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New Vanadium and Zinc Complexes with Schiff Base Ligand *N*,*N*'-bis(3-Ethoxy-2-Hydroxybenzylidene)ethylenediamine: Synthesis, Structures, and Biochemical Properties[1]

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Abstract—The Schiff base ligand *N*,*N*'-bis(3-ethoxy-2-hydroxybenzylidene)ethylenediamine (H_2L) reacting with vanadyl acetylacetonate and zinc chloride, respectively, in methanol gave the complexes [VOL] · H_2O (**I**) and [ZnL(OH_2)] (**II**). Both complexes were characterized by elemental analyses and IR spectroscopic method in the solid state. Single crystal X-ray analysis was performed, which reveals that both of them are mononuclear complexes. Complex **I** crystallizes in the monoclinic space group $P2_1/c$ with unit cell dimensions $a = 9.4387(7)$, $b = 16.996(1)$, $c = 12.758(1)$ Å, $\beta = 98.269(2)°$, $V = 2025.4(3)$ Å^3, $Z = 4$, $R_1 = 0.0365$, and $wR_2 = 0.0946$. Complex II crystallizes in the tetragonal space group $P\overline{4}2_1m$ with unit cell dimensions $a = b = 22.0489(8)$, $c = 4.9846(4)$ Å, $V = 2423.3(2)$ Å^3, $Z = 4$, $R_1 = 0.0890$, and $wR_2 = 0.2278$. The V atom in **I** and the Zn atom in **II** are in square pyramidal coordination. Anbacterial activities of the Schiff base ligand and the complexes have been studied on the strains *B. subtilis*, *E. coli* and *S. aureus*.

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INTRODUCTION

Schiff bases in general have been shown to be biological active. A great deal of Schiff bases were reported to possess antibacterial, antifungal and antitumor activities [1–3]. The effect of presence of various substituents in the phenyl rings of aromatic Schiff bases on their antibacterial activity has been reported [4]. Due to their multiple implications, the transition metal complexes with Schiff bases, as ligands, are of paramount scientific interest. It has been found that in general the complexation of Schiff bases with most transition metal atoms influences their antibacterial activities [5–7]. With this view and in continuation of work on the study of Schiff bases and their metal complexes, herein we report two new vanadium and zinc complexes, [VOL] · H_2O (**I**) and [ZnL(OH_2)] (**II**), where L is the dianionic form of *N*,*N*'-bis(3-ethoxy-2-hydroxybenzylidene)ethylenediamine (**H_2L**). The antibacterial activity of the Schiff base and their complexes are reported against *B. subtilis*, *E. coli* and *S. aureus*.

EXPERIMENTAL

3-Ethoxysalicylaldehyde and ethylenediamine were purchased from Merck and Fluka, and used as received. The Schiff base ligand was prepared in over 90% yield according to the literature method [8]. All other chemicals and solvents used in this work were of analytical grade available commercially and used without further purification. Elemental analyses (carbon, hydrogen, and nitrogen) of the compounds were obtained from a Carlo ERBA Model EA 1108 analyzer. Infrared spectra were collected by using KBr pellets on a Jasco-5300 FT–IR spectrophotometer. Solution electrical conductivity was measured with a DDS-11A conductivity meter.

Synthesis of I. Vanadyl acetylacetonate (0.01 mmol, 2.65 g) dissolved in methanol (30 mL) was added dropwise to a stirred methanolic solution (30 mL) of H_2L (0.01 mol, 3.56 g). The mixture was gently refluxed for 2 h, then most of the solvent was evaporated by distillation. After cooling, the resulting brown solid was filtered off, washed with cold methanol, and dried in a vacuum containing anhydrous $CaCl_2$. The yield was 3.17 g (72%).

For $C_{20}H_{24}N_2O_6V$			
anal. calcd., %:	C, 54.7;	H, 5.5;	N, 6.4.
Found, %:	C, 54.5;	H, 5.6;	N, 6.3.

Brown block-like single crystals of the complex, suitable for single crystal X-ray diffraction, were obtained by slow evaporation of a methanol solution containing complex **I**.

[1] The article is published in the original.

