

Synthesis, Crystal Structure and DNA-Binding of Lanthanum Complex with Schiff Base Derived from *o*-Vanillin and *p*-Toluidine

XIAO-JU CHEN¹, WEI-JI HU², YI QIN² and GUO-LIANG ZHAO^{1,2,*}

¹College of Chemistry and Life Science, Zhejiang Normal University, Jinhua 321004, P.R. China

²Xingzhi College, Zhejiang Normal University, Jinhua 321004, P.R. China

*Corresponding author: Fax: +86 579 82282269; Tel: +86 579 82282061; E-mail: sky53@zjnu.cn

(Received: 3 August 2012;

Accepted: 22 May 2013)

AJC-13533

A new complex $[\text{La}(\text{NO}_3)_3(\text{C}_2\text{H}_5\text{OH})(\text{C}_{15}\text{H}_{15}\text{NO}_2)_2]$ was synthesized from lanthanum nitrate and Schiff base ($\text{C}_{15}\text{H}_{15}\text{NO}_2$, derived from *o*-vanillin and *p*-toluidine) by refluxing in ethanol. Its crystal structure was determined by single crystal X-ray diffraction method. The complex is crystallize in triclinic, space group P-1, with $a = 0.79851(3)$ nm, $b = 1.47473(5)$ nm, $c = 1.63872(6)$ nm, $\alpha = 73.546(2)^\circ$, $\beta = 86.769(2)^\circ$, $\gamma = 79.767(2)^\circ$, $V = 1.82123(1)$ nm³, $Z = 2$, $M_r = 852.56$, $F(000) = 1862$, $D_c = 1.555$ g cm⁻³, $\mu(\text{MoK}\alpha) = 1.056$ mm⁻¹. It turned out that six oxygen atoms from three nirtate anions, one oxygen atom in ethanol and two phenolate oxygen atoms from two Schiff base ligands coordinate to La(III), forming a 9-coordination distorted monocapped square prism geometry. In addition, DNA-binding of the complex was studied by EtBr fluoescent probe and the results show that the complex interact with DNA by intercalative mode. CCDC:878971.

Key Words: Schiff base, *o*-Vanillin, *p*-Toluidine, Lanthanum complex, Crystal structure, DNA-binding.

INTRODUCTION

It is well know that Schiff bases are important in multiple fields such as chemistry and biochemistry owing to their biological activities^{1,2}. Schiff bases complexes prepared by ligands from substituted *o*-vanillin have been absorbed considerable attention in the past decades due to the intriguing biological activities³⁻⁵. DNA-binding is the critical step for DNA activity. To design effective chemotherapeutic agents and better anticancer drugs, it is essential to explore the interactions of metal complexes with DNA. Great effort has been made to metal complexes binding to DNA through an intercalation mode with their structures containing fully planar intercalating into the adjacent base pairs of DNA⁶⁻¹⁰. In addition, lanthanide ions have high and variable coordination numbers and flexible coordination geometry^{11,12}. Studies on the interaction of lanthanide metal complexes with DNA have been an active field of research. Interested in this field, a new Schiff base complex, $[\text{La}(\text{NO}_3)_3(\text{C}_2\text{H}_5\text{OH})(\text{C}_{15}\text{H}_{15}\text{NO}_2)_2]$ was synthesized and characterized. The DNA-binding experiment of the complex suggest that the complex bind to DNA in an intercalation mode.

EXPERIMENTAL

All reagents were of analytical grade quality and were used without further purification. The FTIR spectra were

obtained from KBr pellets in the range 4000-400 cm⁻¹ with a Nicolet NEXUS 670 FTIR spectrometer. Thermal analyses were carried out using Mettler-Toledo TGA/SDTA 851^e thermal analyzer at a heating rate of 10 °C min⁻¹ from 30 to 800 °C in air atmosphere. Fluorescence spectra were recorded on a 970-CRT spectrofluorophotometer. Diffraction data were collected at 296(2)K on a Bruker APEXII CCD diffractometer with graphite monochromated $\text{M}_0\text{K}\alpha$ radiation ($\lambda = 0.071073$ nm).

