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Synthesis and Crystal Structure of a Novel Trinuclear Schiff Base Cadmium(II) Complex $[Cd_3L_4] \cdot 2ClO_4 \cdot 2CH_3OH$ with Antimicrobial Activity[1]

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Abstract—The Schiff base 2-ethoxysalicylaldehydethiosemicarbazone (HL) derived from 3-ethoxysalicylaldehyde and thiosemicarbazide and its centrosymmetric trinuclear cadmium(II) complex $[Cd_3L_4] \cdot 2ClO_4 \cdot 2CH_3OH$ (**I**), have been successfully prepared. The structure of complex **I** was characterized by elemental analysis, IR spectrum, and single crystal X-ray crystallographic determination. The complex crystallizes in the monoclinic space group $C2/c$ with unit cell dimensions $a = 15.584(2)$, $b = 19.540(2)$, $c = 20.994(3)$ Å, $\beta = 106.632(2)°$, $V = 6125.2(13)$ Å^3, $Z = 4$, $R_1 = 0.0558$, and $wR_2 = 0.1696$. The Schiff base coordinates to the Cd atoms through the phenolate O, ether O, imino N, and S atoms. The central Cd atom of complex **I** is coordinated by eight O atoms from four Schiff base ligands. The terminal Cd atoms of the complex are coordinated by six donor atoms from two Schiff base ligands. The effect of the complex on the antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* were studied.

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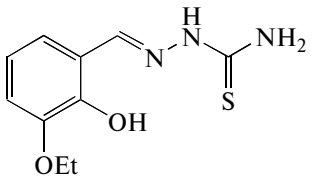
INTRODUCTION

Schiff bases are a kind of versatile ligands in coordination chemistry [1–3]. In recent years, metal complexes of Schiff bases have attracted considerable attention due to their remarkable biological activity, such as antifungal, antibacterial and antitumor [4–6]. It has been shown that the Schiff base complexes derived from salicylaldehyde and its derivatives with primary amines, bearing the N_2O, N_2S, NO_2 or NSO donor sets, have interesting biological activities [6–8]. The search in the Cambridge Crystallographic Database (version 5.31 with addenda up to May 2011) [9] has revealed that the complexes with the Schiff base 2-ethoxysalicylaldehydethiosemicarbazone (HL) have never been reported. In the present paper, the preparation, characterization, and antimicrobial activity of a new cadmium(II) complex $[Cd_3L_4] \cdot 2ClO_4 \cdot 2CH_3OH$ (**I**), derived from HL, is reported.



(HL)

[1] The article is published in the original.

EXPERIMENTAL

Material and methods. 3-Ethoxysalicylaldehyde and thiosemicarbazide were purchased from Fluka. The cadmium perchlorate was prepared by the reaction of basic cupric carbonate with perchloric acid in distilled water, followed by distillation and crystallization. Other reagents and solvents were analytical grade and were used without further purification. Elemental (C, H, and N) analyses were made on a PerkinElmer Model 240B automatic analyser. Infrared spectra were recorded on an IR-408 Shimadzu 568 spectrophotometer. X-ray diffraction was carried out on a Bruker SMART 1000 CCD diffractometer.

Synthesis of HL. The Schiff base ligand HL was prepared by the condensation of equimolar quantities of 3-ethoxysalicylaldehyde (0.166 g, 1 mmol) with thiosemicarbazide (0.091 g, 1 mmol) in methanol (30 mL) at ambient temperature for 1 h. Then the methanol was evaporated by distillation, yielding yellow micro-cystalline product of the Schiff base, which was used for the preparation of complex (**I**) without purification.

For $C_{10}H_{13}N_3O_2S$			
anal. calcd., %:	C, 50.19;	H, 5.48;	N, 17.56.
Found, %	C, 50.02;	H, 5.56;	N, 17.72.

