ISSN 1070-3284, Russian Journal of Coordination Chemistry, 2013, Vol. 39, No. 3, pp. 297–300. © Pleiades Publishing, Ltd., 2013.

Synthesis, Crystal Structures, and Biological Activity of Zinc(II) Complexes Derived from 4-Bromo-2-[(3-Diethylaminopropylimino)methyl]phenol[1]

D. H. Shi[a, b, *], Z. L. Cao[a], W. W. Liu[a], R. B. Xu[a], L. L. Gao[a], Q. Zhang[a], and Z. You[c]

[a] *School of Chemical Engineering, Huaihai Institute of Technology, Lianyungang, 222005 P.R. China*

[b] *JiangSu Key Laboratory of Marine Biotechnology, Huaihai Institute of Technology, Lianyungang, 222005 P.R. China*

[c] *Department of Chemistry, Liaoning Normal University, Dalian, 116029 P.R. China*

**e-mail: dahua_shi@126.com*

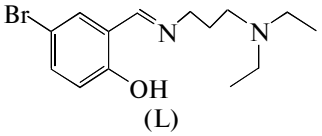
Received September 7, 2011

Abstract—Two new Schiff base zinc(II) complexes, $[ZnBr_2L]$ (**I**) and $[ZnCl_2L]$ (**II**), where L is 4-bromo-2-[(3-diethylaminopropylimino)methyl]phenol, were synthesized and characterized by physico-chemical methods and single crystal X-ray diffraction. The crystal of **I** is monoclinic: space group $P2_1/n$ $a = 7.250$ (2), $b = 16.136$ (3), $c = 15.802$ (3) Å, $\beta = 90.027$ (3)°, $V = 1848.6$ (7) Å^3, $Z = 4$. The crystal of **II** is monoclinic: space group $P2_1/n$, $a = 7.177$ (3), $b = 15.970$ (4), $c = 15.689$ (3), $\beta = 91.674$ (3)°, $V = 1797.5$ (9) Å^3, $Z = 4$. The Zn atom in each complex is four-coordinated by one phenolate O and one imine N atoms of the Schiff base ligand and two halide atoms, forming a tetrahedral coordination. The urease inhibitory activities of the complexes were evaluated.

DOI: 10.1134/S1070328413030111

INTRODUCTION

Schiff bases have been received much attention for their wide application in coordination chemistry [1–3] and biological aspects [4–6]. Recently, we have reported the urease inhibitory activities of some Schiff base complexes [7–9]. In this paper, two new zinc complexes, $[ZnBr_2L]$ (**I**) and $[ZnCl_2L]$ (**II**), where L is 4-bromo-2-[(3-diethylaminopropylimino)methyl]phenol, were synthesized, structurally characterized, and evaluated for their urease inhibitory activities. It is notable that no complexes were reported with the Schiff base ligand (L) to date.



(L)

EXPERIMENTAL

Materials and methods. 5-Bromosalicylaldehyde and N,N-diethylpropane-1,3-diamine with AR grade were purchased from Lancaster. Other chemicals and solvents were purchased from the Beijing Chemical Reagent Company and used as received. Elemental analyses for C, H, and N were performed on a Perkin-Elmer 240C elemental analyzer. The IR spectra were recorded on a Nicolet AVATAR 360 spectrometer as KBr pellets in the 4000–400 cm^{-1} region.

[1] The article is published in the original.

Synthesis of L. To a methanolic solution (20 mL) of 5-bromosalicylaldehyde (1.0 mmol, 201.0 mg) was added a methanolic solution (20 mL) of N,N-diethylpropane-1,3-diamine (1.0 mmol, 130.2 mg) with stirring. The mixture was stirred for 30 min at room temperature to give a yellow solution. Then the methanol was evaporated to give a yellow precipitate of L. The yield was 93%.

For $C_{14}H_{21}N_2OBr$			
anal. calcd., %:	C, 53.7;	H, 6.8;	N, 8.9.
Found, %:	C, 53.5;	H, 6.8;	N, 9.0.

