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Synthesis, characterization and cell imaging properties of rare earth compounds based on hydroxamate ligand☆

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ABSTRACT

Six binuclear rare earth compounds were synthesized through the ligand of 4-Bromo-N-hydroxy-N-methyl-benzamide (sH_2bha). Compounds **1**–**3** are isomorphous, and compound **1** is crystallized in the monoclinic system with the $P2_1/c$ space group. Compounds **4** and **5** are isomorphous, and compound **4** is crystallized in the triclinic system with the *P*-1 space group. Compound **6** is crystallized in the triclinic system with the *P*-1 space group. The compounds were characterized by thermogravimetric analysis (TGA) and IR spectroscopy. The fluorescence spectrum in the visible area shows characteristic peaks of Eu, Tb, and Dy compounds. The efficiency of Eu compound on the viability of PC3 cells was assessed using CCK8 assays. From the CCK8 results, ionic concentration may have a great effect on PC3 cells' proliferation. Eu compound shows red fluorescence in the cytoplasm of PC3 cell. As for Eu compound, it might have potential application in cell imaging technology.

1. Introduction

There has been enormous research interest in the coordination chemistry of rare earth complexes owing to their pronounced luminescence properties.[1–4] Rare earth complexes luminescent material is a research subject that integrates inorganic, organic, and biological luminescence.[5] In view of the fact that lanthanide ions typically show weak absorption of light, luminescent lanthanide complexes exhibit distinctive photophysical properties after the introduction of organic ligands.[6] Lanthanide complexes have successfully replaced the organic chromophore luminescence immunity because of recognizable sharp emission lines over narrow wavelength ranges.[7–9] In order to increase the luminescence efficiency of rare earth ions, most research is devoted to the selection and optimization of rare earth coordination polymers, while Eu(III) complexes have been considered as attractive luminescent materials due to their strong red emission.[5]

Hydroxamic acids are a family of compounds that possess strong chelating properties with various metal ions.[10] Given the important potential applications of lanthanide complexes and the fascinating properties of the hydroxamic acid, we investigated a series of lanthanide-based complexes $[Ln_2(sbha)_2(hfac)_4(H_2O)_2]$ (Ln = Eu (**1**), Tb (**2**), Gd (**3**), Dy (**4**), Ho (**5**), Nd (**6**)) based on 4-Bromo-N-hydroxy-N-methyl-benzamide (sH_2bha) and rare earth hexafluoroacetylacetonacetate $[Ln(hfac)_3]$. The fluorescence spectrum in the visible area shows characteristic peaks of Eu, Tb, and Dy compounds. As seen from the results, Eu compound shows red fluorescence in the cytoplasm of PC3 cell, and Eu compound has entered the cytoplasm, not just on the cell membrane. In further experiments, Eu compound may have potential application in living-animal imaging technology.

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2. Experimental

2.1. Materials and physical measurements

All commercially available chemicals and solvents were of reagent grade and used without further purification. The ligand of 4-Bromo-N-hydroxy-N-methyl-benzamide (sH_2bha) was synthesized according to the method reported previously.[10] Rare earth hexafluoroacetylacetonacetate [Ln(hfac)$_3$] was synthesized according to the method reported previously.[11] The single crystalline powder samples were prepared by crushing the crystals and scanned from 3° to 60° with a scanning speed of 0.02 °/s. Thermogravimetric analysis (TGA) were performed on a NETZSCH TG 209 instrument with a heating rate of 10 °C/min in the N_2 atmosphere. IR spectra were recorded in the range of 4000–400 cm^{-1} on a Perkin–Elmer spectrometer with KBr pellets. Fluorescence spectroscopy data were recorded on a HORIBA Jobin Yvon HJY-FL3-221-TCSPC spectrophotometer.

2.2. Preparation of compounds

Synthesis procedure of [$Ln_2(sbha)_2(hfac)_4(H_2O)_2$] (Ln = Eu (**1**), Tb (**2**), Gd (**3**), Dy (**4**), Ho (**5**), Nd (**6**)) is as follows:

Ln(hfac)$_3$ (0.05 mmol, 0.039 g) was dissolved in n-heptane (10 mL), and the solution was refluxed for 2 h. Then the solution was cooled to 60 °C. A CH_2Cl_2 solution (2 mL) of sH_2bha (0.1 mmol) was added. And then methanol (0.2 mL) was added. The mixture was stirred for 30 min, cooled slowly to room temperature, and solution A was obtained. Ln(hfac)$_3$ (0.05 mmol, 0.039 g) was placed in the bottom of the tube, CH_2Cl_2 (4 mL) was added. Solution A was slowly added, and finally *n*-heptane (4 mL) was slowly added. Via standing, solution diffusion, and slow evaporation of solvents, needle-shaped crystals suitable for X-ray analysis were precipitated after one week. FT-IR (KBr, ν, cm^{-1}): 3338, 2357, 1649, 1460, 1267, 1211, 1147, 910, 804, 663 (7); 3335, 2355, 1651, 1462, 1261, 1215, 1143, 915, 802, 661 (8); 3340, 2362, 1653, 1465, 1260, 1211, 1145, 914, 804, 662 (9); 3344, 2357, 1651, 1462, 1263, 1211, 1141, 914, 806, 663 (10); 3336, 2357, 1653, 1465, 1258, 1210, 1141, 916, 804, 661 (11); 3335, 2358, 1653, 1463, 1257, 1208, 1144, 912, 804, 663 (12).

