

苯磺酰苯丙氨酸构筑的一维链状钙(II) 配位聚合物的合成、结构表征和抗肿瘤活性

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摘要: 在 95%乙醇溶剂中,通过高氯酸钙、苯磺酰苯丙氨酸和 NaOH 反应,合成了一个新型的一维链状钙配位聚合物。对其进行了元素分析和红外光谱分析表征,并用 X-射线单晶衍射测定了它的单晶结构。结果表明:在配合物分子中,每个钙原子分别与配体中羧酸根的 4 个氧原子、配位水中的 2 个氧原子以及配位乙醇分子中的 1 个氧原子配位,形成了畸变的五角双锥构型。配合物分子通过羧酸根的桥联作用形成了一维链状配位聚合物结构。初步研究了配合物对肝癌、肺腺癌、白血病和结肠癌的抗肿瘤活性。

关键词: 苯磺酰苯丙氨酸; Ca(II)配位聚合物; 合成; 结构表征; 抗肿瘤活性

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Synthesis, Crystal Structure and Antitumor Activity of Ca(II) Coordination Polymer Constructed by *N*-Benzenesulphonyl-*L*-phenylalanine

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Abstract: Colourless crystals of 1D coordination polymer, $[\text{Ca}(\text{L})_2(\text{H}_2\text{O})_2(\text{CH}_3\text{CH}_2\text{OH})]_n$ ($\text{L}=\text{N}$ -benzenesulphonyl-*L*-phenylalanine), were obtained by the reaction of calcium perchlorate and *N*-benzenesulphonyl-*L*-phenylalanine in the 95% $\text{CH}_3\text{CH}_2\text{OH}$ solution, and characterized by elemental analysis, IR and X-ray single crystal diffraction analysis. The single-crystal X-ray analysis of the title complex reveals that each Ca(II) atom is seven-coordinated in a distorted pentagonal bipyramid coordination environment by seven oxygen atoms from the *N*-benzenesulphonyl-*L*-phenylalanine ligand, the coordinated water molecule and the coordinated $\text{CH}_3\text{CH}_2\text{OH}$ molecule, respectively. The molecular structure is 1D coordination polymer by the interaction of bridged carboxylato groups. The antitumor activity against SMMC-7721, A549, WiDr and P388 cancer cells of the Ca(II) complex also was investigated. CCDC: 890991.

Key words: *N*-benzenesulphonyl-*L*-phenylalanine; Ca(II) coordination polymer; synthesis; crystal structure; antitumor activity

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0 Introduction

The chemistry of metal-organic coordination polymers has been enriched enormously in the past two decades owing to their interesting framework topologies and their wide range of potential applications in adsorption, separation, catalysis, magnetism and fluorescence [1-7]. A large number of coordination polymers constructed by transition metal ions with carboxylate ligands have been extensively investigated. These complexes exhibit extraordinary structural diversity and provide facile accessibility to functionalized new materials [8-10]. Calcium is an indispensable element in biology. It is involved in several biochemical processes and is an essential cofactor required for the activation of a variety of enzymes [11]. Amino acid is also an important physiological active substance in biological processes. To the best of our knowledge, the calcium(II) complex materials with amino acid ligands have been much less extensively studied than other metal complexes. In this paper, we report the synthesis and structure of $[\text{Ca}(\text{L})_2(\text{H}_2\text{O})_2(\text{CH}_3\text{CH}_2\text{OH})]_n$, which was constructed from calcium perchlorate and *N*-benzenesulphonyl-*L*-phenylalanine. The antitumor activity against SMMC-7721, A549, WiDr and P388 cancer cells of the Ca(II) complex also was investigated.

1 Experimental

1.1 Materials and measurements

Calcium perchlorate, benzene sulfonyl chloride, *L*-phenylalanine and other chemicals were obtained commercially and used without further purification.

Elemental analyses were determined on a Elementar Vario III EL elemental analyzer. Infrared spectra were recorded with KBr optics on a Nicolet AVATAR 360 FTIR spectrophotometer in the range of 4,000~400 cm^{-1} . Mass spectrum was performed on VG ZAB-HS Fast-atom bombardment (FAB) instrument. The crystal data were collected on a Bruker smart CCD Area Detector.