Synthesis of I. The Schiff base L (0.1 mmol, 31.3 mg) and $ZnBr_2$ (0.1 mmol, 22.5 mg) were mixed and stirred in a methanolic solution (15 mL) for 30 min at room temperature. The mixture was filtered, and the colorless block-shaped crystals of **I** suitable for X-ray diffraction, were formed on slow evaporation of the filtrate in air. The yield was 72%.

For $C_{14}H_{21}N_2OBr_3Zn$			
anal. calcd., %:	C, 31.2;	H, 3.9;	N, 5.2.
Found, %:	C, 31.5;	H, 4.0;	N, 5.1.

Synthesis of II. The complex was prepared by a similar procedure as that described for **I**, with $ZnBr_2$

Table 1. Crystallographic data and experimental details for complexes **I** and **II**

Parameter	Value	
	I	**II**
F_w	538.4	449.5
Crystal shape/colour	Block/colorless	Block/colorless
Ctystal size, mm	0.30 × 0.28 × 0.27	0.30 × 0.27 × 0.27
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/n$	$P2_1/n$
a, Å	7.250(2)	7.177(3)
b, Å	16.136(3)	15.970(4)
c, Å	15.802(3)	15.689(3)
β, deg	90.027(3)	91.674(3)
V, Å	1848.6(7)	1797.5(9)
Z	4	4
$\mu(MoK_\alpha)$, cm^{-1}	7.813	3.886
T_{min}	0.203	0.388
T_{max}	0.227	0.420
ρ_{calcd}, g cm^{-3}	1.935	1.661
Measured reflections	14358	14861
Unique reflections, R_{int}	3958 (0.0898)	3914 (0.0411)
Observed reflections	2246	2825
Restraints	10	16
Parameters	213	213
Goodness of fit on F^2	1.089	1.020
Final R indices ($I \geq 2\sigma(I)$)	$R_1 = 0.0747$; $wR_2 = 0.1618$	$R_1 = 0.0440$; $wR_2 = 0.0962$
R indices, all data	$R_1 = 0.1354$; $wR_2 = 0.1847$	$R_1 = 0.0700$; $wR_2 = 0.1081$
Large diff. peak and hole, e $Å^{-3}$	1.050, −0.999	0.715, −0.443

replaced by $ZnCl_2$ (0.1 mmol, 13.6 mg). The yield was 67%.

For $C_{14}H_{21}Cl_2N_2OBrZn$

anal. calcd., %:	C, 37.4;	H, 4.7;	N, 6.2.
Found, %:	C, 37.2;	H, 4.8;	N, 6.4.

X-ray structure determination. Diffraction intensities for the two complexes were collected at 298(2) K using a Bruker SMART 1000 CCD area-detector with MoK_α radiation (λ = 0.71073 Å). The collected data were reduced with the SAINT program [10], and multi-scan absorption corrections were applied using the SADABS program [11]. Both structures of the complexes were solved by direct methods. The complexes were refined against F^2 by full-matrix least-squares methods using the SHELXTL program [12]. All of the non-hydrogen atoms were refined anisotropically. The amino H atoms were located from difference Fourier maps and refined isotropically, with N–H distances restrained to 0.90(1) Å. Other hydrogen atoms were placed in calculated positions and constrained to ride on their parent atoms. One of the ethyl groups in each complex is disordered over two distinct sites with occupancies of 0.622(2) and 0.378(2) for **I** and 0.623(2) and 0.377(2) for **II**. The crystallographic data for both complexes are summarized in Table 1. Selected bond lengths and angles are given in Table 2. Crystallographic data for the complexes have been deposited with the Cambridge Crystallographic Data Centre (nos. 750907 (**I**) and 750908 (**II**); deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

Urease inhibition assay. The urease inhibitory activities were measured according to the literature method [13]. Generally, the assay mixture containing 25 μL of jack bean urease (10 kU/1) and 25 μL of the tested complexes of various concentrations (dissolved in a solution of DMSO : H_2O = 1 : 1 (v/v)) was prein-

cubated for 1 h at 37°C in a 96-well assay plate. Then 0.2 mL of a 100 mM phosphate buffer at pH 6.8 [14] containing 500 mmol urea and 0.002% Phenol Red were added and incubated at 37°C. The reaction time, which was required to produce enough ammonium carbonate to raise the pH of a phosphate buffer from 6.8 to 7.7, was measured by a microplate reader (570 nm) with the end-point, being determined by the color of Phenol Red indicator. The acetohydroxamic acid was used as the standard reference. All the tests were carried out for three times.

