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喹啉缩氨基硫脲 Co(Ⅲ)/Cd(Ⅱ)配合物的合成、结构和 DNA 结合性质

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摘要:合成并通过单晶衍射、元素分析、红外光谱表征了配合物 $[CoL_2]Cl\cdot 2CH_3OH$ (**1**)和$[CdL_2]$ (**2**)的结构(HL 为喹啉-8-甲醛缩硫代氨基脲)。单晶衍射结果表明,配合物 **1** 和 **2** 中金属离子采取相同的配位模式,分别与来自硫醇化脱质子的配体 L^-的 4 个 N 原子和 2 个 S 原子配位,采取扭曲的八面体配位构型。配合物 **1** 和 **2** 能够与 DNA 结合,结合模式分别为静电结合和部分插入。

关键词:喹啉;缩氨基硫脲;配合物;晶体结构;DNA 结合性质

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Syntheses, Crystal Structures and DNA-Binding Properties of Co(Ⅲ)/Cd(Ⅱ) Complexes with Quinoline Thiosemicarbazone Ligand

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Abstract: Two complexes $[CoL_2]Cl\cdot 2CH_3OH$ (**1**) and $[CdL_2]$ (**2**) (HL=(quinolin-8-ylmethylene)thiosemicarbazide) have been synthesized and structurally determined by single-crystal X-ray diffraction. The results show that the metal ion in each complex with a distorted octahedron geometry is surrounded by two anionic thiosemicarbazone ligand with N_2S donor set. Complexes **1** and **2** can bind to DNA via electrostatic intercalation and partial intercalation modes, respectively. CCDC: 1436092, **1**; 1436093, **2**.

Keywords: quinoline; thiosemicarbazone; complex; crystal structure; DNA-biding property

Thiosemicarbazones (TSCs) and their metal complexes, especially the transition metal, have attracted intensity attention in the coordination chemistry because of their high biological and pharmaceutical activities, such as antibacterial, antiviral, antifungal, and antitumor activity[1]. In fact, the mechanism of antitumor action is still controversial in many respects and has been identified including ribonucleotide reductase inhibition, metal dependent radical damage, DNA binding and inhibition of protein synthesis[1-10]. Up to now, a large amount of TSCs metals containing six-member heterocycles have been found to possess considerable antitumor activity[2,4-10]. However, the studies on the complexes with TSCs bearing condensed heterocycles are relatively few[3,11-13]. Recently, several Cu(Ⅱ) complexes with quinolin-8-ylmethylene) thiosemicarbazide have been reported to be potential antitumor agents[12-13]. In this paper, the structures and

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DNA-binding properties of its Co(Ⅲ)/Cd(Ⅱ) complexes have been discussed in detail.

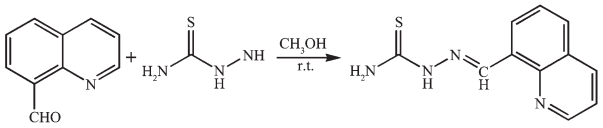
1 Experimental

1.1 Materials and measurements

Solvents and starting materials for syntheses were purchased commercially and used as received. Elemental analyses were carried out on an Elemental Vario EL analyzer. The IR spectra (ν=4 000~400 cm^{-1}) were determined by the KBr pressed disc method on a Bruker V70 FT-IR spectrophotometer. DNA-Binding Properties of both complexes are measured using literature method via absorption and emission spectra[14]. The UV spectra were recorded on a Purkinje General TU-1800 spectrophotometer. Fluorescence spectra were determined on a Varian CARY Eclipse spectrophotometer, in the measurements of emission and excitation spectra the pass width is 5 nm.

1.2 Preparations of the ligand and complexes 1 and 2

The TSC ligand HL (Scheme 1) was produced according to the literature method[13]. The complexes **1** and **2** were generated by reaction of HL (5mmol) with equimolar of $CoCl_2$ or $Cd(NO_3)_2$ in CH_3OH (10 mL) solution, respectively. Crystals of **1** and **2** suitable for X-ray diffraction analysis were obtained by evaporating the corresponding reaction solutions at room temperature.



Scheme 1 Synthetic route for HL

1: purple block. Anal. Calcd. For $C_{24}H_{26}N_8O_2S_2ClCo$ (%): C 46.72; H 4.25; N 18.16. Found (%): C 46.62; H 4.44; N 18.03. FT-IR (cm^{-1}): ν(C=N) 1 590, $\nu(N=C)_{quinoline}$ 1 482, ν(C-S) 768.