1.2 Synthesis of the ligand (L)

The ligand was prepared according to the

literature [12]. Yield may reach up to over 65%. Anal. Calcd. for $\text{C}_{15}\text{H}_{15}\text{NSO}_4$ (%): C, 58.96; H, 5.00; N, 4.52. Found (%): C, 59.02; H, 4.92; N, 4.59. IR $\nu_{\text{max}}(\text{cm}^{-1})$: $\nu_{\text{as}}(\text{COOH})$: 1 659, $\nu_{\text{s}}(\text{COOH})$: 1 437, $\nu(\text{-SO}_2\text{-NH-})$: 3 247, 1 321, 1 154. FAB-MS: $m/z=306$ $[\text{M}+\text{H}]^+$.

1.3 Synthesis of the complex

1.0 mmol (0.305 g) of *N*-benzenesulphonyl-*L*-phenylalanine and 1.0 mmol (0.04 g) of sodium hydroxide were added to the 10 mL of 95% $\text{CH}_3\text{CH}_2\text{OH}$ solution. After being dissolved, 0.5 mmol (0.119 5 g) of calcium perchlorate was added to the above solution. The mixture was continuously stirred for 4 h at refluxing temperature.

The mixture was cooled at room temperature, and was collected by filtration. By evaporation in air at room temperature, the single crystal suitable for X-ray determination was obtained from 95% ethanol solution after 7 d. Anal. Calcd. for $\text{C}_{32}\text{H}_{38}\text{CaN}_2\text{O}_{11}\text{S}_2$ (%): C, 52.59; H, 5.24; N, 3.83; Found (%): C, 52.78; H, 5.59; N, 3.72%. IR $\nu_{\text{max}}(\text{cm}^{-1})$: $\nu_{\text{as}}(\text{COO})$: 1 586, $\nu_{\text{s}}(\text{COO})$: 1400, $\nu(\text{-SO}_2\text{-NH-})$: 3 246, 1 322, 1,153, $\nu(\text{H}_2\text{O})$: 3350~3467, $\nu(\text{Mg-O})$: 423.

1.4 Crystal structure determination

A colourless block single crystal was placed on a glass fiber and mounted on a CCD area detector. Diffraction data were collected by φ - ω scan mode using a graphite-monochromatic Mo $K\alpha$ radiation ($\lambda=0.071\ 073$ nm) at 291(2) K. A total of 15 466 reflections were collected, of which 6 656 were unique ($R_{\text{int}}=0.015\ 2$) and 4 989 were observed with $I>2\sigma(I)$. The data were corrected for Lp factors. The structure was solved by direct methods and refined by full-matrix least-squares techniques on F^2 using SHELXL-97 [13] and Fourier techniques. All non-hydrogen atoms and hydrogen atoms were refined anisotropically and isotropically, respectively. The final refinement by full-matrix least squares method was converged at $R=0.059\ 6$, and $wR=0.1431$ ($w=1/[\sigma^2(F_o^2)+(0.06P)^2+1.99P]$, $P=(F_o^2+2F_c^2)/3$, $S=1.108$, $(\Delta/\sigma)_{\text{max}}=0.000$). Molecular graphics were drawn with the program package SHELXTL-97 crystallographic software package [14]. The most relevant crystal data for complex are quoted in Table 1.

CCDC: 890991.

Table 1 Crystal structure parameters of the title complex

Formula	C ₃₂ H ₃₈ CaN ₂ O ₁₁ S ₂	<i>V</i> / nm ³	3.447 6(13)
Formula weight	730.84	Calculated density / (g·cm ⁻³)	1.408
Crystal system	Orthorhombic	Crystal size / mm ³	0.32×0.30×0.28
Space group	<i>P</i> 2 ₁ 2 ₁ 2 ₁	θ Range for data collection / (°)	1.56~26.00
<i>a</i> / nm	0.519 06(18)	Limiting indices	-6 ≤ <i>h</i> ≤ 6, -31 ≤ <i>k</i> ≤ 13, -31 ≤ <i>l</i> ≤ 31
<i>b</i> / nm	2.541 1(2)	Reflections collected / unique	15 466/6 656
<i>c</i> / nm	2.613 9(3)	<i>R</i> ₁ , <i>wR</i> ₂ (all data)	0.067 0, 0.144 7
<i>Z</i>	4	<i>R</i> ₁ , <i>wR</i> ₂ (<i>I</i> > 2σ(<i>I</i>))	0.059 6, 0.143 1
<i>F</i> (000)	1536	Largest diff. peak and hole / (e·nm ⁻³)	345 and -345
Temperature / K	291(2)		

