

N,N'-苄基-1,2 二胺合铜的合成和晶体结构及与 DNA 的相互作用

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关键词: 金属配合物; 晶体结构; 合成; 小牛胸腺 DNA

中图分类号: O614.121

文献标识码: A

文章编号: 1001-4861(2007)12-2119-04

Synthesis, Crystal Structure and Interaction with DNA of (*N,N'*-dibenzylethane-1,2-diamine) Copper(II)

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Abstract: A ligand, (*N,N'*-dibenzylethane-1,2-diamine) (L), and its complex with copper acetate was synthesized and characterized by some spectral analyses. The copper (II) ion is six-coordinated and exhibits octahedral coordination geometry, the coordination atoms are four nitrogen atoms from two (L) ligands and two carboxyl oxygen atoms from two acetic acid groups, respectively. After studying the interaction of the complex with calf thymus DNA through UV and fluorescence spectra, we can find that there is a strong binding and a large affinity between the complex and calf thymus DNA. CCDC: 649416.

Key words: metal complex; crystal structure; synthesis; calf thymus DNA

In the past few years, many researchers paid much attention to the molecular structure and biological activity of coordinated complexes in inorganic chemistry field. Cu(II) is one of the commonest transition metals with four or six coordination numbers^[1,2]. Its complex coordination mode depends on the structure of ligand, solvent and reaction conditions. The ligand plays a decisive role and determines not only the molecular structure of the complex but also the aggregation pattern of small molecule. These complexes are widely used in chemical biology, medicine and gene therapy *via*

DNA^[3-6]. Binding studies of small molecule with DNA are very important for the development of new therapeutic reagents and DNA probes. Here, we report the synthesis and crystal structure of (*N,N'*-dibenzylethane-1,2-diamine) Copper (II), X-ray diffraction structural analysis suggests that Cu(II) presents an octahedral coordination geometry. After studying the interaction of the complex with calf thymus DNA through UV and fluorescence spectra, we can find that there is a strong binding between the complex and calf thymus DNA, and the complex cause the slight change of the confor-

收稿日期:2007-07-23。收修改稿日期:2007-09-29。

国家自然科学基金(No.20361003)和国家 863 引导项目(No.2005AA001240)共同资助。

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mation of DNA.

1 Experimental

1.1 Materials and instruments

Chemicals obtained from commercial sources were of analytical grade and used without further purification. Melting point was determined with an XT4 Digital melting point apparatus. IR spectrum was recorded on a Burker T27 FTIR Spectrometer. ^1H NMR spectrum was taken on a Bruker AV400 spectrometer. Elementary analysis was performed on a Vario EL III elementary analysis instrument. A UV-2450 spectrometers (Shimadzu, Japan) and RF-540 spectrofluorometer (Shimadzu, Japan) were used for spectral analysis of the complex with DNA.

1.2 Complex synthesis

1,2-diaminoethane (10 mmol) was dissolved in 10 mL absolute methanol, followed by the addition of methanol solution (10 mL) of benzaldehyde (10 mmol). After continuous stirring for 2 h at room temperature, potassium borohydride (40 mmol) was added to the solution in several times, stirred and refluxed for 3 h at 60 $^{\circ}\text{C}$, a yellowish solution was obtained. After cooled, 50 mL distilled water was poured, then the turbid solution was extracted by 50 mL chloroform for three times. Organic phase was washed with water. After removing the solvent thoroughly, liquid residue appear, which eventually form white powder (*N,N'*-dibenzylethane-1,2-diamine). Yield: 72.5%. m.p.: 79.5~82 $^{\circ}\text{C}$. FAB-MS: m/z 241.3(MH^+ , $[\text{C}_{16}\text{H}_{21}\text{N}_2]^+$); Elemental analysis, Found(%): C, 79.56; H, 4.38; N, 16.05. Calculated for $\text{C}_{16}\text{H}_{20}\text{N}_2$ (%): C, 79.90; H, 4.17; N, 11.65.