2: yellow plate. Anal. Calcd. for $C_{22}H_{18}N_8S_2Cd$(%): C 46.28; H 3.18; N 19.63. Found (%): C 46.44; H 3.29; N 19.48. FT-IR (cm^{-1}): ν(C=N) 1 591, $\nu(N=C)_{quinoline}$ 1 437, ν(C-S) 730.

1.3 X-ray crystallography

The X-ray diffraction measurement for complexes **1** (size: 0.10 mm×0.08 mm×0.08 mm) and **2** (size: 0.15 mm×0.14 mm×0.06 mm) was performed on a Bruker SMART APEX Ⅱ CCD diffractometer equipped with a graphite monochromatized Mo $K\alpha$ radiation (λ= 0.071 073 nm) by using φ-ω scan mode. Semi-empirical absorption correction was applied to the intensity data using the SADABS program[15]. The structures were solved by direct methods and refined by full matrix least-square on F^2 using the SHELXTL-97 program[16]. All non-hydrogen atoms were refined anisotropically. All H atoms were positioned geometrically and refined using a riding model. Details of the crystal parameters, data collection and refinements for complexes **1** and **2** are summarized in Table 1.

CCDC: 1436092, **1**; 1436093, **2**.

Table 1 Crystal data and structure refinement for complexes 1 and 2

	1	2
Empirical formula	$C_{24}H_{26}N_8O_2S_2ClCo$	$C_{22}H_{18}N_8S_2Cd$
Formula weight	645.66	570.96
T / K	296(2)	296(2)
λ / nm	0.071 073	0.071 073
Crystal system	Monoclinic	Monoclinic
Space group	*C*2/*c*	*P*2/*c*
a / nm	1.579(4)	1.745(2)
b / nm	1.156(3)	0.809 4(11)
c / nm	1.762(5)	1.581(2)
β / (°)	112.55(5)	109.34(2)
V / nm^3	2.970(14)	2.107(5)
Z	4	4

Continued Table 1

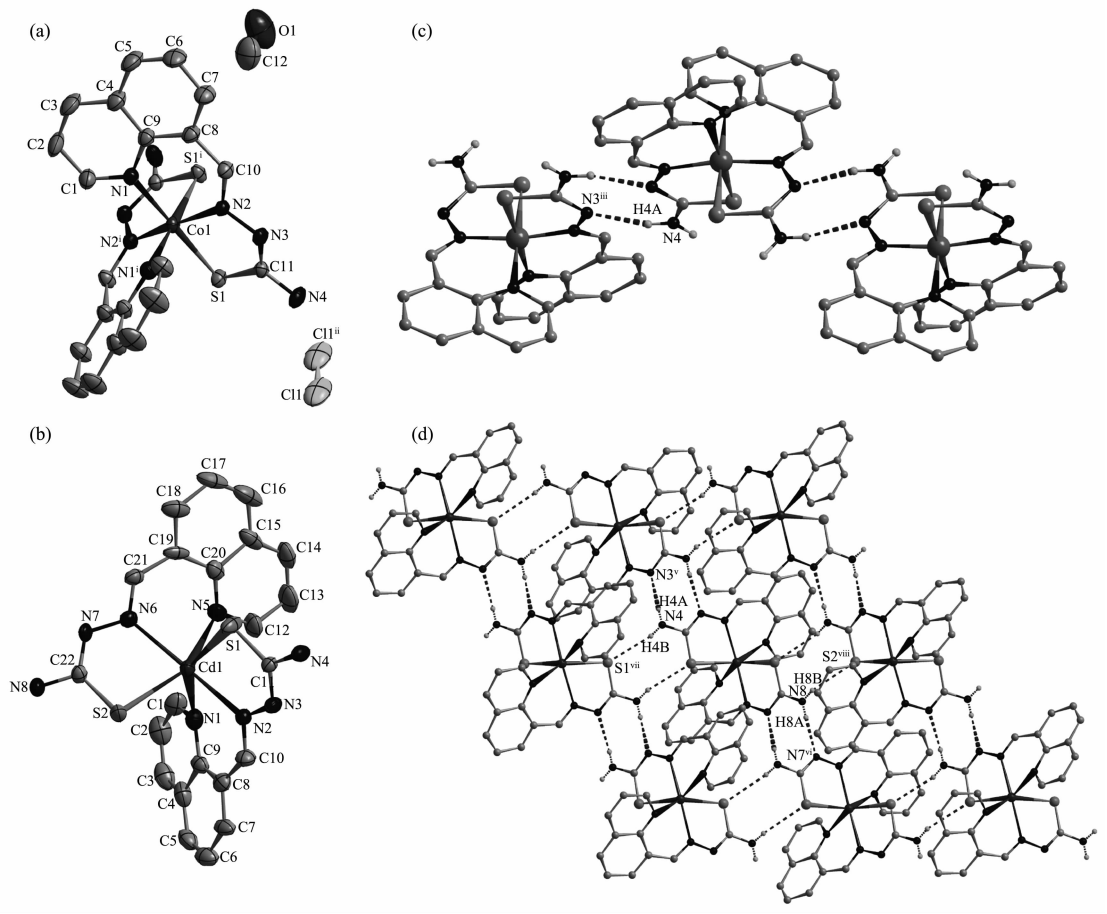
D_c / (g·cm^{-3})	1.380	1.800
Absorption coefficient / mm^{-1}	0.844	1.265
F(000)	1 272	1 144
Reflection collected, unique (R_{int})	7 337, 2 611 (0.056 5)	10 313, 3 696 (0.063 6)
Data, restraints, parameters	2 611, 0, 179	3 696, 0, 298
Goodness-of-fit (GOF) on F^2	1.069	1.021
Final R indices [$I>2\sigma(I)$]	R_1=0.065 8, wR_2=0.198 1	R_1=0.053 4, wR_2=0.100 7
R indices (all data)	R_1=0.094 8, wR_2=0.223 8	R_1=0.101 8, wR_2=0.120 9
Largest peak and hole / (e·nm^{-3})	1 088 and −365	1 388 and −827