Synthesis of complex I. The Schiff base HL (0.120 g, 0.5 mmol) was dissolved by methanol (20 mL), to which was added with stirring a methanol solution (10 mL) of cadmium perchlorate hexahydrate (0.210 g,

0.5 mmol). The mixture was stirred for 1 h at ambient temperature to give a colorless solution. Colorless block-shaped single crystals suitable for X-ray diffraction were formed by slow evaporation of the solution in air for a week. The yield was 53% (based on HL). IR data (ν, cm^{-1}): 3395 w, 3296 m, 3176 w, 3061 w, 2973 w, 2935 w, 2882 w, 1601 s, 1578 m, 1550 w, 1455 s, 1326 m, 1292 m, 1245 m, 1210 s, 1097s, 1023 w, 971 w, 893 w, 845 w, 780 m, 737 m, 662 w, 613 w, 569 w, 455 m.

For $C_{41}H_{52}N_{12}O_{17}S_4Cl_2Cd_3$			
anal. calcd., %:	C, 32.37;	H, 3.45;	N, 11.05.
Found, %	C, 32.13;	H, 3.53;	N, 11.21.

X-ray structure ditermination. Data were collected from selected crystals mounted on a glass fibre. The data for the complex was processed with SAINT [10] and corrected for absorption using SADABS [11]. Semi-empirical absorption correction was applied with ψ-scans [12]. The structure was solved by direct method using the program SHELXS-97 and was refined by full-matrix least-squares techniques on F^2 using anisotropic displacement parameters [13]. The amino hydrogen atoms were located from a difference Fourier map and refined isotropically with N–H and H···H distances restrained to 0.90(1) and 1.43(2) Å, respectively. The remaining hydrogen atoms were placed at the calculated positions. Idealized H atoms were refined with isotropic displacement parameters set to 1.2 (1.5 for methyl groups and hydroxy groups) times the equivalent isotropic U values of the parent carbon and oxygen atoms. The crystallographic data for the complex are listed Table 1. Supplementary material for structure **I** has been deposited with the Cambridge Crystallographic Data Centre (no. 842603; deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

Table 1. Crystallographic data and details of the experiment and refinement of **I**

Parameter	Value
Colour, habit	Block, colorless
Formula weight	1521.29
Temperature, K	298(2)
Crystal size, mm	0.18 × 0.17 × 0.16
Radiation (λ, Å)	MoK_α (0.71073)
Crystal system	Monoclinic
Space group	$C2/c$
Unit cell dimensions:	
a, Å	15.5838(18)
b, Å	19.540(2)
c, Å	20.994(3)
β, deg	106.632(2)
V, Å	6125.2(13)
Z	4
ρ, mg cm^{-3}	1.650
Absorption coefficient, mm^{-1}	1.327
θ Range for data collection, deg	2.18–27.00
Index ranges (h, k, l)	$-19 \le h \le 19$, $-24 \le k \le 15$, $-26 \le l \le 26$
Reflections collected	18874
Independent reflections	6614
Observed reflections ($I > 2\sigma(I)$)	4933
Parameters	377
Restraints	40
Final R indices ($I > 2\sigma(I)$)	0.0558
R indices (all data)	0.1696
Goodness-of-fit	1.060
Largest diff. peak and hole, e $Å^{-3}$	1.583 and −1.937

RESULTS AND DISCUSSION

A new Schiff base 2-ethoxysalicylaldehydethiosemicarbazone and its cadmium(II) complex **I** have been prepared. The Schiff base prepared in this way is formed in nearly quantitative yield and is of high purity. Both the Schiff base and complex **I** are very stable at room temperature in the solid state. The results of the elemental analyses are in accord with the composition suggested for the ligand and complex **I**.