Solution of $\text{Cu}(\text{Ac})_2 \cdot 5\text{H}_2\text{O}$ (0.2 mmol) in 10 mL methanol was added dropwise to a solution of *N,N'*-dibenzylethane-1,2-diamine (0.1 mmol) in 20 mL methanol, after stirring for 2 h at room temperature. Then the mixture was condensed, 10 mL blue clear concentrated solution was got with rotary evaporation, kept at ambient temperature, and then transparent crystals were obtained by slowly evaporating in 6 days. Yield: 87.3%. (Based on Cu); IR (KBr, cm^{-1}): 3 424, 3 354, 1 602.05, 1 421, 612.16. Elemental analysis, calculated for $\text{C}_{36}\text{H}_{50}\text{N}_4\text{O}_6\text{Cu}$ (%): C, 61.86; H, 7.16, N,

8.02; found(%): C, 61.45; H, 7.42, N, 8.36.

1.3 Solution preparation of DNA

Calf thymus DNA was obtained from Huamei Chemical Co.(Beijing), solutions of DNA in $5.00 \times 10^{-3} \text{ mol} \cdot \text{L}^{-1}$ Tris, $5.00 \times 10^{-2} \text{ mol} \cdot \text{L}^{-1}$ NaCl (pH=7.2) gave the ratio of UV absorbance at 260 and 280 nm, A_{260}/A_{280} of=1.9, indicating that the DNA ($C_{\text{DNA}}=9.45 \times 10^{-3} \text{ mol} \cdot \text{L}^{-1}$) was sufficiently free of protein^[7]. Stock solution were stored at 4C and used in no more than 4 days.

1.4 Crystal structure determination

Some crystals of complex suitable for X-ray diffraction crystal structure analysis were obtained from methanol. A crystal with the dimensions of 0.32 mm \times 0.22 mm \times 0.13 mm was selected for the X-ray diffraction experiment. Diffraction data were collected at 293 (2) K with a Siemens Smart CCD area detector diffractometer using Mo $K\alpha$ radiation ($\lambda=0.071\ 073$ nm) with an ω -scan mode. The structure was solved by direct methods with SHELXS-97 and refined by full-matrix least squares on F^2 with SHELXL-97. 35 125 reflections were collected, of which 8 492 unique ($R_{\text{int}}=0.071\ 4$). At convergence, $R_1=0.049\ 8$, $wR_2=0.107\ 7$ [$I \geq 2\sigma(I)$] and $R_1=0.077\ 6$, $wR_2=0.119\ 4$ (all data), for 462 parameters. In the final difference Fourier map the maximum and minimum residual electron density were 623 and $-365 \text{ e} \cdot \text{nm}^{-3}$ respectively. Crystallographic data: $\text{C}_{36}\text{H}_{50}\text{N}_4\text{O}_6\text{Cu}$; Orthorhombic, space group $P2_12_12_1$; $a=1.067\ 47(17)$ nm, $b=1.250\ 1(3)$ nm, $c=3.786\ 7(6)$ nm; $V=3.718\ 7(1) \text{ nm}^{-3}$, $Z=4$, $D_c=1.247 \text{ Mg} \cdot \text{m}^{-3}$, $\mu=0.634 \text{ mm}^{-1}$, $F(000)=1\ 484$.

CCDC: 649416.

2 Results and discussions

2.1 Crystal structure

The selected bond distances and bond angles are presented in Table 1. The coordination environment of Cu(II) is shown in Fig.1. Each copper(II) ion is six-coordinated with four nitrogen atoms from *N,N'*-dibenzylethane-1,2-diamine and two carboxyl oxygen atoms of two acetic acid groups. These nitrogen atoms belong to two same ligands, the carboxyl oxygen groups coordinate with Cu(II) ion in an unidentate mode and one of the acetic acid is disordered, because the coordinating

Table 1 Selected bond lengths (nm) and bond angle (°)