2　Results and discussion

2.1　Crystal structures description

The ORTEP drawing of complexes **1** and **2** is shown in Fig.1. Selected bond distances and angles are listed in Table 2. Hydrogen bonds information is in Table 3. The lengths of C-S bond are in the range of 0.166 7(7)~0.171 5(6) nm in complexes **1** and **2**, showing that the ligand HL has thiolated and deprotonated in both complexes[14].

As shown in Fig.1a, the asymmetric unit of complex **1** contains a half of the molecule with the



Hydrogen bonds shown in dashed line; H atoms for C-H bonds are ommited for clarity; Symmetry code: [i] 1−x, y, 0.5−z; [ii] 1.5−x, 1.5−y, 1−z; [iii] −0.5+x, 1.5−y, −0.5+z; [v] −x, y, 0.5−z; [vi] 1−x, y, 1.5−z; [vii] −x, 2−y, 1−z; [viii] 1−x, 2−y, 1−z

Fig.1　ORTEP drawing of **1** (a) and **2** (b) with 30% thermal ellipsoids; (c) Chain-like structure along c axis formed via pairs of N−H···N hydrogen bonds in complex **1**; (d) Extended 2D supermolecular structure in complex **2**

Table 2 Selected bond lengths (nm) and angles (°) in complexes 1 and 2

			1		
Co1-N1	0.199 5(6)	Co1-N2	0.188 0(6)	Co1-S1	0.220 4(4)
N2^{i}-Co1-N2	171.0(3)	N1-Co1-N1^{i}	90.7(3)	N2-Co1-S1	86.2(2)
N2^{i}-Co1-N1	92.5(2)	N2-Co1-S1^{i}	87.6(2)	N1-Co1-S1	179.31(15)
N2-Co1-N1	93.8(2)	N1-Co1-S1^{i}	88.6(2)	S1i-Co1-S1	92.1(2)
			2		
Cd1-N1	0.244 0(7)	Cd1-N2	0.229 8(6)	Cd1-S1	0.253 3(3)
Cd1-N5	0.241 9(7)	Cd1-N6	0.230 7(6)	Cd1-S2	0.251 3(3)
N2-Cd1-N6	170.1(2)	N5-Cd1-N1	85.0(3)	N2-Cd1-S1	75.51(16)
N2-Cd1-N5	110.4(2)	N2-Cd1-S2	101.47(16)	N6-Cd1-S1	98.42(16)
N6-Cd1-N5	76.2(2)	N6-Cd1-S2	75.04(16)	N5-Cd1-S1	83.71(19)
N2-Cd1-N1	76.8(2)	N5-Cd1-S2	143.24(16)	N1-Cd1-S1	144.12(16)
N6-Cd1-N1	111.7(2)	N1-Cd1-S2	84.83(18)	S2-Cd1-S1	122.76(12)

