1,10-邻菲咯啉-5,6-二酮铁(Ⅱ)配合物的合成、结构及与 DNA 相互作用的研究

赵海燕*,1   马晶军 2   杨芙丽 3

(1 河北科技大学理学院,石家庄   050018)

(2 河北农业大学理学院,保定   070001)

(3 河北化工医药职业技术学院化学与环境工程系,石家庄   050026)

摘要: 在乙腈体系中合成了 Fe(Ⅱ)的配合物[Fe(phon)₃](ClO₃)₂·2CH₃CN(phon=1,10-邻菲咯啉-5,6-二酮)。X-射线衍射单晶结构表明:配合物[Fe(phon)₃](ClO₃)₂·2CH₃CN 属于正交晶系,$P2_12_12_1$ 空间群,Fe(Ⅱ)与 3 个 phon 配体的 6 个氮原子配位,形成变形的八面体结构。配合物[Fe(phon)₃](ClO₃)₂·2CH₃CN 中的氢键和 C=O…π 相互作用将配合物连接成二维网络结构。用红外光谱、紫外–可见光谱对配合物[Fe(phon)₃](ClO₃)₂·2CH₃CN 进行了表征,并用紫外光谱法对配合物与 ct-DNA 的相互作用做了初步研究,结果表明配合物与 ct-DNA 的结合常数(K_b)为 2.2×10⁵ L·mol⁻¹。

关键词: 1,10-邻菲啰啉-5,6-二酮;铁(Ⅱ)配合物;晶体结构;弱相互作用;ct-DNA

中图分类号: O614.81⁺1   **文献标识码:** A   **文章编号:** 100-4861(2012)11-2468-05

Synthesis, Crystal Structure and the Interaction with DNA of the Fe(Ⅱ) Complex with Tris-(1,10-phenanthroline-5,6-dione)

ZHAO Hai-Yan*,1   MA Jing-Jun2   YANG Fu-Li3

(1College of Science, Hebei University of Science and Technology, Shijiazhuang 050018, China)

(2College of Science, Hebei University of Agriculture, Baoding, Hebei 070001, China)

(3Department of Chemical and Environmental Engineering, Hebei Chemical & Pharmaceutical College, Shijiazhuang 050026, China)

Abstract: The crystal structure of the complex [Fe(phon)₃](ClO₃)₂2CH₃CN (phon=1,10-phenanthroline-5,6-dione) has been determined via the X-ray diffraction method and refined via the full-matrix least-squares methods to R=0.069 1 and wR_2=0.143 7 using 4 966 reflections with $I>2\sigma(I)$. This complex crystallizes in the orthorhombic system, space group $P2_12_12_1$ with a=1.381 8(4), b=1.416 7(4), c=2.053 3(6) nm and Z=4. The X-ray analysis revealed that the Fe(Ⅱ) ion is coordinated by the six nitrogen atoms from three ligands in a slightly distorted octahedral arrangement. The C−H…O and C=O…π interactions extend the complex into a quasi 2D networks, and such weak interactions further stabilized the complex. The complex was characterized via FT-IR and UV-Vis. The interaction between the complex and calf thymus DNA was investigated using UV spectra. The intrinsic binding constant (K_b) for the complex to DNA was calculated to be 2.2×10⁵ L·mol⁻¹. CCDC: 672079.

Key words: 1,10-phenanthroline-5,6-dione; Fe(Ⅱ) complex; crystal structure; weak interactions; calf thymus DNA

As a versatile ligand for the assembly of metal organic materials, 1,10-phenanthroline-5,6-dione (phon) is linked to metals with an N-N chelate with a free *o*-quinoid group or an O-O chelate with two free diiminic nitrogen atoms and a bridging mode with two different coordination sites[1-6]. This ligand has the ability to form stable complexes with a wide variety of metal inos and carries an *o*-quinone moiety with pH-dependent electroactivity[7-8].

Metal complexes of the type $[M(LL)_3]^{n+}$, where LL is either phon or 1,10-phenanthroline ligand, are particularly attractive species for the development of new diagnostic and therapeutic agents that can recognize and cleave DNA. The ligand or the metal in these complexes can be varied in an easily controlled manner to facilitate an individual application, thus providing an easy access to the details involved in DNA-binding and cleavage[9-11]. In the present study, the synthesis, characterization, crystal structure, and the interaction with DNA of the complex $[Fe(phon)_3]$ $(ClO_3)_2 \cdot 2CH_3CN$ is reported.