For the IR spectrum of complex **I**, the weak band at 3395 cm^{-1} proved the presence of methanol molecules. The middle and sharp band at 3296 cm^{-1} is assigned to the streching vibrations of the N–H groups. The strong band at 1601 cm^{-1} is assigned to the azomethine groups [14, 15]. The characteristic intense absorption band for the perchlorate anions in complex **I** is at 1097 cm^{-1}. The bands in the region 613–455 cm^{-1} are assigned to the Cd–S, Cd–N, and Cd–O vibrations [16].

The molecular structure of complex **I** is shown in Fig. 1. Selected bond distances and angles are listed in Table 2.

The compound contains a centrosymmetric trinuclear cadmium complex cation, two perchlorate anions, and two methanol molecules of crystallization. The Cd···Cd separation is 3.540(1) Å. The Cd(1) atom, located at the inversion center, is coordinated by four phenolate O and four ether O atoms from four Schiff base ligands. The terminal Cd(2) atom is coordinated by two phenolate O, two imino N, and two S atoms from two Schiff base ligands. The phenolate O atom acts as a bridging group and coordinates to two Cd atoms, forming a slightly roof-shaped four-membered

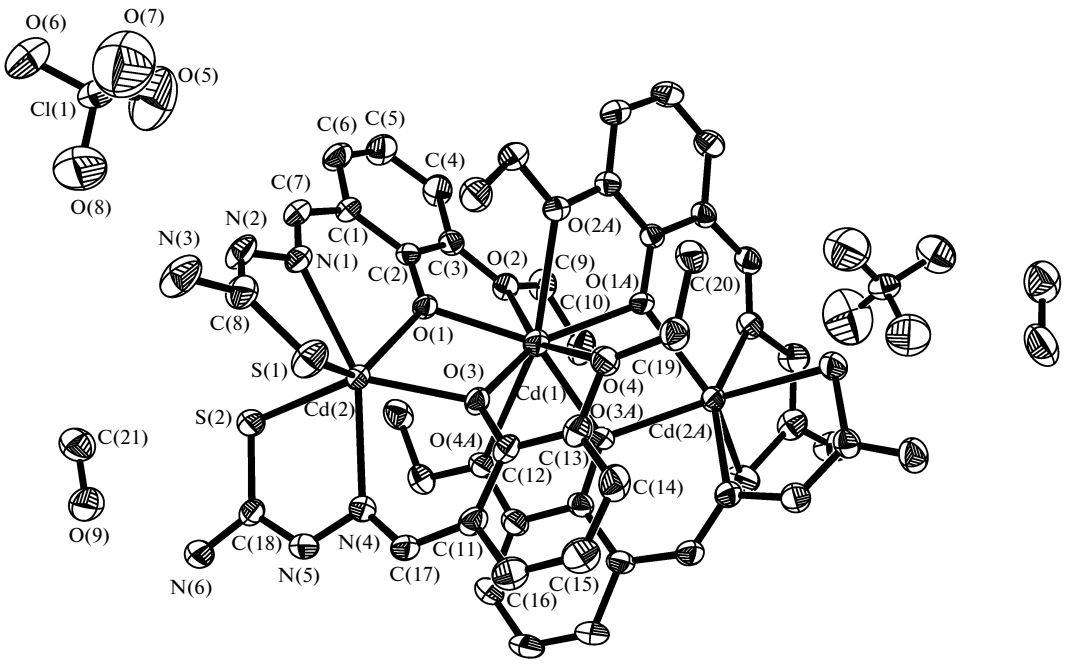


Fig. 1. Perspective view of complex **I** with 30% probability thermal ellipsoids. Unlabeled atoms and those labeled with the suffix *A* are related to the symmetry position $1 - x, y, 3/2 - z$.