Synthesis of the complex: A solution of lanthanum(III) nitrate hexahydrate salt (0.5 mmol) in ethanol (10 mL) was added to a boiling solution of the Schiff base (1 mmol) in ethanol (30 mL). The mixture was gently heated on a water bath for 2 h and then left to stand overnight. The complex that crystallized out of the reaction mixture were filtered off washed with ethanol and dried in a desiccator over anhydrous silica gel. Yield 80 % based on metal. Anal. calcd. (%) for $\text{C}_{32}\text{H}_{36}\text{N}_5\text{O}_{14}\text{La}$: C, 45.16; H, 4.11, N, 8.15. Found (%): C, 45.04; H, 4.11; N, 8.21. IR (KBr, ν_{max} , cm⁻¹): 3441(m), 3414 (m), 3044(w), 2946 (w), 2843(w), 1637 (s), 1549 (s), 1502(s), 1384 (s), 1305(s), 1233(s), 1032 (s), 823(w), 731(w), 491(m).

DNA-binding experiments: 2 mL EB solution (100 $\mu\text{g mL}^{-1}$) and 1.0 mL DNA solution (200 $\mu\text{g mL}^{-1}$) were added to 10 mL colourimetric tube, the DNA-binding ability of the complex to EB-DNA were studied in 2 mL *tris*-HCl/NaCl buffer (pH = 7.4). After standing for 2 h, gradually with adding a certain amount of the complex solutions to the mixture and

reacting for 12 h at 4 °C. The excitement wavelength was aroused at 251 nm and each sample solution was scanned in the range 520-700 nm.

Crystal structure determination: A single crystal of the title complex with dimensions of 0.202 mm × 0.192 mm × 0.168 mm was selected and mounted on a glass fiber and collected diffraction data on a Bruker Smart APEX II CCD diffractometer with graphite monochromated $M\alpha$ radiation ($\lambda = 0.071073$ nm). Structure was solved by direct methods using SHELXS-97¹³ and refined on the F^2 by full-matrix least-square method with SHELXL-97¹⁴. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed in geometrically calculated positions and refined by using a riding mode. Experimental details for X-ray data collection are presented in Table-1 and the selected bond lengths and angles are listed in Table-2. CCDC No. 878971 of **1** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge crystallographic data centre.

TABLE-1
CRYSTALLOGRAPHIC DATA FOR THE COMPLEX

Empirical formula	$C_{32}H_{36}N_5O_{14}La$
Formula weight	852.56
Temperature / K	296(2)
Wavelength / Å	0.71073
Crystal system,	Triclinic
Space group	P-1
a (nm)	0.79851(3)
b (nm)	1.47473(5)
c (nm)	1.63872(6)
α (°)	73.546(2)
β (°)	86.769(2)
γ (°)	79.767(2)
V (nm ³)	1.82123(1)
Z	2
Dc (g cm ⁻³)	1.555
Absorption coefficient (mm ⁻¹)	1.246
F(000)	862
Crystal size (mm)	0.202 × 0.192 × 0.168
Theta range for data collection (°)	1.66 to 27.52
Limiting indices	-10 ≤ h ≤ 10, -19 ≤ k ≤ 19, -20 ≤ l ≤ 21
Reflections collected (unique)	29358/8305 [R(int) = 0.0268]
Completeness to $\theta = 27.52$ (%)	98.9
Max. and min. transmission	0.809 and 0.779
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	8305/600/465
Goodness-of-fit on F^2	1.009
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0308$, $wR_2 = 0.0842$
R indices (all data)	$R_1 = 0.0364$, $wR_2 = 0.0885$
Largest diff. peak and hole (e nm ⁻³)	576 and -534