Cu(1)-N(4)	0.205 6(3)	Cu(1)-N(1)	0.207 0(3)	Cu(1)-N(3)	0.207 3(2)
Cu(1)-N(2)	0.208 1(3)	Cu(1)-O(3)	0.244(3)	Cu(1)-O(1)	0.246 2(2)
N(1)-C(8)	0.147 7(4)	N(1)-C(7)	0.148 1(4)	N(2)-C(9)	0.147 9(4)
N(3)-C(23)	0.147 2(4)	N(3)-C(24)	0.148 2(4)	N(2)-C(10)	0.148 9(4)
N(4)-C(25)	0.148 9(5)	N(4)-C(26)	0.145 0(4)		
N(1)-Cu(1)-N(2)	84.57(10)	N(3)-Cu(1)-N(2)	95.70(10)	N(4)-Cu(1)-N(3)	84.39(10)
N(4)-Cu(1)-N(1)	95.36(10)	N(4)-Cu(1)-O(1)	86.02(10)	N(3)-Cu(1)-O(1)	93.66(10)
N(4)-Cu(1)-O(3)	93.6(7)	N(3)-Cu(1)-O(3)	90.4(4)	N(1)-Cu(1)-O(1)	89.70(10)
N(2)-Cu(1)-O(1)	93.64(9)	N(1)-Cu(1)-O(3)	86.3(4)	N(2)-Cu(1)-O(3)	86.8(7)

Table 2 Parameters of hydrogen bonds for the Cu(II) complex

D-H...A	<i>d</i> (D-H) / nm	<i>d</i> (H...A) / nm	<i>d</i> (D...A) / nm	∠(DHA) / (°)
N(1)-H(1N)...O(4)	0.091	0.209	0.297(3)	160.9
N(1)-H(1N)...O(4')	0.091	0.207	0.292(3)	154.2
N(2)-H(2N)...O(6)	0.091	0.202	0.290 6(4)	165.9
N(3)-H(3N)...O(5)	0.091	0.217	0.3042(4)	161.3
N(4)-H(4N)...O(2)	0.091	0.196	0.281 2(4)	155.4
O(5)-H(5A)...O(3)	0.0816(10)	0.206(3)	0.285(2)	162(4)
O(5)-H(5A)...O(3')	0.081 6(10)	0.178(2)	0.258(2)	167(4)
O(5)-H(5B)...O(4)#1	0.082 3(10)	0.179(3)	0.261(3)	171(4)
O(5)-H(5B)...O(4')#1	0.082 3(10)	0.203(3)	0.285(2)	178(4)
O(6)-H(6A)...O(1)	0.082 3(10)	0.197(2)	0.2747(4)	156(4)
O(6)-H(6B)...O(2)#2	0.082 1(10)	0.204(3)	0.281 8(4)	158(7)

Symmetry transformations used to generate equivalent atoms: #1: $x+1/2, -y+1/2, -z+1$; #2: $-x+1, y+1/2, -z+3/2$.

capability of acetic acid is weaker than the carboxyl oxygen and O3, O4, C35 and C36 are 50% respectively in this crystal. Two free water molecules are not coordinated with the Cu ion. Cu(II), N(1), N(2), N(3) and N(4) are in the plane position and Cu-N distances are in the range of 0.205 6 nm to 0.208 1 nm. O(1)-Cu(1)-O(2) is vertical to the coordinate plane and the Cu-O distance is 0.247 4 nm. So the Cu(II) has an octahedral coordina-

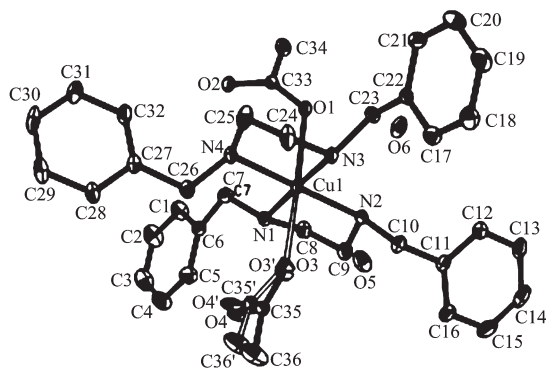


Fig.1 Molecular structure of the title complex

tion environment. The crystal-packing pattern of the complex is shown in Fig.2, in which the hydrogen-bond interactions can be seen. Hydrogen bonds are represented as dashed lines in Fig.2 and listed in Table 2.