1　Experimental

1.1　Materials and methods

All reagents for syntheses and analyses were of analytical grade and the aqueous solution was prepared using doubly distilled water. Phon was synthesized according to the method described in a previous study[12]. Elemental analyses were conducted using a Perkin-Elmer 240C analyzer. FT-IR spectra (KBr pellet) were obtained using a FT-IR 170 SX (Nicolet) spectrometer. The electronic absorption spectra were obtained via UV-Vis spectroscopy using a Jasco V-570 spectrophotometer.

1.2　Synthesis of $[Fe(phon)_3](ClO_3)_2 \cdot 2CH_3CN$

A solution of phon (0.063 0 g, 0.3 mmol) in ethanol (5 mL) was added with $Fe(ClO_3)_3 \cdot 9H_2O$ (0.038 5 g, 0.1 mmol) dissolved in 5 mL ethanol. The reaction mixture was stirred at room temperature for 30 min to produce a red solution. An aqueous solution of NaN_3 (0.0070 g, 0.2 mmol) was added to the reaction mixture to obtain the Fe-phon-N_3 mixed-ligand complex. However the product precipitated as a deep

red solid was the title complex. The complex was collected via suction filtration, washed with cold water and diethylether, and then air-dried. Crystals for the determination were prepared by recrystallizing the above material from acetonitrile. Yield: 42%. Anal. Calcd. For $C_{37}H_{24}Cl_2FeN_8O_{14}(\%)$: C, 47.69; H, 2.48; N, 11.23. Found(%): C, 47.19; H, 2.58; N, 11.23. FT-IR (KBr, cm^{-1}): 3 369w, 1 701s, 1 569s, 1 429s, 1 299s, 1 122s, 1 089s, 941m, 813m, 720m, 626s.

1.3　Solution preparation of DNA

Calf thymus DNA (ct-DNA, purchased from Siama) was dissolved in Tris-HCl buffer (5 mmol·L^{-1} Tris-HCl, 50 mmol·L^{-1} NaCl, pH 7.2, Tris =Tris (hydroxymethyl)aminomethane). ct-DNA was purified following standard procedures. A UV-Vis spectrophotometer was employed to check DNA purity ($A_{260}/A_{280}>1.84$)[13] and concentration (ε=6 600 L·mol^{-1}·cm^{-1} at 260 nm)[14]. Stock solution was stored at 4 ℃ and used in no more than 4 d.

1.4　Crystal structure determination

Diffraction intensities for complex $[Fe(phon)_3]$ $(ClO_3)_2 \cdot 2CH_3CN$ was collected on a Bruker Smart 1000 CCD area detector using graphite-monochromatized Mo $K\alpha$ radiation (λ=0.071 073 nm) with ω scan mode at 293 (2) K. Unit cell dimensions were obtained with least-squares refinements. Semiempirical absorption corrections were applied using SADABS program[15]. The structures were solved by direct method using the SHELXS-97[16] and refined by full-matrix least-squares methods on F^2 by SHELXL-97[17]. Hydrogen atoms were included in calculated positions and refined with fixed thermal parameters riding on their parent atoms. Further crystallographic data and experimental details for structural analyses are summarized in Table 1. The selected bond lengths and bond angles are listed in Table 2.

CCDC: 672079.

2　Results and discussion

2.1　Synthesis and characterization

The elemental analyses of the complex $[Fe(phon)_3]$ $(ClO_3)_2 \cdot 2CH_3CN$ is consistent with a 1:2 anion: cation stoichiometry, as confirmed via X-ray crystal structure

Table 1　Crystal data and structure refinement summary for [Fe(phon)$_3$](ClO$_3$)$_2$·2CH$_3$CN