RESULTS AND DISCUSSION

IR spectrum: The broad absorption band at 3414 cm⁻¹ is attributed to the hydroxyl group of the free ligand. The H atoms of the Schiff base ligand migrate to the azomethine N atom *via* N-H...O intramolecular hydrogen bonding and with absorption at 3441 cm⁻¹, showing coordination of oxygen atom of the phenolic hydroxyl with the central La(III) ion as reported in the literature¹⁵. The C-O (Ph-OH) stretching vibration shift from 1257 cm⁻¹ to 1233 cm also supports the coordination of oxygen atoms, which indicating that coordination

TABLE 2
SELECTED BOND LENGTHS (nm) AND ANGLES (°)

Bond	Length	Bond	Length
La(1)-O(6)	0.2651(3)	La(1)-O(13)	0.2481(2)
La(1)-O(11)	0.2432(2)	La(1)-O(14)	0.2530(2)
La(1)-O(5)	0.2669(3)	La(1)-O(7)	0.2648(6)
La(1)-O(9)	0.2708(6)	La(1)-O(7')	0.2710(8)
La(1)-O(2)	0.2777(7)	La(1)-O(2')	0.2802(8)
La(1)-O(1)	0.2586(6)	La(1)-O(1')	0.2577(6)
La(1)-O(9')	0.2769(7)		
Angle	(°)	Angle	(°)
O(11)-La(1)-O(13)	131.36(80)	O(11)-La(1)-O(14)	79.67(80)
O(11)-La(1)-O(1)	118.26(14)	O(13)-La(1)-O(14)	72.30(90)
O(14)-La(1)-O(1)	81.46(15)	O(13)-La(1)-O(10)	96.17(15)
O(11)-La(1)-O(7)	110.70(15)	O(13)-La(1)-O(7)	113.38(14)
O(14)-La(1)-O(7)	150.26(16)	O(11)-La(1)-O(6)	64.71(80)
O(1)-La(1)-O(7)	69.0(20)	O(14)-La(1)-O(6)	133.59(90)
O(13)-La(1)-O(6)	109.50(80)	O(1)-La(1)-O(6)	140.97(16)
O(7)-La(1)-O(6)	73.88(16)	O(11)-La(1)-O(5)	109.61(80)
O(13)-La(1)-O(5)	69.61(80)	O(14)-La(1)-O(5)	135.48(10)
O(7)-La(1)-O(5)	69.00(15)	O(1)-La(1)-O(5)	124.45(13)
O(11)-La(1)-O(9)	67.72(14)	O(6)-La(1)-O(5)	47.12(80)
O(14)-La(1)-O(9)	123.99(14)	O(13)-La(1)-O(9)	159.58(14)
O(1)-La(1)-O(9)	76.2(20)	O(7)-La(1)-O(9)	46.24(18)
O(6)-La(1)-O(9)	69.52(15)	O(5)-La(1)-O(9)	98.80(14)
O(14)-La(1)-O(2)	98.23(17)	O(11)-La(1)-O(2)	164.87(17)
O(1)-La(1)-O(2)	46.8(20)	O(13)-La(1)-O(2)	60.57(16)
O(6)-La(1)-O(2)	123.72(17)	O(7)-La(1)-O(2)	64.3(20)
O(9)-La(1)-O(2)	102.2(20)	O(5)-La(1)-O(2)	82.49(17)

bonds were formed between the metal ion and the oxygen atoms of the phenol hydroxyl¹⁶. The presence of broad band at 3044 cm⁻¹ indicating the hydrogen bonds of the N-H...O. The five absorption bands of 1502, 1305, 1032, 823 and 731 cm⁻¹ can be assigned to the vibrations of the bidentate NO₃⁻. The feature at 1637 cm⁻¹ may be assigned to the $\nu(C=N)$ stretching in the Schiff base ligand. A new band at 491 cm⁻¹ attributed to La-O stretching vibration also appears.

