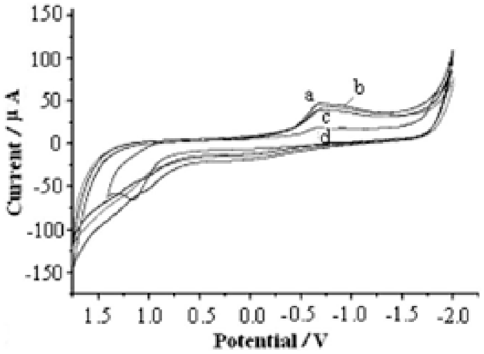

Fig. 2. CV of $CoL\cdot(ClO_4)_2$ with DNA

Fig. 1 shows the cyclic voltammetry curve of $CoL\cdot(ClO_4)_2$ at the optimal condition ($CoL\cdot(ClO_4)_2$ 0.04 mmol/L, phosphate buffer (pH 7), scanning rate 0.3 V s^{-1}, KNO_3 as the supporting electrolyte). In the absence of CT-DNA, there are one oxidation peak and one reduction peak. The Epc, Epa and ΔEp are -0.75, 0.64 and 1.39V, $E_{1/2}$ = (Epc + Epa)/2 is -55 mV. The oxidation peak current almost equal to that of reduction peak indicates that the electrochemical reactions are reversible.

Fig. 2 shows the cyclic voltammetry curves of $CoL\cdot(ClO_4)_2$ in the presence of CT-DNA (a: 0.2, b: 0.4, c: 0.6, d: 0.8 mmol/L) at the optimal condition described above and in an airtight container reaction for 2 h. When DNA was added into the solution, the oxidation peak disappeared and electrochemical reactions from reversible became irreversible. It can be seen that the currents were decreased with the increasing of DNA and the reduction peak potential shifted to more positive values *vs.* the cyclo-voltammetric curve of $CoL\cdot(ClO_4)_2$ without CT-DNA. According to Bard *et al.*[10,11], if the peak potential shifted to more positive value when small molecules interacted with DNA, the binding mode was the intercalation. This indicated that the synthesized tetraazamacrocyclotetradecane cobalt(II) complex could interact with DNA molecules by intercalative binding.

Conclusion

In summary, a tetraazamacrocyclotetradecane cobalt(II) complex, $CoL\cdot(ClO_4)_2$ was obtained and characterized by IR spectra and elemental analysis. The interaction of the complex with DNA were studied by cyclic voltammetry. The experimental results indicate that the macrocyclic Co(II) complex could interact with DNA mainly by intercalative binding mode.

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