Synthesis, Crystal Structure and Antitumor Activity of a Ca(II) Coordination Polymer Based on 4-Acetylphenoxyacetate Ligands①

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ABSTRACT A novel Ca(II) coordination polymer, $[CaL_2(H_2O)_2]_n$ (**1**, HL = 4-acetylphenoxyacetic acid) has been synthesized with 4-acetylphenoxyacetic acid, $Ca(ClO_4)_2·4H_2O$ and NaOH as raw materials. Complex **1** was characterized by elemental analysis and single-crystal X-ray diffraction analysis. The results show that the Ca(II) ion is eight-coordinated in a distorted triangular dodecahedral geometric configuration with six carboxylate O atoms of four L ligands and two O atoms of two coordinated water molecules. Complex **1** forms a one-dimensional chained structure by the bridging effect of carboxylate O atoms. The antitumor activity of HL ligand and complex **1** has also been investigated.

Keywords: 4-acetylphenoxyacetic acid, Ca(II) coordination polymer, synthesis, crystal structure, antitumor activity; DOI: 10.14102/j.cnki.0254–5861.2011–2860

1 INTRODUCTION

The design and synthesis of metal coordination polymers have received considerable attention during the past decades because they show not only structural diversity[1], but also potential widespread applications as functional materials, such as molecular recognition[2], gas storage[3], magneto-caloric effect[4], luminescence[5-7], catalysis[8], magnetic property[9], bioactivity[10], magnetorefrigerant[11], and so on. To our knowledge, many studies on coordination polymers have focused on transition metals in the past years[12-16]. However, few investigations have been done on calcium coordination polymers. In our previous work, some calcium coordination polymers have been synthesized and structurally characterized[17-20]. In order to extend the investigation of novel structures and properties of calcium coordination polymer, in this work, we successfully designed and synthesized a novel 1D Ca(II) coordination polymer, $[CaL_2(H_2O)_2]_n$ (HL = 4-acetylphenoxyacetic acid), by 4-acetylphenoxyacetic acid, $Ca(ClO_4)_2·4H_2O$ and NaOH as raw materials. And its antitumor activity against human hepatoma *SMMC*-7721 cells, human colon carcinoma *WiDr* cells and human lung adenocarcinoma *A549* cells has been investigated. The coordination mode of Ca(II) ion is shown in Fig. 1.

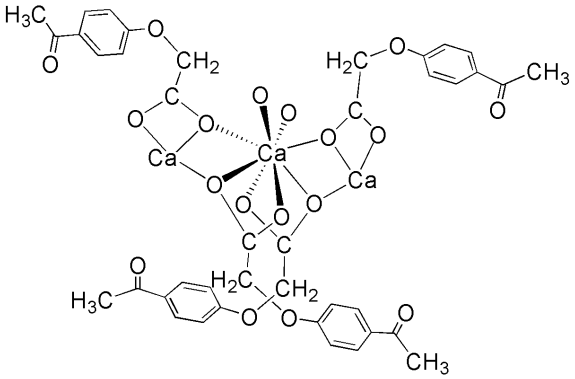

Fig. 1. Coordination mode of Ca(II) ion

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2 EXPERIMENTAL

2. 1 Materials and measurements

4-Acetylphenoxyacetic acid, NaOH, $Ca(ClO_4)_2·4H_2O$ and ethanol solvent were of analytical grade and used directly without further purification. Carbon, hydrogen and nitrogen were determined using an Elementar Vario III EL elemental analyzer. IR spectra were recorded using KBr discs on a Nicolet AVATAR 360 FTIR spectrophotometer (Nicolet Instrument Inc., Madison, WI, USA) (range 4,000～400 cm^{-1}). Single-crystal X-ray diffraction data of $[CaL_2(H_2O)_2]_n$ were collected on a Bruker Smart CCD diffractometer (Bruker, Billerica, MA, USA).

2. 2 Synthesis of $[CaL_2(H_2O)_2]_n$ (1)

4-Acetylphenoxyacetic acid (0.1941 g, 1.0 mmol) and sodium hydrate (0.040 g, 1.0 mmol) were dissolved into 10 mL ethanol solution at room temperature. Then 5 mL of aqueous solution containing 0.1195 g $Ca(ClO_4)_2·4H_2O$ (0.5 mmol) was dropped into the above solution. The mixture was heated at 70 °C for 6.5 h with stirring, cooled to room temperature and filtered. Colourless crystals of $[CaL_2(H_2O)_2]_n$ were obtained in 25 days by slowly volatilizing the filtrate at room temperature. Anal. Calcd. for $C_{20}H_{22}O_{10}Ca$: C, 51.90; H, 4.76%. Found: C, 51.65; H, 5.09. IR ν_{max} (cm^{-1}): ν (COO^-): 1675 cm^{-1}.

2. 3 Antitumor activity

The culture of tumor cells (Human hepatoma *SMMC*-7721 cells, human colon carcinoma *WiDr* cells and human lung adenocarcinoma *A*549 cells) and the test procedure for the antitumor activity are consistent with the literature[21, 22].