Empirical formula	C$_{40}$H$_{24}$Cl$_2$FeN$_8$O$_{14}$	$F(000)$	1968
Formula weight	967.42	Crystal size / mm	0.22×0.18×0.16
Temperature / K	293(2)	Range of θ / (°)	1.75~26.45
Crystal system	Orthorhombic	Range of h, k, l	−17/17, −17/11, −25/25
Space group	$P2_12_12_1$	Reflections collected	23 423
a / nm	1.381 8(4)	Independent reflections (R_{int})	8 238 (0.077 5)
b / nm	1.416 7(4)	Reflections observed ($I>2\sigma(I)$)	4 966
c / nm	2.053 3(6)	Flack	0.44
Volume / nm^3	4.020(2)	Goodness-of-fit on F^2	1.016
D_c / (g·cm^{-3})	1.5909	R_1, wR_2 ($I>2\sigma(I)$)	0.069 1, 0.143 7
Z	4	R_1, wR_2 (all data)	0.133 4, 0.1692
μ / mm^{-1}	0.59	Largest diff. Peak and hole / (e·nm^{-3})	549 and −468

Table 2　Selected bond lengths (nm) and angles (°) for [Fe(phon)$_3$](ClO$_4$)$_2$·2CH$_3$CN

Fe(1)-N(1)	0.198 0(5)	Fe(1)-N(3)	0.196 1(5)	Fe(1)-N(5)	0.197 6(5)
Fe(1)-N(2)	0.197 2(5)	Fe(1)-N(4)	0.197 1(5)	Fe(1)-N(6)	0.198 0(5)
N(3)-Fe(1)-N(4)	82.3(2)	N(2)-Fe(1)-N(5)	177.3(2)	N(3)-Fe(1)-N(6)	173.3(2)
N(3)-Fe(1)-N(2)	89.1(2)	N(3)-Fe(1)-N(1)	98.0(2)	N(4)-Fe(1)-N(6)	93.4(2)
N(4)-Fe(1)-N(2)	93.4(2)	N(4)-Fe(1)-N(1)	174.7(2)	N(2)-Fe(1)-N(6)	96.3(2)
N(3)-Fe(1)-N(5)	92.9(2)	N(2)-Fe(1)-N(1)	81.33(18)	N(5)-Fe(1)-N(6)	81.9(2)
N(4)-Fe(1)-N(5)	88.72(19)	N(5)-Fe(1)-N(1)	96.5(2)	N(1)-Fe(1)-N(6)	86.7(2)

determination, which indicates Fe(II) regardless of starting from Fe(ClO$_3$)$_3$·9H$_2$O.

The IR spectrum of phon clearly exhibits a band at 1 675 cm^{-1} that is ascribable to a stretching frequency of the C=O bands on the ligand[2,10]. This band was observed to be not shifted much in the corresponding complexes, which is reasonable because the C=O moieties are far from the coordination site of the ligand with the metal ion[1,6]. The IR spectrum of the complex showed a band approximately 1 701 cm^{-1}, which was assigned to the ν(C=O) band of an o-quinoid group of the phon ligand. In the M(O,O′-phon)$_3$ (M=V and Ti) and M(O,O′-phon)$_3$(M′L$_n$)$_3$ (M=V, M′L$_n$= TiCl4, M=Ti, M′L$_n$=TiCp2 and M=V, M′L$_n$=TiCp2), phon ligand was coordinated to the metal ion as a phen-semiquinonate or phen-diolate via oxygen atoms. In these complexes, the carbon-oxygen stretching vibration of approximately 200 to 300 cm^{-1} shifted to the lower wave number[3]. The strong absorption bands at 1 089 and 626 cm^{-1} were assigned to ClO$_4^-$ and demonstrated the presence of ClO$_4^-$ as a counter ion.

The electronic spectrum of the complex [Fe(phon)$_3$](ClO$_3$)$_2$2CH$_3$CN recorded in dimehtylformamide solution exhibited three absorption bands in the UV region and one band in the visible region. These bands centered at 257, 298 and 311 nm and were assigned to ligand-centered ($\pi{\rightarrow}\pi^*$) transition[18-19]. The absorption band centered at 485 nm was assigned to the intense $d{\rightarrow}\pi^*$ metal-to-ligand charge transition. This band is similar to that of the corresponding phenanthroline complexes except that there is a blue shift in the maximum wavelength of absorption[20]. This effect essentially reflects the enhanced π acidity of the phon ligand relative to that of phenanthroline[1].