Description of the structure: The crystal structure of the complex is shown in Fig. 1. Four O atoms (O1, O2, O7, O9) in two nitrate anions are disordered over two sites (all assigned in a 50:50 ratio), in order to make it clear, we don't show it in Fig. 1. Nine O atoms coordinate to La(III) ion, six of which come from three nitrate radical anions, one comes from ethanol and the other two come from the Schiff base ligands (HL). The Schiff base HL ligand coordinate to La(III) ion in monodentate mode, using O atoms from deprotonated phenolic hydroxyl groups. The bond lengths of La-O (phenolic) are 0.2432(2) and 0.2481(2) nm, which are shorter than La-O (methoxy) (0.2811(2) and 0.3001(3) nm for La-O12 and La-O10), so we know that there exist a weak interaction between La(III) and the O12, O10 atoms. The nitrate anions coordinate to La(III) with the distances ranging from 0.2577(6) to 0.2777(7) nm, which are intermediate between the La-O (phenolic) and the La-O (methoxy) bond lengths. The La-O (methoxy) bond length is only slightly longer than the La-O (phenolic), which are similar with the reported complex¹⁵.

The coordination geometry of La(III) can be described as a distorted monocapped square prism geometry (Fig. 2), Atoms O2, O6, O7 and O13 form a similar square plane with a mean deviation of 0.1321 nm. The other square plane is defined by O1, O9, O11 and O14 and its mean deviation from

plane is 0.0182 nm. The dihedral angle is $15.140(86)^\circ$ between the two plane. Atom O5 is located as the cap to complete the coordination environment of the La center.

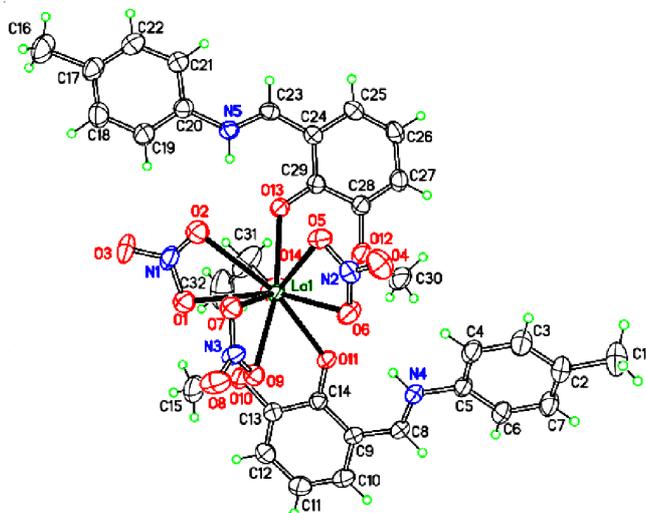


Fig. 1. Molecular structure of the title complex with thermal ellipsoids shown at the 30 % level

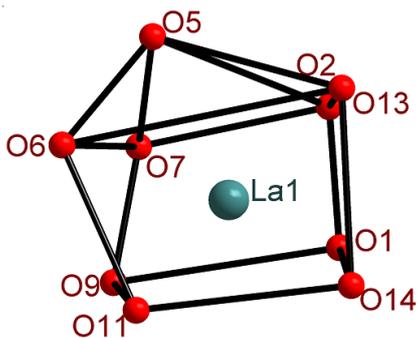


Fig. 2. Coordinate of the title complex

The hydrogen bonds and $\pi \cdots \pi$ weak non-covalent interactions tend to stability to the crystal structure. The hydrogen bonds are listed in Table-3 and the stacking plot of this complex is shown in Fig. 3. In each Schiff base ligand, the proton of phenolic hydroxyl group is transferred to the imine N atom, which is involved in the formation of intramolecular hydrogen bonds.