2.3. X-ray crystallography

Diffraction data for compounds **1**–**6** was collected with a Bruker SMART APEX CCD instrument with graphite monochromatic Mo Kα radiation (λ = 0.071073 nm). The data were collected at 293 (2) K. The absorption corrections were made by multi-scan methods. The structure was solved by charge flipping methods with the program Olex2 and refined by full-matrix least-squares methods on all F2 data with Olex2. Selected bond lengths and angles for **1**–**6** are given in Tables S1–S6 (supporting information). The crystallographic details are provided in Table 1.

2.4. Cell culture

Prostate Cancer PC3 cells and Hela cells were provided by the Chinese Academy of Sciences (Shanghai, China). The cells were routinely cultured with RPMI-1640 supplemented with 10% fetal bovine serum (FBS), 100 units/mL penicillin, and 100 μg/mL streptomycin in a humidified atmosphere of 5% CO_2 at 37 °C. To maintain cells in the exponential growth phase, they were passaged at a ratio of 1:3 every 3 days. Before use, the cells were trypsinized, resuspended, and then precultured. Caution was used in handling all human biological material.[12,13]

2.5. In vitro cytotoxicity of compound *1*

To evaluate the cell cytotoxicity of compound **1**, we performed CCK8 (method of transcriptional and translational) assays to

Table 1
Crystallographic Data for compounds **1**–**6**.

Identification	1	2	3	4	5	6
Empirical formula	$C_{17}H_8BrEuF_{12}NO_7$	$C_{17}H_8BrF_{12}NO_7Tb$	$C_{17}H_8BrF_{12}NO_7Gd$	$C_{17}H_8BrF_{12}NO_7Dy$	$C_{17}H_8BrF_{12}NO_7Ho$	$C_{17}H_8BrF_{12}NO_7Nd$
Formula weight	798.11	805.07	803.40	808.65	811.08	790.39
T (K)	113.15	113.15	113.15	113.15	113.15	113.15
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic	Triclinic	Triclinic
Space group	$P2_1/c$	$P2_1/c$	$P2_1/c$	P-1	P-1	P-1
a (nm)	0.80093 (8)	0.80095 (7)	0.80135 (8)	0.7964 (3)	0.79735 (18)	0.80995 (13)
b (nm)	2.3150 (2)	2.3030 (2)	2.3106 (3)	1.2454 (5)	1.2444 (2)	1.07697 (17)
c (nm)	1.29455 (12)	1.29229 (12)	1.29373 (12)	1.3198 (2)	1.3185 (2)	1.4528 (2)
α(°)	90	90	90	66.82 (4)	66.394 (8)	95.082 (2)
β(°)	95.151	95.473 (2)	95.351 (2)	80.29 (3)	80.447 (11)	103.383 (3)
γ(°)	90	90	90	87.01 (4)	87.204 (12)	97.243 (3)
Volume/nm^3	2.3906 (4)	2.3728 (4)	2.3850 (4)	1.1860 (8)	1.1819 (4)	1.2139 (3)
Z	4	4	4	2	2	2
ρ (mg/mm^3)	2.218	2.254	2.237	2.264	2.279	2.162
F (000)	1516	1524.0	1520.0	764.0	766.0	752.0
Theta range for data collection	6.022°–56.632°	6.02°–55°	6.014°–54.996°	6.05°–55.158°	6.052°–55.33°	6°–55.02°
Index ranges	$-10 \le h \le 10$, $-30 \le k \le 30$, $-17 \le l \le 15$	$-10 \le h \le 10$, $29 \le k \le 29$, $-16 \le l \le 16$	$-10 \le h \le 10$, $-30 \le k \le 30$, $-16 \le l \le 16$	$-10 \le h \le 10$, $15 \le k \le 15$, $-17 \le l \le 16$	$-10 \le h \le 10$, $-16 \le k \le 16$, $-17 \le l \le 16$	$-10 \le h \le 10$, $-13 \le k \le 13$, $-18 \le l \le 18$
Reflections collected	31,742	30,137	30,450	15,434	14,242	14,423
Independent reflections	5908 [R_{int} = 0.0262]	5422 [R_{int} = 0.0288]	5746 [R_{int} = 0.0307]	5374 [R_{int} = 0.0288]	5375 [R_{int} = 0.0245]	5473 [R_{int} = 0.0209]
Data/restraints/parameters	5908/0/353	5422/0/353	5476/0/353	5374/0/353	5375/0/353	5473/0/353
Goodness-of-fit on F^2	1.039	1.031	1.043	1.031	1.135	1.282
Final R indexes [$I \ge 2\sigma$ (I)]	R_1 = 0.0160, wR_2 = 0.0409	R_1 = 0.0164, wR_2 = 0.0412	R_1 = 0.0160, wR_2 = 0.0406	R_1 = 0.0206, wR_2 = 0.0562	R_1 = 0.0208, wR_2 = 0.0532	R_1 = 0.0334, wR_2 = 0.0863
R indices (all data)	R_1 = 0.0187, wR_2 = 0.0416	R_1 = 0.0187, wR_2 = 0.0418	R_1 = 0.0185, wR_2 = 0.0411	R_1 = 0.0220, wR_2 = 0.0566	R_1 = 0.0222, wR_2 = 0.0535	R_1 = 0.0353, wR_2 = 0.0867
Largest diff. peak/hole/(e/nm^3)	930/-520	970/-490	850/-710	1280/-940	750/-700	2070/-930

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