# 双核钒席夫碱配合物[VO($\mu_2$-O)(*o*-Vanillin-en)]$_2$的合成、结构及与 DNA 相互作用

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**摘要**:在甲醇体系中乙酰丙酮氧钒与邻香草醛缩牛磺酸钾席夫碱在乙二胺存在下反应得到一个双核钒配合物。通过红外光谱和 X-射线单晶衍射对其进行了表征。晶体结构表明该化合物的晶体属于三斜晶系,$P\bar{1}$空间群,晶胞参数为 $a$=0.898 67(19)nm,$b$=1.159 3(3) nm,$c$=1.200 0(3) nm,$\alpha$=106.872(3)°,$\beta$=102.718(4)°,$\gamma$=94.905(3)°,$Z$=2。通过紫外吸收光谱法和循环伏安法研究了钒配合物与小牛胸腺 DNA 间的相互作用。紫外吸收光谱法得到配合物与 DNA 的结合常数为 1.77×10$^4$ dm$^3$·mol$^{-1}$。

**关键词**:钒配合物;席夫碱;晶体结构;小牛胸腺 DNA
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## Synthesis, Structure and the Interaction with DNA of Binuclear Vanadium Schiff Base Complex [VO($\mu_2$-O)(*o*-Vanillin-en)]$_2$

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**Abstract:** The reaction of VO(acac)$_2$ with taurine *o*-vanillin schiff base ligand and ethylenediamine in $CH_3OH$ yields a binuclear vanadium compound [VO($\mu_2$-O)(*o*-Vanillin-en)]$_2$. The complex was characterized by IR spectroscopic method and X-ray crystal structure determination. It crystallizes in the triclinic space group $P\bar{1}$ with $a$=0.898 67(19) nm, $b$=1.159 3(3) nm, c=1.200 0(3) nm, $\alpha$=106.872(3)°, $\beta$=102.718(4)°, $\gamma$=94.905(3)° and $Z$=2. The interaction between the vanadium complex and calf thymus DNA has been investigated by UV-Vis absorption spectrophotometry and cyclic voltammetry. In UV-Vis spectrophotometry studies, the binding constant of the complex to DNA is 1.77×10$^4$ dm$^3$·mol$^{-1}$. CCDC: 658848.

**Key words:** vanadium complex; schiff base; crystal structure; calf thymus DNA

The notion that vanadium plays an important role in biological systems and vanadium complexes with organic ligands might be candidates for therapy of diabetes has invoked great interest in the design, synthesis and study of new vanadium complexes[1,2]. The coordination environment of vanadium in vanadium nitrogenase and vanadate-dependent haloperoxidases is modeled by complexes with ligand sets containing similar function groups like phenolate, alkoxide, carboxylate, enamine, etc. The insulin-like in vitro and in vivo activity of vanadium compouds has also stimulated research on vanadium compounds that may have important application in the treatment of diabetes mellitus. Schiff bases and their first-row transition metal complexes were reported to exhibit fungicidal, bactericidal, antiviral, and antitubercular activity.

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Study on schiff base complexes helps us understand the metal-protein binding in organism. Taurine is a kind of nonprotein amino acids, but it is essential to the lives and rich in organism. It exerts an influence on comprehensive circadian functions[3,4]. Therefore, schiff base complexes derived from taurine would allow us to focus on the relevance effects. Unfortunately, schiff bases of amino acid were unstable and decomposed in the existense of amine, so we didn't obtain expected vanadium complex of taurine schiff base, but a new binuclear *o*-vanillin ethylenediamine vanadium complex [VO($\mu_2$-O)(*o*-vanillin-en)]$_2$. The interaction between the vanadium complex and calf thymus DNA has been investigated by UV-Vis absorption spectrophotometry and cyclic voltammetry.

## 1 Experimental

### 1.1 Reagents and instruments

Infrared spectra was recorded on an EQUINO55 spectrometer with samples prepared as KBr pellets. UV-Vis spectra was recorded on a LENG GUANG 756 CRT spectrophotometer. X-ray intensity data was measured on a Bruker Smart-1000CCD diffractometer. Cyclic voltammetry (CV) was performed on a M273 electrochemical workstation. The three-electrode system consisted of a glassy carbon (GC) working electrode, a platinum wire counter electrode and a saturated Ag/AgCl reference electrode.