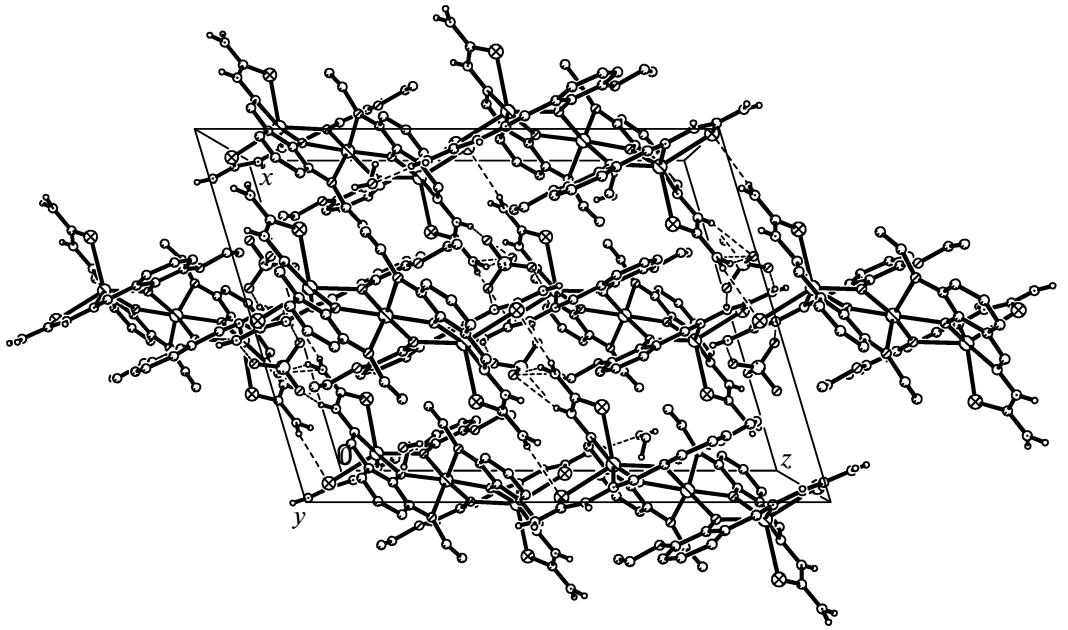


Fig. 2. Molecular packing of complex **I**, viewed along the *y* axis. Hydrogen bonds are shown as dashed lines. H atoms not related to the hydrogen bonding are omitted for clarity.

chelate ring Cd(1)–O(1)–Cd(2)–O(3). The exsistence of a number of four- and five-membered chelate rings in the complex leads to the formation of severely distorted coordination geometries. The coordinate bond distances and angles in the complex are comparable to those observed in the similar cadmium(II) complexes [17–19].

In the crystal structure of complex **I**, the cadimium complex cations, the perchlorate anions, and the methanol molecules are linked *via* intermolecular N–H···O, O–H···S, and N–H···S hydrogen bonds (Table 3), forming a three-dimensional network, as shown by Fig. 2.

Table 2. Coordinate bond distances (Å) and angles (deg) for complex **I***

Bond	*d*, Å	Bond	*d*, Å
Cd(1)–O(1)	2.192(4)	Cd(1)–O(2)	2.566(4)
Cd(1)–O(3)	2.198(4)	Cd(2)–O(1)	2.254(4)
Cd(2)–O(3)	2.230(4)	Cd(2)–N(1)	2.390(5)
Cd(2)–N(4)	2.382(5)	Cd(2)–S(1)	2.613(2)
Cd(2)–S(2)	2.5979(19)		
Angle	ω, deg	Angle	ω, deg
O(1)Cd(1)O(1*A*)	137.9(2)	O(1)Cd(1)O(3*A*)	141.18(15)
O(1)Cd(1)O(3)	74.48(15)	O(1)Cd(1)O(2)	66.00(14)
O(3)Cd(1)O(3*A*)	89.2(2)	O(3)Cd(1)O(2*A*)	111.18(16)
O(1)Cd(1)O(2*A*)	81.67(15)	O(1)Cd(1)O(2*A*)	81.67(15)
O(3)Cd(1)O(2)	137.07(14)	O(2)Cd(1)O(2*A*)	79.7(2)
O(3)Cd(2)O(1)	72.65(15)	O(3)Cd(2)N(4)	75.95(17)
O(1)Cd(2)N(4)	127.55(17)	O(3)Cd(2)N(1)	126.74(18)
O(1)Cd(2)N(1)	74.98(17)	N(4)Cd(2)N(1)	154.70(19)
O(3)Cd(2)S(2)	141.60(13)	O(1)Cd(2)S(2)	106.63(12)
N(4)Cd(2)S(2)	75.22(14)	N(1)Cd(2)S(2)	87.88(14)
O(3)Cd(2)S(1)	97.54(12)	O(1)Cd(2)S(1)	131.45(13)
N(4)Cd(2)S(1)	93.19(14)	N(1)Cd(2)S(1)	74.33(15)
S(2)Cd(2)S(1)	108.84(7)		