Table 1. Crystallographic data and refinement parameters for complexes **I** and **II**

Parameter	Value	
	I	**II**
Formula weight	439.35	437.78
Crystal system	Monoclinic	Tetragonal
Space group	$P2_1/c$	$P\overline{4}2_1m$
Unit cell dimensions:		
a, Å	9.4387(7)	22.0489(8)
b, Å	16.996(1)	22.0489(8)
c, Å	12.758(1)	4.9846(4)
β, deg	98.269(2)	
V, Å^3	2025.4(3)	2423.3(2)
Z	4	4
ρ, g cm^{-3}	1.441	1.200
μ, mm^{-1}	0.529	1.041
T_{min}, T_{max}	0.8880, 0.9016	0.7736, 0.8188
Reflections collected	19368	21635
Reflections unique	3769	2330
Reflections observed ($I > 2\sigma(I)$)	3165	1732
Parameters	270	134
Restraints	2	1
R_1, wR_2 ($I > 2\sigma(I)$)	0.0365, 0.0946	0.0890, 0.2278
R_1, wR_2 (all data)	0.0459, 0.1028	0.1258, 0.2452
Goodness-of-fit on F^2	1.040	1.203
Largest diff. peak and hole, e Å^{-3}	0.297, –0.236	0.726, –0.603

Synthesis of II. Zinc chloride (0.01 mmol, 1.36 g) dissolved in methanol (30 mL) was added dropwise to a stirred methanolic solution (30 mL) of H_2L (0.01 mol, 3.56 g). The mixture was gently refluxed for 2 h, then most of the solvent was evaporated by distillation. After cooling, the resulting colorless solid was filtered off, washed with cold methanol, and dried in a vacuum containing anhydrous $CaCl_2$. The yield was 2.82 g (64%).

For $C_{20}H_{24}N_2O_5Zn$			
anal. calcd., %:	C, 54.9;	H, 5.5;	N, 6.4.
Found, %:	C, 54.7;	H, 5.7;	N, 6.5.

Colorless block-like single crystals of the complex, suitable for single crystal X-ray diffraction, were obtained by slow evaporation of a methanol solution containing complex **II**.

X-ray crystallography. Suitable X-ray quality crystals of the complexes were pick up under a microscope and investigated in a diffraction experiment at 298(2) K on a Bruker Apex II diffractometer with monochromated MoK_α radiation (λ = 0.71073 Å) obtained from a graded multilayer X-ray optics. The structures were solved by direct methods with SHELXS-97 [9], and refined with full-matrix least-squares techniques on F^2 with SHELXL-97 [9]. The C- and O-bonded hydrogen atoms were calculated in an idealized geometry, riding on their parent atoms, with distances restrained to 0.93–0.97 Å for C–H. The water hydrogen atoms were located from difference Fourier maps and refined isotropically with O–H distances restrained to 0.85(1) Å. The crystal data and refinement parameters are listed in Table 1. Selected bond lengths and angles are given in Table 2. The O–H···O hydrogen bonds in complexes **I** and **II** are listed in Table 3.

Supplementary material for structure **I** and **II** has been deposited with the Cambridge Crystallographic Data Centre (nos. 935001 (**I**) and 935002 (**II**); deposit@ccdc.cam.ac.uk or http://www.ccdc.cam. ac.uk).

Antibacterial assay. The antibacterial activities were tested against *B. subtilis*, *E. coli*, and *S. aureus* using Mueller-Hinton medium. The MICs (minimum inhibitory concentrations) of the test compounds were determined by a colorimetric method using the dye MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide]. A stock solution of the synthesized compound (50 μg mL^{-1}) in DMSO was prepared and quantities of the test compounds were incorporated in specified quantity of sterilized liquid Mueller-Hinton medium. A specified quantity of the medium containing the compound was poured into microtitration

Table 2. Selected bond lengths (Å) and angles (deg) for complexes **I** and **II**

Bond	*d*, Å	Bond	*d*, Å
	I		
V(1)–O(1)	1.9326(14)	V(1)–O(2)	1.9234(14)
V(1)–O(5)	1.5939(15)	V(1)–N(1)	2.0619(17)
V(1)–N(2)	2.0563(17)		
	II		
Zn(1)–O(1)	1.989(7)	Zn(1)–O(3)	2.021(10)
Zn(1)–N(1)	2.081(9)		
Angle	ω, deg	Angle	ω, deg
	I		
O(5)V(1)O(2)	112.89(7)	O(5)V(1)O(1)	107.16(7)
O(2)V(1)O(1)	87.60(6)	O(5)V(1)N(2)	102.35(8)
O(2)V(1)N(2)	86.57(6)	O(1)V(1)N(2)	149.85(7)
O(5)V(1)N(1)	108.49(7)	O(2)V(1)N(1)	138.13(6)
O(1)V(1)N(1)	86.25(6)	N(2)V(1)N(1)	78.64(7)
	II		
O(1)Zn(1)O(1*A*)	90.0(4)	O(1)Zn(1)O(3)	106.3(3)
O(1)Zn(1)O(3*A*)	106.3(3)	O(1)Zn(1)N(1*A*)	150.7(4)
O(3)Zn(1)N(1*A*)	101.9(4)	O(1)Zn(1)N(1)	89.5(3)
N(1)Zn(1)N(1*A*)	77.0(6)		