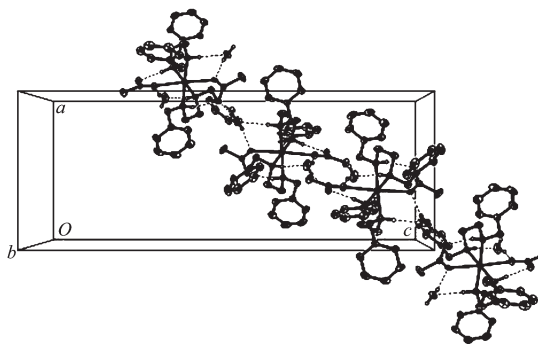
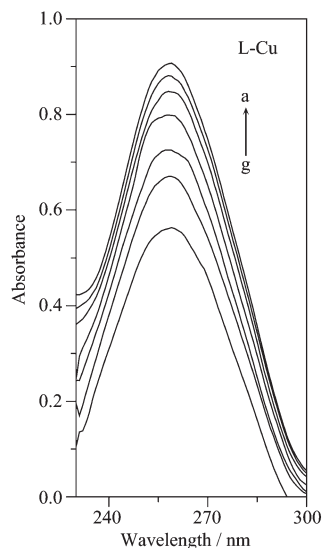


Fig.2 1D chain structure of the title complex

2.2 Electronic and fluorescence spectra

At room temperature, the absorption spectra of calf thymus DNA are scanned from 230 to 300 nm. The maximal absorption peak of DNA is at 260 nm, but the complex has no absorption at 200 to 300 nm. The emis-

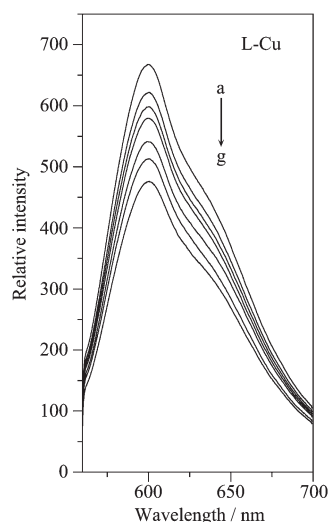
sion intensity of DNA solution increases with the concentration of the complex increasing. The phenomenon indicates that there is a strong binding and a large affinity between the complex and calf thymus DNA, this kind of binding may cause the slight change of the conformation of DNA^[8]. The results are shown in Fig.3.



a: DNA ($9.45 \times 10^{-3} \text{ mol} \cdot \text{L}^{-1}$), b: a+1.0 μL ($2.0 \times 10^{-3} \text{ mol} \cdot \text{L}^{-1}$) Cu-L, c: a+2.0 μL Cu-L, d: a+4.0 μL Cu-L, e: a+8.0 μL Cu-L, f: a+16.0 μL Cu-L; g: a+32.0 μL Cu-L

Fig.3 UV Absorbance spectra of the interaction the between Cu(II) complexes and DNA

Moreover, the mechanism of the interaction between the complex and DNA is also investigated by using ethidium bromide (EB) as a fluorescence probe. Fig. 4 displays the emission spectra of the EB-DNA system in the absence and presence of the complex. As the concentration of the complex increasing, the emission intensity of EB-DNA system decreases. This phenomenon indicates that the complex can not substitute for EB in the EB-DNA system which leads to a constant emission intensity for the EB-DNA system, but it causes the slight change of the conformation of DNA^[9].



a: DNA ($9.45 \times 10^{-3} \text{ mol} \cdot \text{L}^{-1}$), EB ($4.5 \times 10^{-3} \text{ mol} \cdot \text{L}^{-1}$), b: a+1.0 μL ($2.0 \times 10^{-3} \text{ mol} \cdot \text{L}^{-1}$) Cu-L c: a+2.0 μL Cu-L, d: a+4.0 μL Cu-L, e: a+8.0 μL Cu-L, f: a+16.0 μL Cu-L; g: a+32.0 μL Cu-L

Fig.4 Effects of the Cu(II) complexes fluorescence spectra of DNA-EB system

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