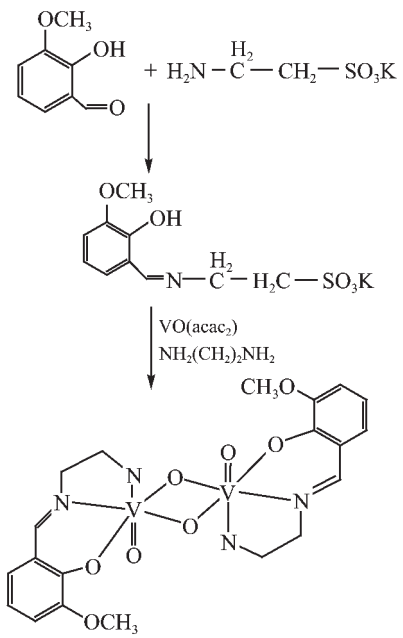
Ct-DNA was biochemicals, purchased from Sigma and used as received. The concentration of the nucleotide was determined by UV absorption spectroscopy using the molar absorption coefficient at 260 nm ($\varepsilon$=6600 L·mol$^{-1}$·cm$^{-1}$, concentration=1.935×10$^{-3}$ mol·dm$^{-3}$)[5,6].A solution of ct-DNA in the tris-HCl buffer (pH 7.4) gave an absorbance ratio, A260/A280, between 1.8 and 1.9, indicating that the DNA was sufficiently free of protein[7]. This DNA solution was not purified further. All other chemicals were of AR grade and were used without further purification. Bis (acetylacetonato) oxovanadium(Ⅳ)[8] was prepared according to reported method.

### 1.2 Preparation of L

L was synthesized by the reaction of taurine and *o*-vanillin[9] with 90% high yield. Taurine (1 250 mg, 10 mmol) and KOH (560 mg, 10 mmol) were dissolved in 15 mL of methanol and stirred for 10 min. Then a solution of *o*-vanillin (1 520 mg, 10 mmol) in 15 mL of methanol was added to yield a yellow solution. The reaction mixture was rapidly stirred for 2 h. After that light yellow precipitate was collected by filtration, washed with MeOH and dried in vacuo to afford L for further use.

### 1.3 Synthesis of complex

Methanol solution of VO(acac)$_2$ (132 mg, 0.5 mmol) was added dropwise to the solution of L (160 mg, 0.5 mmol) dissolved in methanol and DMSO with stirring, followed by the addition of little ethylenediamine. The reaction mixture was stirred for 12 h at r.t. and the resulting light brown solution was filtered off. Golden crystals of the title complex were obtained by slow diffusion of diethyl ether vapor into the mother liquor.




Scheme 1

### 1.4 Crystal structure determination

A single crystal of suitable size was selected and data were collected on a Bruker Smart-1000CCD diffractometer with graphite monochromatized Mo $K\alpha$ radiation ($\lambda$=0.071 073 nm) using the $\varphi$-$\omega$ scan technique in the range of 1.83°≤$\theta$≤ 25.02° at 294 (2) K. A total of 5 898 reflections were collected, of which 4 046