plates. A suspension of the microorganism was prepared to contain approximately 10^5 cfu mL^{-1} and applied to microtitration plates with serially diluted compounds in DMSO to be tested and incubated at 37°C for 24 h. After the MICs were visually determined on each of the microtitration plates, 50 μL of PBS (phosphate buffered saline 0.01 mol L^{-1}, pH 7.4: $Na_2HPO_4 \cdot 12H_2O$ 2.9 g, KH_2PO_4 0.2 g, NaCl 8.0 g, KCl 0.2 g, distilled water 1000 mL) containing 2 mg of MTT/mL was added to each well. Incubation was continued at room temperature for 4–5 h. The content of each well was removed and 100 μL of isopropanol containing 5% 1 mol L^{-1} HCl was added to extract the dye. After 12 h of incubation at room temperature, the optical density was measured with a microplate reader at 550 nm. The antibiotics kanamycin and penicillin were used as standard drugs. The observed MIC values are given in Table 4.

RESULTS AND DISCUSSION

Reaction of H_2L with vanadyl acetylacetonate and zinc chloride, respectively, under aerobic conditions afforded mononuclear vanadium complex **I** and mononuclear zinc complex **II**. Both complexes were obtained as single crystals, stable in air and soluble in polar organic solvents, such as ethanol, methanol, DMF, and DMSO. Elemental analyses of the complexes are consistent with the general molecular formulae proposed by single crystal X-ray determination. The molar conductivity of the complexes in absolute methanolic solution confirms the non-electrically nature [10].

Comparison of the IR spectra of the complexes with that of the free Schiff base ligand gives information about the coordination. The IR spectra of the complexes exhibit broad bands in the range 3200–3600 cm^{-1} due to the water O–H stretching vibrations. The complexes display strong peaks at 1631 cm^{-1} for **I** and 1639 cm^{-1} for **II** due to the azomethine (C=N) stretching [11]. The azomethine ν(C=N) bands in the complexes are shifted by about 6–14 cm^{-1} to lower wave numbers compared to the free Schiff base ligand. For the spectrum of the Schiff base ligand, the strong band at 1282 cm^{-1} are due to ν(C–O)(phenolic) [12]. While for the complexes, the C–O stretching bands are observed at about 1230 cm^{-1} for **I** and 1226 cm^{-1} for **II**. These spectra assignments show that the Schiff base ligand is coordinated to the metal atoms through azomethine nitrogen and phenolic oxygen. Conclusive evidence of the bonding is also shown by the presence of new bands in the spectra of the complexes at low wave numbers 450–580 cm^{-1}, which can be attributed to M–O and M–N stretching vibrations. The spectrum of complex **I** displays a typical and intense band at

Table 3. Geometric parameters of hydrogen bonds for complexes **I** and **II***

D–H···A	Distance, Å			Angle D–H···A, deg
	D–H	H···A	D···A	
		I		
O(6)–H(6*wA*)···O(4)	0.85(1)	2.29(2)	3.037(3)	147(3)
O(6)–H(6*wA*)···O(2)	0.85(1)	2.26(2)	2.983(2)	143(3)
O(6)–H(6*wB*)···O(1)	0.85(1)	2.36(3)	3.012(2)	134(3)
O(6)–H(6*wB*)···O(3)	0.85(1)	2.20(2)	2.984(2)	153(4)
		II		
O(3)–H(3)···O(1)^{i}	0.85(1)	2.00(6)	2.756(10)	147(10)
O(3)–H(3)···O(2)^{i}	0.85(1)	2.32(8)	2.986(7)	136(9)

* Symmetry code: ^{i} $-1/2 + y$, $1/2 + x$, $-1 + z$.

972 cm^{-1} which is assignable to the typical stretch of the V=O bond [13].