2.2　Crystal structure

The ORTEP structure of [Fe(phon)$_3$](ClO$_3$)$_2$·2CH$_3$CN with atom labeling is shown in Fig.1. The complex [Fe(phon)$_3$](ClO$_3$)$_2$2CH$_3$CN crystallizes in the orthorhombic $P2_12_12_1$ space group. The analogous complex [Fe(phon)$_3$](ClO$_3$)$_2$·H$_2$O crystallizes in the same space group. However, [Fe(phon)$_3$](ClO$_3$)$_2$·H$_2$O was weekly reflecting[21]. The complex [Fe(phon)$_3$]
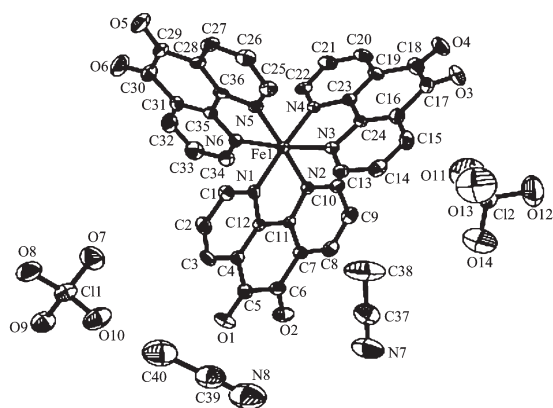
Fig.1 ORTEP view of the complex [Fe(phon)$_3$](ClO$_3$)$_2$·2CH$_3$CN showing the labeling of atoms with thermal ellipsoids at 30% probability

(ClO$_3$)$_2$·2CH$_3$CN consists of a chiral octahedral [Fe(phon)$_3$]$^{2+}$ cation, non-coordinated ClO$_4^-$ counterious and acetonitrile molecules. The crystal structure of the complex [Fe(phon)$_3$](ClO$_3$)$_2$·2CH$_3$CN is not resoluted and racemic mixtures, which is confirmed by the Flack parameter (0.44). The Fe (II) atom is six-coordinated with an approximately ideal octahedral geometry, by six nitrogen donors of three ligands. In the complex cation, the Fe(II) atom is constrained to lie on the least-squares plane defined by N (1), N(3), N(4) and N(6) set of atoms with the largest deviation being 0.008 40 nm at the N(1) atom, which deviates by only 0.000 86 nm form the mean plane. The sum of the bond angles within the plane is very close to 360°with N(1)-Fe(1)-N((6) 87.6(2)°, N(6)-Fe(1)-N(4) 93.4(2)°, N(4)-Fe(1)-N(3) 82.2(2)° and N(1)-Fe-N(1) 98.0(2)°, respectively. The N(5)-Fe(1)-N(2) bond angle deviates from linearity (180°) by only 2.7° in this complex, which can be defined as the apex of the octahedron. The bite angles for all three bidentate ligands are in the range of 81.33° to 82.3°. The Fe(II)-N bond lengths range from 0.196 1(5) to 0.198 0(5) nm, with an average of 0.197 3 nm. The mean Fe-N distances and the N-Fe-N angles are in the range usually found in other Fe-phenanthroline derivatives[22-23].

The most interesting feature of the crystal structure of the complex is the presence of intermolecular hydrogen bonds and C=O···π interactions. The CH$_2$ group of one ligand and the O atom of the adjacent C=O group form the intermolecular C–H···O

hydrogen bond . The C···O and H···O distances are 0.300 5 and 0.235 0 nm, respectively, falling into the normal range of hydrogen bond interactions. The bond angle is 127.2°. The C=O group of one ligand and the adjacent aromatic cycle (the ring, comprising atoms C16-C19, C23 and C24, is designated as ring **1** with centroid Cg) involved in the C=O···π interactions. The C···centroid and O···centroid distance is 0.423 1 and 0.320 1 nm, respectively, wherein the angle at the O atom is 145.5°, which fall into the normal range of C=O···π interactions[24]. The C–H···O hydrogen bonds are responsible for the formation of infinite chains along the b axis; the C=O···π interactions join along the c axis, producing 2D layers to the a axis of the crystal (Fig.2).
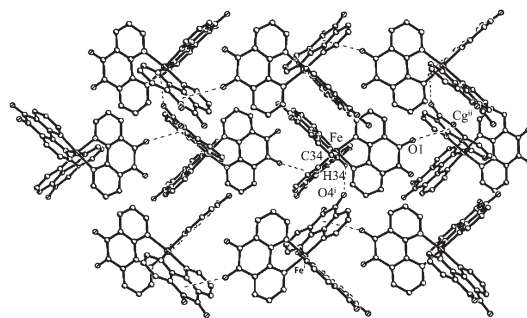
Symmetry codes: ^{i} 0.5+x, $-y$+2.5, $-z$; ^{ii} 1.5-x, $-y$+2, 0.5+z