Symmetry code: ^{i} 1–x, y, 0.5–z

Table 3 Hydrogen bonds information in complexes 1 and 2

D–H···A	d(D-H) / nm	d(H···A) / nm	d(D···A) / nm	∠DHA / (°)
		1		
N4–H4B···Cl1	0.086	0.233	0.314 0(9)	157.7
O1–H1A···Cl1^{i}	0.082	0.249	0.325 1(13)	153.9
N4–H4B···Cl1^{ii}	0.086	0.246	0.326 6(9)	156.2
N4–H4A···N3^{iii}	0.086	0.213	0.297 3(8)	167.5
O1–H1A···Cl1^{iv}	0.082	0.294	0.342 2(15)	119.3
		2		
N4–H4A···N3^{v}	0.086	0.226	0.302 3(9)	148.5
N8–H8A···N7^{vi}	0.086	0.224	0.306 0(9)	160.3
N4–H4B···S1^{vii}	0.086	0.266	0.348 3(7)	161
N8–H8B···S2^{viii}	0.086	0.271	0.349 8(7)	153

Symmetry code: ^{i} 1–x, y, 0.5–z; ^{ii} 1.5–x, 1.5–y, 1–z; ^{iii} –0.5+x, 1.5–y, –0.5+z; ^{iv} 1–x, 1–y, 1–z; ^{v} –x, y, 0.5–z; ^{vi} 1–x, y, 1.5–z; ^{vii} –x, 2–y, 1–z; ^{viii} 1–x, 2–y, 1–z

Co(Ⅲ) ion situated on a two-fold rotational axis. The centre Co(Ⅲ) ion is coordinated by two anionic TSC ligands with N_2S donor sets, and thus possesses a distorted octahedron coordination geometry. There exists one free chloride anion (occupying two positions) in the outside of the complex for charge balance, although complex **1** is prepared by the reaction of the TSC ligand HL with $CoCl_2$ in methanol medium. This is a normal phenomenon in the Co(Ⅲ) complexes with TSC ligands reported in literature[14]. The distances of Co-N/S bonds were in the range of 0.188 0(6)~0.220 4(4) nm, which were comparable with those found in the reported complexes with similar donor set. In the crystal, pairs of intermolecular N–H···N hydrogen bonds link the complex cations into one-dimentional chains along c axis (Fig. 1c). Furthermore, a 3D supermolecular network is formed via the N–H···Cl hydrogen bonds between the chains and free chlorides. The intermolecular O–H···Cl hydrogen bonds between the crystal methanol molecules and chloride anions are also present (Table 3).

The coordination environment of central Cd(Ⅱ) ion in complex **2** (Fig.1b) is quite similar as that of

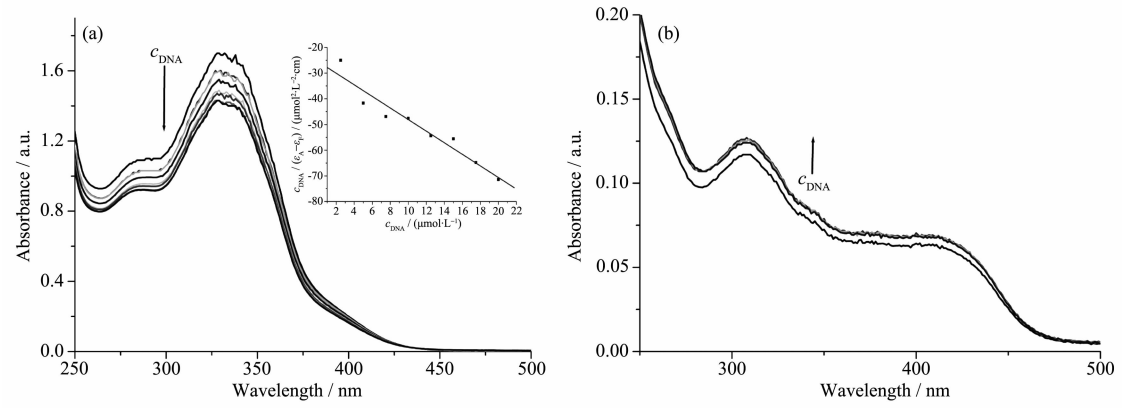
Co(Ⅲ) ion in complex **1**. The distances of Cd-N/S bonds were in the normal range (0.229 8(6)~0.253 3(3) nm). In the crystal of **2**, the intermolecular N–H⋯N hydrogen bonds link the complexes into chains, which were further linked with each other via intermolecular N–H⋯S hydrogen bonds to form extended 2D supermolecular network, as illustrated in Fig.1d.

2.2 IR spectra

The infrared spectral bands most useful for determining the mode of coordination of the ligands are the ν(N=C), ν(N=C, pyrazine) and ν(S=C) vibrations. Such three bonds of the free TSC ligand is found at 1 594, 1 532 and 816 cm^{-1}, while they shifts to lower frequency in complexes **1** and **2**, clearly indicating the coordination of imine nitrogen, quinoline nitrogen and sulfur atoms[14]. It is in accordance with the X-ray diffraction analysis result.