2. 4 Crystal data and structure determination

A single crystal of **1** (0.12mm × 0.11mm × 0.10mm) was placed on a Bruker SMART APEX CCD X-ray diffractometer equipped with graphite-monochromated Mo$K\alpha$ radiation (λ = 0.71073 Å) at 99.99(10) K. 4441 reflections (R_{int} = 0.0245) were independent for **1**. The structure was solved by direct methods using *SHELXL*-2014/7 program[23]. The *OLEX2*[24] program was used to refine the structure. The non-hydrogen atoms were refined anisotropically and the hydrogen atoms were generated by theoretical calculations. Crystal data for complex **1**: monoclinic system, space group *C*2/*c* with a = 24.4894(11), b = 11.3416(5), c = 7.7164(4) Å, β = 94.750(5)°, V = 2135.88(17) $Å^3$, Z = 4, $C_{20}H_{22}O_{10}Ca$, M_r = 462.45, D_c = 1.438 Mg/m^3, F(000) = 968 and μ(Mo$K\alpha$) = 0.348 mm^{-1}. The final R = 0.0319, wR = 0.0753 ($w = 1/[\sigma^2(F_o^2) + (0.0342P)^2 + 1.4584P]$, where $P = (F_o + 2F_c^2)/3$), S = 1.067. The maximum and minimum peaks are 0.229 and –0.333 e/$Å^3$, respectively.

3 RESULTS AND DISCUSSION

3. 1 Structural description of $[CaL_2(H_2O)_2]_n$ (1)

Single-crystal X-ray structural analyses show that complex **1** crystallizes in monoclinic space group *C*2/*c*. Selected bond distances and bond angles of complex **1** are shown in Table 1. The average distance of the Ca–O bonds is 2.465 Å (ranging from 2.3384(12) to 2.6308(12) Å), which are consistent with those reported[16-21]. And the bond angles of O–Ca–O vary from 50.82(4) to 157.67(4)°.

Table 1. Selected Bond Lengths (Å) and Bond Angles (°)

Bond	Dist.	Bond	Dist.
Ca(1)–O(4)	2.3384(12)	Ca(1)–O(5)	2.3828(12)
Ca(1)–O(4A)	2.6308(12)	Ca(1)–O(5A)	2.3827(12)
Ca(1)–O(4B)	2.6308(12)	C(8)–O(4)	1.259(2)
Ca(1)–O(4C)	2.3384(12)	C(4)–O(2)	1.363(2)
Ca(1)–O(3B)	2.5069(12)	C(7)–O(2)	1.427(2)
Ca(1)–O(3C)	2.5069(12)	C(8)–O(3)	1.252(2)
C(9)–O(1)	1.224(2)		
Angle	(°)	Angle	(°)
O(4)–Ca(1)–O(4C)	122.51(4)	O(4)–Ca(1)–O(3B)	122.51(4)
O(4)–Ca(1)–O(4B)	72.94(4)	O(4A)–Ca(1)–O(3B)	77.99(4)
O(4A)–Ca(1)–O(4C)	72.94(4)	O(4A)–Ca(1)–O(3C)	122.51(4)
O(4B)–Ca(1)–O(4C)	108.23(5)	O(4)–Ca(1)–O(3C)	77.99(4)
O(4A)–Ca(1)–O(4B)	122.51(4)	O(4A)–Ca(1)–O(5A)	78.78(4)
O(4)–Ca(1)–O(4A)	155.97(6)	O(4)–Ca(1)–O(5A)	84.74(4)
O(4)–Ca(1)–O(5)	78.78(4)	O(4B)–Ca(1)–O(3C)	72.78(4)
O(4A)–Ca(1)–O(5)	84.74(4)	O(4B)–Ca(1)–O(3B)	50.82(4)
O(4C)–Ca(1)–O(3B)	72.78(4)	O(3B)–Ca(1)–O(3C)	75.37(5)

To be continued

O(4C)–Ca(1)–O(3C)	50.82(4)	O(4C)–Ca(1)–O(5A)	83.18(4)
O(4B)–Ca(1)–O(5)	83.18(4)	O(3C)–Ca(1)–O(5A)	102.61(4)
O(4C)–Ca(1)–O(5)	157.67(4)	O(3B)–Ca(1)–O(5)	102.61(4)
O(4B)–Ca(1)–O(5A)	157.67(4)	O(3C)–Ca(1)–O(5)	150.49(4)
O(3B)–Ca(1)–O(5A)	150.49(4)	O(5)–Ca(1)–O(5A)	93.09(6)

Symmetry transformation: A: 1 – *x*, *y*, 1/2 – *z*; B: 1 – *x*, 1 – *y*, 1 – *z*; C: *x*, 1 – *y*, –1/2 + *z*