Fig.2 2D structure linked by C–H···O and C=O···π interactions in [Fe(phon)$_3$](ClO$_3$)$_2$·2CH$_3$CN

2.3 Interaction with ct-DNA

DNA binding is a critical step in DNA cleavage. Therefore, the potential DNA binding caability of the complex [Fe(phon)$_3$](ClO$_3$)$_2$·2CH$_3$CN was studied via UV spectroscopy following the intensity changes of the π-π* transition band at 225 nm. The electronic spectra of the complex [Fe(phon)$_3$](ClO$_3$)$_2$·2CH$_3$CN in the absence and the presence of ct-DNA are illustrated in Fig.3. Upon the addition of an increasing amount of DNA (from 0 to 6.95×10^{-6} mol·L^{-1}) to the complex (1.00×10^{-5} mol·L^{-1}), a 74% hypochromism and a red shift (of 5 nm) were observed. These spectral changes are consistent with the intercalation of the Fe(II) complex into the DNA base stack[25].

The intrinsic binding constant (K_b) was determined according to the following equation[26]:

$$c_{DNA}/(\varepsilon_a-\varepsilon_f)=c_{DNA}/(\varepsilon_b-\varepsilon_f)+1/[K_b(\varepsilon_b-\varepsilon_f)] \qquad (1)$$

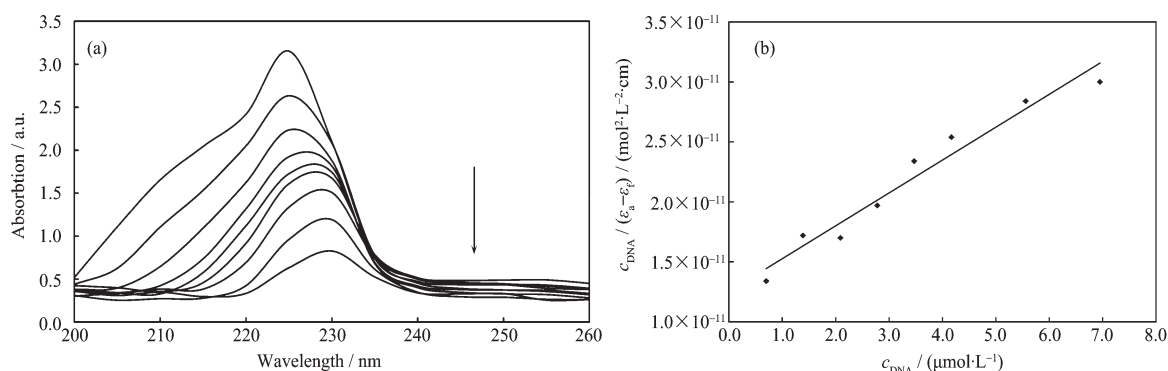Fig.3　(a) Change in the absorbance peak of $[Fe(phon)_3](ClO_3)_2 \cdot 2CH_3CN$ titrated with increasing DNA;
(b) Plot of $c_{DNA}/(\varepsilon_a-\varepsilon_f)$ versus c_{DNA}

where c_{DNA} is the total concentration of base pairs, and ε_a, ε_f and ε_b correspond to the extinction coeffi-cients for the absolutely bound Fe(II) complex, free Fe(II) complex, and the actually bound Fe(II) complex, respectively. In the plots of $c_{DNA}/(\varepsilon_a-\varepsilon_f)$ versus c_{DNA}, K_b is given by the ratio of the slope to the intercept. The K_b value obtained for the complex is 2.2×10^5 L·mol^{-1}, which is higher than those observed for $[Fe(phen)_3]^{2+}$ (4.68×10^3 L·mol^{-1})[27] and $[Ru(phen)_3]^{2+}$ (5.5×10^3 L·mol^{-1})[28]. This result is expected, since phon possesses a greater planar area and extended π system than that of phen, leading to phon penetrating more deeply into and makes stacking more strongly.