Symmetry code: A: *x*+1, *y*, *z*

1.5 Antitumor activity

SMMC-7721, A549, WiDr and P388 cancer cells were propagated continuously in culture and grown in RPMI 1640 medium with 10% inactivated fetal calf serum and antibiotics. Cell harvested from exponential phase were seeded equivalently into 96 well plates and incubated for 24 h, then compounds studied were added in a concentration gradient. The final concentrations were maintained at *c* (μg·mL⁻¹) 5, 10, 20, respectively. The plates were maintained at 37 °C in a humidified 5% CO₂-90% N₂-5% O₂ atmosphere and incubated for 48 h, the MTT solution was added, the following procedure referred to^[15]. The measurements of absorption of the solution concerned with the number of live cells were performed on spectrophotometer at 570 nm.

2 Results and discussion

2.1 IR spectra

In the IR spectra, the characteristic bands at 1 659 and 1 437 cm⁻¹ are assigned to the asymmetric

stretching and symmetric stretching of COOH group, respectively. For the complex, the asymmetric stretching and symmetric stretching of COO⁻ group are observed at 1 586 and 1 400 cm⁻¹. It can be explained that the oxygen atoms of carboxylate group take part in the coordination with calcium atom^[16]. The value of Δ*ν* (*ν*_{as}(COO⁻)-*ν*_s(COO⁻)) is 186 cm⁻¹ and reveals that the carboxylate groups are coordinated in bidentate fashion, which is consistent with the results of the X-ray analysis. In addition, the broad and strong absorption bands at 3 350~3 467 cm⁻¹ correspond to the presence of water molecules in the complex, which are accordance with the results of elemental analysis.

2.2 Crystal structure

Colourless block crystals of the Ca (II) complex were obtained and its structure was determined by a single-crystal X-ray diffraction study. The selected bond lengths and angles with their estimated standard deviations are listed in Table 2. As depicted in Fig.1, the coordination environment of the Ca(II) atom consists

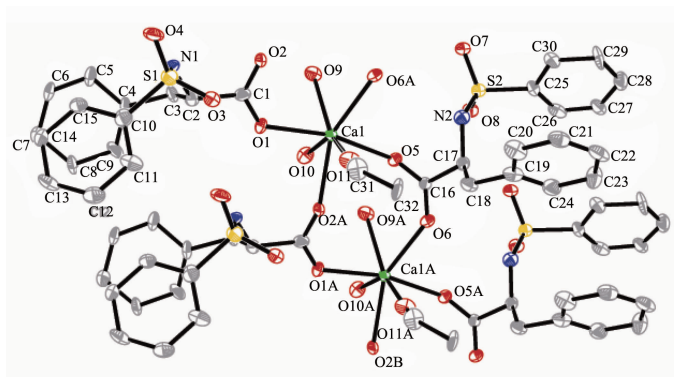


Fig.1 Coordination environment of Ca (II) in the title complex

Table 2 Selected bond lengths (nm) and angles (°) of complex

Ca1-O1	0.2341(3)	Ca1-O10	0.2446(4)	S1-O3	0.1426(4)
Ca1-O2A	0.2377(3)	Ca1-O6A	0.2428(4)	S1-O4	0.1416(4)
Ca1-O5	0.2380(3)	Ca1-O11	0.2430(4)	S2-O7	0.1430(3)
Ca1-O9	0.2448(3)				
O1-Ca1-O2A	87.04(11)	O9-Ca1-O10	69.61(12)	O5-Ca1-O11	92.60(13)
O1-Ca1-O5	167.31(12)	O1-Ca1-O6A	107.25(12)	O9-Ca1-O11	144.19(13)
O5-Ca1-O2A	80.48(11)	O2A-Ca1-O6A	144.60(13)	O10-Ca1-O11	144.99(13)
O1-Ca1-O9	83.50(12)	O5-Ca1-O6A	84.51(11)	O11-Ca1-O6A	78.16(12)
O5-Ca1-O9	104.99(12)	O9-Ca1-O6A	72.91(11)	C2-N1-S1	119.7(3)
O1-Ca1-O10	92.60(13)	O10-Ca1-O6A	134.91(12)	O4-S1-O3	118.4(2)
O10-Ca1-O2A	74.24(12)	O1-Ca1-O11	85.39(13)	O4-S1-N1	106.4(2)
O5-Ca1-O10	81.86(12)	O11-Ca1-O2A	70.75(12)	O4-S1-C10	107.0(2)