RESULTS AND DISCUSSION

The two complexes were readily synthesized in methanol with the same synthetic procedures and with the same Schiff base ligand but with different zinc halides. Both complexes and the Schiff base ligand are stable in air at room temperature, soluble in methanol, ethanol, acetonitrile but insoluble in water.

Figure 1 gives perspective views of the complexes **I** and **II**, respectively. Both complexes are isostructural mononuclear zinc compounds. The Zn atom in each complex has a tetrahedral coordination and is coordinated by one phenolate O and one imine N atoms of the Schiff base ligand, and by two halide atoms, Br for **I** and Cl for **II**.

The coordinate bond lengths and angles in both complexes are comparable to each other and also comparable to those observed in other similar Schiff base zinc complexes [15–17]. The coordinate bond angles are in the range 93.3(3)°–114.4(3)° for **I** and 93.0(2)°–114.2(1)° for **II**.

The molecular packing diagrams for **I** and **II** are shown in Fig. 2. Both crystals are stabilized by intermolecular N–H···O hydrogen bonds, forming chains running along the *z* axis (N(2)–H(2)···O(1)$^{\#1}$ ($^{\#1}$ $1/2 + x, 3/2 - y, -1/2 + z$) with N···A 2.920(14) Å and D–H...A angle 155(12)° for **I** and N(2)–H(2)···O (1)$^{\#2}$ ($^{\#2}$ $1/2 + x, 1/2 - y, -1/2 + z$) with N···A 2.837(5) Å and D–H···A angle 171(5)° for **II**).

The weak absorption at 3382 cm^{-1} is assigned to the stretching vibration of the phenol group in the Schiff base L. The strong absorption bands at 1638 cm^{-1} for L is assigned to the azomethine group, ν(C=N), which is shifted to lower wave numbers in both complexes, 1622 cm^{-1} for **I** and 1621 cm^{-1} for **II**, respectively. The lower shift of the absorption bands indicating that the coordination of the azomethine N atoms to the Zn atoms. The phenolic ν(Ar–O) in the free ligand exhibits strong band at 1203 cm^{-1}, while in the complexes, the bands appear at 1180 cm^{-1}, which can be assigned to the skeletal vibrations related to the phenolic oxygen atom of L, and the bands are known to shift to lower frequency when the phenolic oxygen atom coordinates to metal ions [18].

The close resemblance of the shapes and the positions of the bands suggest similar coordination modes for the complexes.

Table 2. Selected bond lengths and angles for complexes **I** and **II**

Bond	*d*, Å	Bond	*d*, Å
	I		
Zn(1)–O(1)	1.942(7)	Zn(1)–N(1)	2.015(9)
Zn(1)–Br(2)	2.3487(19)	Zn(1)–Br(3)	2.3538(19)
	II		
Zn(1)–O(1)	1.967(3)	Zn(1)–N(1)	2.022(3)
Zn(1)–Cl(1)	2.2297(14)	Zn(1)–Cl(2)	2.2101(14)
Angle	ω, deg	Angle	ω, deg
	I		
O(1)Zn(1)N(1)	93.3(3)	N(1)Zn(1)Br(2)	110.0(3)
N(1)Zn(1)Br(3)	114.4(3)	O(1)Zn(1)Br(2)	110.3(2)
O(1)Zn(1)Br(3)	112.9(3)	Br(2)Zn(1)Br(3)	114.1(1)
	II		
O(1)Zn(1)N(1)	93.0(1)	N(1)Zn(1)Cl(1)	113.3(1)
N(1)Zn(1)Cl(2)	111.1(1)	O(1)Zn(1)Cl(1)	113.0(1)
O(1)Zn(1)Cl(2)	110.5(1)	Cl(2)Zn(1)Cl(1)	114.2(1)