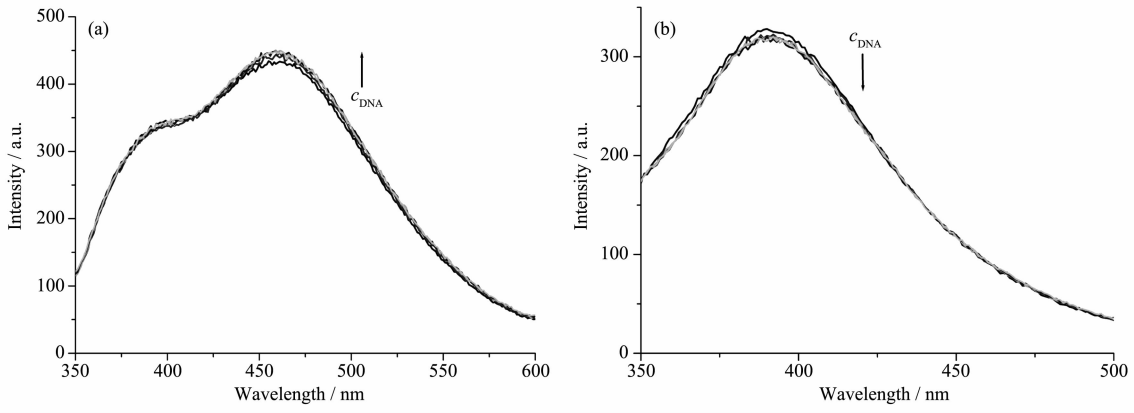
2.3 DNA-binding studies

The application of electronic absorption spectroscopy is one of the most useful techniques in DNA-binding studies. The UV absorption spectra would change in accordance with the environmental condition changes, since the stacking interactions happened between the complexes and DNA[14,17-18]. As shown in Fig.2, with increasing DNA concentration, hypochromic (**1**) or hyperchromic (**2**) effect was observed, which indicated molecular level interactions between the complexes and DNA. In addition, the lack of the red shift suggests that the major binding modes of both complexes with DNA are not classical intercalative interaction[18]. The intrinsic binding constant (K_b) of **1** was determined to be 8.81×10^3 L·mol^{-1} according to the literature method[14,17], which is comparable with some Co(Ⅲ) complexes with TSCs ligands[14]. However,



Inset: plots of $c_{DNA}/(\varepsilon_A-\varepsilon_F)$ vs c_{DNA} of the titration of DNA with the complex **1**, where ε_A and ε_F corresponded to the apparent extinction coefficient and the extinction coefficient for free complex **1**, respectively; $c_{complex}$=10 μmol·L^{-1}, c_{DNA}=0~20 μmol·L^{-1}

Fig.2　Electronic spectra of the complexes **1** (a) and **2** (b) in Tris-HCl buffer (pH=7.2) upon addition of CT-DNA



$c_{complex}$=10 μmol·L^{-1}, c_{DNA}=0~10 μmol·L^{-1}

Fig.3　Emission enhancement spectra of the complexes **1** (a) and **2** (b) in Tris-HCl buffer (pH=7.2) upon addition of CT-DNA

the absorption intensities change of **2** is obscure, thus its binding constant cannot be obtained reasonably.

The emission experiment has been widely used to further confirm the interaction between the complexes and CT-DNA. The results of fluorescence titration spectra have also been confirmed to be effective for characterizing the binding mode of the metal complexes to DNA[17-18]. Fig.3 shows the results of the emission titration curve of the complexes with CT-DNA. An increase in DNA concentration resulted slight increase and decrease in the emission intensity of complexes **1** and **2**, respectively. Combining with the electronic absorption spectroscopy titration results and according to the literature, it can be roughly concluded that complexes **1** and **2** bind to DNA via electrostatic intercalation[17] and partial intercalation[18] modes, respectively.

3 Conclusions

In summary, two transition metal complexes $[CoL_2]Cl\cdot 2CH_3OH$ (**1**) and $[CdL_2]$ (**2**) were synthesized and characterized. The metal ion in each complex with a distorted octahedron geometry is surrounded by two anionic thiosemicarbazone ligand with N_2S donor set. Complexes **1** and **2** can bind to DNA via electrostatic intercalation and partial intercalation modes, respectively. This indicates that both complexes have potential pharmaceutical activity.

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