



NOTE

Synthesis and DNA-Binding Properties of the Ni(II) Complex with Tetraazamacrocyclotetradecane

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A tetraazamacrocyclotetradecane complex of Ni(II) with composition $\text{NiL}(\text{ClO}_4)_2$ (L = 5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazamacrocyclotetradecane) was synthesized and characterized by elemental analysis and IR spectra. The reciprocities of the $\text{NiL}(\text{ClO}_4)_2$ with DNA were studied by cyclic voltammetry. In the presence of DNA, the redox peaks of $\text{NiL}(\text{ClO}_4)_2$ shifted to more negative values and the peak current decreased. The experimental results illustrate that the $\text{NiL}(\text{ClO}_4)_2$ could interact with DNA by electrostatic combining mode.

Key Words: Nickel(II) complex, Tetraazamacrocycle, Synthesis, DNA, Cyclic voltammetry, Electrostatic combining mode.

There has been increasing interest in the field of azamacrocyclic complexes interacting with DNA¹⁻³. Because the complex molecules can interact with DNA to prevent the growth of cancer cells and cause cancer cell death. Therefore, researching the mechanism of azamacrocyclic complexes acting on DNA, can open a new way for synthetic anticancer drugs⁴⁻⁶.

In this paper, the tetraazamacrocyclotetradecane complex, $\text{NiL}(\text{ClO}_4)_2$ (L = 5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazamacrocyclotetradecane) was synthesized and characterized by elemental analysis and IR spectra. The reciprocities of the $\text{NiL}(\text{ClO}_4)_2$ with DNA have been studied by cyclic voltammetry.

All the reagents were of AR grade and used without further purification. Elemental analyses for C, H and N were detected on a Elementar Vario EL-III analyzer. IR spectra was record on a Nexus-870 spectrophotometer. Cyclic voltammetric measurements of $\text{NiL}(\text{ClO}_4)_2$ was accomplished with LK2005 (Electrochemical 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 electrode as auxiliary electrode. Calf thymus DNA obtained from Huamei Chemical (China). All electrochemistry experiments were carried out at 25 °C. All solutions were deoxygenated *via* purging with N_2 for 10 min prior to measurement. Water used was double distilled.

Synthesis of $\text{NiL}(\text{ClO}_4)_2$: The 5,5,7,12,12,14-Hexamethyl-1,4,8,11-tetraazamacrocyclotetradecane (L)(ClO_4)₂ was synthesized according to the literature^{7,8}. To 20 mL methanol solution of the ligand (1 mmol) was added 20 mL aqueous solution of $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (1 mmol), then refluxed for 6 h and standing at room temperature for 0.5 h. The green powder solids was obtained separately. Yield 70.5 %. IR spectrum (KBr, ν_{max} , cm^{-1}): 3405, 3190 (O-H, N-H); 2973, 1448 (C-H); 1291(C-N); 1087, 624 (ClO_4^-). Elemental analysis (%): Calcd. (Found); C, 35.45 (35.50), H, 6.69 (6.28), N, 10.34 (10.47).

Electrochemical studies of the reciprocities of $\text{NiL}(\text{ClO}_4)_2$ with DNA: Different quantities of $\text{NiL}(\text{ClO}_4)_2$ and the differential pulse voltammetry and cyclic voltammetry curves were recorded on a LK2005 electrochemical analyzer in water solution. Then different quantities of DNA were added to the solution followed by recording the cyclic voltammetric curves. The potential scanning range is from -2.25 to 2.25 V. The sample interval is 0.001 V and the quiet time is 2 s.

Effect of the complex concentration: Different concentrations of the complex were used. Scanning results show that 0.04 mmol/L was best.

Effect of scanning rate: The relationship of I_{pa} and scanning rate was researched. Using different scanning rate (0.1 V/S, 0.3 V/S, 0.5 V/S, 0.7 V/S, 0.9 V/S) to observ the I_{pa} of $[\text{NiL}]^{2+}$ was directly proportional to the square root of the scanning rate, which shows that 0.5 V/S is suitable scanning rate for the electrode reactions.

Effect of supporting electrolyte: When three different supporting electrolyte (KCl, NH_4Cl and KNO_3) add to the aqueous solution, the experiment results indicate that clear redox peak currents appeared when use KNO_3 as the supporting electrolyte for the solution of $\text{NiL}(\text{ClO}_4)_2$ and the solution of $\text{NiL}(\text{ClO}_4)_2$ with DNA.