Table 3. Inhibitory activities of urease

Tested material	Inhibition rate, %
I	39.98 ± 1.35
II	7.09 ± 2.36
L	1.57 ± 0.38
$ZnBr_2$	17.82 ± 1.07
$ZnCl_2$	9.30 ± 1.33
Acetohydroxamic acid	88.23 ± 2.08

The urease inhibitory activities with 10 μg mL^{-1} of the two complexes, the Schiff base L, $ZnBr_2$, $ZnCl_2$, and the standard reference acetohydroxamic acid are summarized in Table 3. It can be seen that even though the structures of the complexes are similar to each other, the urease inhibitory activity of **I** is much stronger than that of **II**. The urease inhibitory activity of **I** is also stronger than those of the Schiff base L and the $ZnBr_2$ used in the preparation of **I**. When compared with the Schiff base cadmium and cobalt complexes we reported previously [7, 8], it can be seen that the urease inhibitory activity of the zinc complexes in this paper is much weak.

ACKNOWLEDGMENTS

This work was financially supported by the Natural Science Foundation of Jiangsu Province

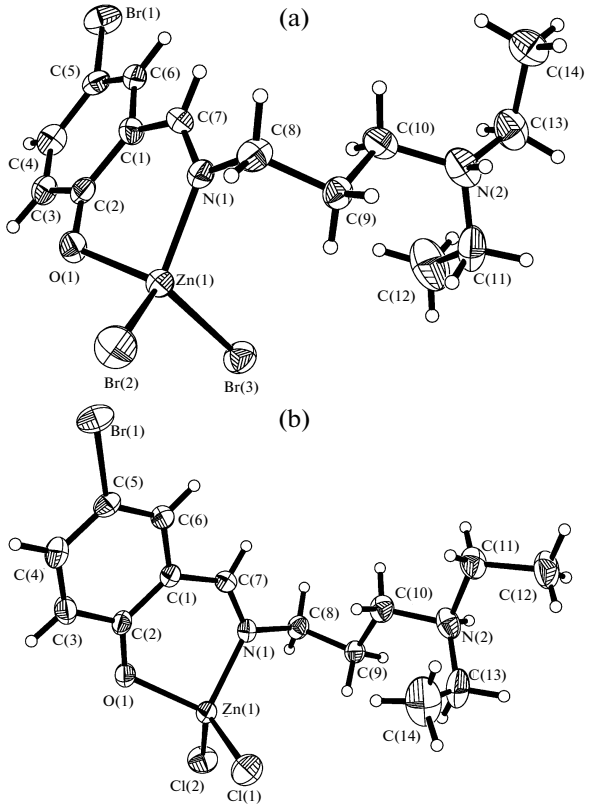


Fig. 1. Molecular structure of **I** (a) and **II** (b) at 30% probability ellipsoids. Only the major component of the disordered ethyl group is shown.

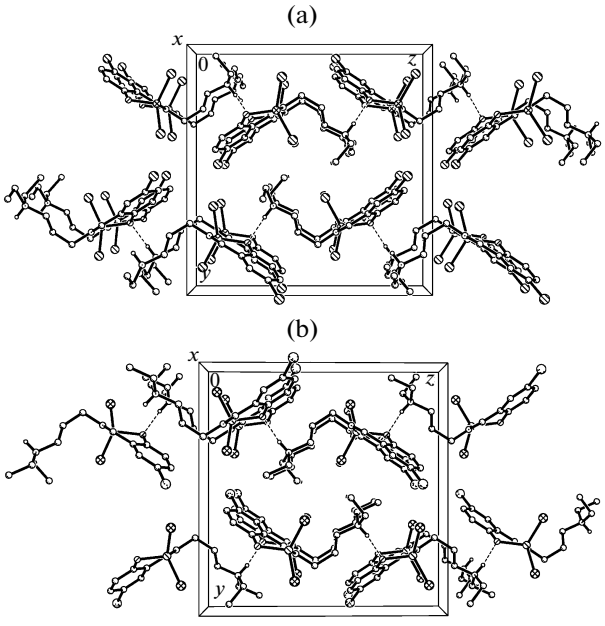


Fig. 2. Molecular packing of **I** (a) and **II** (b). Hydrogen bonds are shown as dashed lines.