TABLE-3 HYDROGEN BOND GEOMETRY FOR TITLE COMPLEX (nm, $^\circ$)				
D—H...A	D—H	H...A	D...A	D—H...A
N5—H5A...O13	0.086	0.198	2.648(3)	134.2
N4—H4A...O11	0.086	0.204	2.687(3)	131.2

Thermogravimetric analysis: The TG curve of complex 1 is shown in Fig. 4. The first stage decomposition temperature is in the range of 220-300 $^\circ\text{C}$, with a mass loss of 27.09 %, which corresponds to the elimination of one $\text{CH}_3\text{CH}_2\text{OH}$ and three NO_3^- (calcd. 27.39 %). In the second to third stage of decomposition in the 300 $^\circ\text{C}$ - 735 $^\circ\text{C}$ temperature range, the Schiff base ligands are lost, with a mass loss of 53.81 % (calcd. 53.49 %). The final product is the metal oxide La_2O_3 (19.10 %, calcd. 19.12 %). The result is in good accordance with the composition of the complex.

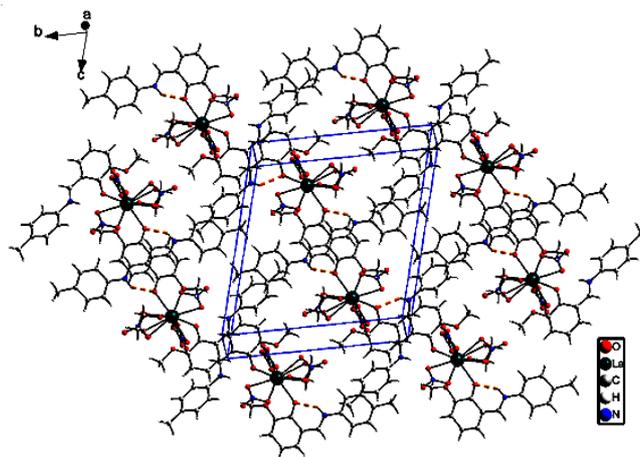


Fig. 3. Packing plot of the title complex

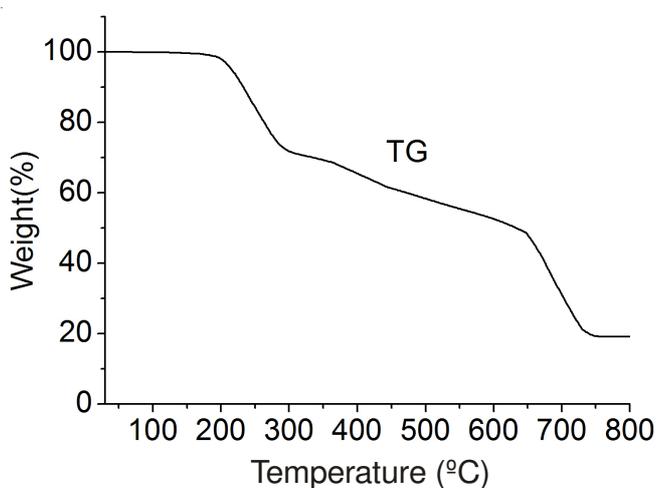


Fig. 4. TG of the complex

Fluorescence quenching studies: Fig. 5 shows that the effects of the complex on the fluorescence spectra of EB-DNA system. Upon addition of the tested complex, the emission intensity at 592 nm of EB-DNA system decreased in different degrees, indicating that the complex competes with EB to bind with DNA. The fluorescence quenching constant (K_{sq}) of the