**Table 1 Crystallographic data of $[VO(\mu_2\text{-}O)(o\text{-vanillin-en})]_2$**

| | | | |
|---|---|---|---|
| Empirical formula | $C_{20}H_{26}N_4O_8V_2$ | $V$ / nm$^3$ | 1.152 0(4) |
| Formula weight/ (g·mol$^{-1}$) | 552.33 | $Z$ | 2 |
| Temperature / K | 294(2) | Calculated density / (Mg·m$^{-3}$) | 1.592 |
| Wavelength / nm | 0.071 073 | $F$(000) | 568 |
| Crystal system | Triclinic | Absorption coefficient / mm$^{-1}$ | 0.865 |
| Space group | $P\bar{1}$ | Crystal size / mm | 0.24 × 0.20 × 0.16 |
| $a$ / nm | 0.898 67(19) | $\theta$ range for data collection / (°) | 1.83~25.02 |
| $b$ / nm | 1.159 3(3) | Reflections collected / unique ($R_{int}$) | 5 898 / 4 046 (0.023 5) |
| $c$ / nm | 1.200 0(3) | Final $R$ indices ($I>2\sigma(I)$) | $R_1$=0.035 1, $wR_2$=0.079 7 |
| $\alpha$ / (°) | 106.872(3) | $R$ indices (all data) | $R_1$=0.059 7, $wR_2$=0.091 8 |
| $\beta$ / (°) | 102.718(4) | Largest diff. peak and hole/ (e·nm$^{-3}$) | 274, −281 |
| $\gamma$ / (°) | 94.905(3) | | |

reflections were indepent and 2 943 were observed with $I>2\sigma(I)$. Absorption correction was performed by using the SADABS program. The structure was solved by direct methods with SHELXS-97[10]. Most non-hydrogen atoms were determined from an E-map, and the others were determined with successive difference Fourier syntheses. The hydrogen atoms were located with theoretical calculations. The final refinement by full-matrix least-squares method with SHELXL-97[11] based on all data gave $R$=0.059 7, $wR$=0.091 8 [$w$=1/[$\sigma^2(F_o^2)$ + (0.041 1$P$)$^2$ + 0.224 1$P$], where $P$=($F_o^2$+2$F_c^2$)/3], $(\Delta/\sigma)_{max}$= 0.001, $S$=1.026, $(\Delta\rho)_{max}$= 274 e·nm$^{-3}$ and $(\Delta\rho)_{min}$=−281 e·nm$^{-3}$.

CCDC: 658848.

## 2 Results and discussion

### 2.1 IR Spectroscopic study

The IR spectra data show that V=O stretches at 917 cm$^{-1}$ in agreement with previously described complexes containing the pervanadyl moiety [12]. Another strong and sharp peak at 1 647 cm$^{-1}$ corresponds to the stretch vibration of -C=N- group which forms conjugated bond with benzene ring, which suggests the formation of schiff base group. The peak at 1 251 cm$^{-1}$ is assigned to the phenoxyl group coordinated to vanadium(Ⅴ).

### 2.2 Description of the structure

Reaction of $VO(acac)_2$ with taurine o-vanillin schiff base ligand and a little ethylenediamine in methanolic solution yields directly the weakly associated dimer. This compound represents the example of two pervanadyl units forming a bis ($\mu$-oxo)-bridged V(Ⅴ) schiff base dimer. An ORTEP diagram of the complex is given in Fig.1, and selected bond lengths and angles are presented in Table 2. The structure demonstrates that each V(Ⅴ) ion is six-coordinate with two distinct oxo groups being apparent. The first of these (V1-O3) is a typical V=O distance of 0.161 8 nm. The second oxo group is involved in the bridge between V1 and V1A. It is strongly coordinated to V1(V1-O4, 0.167 0 nm) and is weakly associated with V1A (V1A-O4, 0.234 6 nm). The remaining three coordinated sites are occupied by the phenolate oxygen(V1-O2, 0.190 2 nm), imine nitrogen (V1-N1, 0.216 5 nm), and amine nitrogen (V1-N2, 0.213 6 nm) atoms of the ligand. Thus, the coordination sphere of the vanadium ions are composed of six unique heteroatom types: a vanadyl oxo atom, two bridging oxo atoms at short and long distances, a phenoalte oxygen atom, and imine and amine nitrogen atoms. The polyhedron that is described resembles two edge shared