Symmetry code: A: $x+1, y, z$

of seven oxygen atoms from the *N*-benzenesulphonyl-*L*-phenylalanine ligand, the coordinated water molecules and the coordinated $\text{CH}_3\text{CH}_2\text{OH}$ molecule, making up a distorted pentagonal pyramid coordination environment. The distances of the Ca-O bonds are in the range of 0.234 2(3)~0.244 8(3) nm. The bonds lengths of Ca-O are consistent with those in reported previously^[17-18]. The

bond lengths and bond angles of benzyl rings in the molecules are within the range of normal values. The benzyl rings (C4-C9 and C25-C30) and the $\text{CH}_3\text{CH}_2\text{OH}$ are disordered.

The molecular structure is one dimensional chain structure by the interaction of bridged carboxylato groups and result in an 1D coordination polymer (Fig.2).

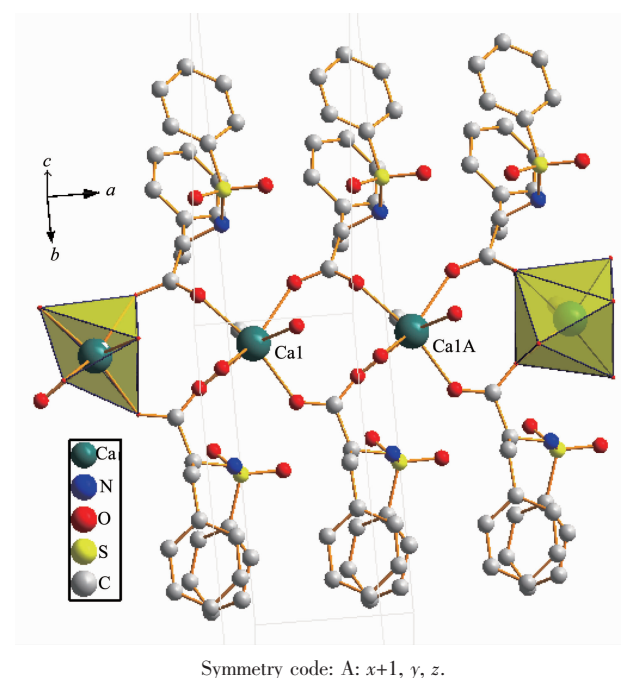


Fig.2 One dimensional chain structure of Ca (II) coordination polymer

2.4 Antitumor activity

The data of the antitumor activities of Ca (II) complex and *N*-benzenesulphonyl-*L*-phenylalanine are

given in Table 3. The concentration of DMSO was controlled under 1% to assure not to affect the results. As can be seen, the Ca (II) complex and *N*-

Table 3 Cytotoxicity of Ca(II) complex

Complex	IC ₅₀ / (μg·mL ⁻¹)			
	SMMC-7721	A549	WiDr	P388
Ca(II) complex	88±1.6	71±0.2	76±0.8	36±0.9
<i>N</i> -benzenesulphonyl- <i>L</i> -phenylalanine	73±2.7	60±0.3	68±0.13	31±1.16

benzenesulphonyl-*L*-phenylalanine exerted cytotoxic effect against SMMC-7721, A549, WiDr and P388 cancer cells, however the better cytotoxicity against P388 cancer cell with lower IC₅₀ value (<50 μg·mL⁻¹) than other cancer cell, and the complex displays the weaker cytotoxic activity than that of *N*-benzenesulphonyl-*L*-phenylalanine. Further structure modification to enhance the cytotoxic activity of the Ca(II) complexes is desirable.

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