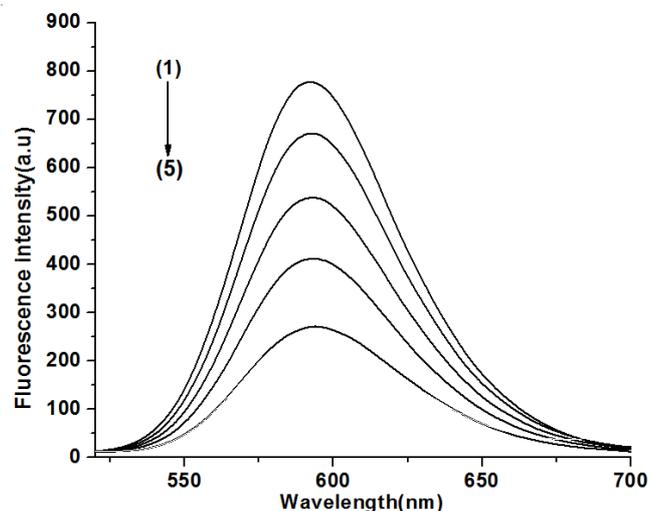


Fig. 5. Effects of the complex on the fluorescence spectra of EB-DNA system; ($r_1 = 0$; $r_2 = 0.059$; $r_3 = 0.118$; $r_4 = 0.177$; $r_5 = 0.236$)

title complex is 5.49. The quenching plots illustrate that the quenching of EB-bound EB-DNA system by the complex agree well with the Stern-Volmer equation¹⁶: $I_0/I = 1 + K_sqr$. It indicating that interaction of the complex with DNA was strong and could release some free EB from EB-DNA¹⁷, which may be due to the five chelating rings created by the ligand and metal. These rings strong the planarity of Schiff base HL ligand, at the same time the Schiff base HL ligand possessing a great conjugated structure can effectively improve the DNA-binding affinity of the complex. so it is easy for the complex to insert to the base of DNA molecule to compete with the combination of EB-DNA sites.

REFERENCES

1. J.E. Kovacic, *Spectrochim. Acta A*, **23**, 183 (1967).
2. R. Atkins, G. Brewer and E. Kokot, G.M. Mockler and E. Sinn, *Inorg. Chem.*, **24**, 127 (1985).
3. G.L. Zhao, P.H. Zhang and Y.L. Feng, *Chin. J. Inorg. Chem.*, **21**, 421 (2005).
4. R.C. Burrows and J.C. Bailar, *J. Am. Chem. Soc.*, **88**, 4150 (1966).
5. C. Metcalfe and J.A. Thomas, *Chem. Soc. Rev.*, **32**, 215 (2003).
6. K.K. Patel, E.A. Plummer, M. Darwish, A. Rodger and M.J. Hannon, *J. Inorg. Biochem.*, **91**, 220 (2002).
7. N. Shahabadi, S. Kashanian and F. Darabi, *Eur. J. Med. Chem.*, **45**, 4239 (2010).
8. C. Stinner, M.D. Wightman, S.O. Kelley, M.G. Hill and J.K. Barton, *Inorg. Chem.*, **40**, 5245 (2001).
9. X. Li, Y.T. Li, Z.Y. Wu, Y.-J. Zheng and C.-W. Yan, *Inorg. Chim. Acta*, **385**, 150 (2012).
10. P.U. Maheswari and M. Palaniandavar, *Inorg. Chim. Acta*, **354**, 901 (2004).
11. H.B. Zhang, N. Li, C.B. Tian, T.F. Liu, F.L. Du, P. Lin, Z.H. Li and S.-W. Du, *Cryst. Growth Des.*, **12**, 670 (2012).
12. H.B. Zhang, Y. Peng, X.C. Shan, C.-B. Tian, P. Lin and S.-W. Du, *Inorg. Chem. Comm.*, **14**, 1165 (2011).
13. G.M. Sheldrick, SHELXS-97. Program for the Solution of Crystal Structures. University of Göttingen, Germany (1997).
14. G.M. Sheldrick, SHELXL-97. Program for the Refinement of Crystal Structures. University of Göttingen, Germany (1997).
15. J.L. Liu, H.T. Cai and G.L. Zhao, *Acta Cryst. E.*, **E66**, m1332 (2010).
16. J.R. Lakowicz and G. Weber, *Biochemistry*, **12**, 4161 (1973).
17. N. Wang, Q.-Y. Lin, J. Feng, Y.-L. Zhao, Y.-J. Wang and S.-K. Li, *Inorg. Chim. Acta*, **363**, 3399 (2010).