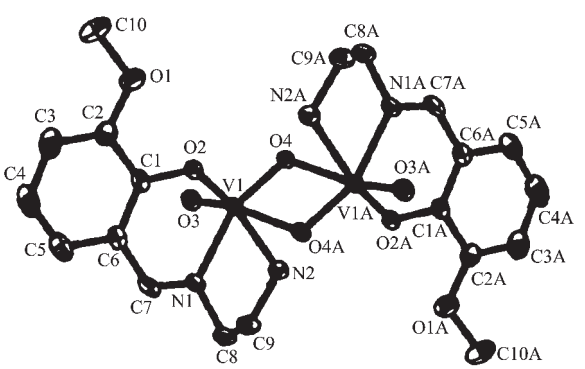



Fig.1 Molecular structure of title complex

**Table 2　Selected bond lengths (nm) and angles (°) of [VO($\mu_2$-O)(*o*-vanillin-en)]$_2$**

| | | | | | |
|---|---|---|---|---|---|
| V(1)-O(3) | 0.161 8(2) | V(1)-O(4) | 0.167 00(18) | V(1)-O(2) | 0.190 2(2) |
| V(1)-N(2) | 0.213 6(2) | V(1)-N(1) | 0.216 5(2) | V(1)-O(4A) | 0.234 62(19) |
| O(4)-V(1A) | 0.234 62(19) | V(1A)-O(3A) | 0.161 8(2) | | |
| O(3)-V(1)-O(4) | 106.50(10) | O(3)-V(1)-O(2) | 101.94(10) | O(4)-V(1)-O(2) | 99.28(9) |
| O(3)-V(1)-N(2) | 91.90(10) | O(4)-V(1)-N(2) | 93.14(9) | O(2)-V(1)-N(2) | 157.85(9) |
| O(3)-V(1)-N(1) | 96.28(10) | O(4)-V(1)-N(1) | 155.59(9) | O(2)-V(1)-N(1) | 84.13(9) |
| N(2)-V(1)-N(1) | 77.17(9) | O(3)-V(1)-O(4A) | 170.53(9) | O(4)-V(1)-O(4A) | 78.98(9) |
| O(2)-V(1)-O(4A) | 84.47(8) | N(2)-V(1)-O(4A) | 79.96(8) | N(1)-V(1)-O(4A) | 77.30(8) |
| V(1)-O(4)-V(1A) | 101.02(9) | | | | |

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

octahedra that are very significantly distorted. The O4-V1-O3 angle is 106.5°, a value that is close to that observed for $VO_2$EDTA [13,14], $VO_2$(8-Q)$_2$ [15], and many other *cis*-$VO_2^+$(pervanadyl) units[16]. Angles described by trans substituents are far from 180°, ranging from 155.6° to 170.5°. The two $VO_2$L units are related by an inversion center with a V-V distance of 0.308 6 nm.

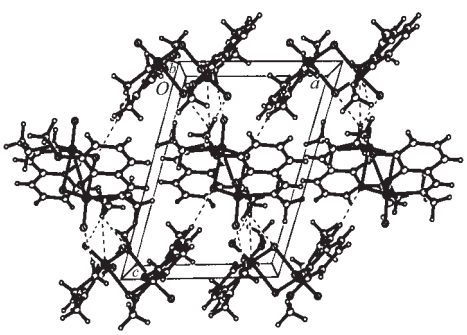



Fig.2　Packing drawing of title complex viewed along axis *b*

## 2.3　Interaction with ct-DNA

### 2.3.1　Absorption spectroscopic studies

The interaction of the complex with DNA was investigated using absorption spectra. The electronic spectra of the complex in the absence and the presence of calf thymus (with subtraction of DNA absorbance for the latter) are illustrated in Fig.3. The complex shows a individual strong peak under the experimental conditions and the addition of DNA yielded obvious absorption hypochromism of 14.86% and slight red shift (2~3 nm), which suggested that the vanadium complex could intercalate into the double helix structure of DNA. The hyperchromic effect around 220 nm after adding DNA might be ascribed to that vanadium could uncoil the helix structure of DNA and made more bases embedding in DNA be exposed[17~19].

