



NOTE

Synthesis of Tetraazamacrocyclic Crown Ether Ni(II) Complex and Electrochemical Study of its Interaction with DNA

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A tetraazamacrocyclic crown ether complex of Ni(II) with the composition $[\text{NiL}](\text{ClO}_4)_2$ (L = 5,12-dimethyl-7,14-diphenyl-1,4,8,11-tetraazamacrocyclotetradecane) was synthesized and characterized by IR spectra and elemental analysis. The mutual effects of the $[\text{NiL}](\text{ClO}_4)_2$ with DNA were studied by electrochemical method. In the presence of DNA, the redox peaks of $[\text{NiL}](\text{ClO}_4)_2$ shifted to more positive values and the peak current increased greatly. The experimental results demonstrate that the $[\text{NiL}](\text{ClO}_4)_2$ could interact with DNA by intercalation binding mode.

Key Words: Tetraazamacrocyclic crown ether, Nickel(II) complex, Synthesis, DNA, Cyclic voltammetry, Intercalation.

Azamacrocyclic crown ether metal complexes have the function of cutting DNA and improving nucleic acid enzymatic activity, so that they can be used to treat cancer, *etc.*¹⁻³. Therefore, study of these compounds interaction with nucleic acid will help to develop the azamacrocyclic crown ether and their metal complexes in medical applications⁴⁻⁶.

In this paper, a tetraazamacrocyclic crown ether complex of Ni(II), *i.e.*, $[\text{NiL}](\text{ClO}_4)_2$ (L = 5,12-dimethyl-7,14-diphenyl-1,4,8,11-tetraazamacrocyclotetradecane) was synthesized and characterized by IR spectra and elemental analysis. The interaction of the $[\text{NiL}](\text{ClO}_4)_2$ with DNA were studied by cyclic voltammetry.

All reagents were of AR grade and used without further purification. The 5,12-dimethyl-7,14-diphenyl-1,4,8,11-tetraazamacrocyclotetradecane (L) was synthesized according to the literature^{7,8} and characterized by IR spectra and elemental analysis. $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ was prepared in our laboratory. IR spectra were record on a Nexus-870 spectrophotometer. Elemental analyses were performed on a Elementar Vario EL-III elemental analyzer.

Cyclic voltammetric measurements of $[\text{NiL}](\text{ClO}_4)_2$ was accomplished with LK2005 (Electrochemical Analyzer, Tianjin Lanlike Instrument Company, China) and CHI 660B (CHI Instrument, Shanghai, 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. All solutions were

deoxygenated *via* purging with Ar about 1 min prior for measurement. All experiments were carried out at 25 °C.

Synthesis of $[\text{NiL}](\text{ClO}_4)_2$: Take 10 mmol of L in 20 mL methanol, 10 mmol of $\text{Ni}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ in 20 mL water was added with stirring. After the yellowish-brown turbid solution formed, the yellow powder precipitated upon standing, then collected and air dried at room temperature. Yield 50 %. IR(KBr, ν_{max} , cm^{-1}): 3431 (N-H), 1087 (ClO_4^-), 767, 704 (Ar-H). Elemental anal. calcd.: C, 45.46; H, 5.09; N, 8.86 %; Found: C, 45.50; H, 4.96; N, 8.73 %.

Cyclic voltammetric measurements of $[\text{NiL}](\text{ClO}_4)_2$ interaction with DNA: Typical cyclic voltammetry behaviour of $[\text{NiL}]^{2+}$ without DNA and in the presence of DNA are shown in Figs. 1 and 2, respectively.

Fig. 1 shows the cyclic voltammetry curve of $[\text{NiL}](\text{ClO}_4)_2$ at the optimal condition: $[\text{NiL}](\text{ClO}_4)_2$ 5 mmol/L acetonitrile solution, scanning rate 0.2 V/S, tetrabutyl ammonium perchlorate (TBAP) as the supporting electrolyte. The potential scanning range is from -0.25 to 1.2 V. The sample interval is 0.001 V and the quiet time is 2 s. In the absence of DNA, there are one oxidation peak and one reduction peak. The E_{pa} , E_{pc} and ΔE_{p} are 0.375, 0.45 and 75 mV, $E_{1/2} = (E_{\text{pc}} + E_{\text{pa}})/2$ is 413 mV. The little difference from oxidation peak current and reduction peak current indicates that the electrochemical reaction is part reversible.

Fig. 2 shows the cyclic voltammetry curves of $[\text{NiL}](\text{ClO}_4)_2$ in the presence of DNA (0.3 g/L) at the optimal

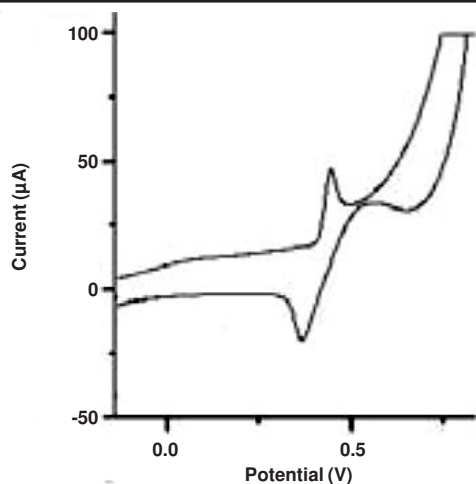


Fig. 1. CV of $[\text{NiL}](\text{ClO}_4)_2$ in optimal condition

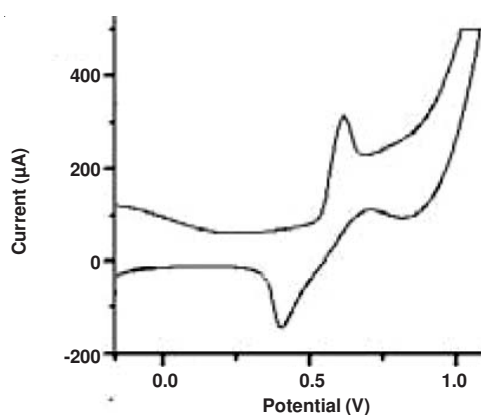


Fig. 2. CV of $[\text{NiL}](\text{ClO}_4)_2$ with DNA

condition described above. The E_{pa} , E_{pc} and ΔE_{p} are 0.417, 0.625 and 208 mV. It can be seen that the oxidation peak current of $[\text{NiL}]^{2+}$ were increased greatly and the redox peaks potential shifted to more positive values vs. a solution without DNA. This indicated that the tetrazamacrocyclic crown ether complex could interact with DNA molecules. According to Bard *et al.*⁹ reported, if the peak potential shifted to more positive value when small molecules interacted with DNA, the binding mode was the intercalation. The experimental results suggested that $[\text{NiL}](\text{ClO}_4)_2$ could interact with DNA mainly by intercalative binding, which afford useful information for further study on medical applications.

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