References:

[1] Hadadzadeh H, Olmsted M M, Rezvani A R, et al. *Inorg. Chim. Acta*, **2006**,**359**:2154-2158

[2] Goss C A, Abruna H D. *Inorg. Chem.*, **1985**,**24**:4263-4267

[3] Calderazzo F, Pampaloni G, Passarelli V. *Inorg. Chim. Acta*, **2002**,**330**:136-142

[4] Nargiotta N, Vertolasi V, Capitelli F, et al. *Inorg. Chim. Acta*, **2004**,**357**:149-158

[5] Fujihara T, Okamuka R, Wada T, et al. *J. Chem. Soc., Dalton Trans.*, **2003**:3221-3226

[6] Saravani H, Rezvani A R, Mansouri G, et al. *Inorg. Chim. Acta*, **2007**,**3609**:2829-2834

[7] Yamada Y, Sakurai H, Miyashita Y, et al. *Inorg. Chim. Acta*, **2006**,**359**:807-814

[8] Fox G A, Bhattacharya S, Pierpont C G. *Inorg. Chem.*, **1991**, **30**:2895-2899

[9] Bhattacharya P K, Lawson H J, Barton J K. *Inorg. Chem.*, **2003**,**42**:8811-8817

[10]Boghaei D M, Behzadian A F. *J. Coord. Chem.*, **2007**,**60**: 1629-1635

[11]Pascaly M, Yoo J, Barton J K. *J. Am. Chem. Soc.*, **2002**,**124**: 9083-9092

[12]Hiort C, Lincoln P, Norden B. *J. Am. Chem. Soc.*, **1993**, **115**:3448-3454

[13]Marmur J. *J. Mol. Biol.*, **1961**,**3**:208-211

[14]Reichmann M E, Rice S A, Thomas C A, et al. *J. Am. Chem. Soc.*, **1954**,**76**:3047-3053

[15]Sheldrick G M. *SADABS: Program for Expirical Absorption Correction of Area Detector Data*, University of Göttingen, Germany, **1996**.

[16]Sheldrick G M. *SHELXL-97, Program for X-ray Crystal Structure Solution*, Gottingen University, Germany, **1997**.

[17]Sheldrick G M. *SHELXL-97, Program for X-ray Crystal Structure Refinement*, Gottingen University, Germany, **1997**.

[18]Stephenson M D, Prior T J. Hardie M. *J. Cryst. Growth. Des.*, **2008**,**8**:643-653

[19]Larsson K, Ohrstrom L. *Inorg. Chim. Acta*, **2004**,**357**:657-664

[20]Mudasir, Wijaya K, Yoshioka N, et al. *J. Inorg. Biochem.*, **2003**,**94**:263-271

[21]Gaspar A B, Muoz M, Real J A. *C. R. Acad. Sci. Paris, Chimie/Chemistry*, **2001**,**4**:193-196

[22]Kulkarni P, Padhye S, Sinn E. *Polyhedron*, **1998**,**17**:2623-2626

[23]Filippova I G, Simonov Y A, Gdanets M, et al. *Journal of Structure Chemistry*, **2005**,**46**:1095-1098

[24]Ma Q, Zhu M L, Yuan C X. *Cryst. Growth. Des.*, **2010**,**10**: 1706-1714

[25]Tysoe S A, Morgan R J, Baker A D, et al. *J. Phys. Chem.*, **1993**,**97**:1707-1711

[26]Wolf A, Shimer Jr G H, Meehan T. *Biochemistry*, **1987**,**26**: 6392-6396

[27]Mudasir, Yoshioka N, Inoue H. *J. Inorg. Biochem.*, **1999**,**77**: 239-247

[28]Pyle A M, Rehmann J P, Meshoyrer R, et al. *J. Am. Chem. Soc.*, **1989**,**111**:3051-3058