* Symmetry code for *A*: $1 - x, y, 3/2 - z$.

Qualitative determination of the antimicrobial activity was done using the disk diffusion method [20, 21]. The results are summarized in Table 4. A comparative study of minimum inhibitory concentration (MIC) values of the Schiff base ligand and the complex indicates that the complex has much more effective activity than the free Schiff base ligand. Generally, this is caused by the greater lipophilic nature of the complex than the ligand. Such increased activity of the metal chelates can be explained on the basis of chelating theory [22]. On chelating, the polarity of the metal atoms will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of positive charge of the metal atoms with donor atoms. Further, it increases the delocalization of *p*-electrons over the whole chelate ring and enhances the lipophilicity of the complexes. This increased lipophilicity enhances the penetration of the complexes into lipid membrane and blocks the metal binding sites on enzymes of microorganisms.

From Table 4, it is obvious that the complex shows stronger antibacterial activities against *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* when compared to the free Schiff base. However, when compared with the reference drug Tetracycline, the activities of complex **I** are relatively weak. For *Staphylococcus aureus* and *Escherichia coli*, even though the activity of complex **I** is stronger than the free Schiff base, it is less than the control drug Tetracycline. But for *Candida*

Table 3. Geometric parameters of hydrogen bonds for complex **I***

Contect D–H···A	Distance, Å			Angle D–H···A, deg
	D–H	H···A	D···A	
N(3)–H(3*A*)···S(2)$^{\#1}$	0.90(1)	2.82(6)	3.568(7)	142(7)
N(5)–H(5*A*)···O(7)$^{\#2}$	0.90(1)	2.55(3)	3.436(18)	170(9)
N(3)–H(3*B*)···O(8)	0.90(1)	2.09(4)	2.909(13)	152(8)
O(9)–H(9*C*)···S(1)$^{\#3}$	0.82	2.97	3.617(13)	137
N(6)–H(6*B*)···O(9)	0.86	2.09	2.946(14)	173
N(6)–H(6*A*)···O(6)$^{\#2}$	0.86	2.16	2.968(10)	158
N(2)–H(2)···Cl(1)	0.86	2.90	3.708(6)	157
N(2)–H(2)···O(5)	0.86	2.43	3.208(13)	152
N(2)–H(2)···O(8)	0.86	2.40	3.159(12)	147

* Symmetry codes: $^{\#1}$ $3/2 - x, 1/2 - y, 1 - z$; $^{\#2}$ $-1/2 + x, 1/2 + y, z$; $^{\#3}$ $-1/2 + x, 1/2 - y, -1/2 + z$.

Table 4. MIC values (μg/mL) for the antimicrobial activities of the tested compounds

Compound	*Staphylococcus aureus*	*Escherichia coli*	*Candida albicans*
HL	16	128	256
Complex **I**	2	8	32
Tetracycline	0.32	2.12	>1024

albicans, both the Schiff base and complex **I** shown stronger activities than the Tetracycline. The results are in accordance with that we reported recently [23].

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