Effect of pH: The relationship of the pH values and the peaks current changes (ΔI_{pa}) of $[\text{NiL}]^{2+}$ before and after adding DNA were measured in phosphate buffer. Consequently, about 8 was chosen for $[\text{NiL}]^{2+}$ as the best pH values for the measurements.

Electrochemical reciprocities of $\text{NiL}(\text{ClO}_4)_2$ with DNA: Typical cyclic voltammetric behaviour of $[\text{NiL}]^{2+}$ for a solution without and presence of DNA are shown in Figs. 1 and 2, respectively.

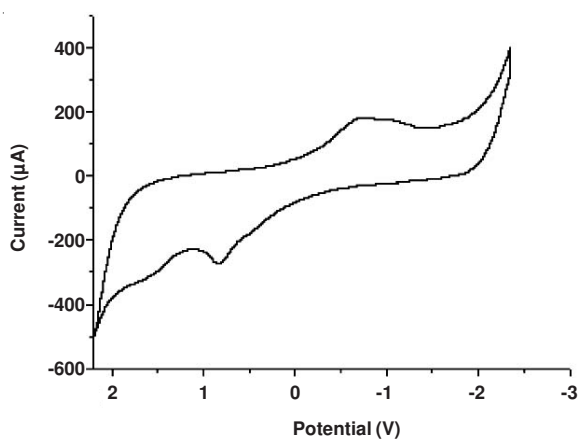


Fig. 1. CV of $\text{NiL}(\text{ClO}_4)_2$ in optimal condition

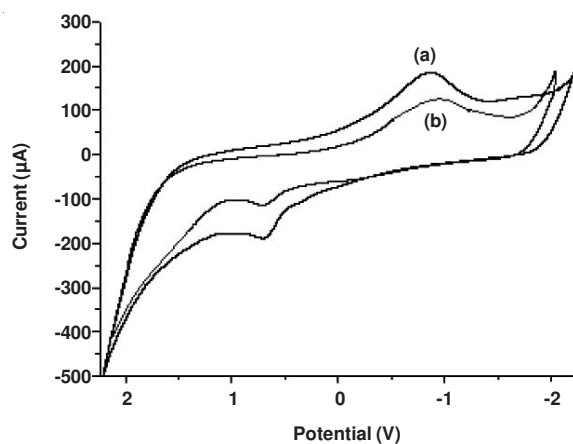


Fig. 2. CV of $\text{NiL}(\text{ClO}_4)_2$ with DNA

Fig. 1 shows the cyclic voltammogram curve of $\text{NiL}(\text{ClO}_4)_2$ at the first-rank condition: $\text{NiL}(\text{ClO}_4)_2$ 0.04 mmol/L, phosphate

buffer (pH \approx 8), scanning rate 0.5V/S, KNO_3 as the supporting electrolyte. In the absence of DNA, there are one oxidation peak and one reduction peak. The E_{pa} , E_{pc} and ΔE_{p} are 0.8395, -0.7543 and 1.5938 V, $E_{1/2} = (E_{\text{pc}} + E_{\text{pa}})/2$ is 42.6 mV. The little difference from oxidation peak current and reduction peak current indicates that the electro-chemical reaction is part reversible.

Fig. 2 shows the cyclic voltammogram curves of $\text{NiL}(\text{ClO}_4)_2$ in the presence of DNA (a: 0.4, b: 0.6 mmol/L) at the first-rank condition described above and in an airtight container reaction for 2 h. The E_{pa} , E_{pc} and ΔE_{p} (Fig. 2,a) are 0.682, -0.878 and 1.56 V. It can be seen that the redox peaks current of $[\text{NiL}]^{2+}$ was decreased and the redox peaks potential shifted to more negative values vs. a solution without DNA. This indicated that the macrocyclic nickel(II) complex could interact with DNA molecules. The currents was decreased with the increasing of DNA (Fig. 2,b) and the redox peaks potential shifted to more negative values. According to Bard *et al.*^{9,10} reported, if the peak potential shifted to more negative value when small molecules interacted with DNA, the binding pattern was the electrostatic combination. This indicated that the synthesized $\text{NiL}(\text{ClO}_4)_2$ could interact with DNA molecules by electrostatic combining mode.

Conclusion

In summary, a tetraazamacrocyclotetradecane complex, $\text{NiL}(\text{ClO}_4)_2$ was obtained and characterized by elemental analysis and IR spectra. The reciprocities of the complex with DNA were studied by cyclic voltammogram. The experimental results indicate that $\text{NiL}(\text{ClO}_4)_2$ could interact with DNA mainly by electrostatic combining mode.

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