

Synthesis and *in vitro* evaluation of anti-breast cancer activity of a novel Dy (II) coordination polymer.

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Abstract

Discuss here is a kind of novel Dy-based Metal Organic Frameworks (MOF) material, ((Dy(H₂O)(PBA)(SO₄))(DMA)₂(H₂NC₂H₆)_n(1 H₂PBA=4-Hydroxybenzoic acid; the DMA=N,N-Dimethylacetamide), from the solvothermal synthesis conditions and using sulfuric acid as the PH controller and template. The X-ray studies shown that 1 is a 3D two-fold interpenetrated MOF built up from 1D-Dy (III) ribbon chains and PBA²⁻ ligands. 1 title compound anti-breast cancer activity and organic ligand (H₂PBA) survey of four kinds of human breast tumor cell line (BT474, ZR-75-30, MDA-MB-453 and Hs-578T) determined by MTT test. Found that compared with organic ligands, compound 1 exerted rather potent activity against all of these cell lines.

Keywords: Synthesis, X-ray, Anti-breast cancer.

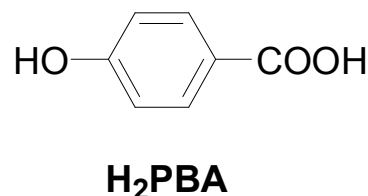
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Introduction

In addition to surgery, radiotherapy and biological therapy, immune therapy and hormone therapy, treatment strategy for cancer treatment in clinical practice is currently focused on cytotoxic drugs as the main form of cancer chemotherapy [1,2]. Very heterogeneous compounds toxicity of cytotoxic drugs to treat cancer is mainly composed of rapid cell growth and division. Because cancer cells often experiencing rapid growth and spread, they are preferred by the agency [3-5]. The material is a traditional free drugs management solution in the form of intravenous injection. Although they use the long history and many more new drug development program to improve clinical success of treatment failure is often encountered, even in patients with malignant tumor is more sensitive to chemotherapy drugs (e.g., breast cancer), clinical results is usually lower than expected [6,7].

Coordination Polymers (CPs) is in the nature has not found another alternative mode. These compounds by the self-assembly of metal ions and organic ligands experiencing explosive growth because they are interesting topology and great potential applications in the field of luminescence, catalysis, magnetism, gas storage, etc. [8,9].

Biological activities of these compounds, however, have not been reported. In this work, we prepared a novel Dy-based MOF material, ((Dy(H₂O)(PBA)(SO₄))(DMA)₂(H₂NC₂H₆)_n(1 H₂PBA=4-Hydroxybenzoic acid; the DMA=N,N-Dimethylacetamide), by using a linear organic link (Figure 1), and then to evaluate their antitumor activities.

**Figure 1.** Chemical structure of H₂PBA ligand.**Experimental****Apparatus and materials**

All the starting materials and reagents used in this work for commercial and without purification before use. Elemental analysis (C, H, N) determination of element analyser Vairo EL III. Single crystal X-ray diffraction data records in mercury compound 1 CCD diffractometer. Melting point is XT-4 micro melting equipment, thermometer and uncorrected.

Synthesis and characterization of compound 1

A mixture of Dy(NO₃)₃·6H₂O (0.045 g, 0.1 mmol), H₂PBA (0.014 g, 0.1 mmol) and DMA (3 mL) were added to the 10 mL glass containers. Add 5 drops of sulfuric acid (20%, aq), glass container is closed and heated to 105°C to 72 h autogenous pressure. The ship was cooled to room temperature and yellow crystal. 1 yield is 32% (based on Dy(NO₃)₃·6H₂O). Infrared (KBr, cm⁻¹): 3225 (br), 1646 (s), 1382 (vs), 1229 (s), 862 (m), 835 (m), 656 (s), 566 (s). Elemental analysis (%) (C₉H₁₄DyO₈SN): C, 23.56; H, 3.08; N, 3.05; Findings: C: 23.21; H: 23.21; N: 3.12.

Crystal structure determination

Structure of the computer control of mercury measurement (Charge-Coupled Device) CCD diffractometer and graphite-monochromated Mo-K α radiation ($\lambda=0.71073$) at T=293 (2) K absorption correction using the SADABS program. Structure solved using direct method, and improved the matrix least square method using SHELXS F2-97 [10] package. The data and the structure improvement of crystal compound 1 summarized in Table 1.

Table 1. Crystal data and structure refinements for compound 1.