The asymmetric unit of complex **1** is shown in Fig. 2. The fundamental unit of **1** contains one Ca(II) ion, two 4-acetylphenoxyacetate ligands and two coordinated water molecules. Each Ca(II) ion is eight-coordination with six O atoms (O(3B), O(3C), O(4), O(4A), O(4B) and O(4C)) from four 4-acetylphenoxyacetate ligands and two O atoms (O(5) and O(5A)) from two coordinated water molecules, resulting in a distorted triangular dodecahedral geometric configuration. In complex **1,** the carboxylate O atoms of 4-acetylphenoxyacetate ligand adopt different coordination modes with Ca(II) ion (Fig. 3): one O atom adopts a bidentate chelating mode to coordinate to different Ca(II) ions, and the other O atom adopts a monodentate chelating mode to coordinate to the Ca(II) ion. The complex forms a one-dimensional (1D) chain structure by the bridging effect of carboxylate O atoms with adjacent Ca(II) ions (Fig. 4). The 3D network structure is also formed by the interactions of 1D chain (Fig. 5). In addition, four uncoordinated water molecules also exist in the crystal structure.

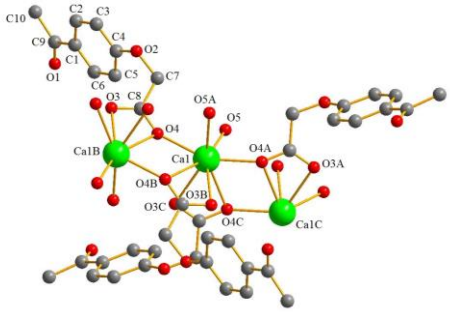

Fig. 2. Asymmetric unit of $[CaL_2(H_2O)_2]_n$

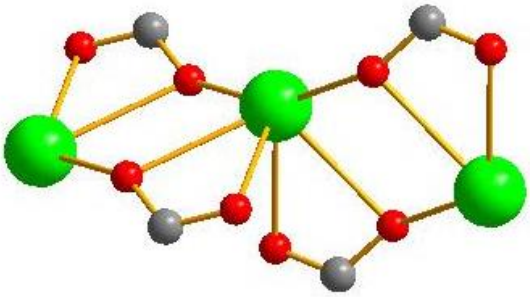

Fig. 3. Coordination mode of carboxylate O atoms

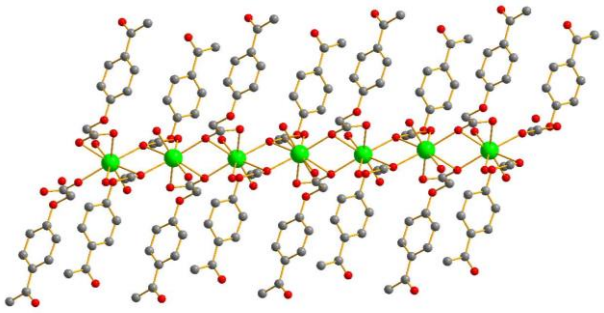

Fig. 4. One-dimension chained structure

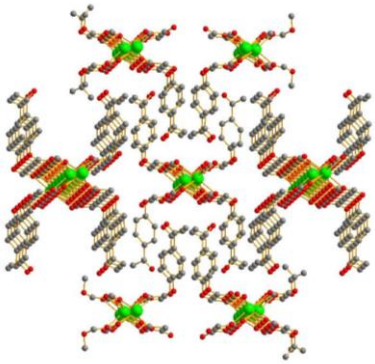

Fig. 5. 3D supramolecular network structure

3. 2 Antitumor activity

The antitumor activity of 4-acetylphenoxyacetic acid and $[CaL_2(H_2O)_2]_n$ was tested against human hepatoma *SMMC*-7721 cells, human colon carcinoma *WiDr* cells and human lung adenocarcinoma *A*549 cells. The data of antitumor activity are given in Table 2. The results show that both 4-acetylphenoxyacetic acid and $[CaL_2(H_2O)_2]_n$ exhibit considerable cytotoxicity, but the antitumor effect of $[CaL_2(H_2O)_2]_n$ is better than that of 4-acetylphenoxyacetic acid. The antitumor effect of $[CaL_2(H_2O)_2]_n$ against WiDr cell is better than that reported[22], while the antitumor effect of $[CaL_2(H_2O)_2]_n$ against SMMC-7721 and A549 cells is weaker than that in document[22].

Table 3. Antitumor Activity of 4-Acetylphenoxyacetic Acid and $[CaL_2(H_2O)_2]_n$

Compound	IC_{50} (μg/mL)		
	SMMC-7721	*WiDr*	*A*549
$[CaL_2(H_2O)_2]_n$	12.5 ±0.2	15.3 ±0.2	19.2 ±0.2
4-Acetylphenoxyacetic acid	15.3 ±0.2	22.6 ±0.2	29.1 ±0.2

4 CONCLUSION

In summary, we have synthesized and structurally characterized a new eight-coordinated Ca(II) coordination polymer, $[CaL_2(H_2O)_2]_n$ (**1**). The antitumor activities of 4-acetylphenoxyacetic acid and the Ca(II) coordination polymer have also been tested. The above results provide a good idea for the synthesis of Ca(II) complexes with antitumor activity in the future.

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