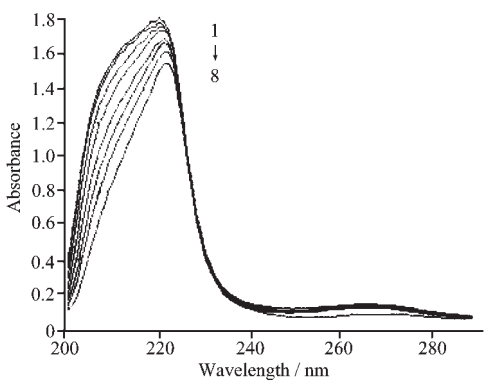



Fig.3　Changes of the electronic absorbance peak of the complex (6.5 μmol·dm$^{-3}$) titrated with increasing concentrations

The addition of certain concentration of NaCl can afford required ionic strength, and the adjustion of the PH of the buffer is to insure the double-stranded structure which is required for binding[20]. The extent of the insertion and the binding strength of the complex and ct-DNA may be evaluated by the index of binding constant $K$.

$K$ can be obtained by monitoring the changes in absorbency of the complex near 220 nm with increasing concentrations of DNA, according to the following equation[21]:

$$\frac{\varepsilon_a-\varepsilon_f}{\varepsilon_b-\varepsilon_f}=\frac{Kc_{DNA}}{Kc_{DNA}+1} \quad (1)$$

where $c_{DNA}$ is a certain concentration of ct-DNA, $\varepsilon_a$ is the extinction coefficient observed for the absorbance band at the corresponding DNA concentration, $\varepsilon_b$ is the extinction coefficient of the fully bound species, $\varepsilon_f$ is

the extinction coefficient for the complex free in solution, and $K$ is the binding constant of the complex to DNA. The transitional form of Eq.**1** is as follows:

$$\frac{\varepsilon_f-\varepsilon_b}{\varepsilon_f-\varepsilon_a}=1+\frac{1}{Kc_{DNA}} \quad (2)$$

Fig.4 is the plot of $(\varepsilon_f-\varepsilon_b)/(\varepsilon_f-\varepsilon_a)$ vs $(1/c_{DNA})\times 10^{-4}$, fitting to Eq.**2** gives value of $K$ $1.77\times10^4$ $dm^3\cdot mol^{-1}$. Comparing the binding constant with that of correlative species reported[22,23], we can conclude that the binding of the complex with ct-DNA is normal.

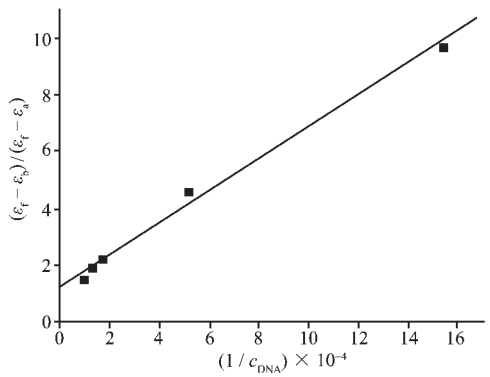



Fig.4 Plot of $(\varepsilon_f-\varepsilon_b)/(\varepsilon_f-\varepsilon_a)$ vs $(1/c_{DNA})\times10^{-4}$ of ct-DNA (0~160 μmol·dm$^{-3}$) in 5 mmol·dm$^{-3}$ tris buffer (pH 7.4) containing 50 mmol·dm$^{-3}$ NaCl

2.3.2 Cyclic voltammetry studies

Cyclic voltammetry of the vanadium complex was recorded in solution in both the absence and presence of ct-DNA.

The results of our investigation suggested that the vanadium complex didnt have obvious interaction with ct-DNA under this condition. Because electrochemical peak potential shift and the change of peak current which is commonly defined as proofs of intercalation between complexes and DNA were not found in the cyclic voltammetry[24,25].

## 3 Conclusions

In summary, a new binuclear vanadium complex, $[VO(\mu_2\text{-}O)(o\text{-vanillin-en})]_2$, was synthesized and its structure was characterized by X-ray crystallography and IR spectrum. The binding properties of the complex to native double stranded DNA were studied by UV-Vis spectrophotometry and cyclic voltammetry. In UV-Vis spectrophotometry studies, the binding constant of the complex to DNA is $1.77\times10^4$ $dm^3\cdot mol^{-1}$.

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