Formula	C ₉ H ₁₄ DyO ₈ SN
Mr	460
Temperature/K	293 (2)
Crystal system	Monoclinic
Space group	P2 ₁ /c
a/Å	7.6118 (3)
b/Å	20.0572 (8)
c/Å	6.4099 (3)
α /°	90
β /°	104.158 (5)
γ /°	90
V/Å ³	948.88 (7)
Z	4
D _{calc} /g/cm ⁻³	2.889
μ (Mo K α)/mm ⁻¹	8.126
θ range/°	3.427 to 26.369
Reflections collected	4091
No. unique data (R (int))	1930 [0.0246]
No. data with $I \geq 2 \sigma (I)$	1748
R ₁	0.0626
ωR_2 (all data)	0.1626

In vitro anticancer activity

The feasibility of the four human tumor cell line (BT474, ZR-75-30, MDA-MB-453 and Hs-578T) was determined using the determined by MTT test. Cells of 70-80% confluency treatment of various concentrations of the synthesized compounds were 1% Dimethyl Sulfoxide (DMSO) as a negative control. After 48 h hatch 20 μ l determined by MTT solution (5 mg/ml of PBS) add and hatch an additional 4 h. After that, the medium is inspiratory carefully, 150 μ l DMSO added. Hatch 15 minutes later, the optical density measurement at 490 nm using FlexStation 3 desktop multimode standard instrument (molecular devices, USA). Data record and analysis to assess the effect of test material cell viability and depress growth.

Results and Discussion

Molecular structure

Single-crystal X-ray diffraction studies indicate that 1 crystallizes in the monoclinic space group P2₁/c, and a two-fold interpenetrated framework with 1D Dy (III) ribbon building units is presented. The asymmetric unit of 1 is composed of one Dy (III) ions, one PBA²⁻ ligand, one SO₄²⁻ ion, one coordinated water molecule and one disordered H₂N(CH₃)₂ cation. The Dy (III) metal center is coordinated by eight O atoms from two PBA²⁻ ligands, three SO₄²⁻ ligands, and one coordinated water molecule, resulting in a [DyO₈] coordinating configuration (Figure 2a). The Dy-O distances are in the range of 2.329 (7) to 2.514 (7) Å. Notably, two Dy (III) centers in the c axis are connected with each other via the SO₄²⁻ ions, and such 1D chains are further inter-linked by the μ_2 -O atoms from the SO₄²⁻ ions along a axis to afford an infinite Dy (III) ribbon building units (Figure 2b). These Dy (III) ribbons are connected by the PBA²⁻ ligands to construct a 3D network with the distances between neighbouring Dy (III) ions in 4.049 Å. Such structural arrangements give large 1D channel with pore diameter ca. 8 Å (Figure 2c). However, due to the two-fold interpenetration, 1 is a dense structure with no residual solvent accessible area in unit cell (Figure 2d). From a topological view point, the structure can then be described as a new 3, 5-connected net by viewing the Dy ion as five connected node and the PBA²⁻ ligand as a three-connected node, and the point symbol for this topology is (42.65.83) (42.6).

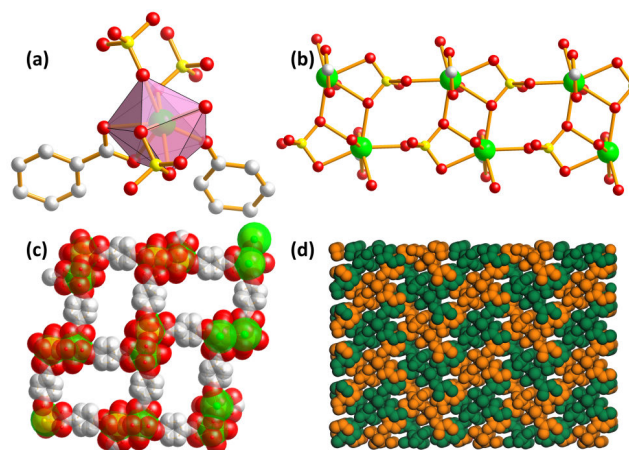


Figure 2. (a) The coordination environment of Dy (III) in 1. (b) The 1D Dy (III) ribbon unit of 1. (c) The square channel in 1. (d) The two-fold interpenetrated network of 1.

Antitumor activity

The cytotoxicity of synthetic compound 1 and organic ligand (H₂PBA) on BT474, ZR-75-30, MDA-MB-453 and Hs-578T cell lines were determined by MTT test evaluation and IC₅₀ value concentration from the experimental data are summarized in Table 2. Comparison, the purpose of a standard anti-cancer drug docetaxel is an assessment under the same conditions.

Obviously, organic ligand (H₂PBA) is not active against all these cell lines (IC₅₀>100 μM). In this concentration, organic ligands should exert high poisonous to the cells of normal cells, so we came to the conclusion that it did not show any living selectivity of these cell lines. However, tumor cells after incubation of compound 1 72 h IC₅₀ value concentration of compound aged 18 to 32 μM, similar reference drug docetaxel, show title compound 1 showed antitumor activity to all of these cell lines to different degrees.

Table 2. Growth inhibitory effects of compound 1, organic ligand (H₂PBA) and docetaxel on BT474, ZR-75-30, MDA-MB-453 and Hs-578T cell lines.

Compounds	IC ₅₀ (μM)			
	BT474	ZR-75-30	MDA-MB-453	Hs-578T
Compound 1	18	20	32	22
H ₂ PBA	>100	>100	>100	>100
Docetaxel	23	25	30	25

Conclusion

All in all, we have successfully synthesized a new Dy (III) based on the framework of infinite Dy (III) ribbon construction units according to a novel topology. Antitumor activity *in vitro* experiments show that the title compound 1 is a potential anticancer drug.

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