(BK2009640), the Open-end Funds of Jiangsu Key Laboratory of Marine Biotechnology, Huaihai Institute of Technology (2010HS04), the Natural Science Foundation of Huaihai Institute of Technology (KQ09029), the Major Program for the Natural Science Research of the Jiangsu Higher Education Institutions of China (grant no. 10KJA170003), and the Six Kinds of Professional Elite Foundation of Jiangsu Province (no. 07-A-024).

REFERENCES

1. Li, Y.G., Dong, X.W., Ai, R., et al., *Russ. J. Coord. Chem.*, 2011, vol. 37, no. 7, p. 523.
2. Khalaji, A.D., Akerdi, S.J., Grivani, G., et al., *Russ. J. Coord. Chem.*, 2011, vol. 37, no. 8, p. 578.
3. Liu, H.Y., Li, G.W., Li, Z.L., et al., *Russ. J. Coord. Chem.*, 2011, vol. 37, no. 9, p. 668.
4. Patil, M., Hunoor, R., and Gudasi, K., *Eur. J. Med. Chem.*, 2010, vol. 45, no. 7, p. 2981.
5. Chohan, Z.H., Sumrra, S.H., Youssoufi, M.H., and Hadda, T.B., *Eur. J. Med. Chem.*, 2010, vol. 45, no. 7, p. 2739.
6. Kumar, G., Kumar, D., Devi, S., et al., *Eur. J. Med. Chem.*, 2010, vol. 45, no. 7, p. 3056.
7. You, Z.-L., Han, X., and Zhang, G.-N., *Z. Anorg. Allg. Chem.*, 2008, vol. 634, no. 1, p. 142.
8. Shi, D.-H., You, Z.-L., Xu, C., et al., *Inorg. Chem. Commun.*, 2007, vol. 10, no. 4, p. 404.
9. Shi, D.H. and You, Z.L., *Russ. J. Coord. Chem.*, 2010, vol. 36, no. 7, p. 535.
10. *SMART (version 5.628) and SAINT (version 6.02)*, Madison (WI, USA): Bruker AXS Inc., 1998.
11. Sheldrick, G.M., *SADABS, Program for Empirical Absorption Correction of Area Detector*, Göttingen (Germany): Univ. of Göttingen, 1996.
12. Sheldrick, G. M., *SHELXTL, Version 5.1, Software Reference Manual*, Madison (WI, USA): Bruker AXS Inc., 1997.
13. Tanaka, T., Kawase, M., and Tani, S., *Life Sci.*, 2003, vol. 73, no. 23, p. 2985.
14. Zaborska, W., Krajewska, B., and Olech, Z., *J. Enzyme Inhib. Med. Chem.*, 2004, vol. 19, no. 1, p. 65.
15. Peng, S.-J., Hou, H.-Y., and Zhou, C.-S., *Synth. React. Inorg. Met.-Org. Nano-Met. Chem.*, 2009, vol. 39, no. 8, p. 462.
16. You, Z.-L., Wang, J., and Han, X., *Acta Crystallogr., Sect. E: Structure Reports Online*, 2006, vol. 62, no. 4, p. m714.
17. Han, X., You, Z.-L., Xu, Y.-T., and Wang, X.-M., *J. Chem. Crystallogr.*, 2006, vol. 36, no. 11, p. 743.
18. Fukuhara, C., Asato, E., Shimoji, T., et al., *Dalton Trans.*, 1987, no. 6, p. 1305.