Figure 1 gives the ORTEP diagram with atomic labeling scheme of complex **I**. The asymmetric unit of compound **I** contains a mononuclear vanadium complex and a water molecule. The two components are linked together by four O–H···O hydrogen bonds (Table 3). The V atom is coordinated in a square pyramidal geometry with two imine nitrogen and two phenolic oxygen defining the basal plane and with the oxo oxygen located at the apical position. The V atom deviates from the basal plane by 0.608(1) Å. The dihedral angle between the two benzene rings of the Schiff base ligand is 16.3(3)°. The azomethine (C=N) bond lengths of 1.289(3) and 1.286(3) Å are within the general vaules of C=N double bonds. The *cis* and *trans* angles at the basal plane are in the range 78.64(7)°–87.60(6)° and 138.13(6)°–149.85(7)°, respectively. The *trans* angles differ by about 30°–42° from the ideal ones because of ligand straints imposed by the adjacent five- and six-membered chelate rings and the effects of the oxo ligand. The average V–O/N distances in complex **I** compare well with those reported for similar vanadium complexes with Schiff bases [14, 15].

Figure 2 gives the ORTEP diagram with atomic labeling scheme of complex **II**. The Zn atom is coordinated in a square pyramidal geometry, with two imine nitrogen and two phenolic oxygen defining the basal plane, and with the water oxygen located at the apical position. The Zn atom deviates from the basal plane by 0.501(1) Å. The dihedral angle between the two benzene rings of the Schiff base ligand is 13.6(5)°. The azomethine (C=N) bond lengths of 1.302(14) Å are within the general vaules of C=N double bonds. The *cis* and *trans* angles at the basal plane are in the range 77.0(6)°–90.0(4)° and 150.7(4)°, respectively. The *trans* angles differ by about 30° from the ideal ones because of ligand straints imposed by the adjacent five- and six-membered chelate rings and the effects of the apical water ligand. The average Zn–O/N distances in the complex compare well with those reported for similar zinc complexes with Schiff bases [16, 17].

Table 4. MIC values (μg mL^{-1}) of the tested compounds

	B. subtilis	*E. coli*	*S. aureus*
H_2L	25	50	25
I	1.56	12.5	3.13
II	3.13	12.5	6.25
Penicillin	0.78	>100	3.13
Kanamycin	0.39	6.25	1.56

The crystal packing of complex **II** is shown in Fig. 3. The molecules are linked by O–H···O hydrogen bonds (Table 3) formed among the water ligands with the adjacent Schiff base ligands, to form 1D chains running along the *z* axis.

The Schiff base ligand H_2L and the the complexes have been tested against the strains *B. subtilis*, *E. coli*, and *S. aureus*. The complexes show from weak to me-

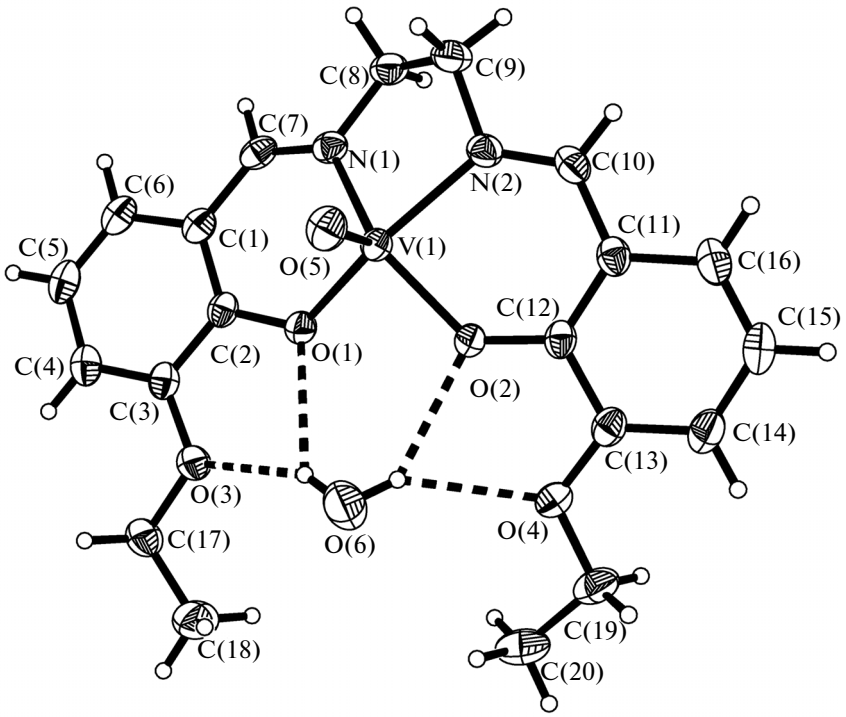

Fig. 1. Structure of complex **I** with the atom labeling scheme. All non-hydrogen atoms are represented at 30% probability thermal ellipsoids. Hydrogen bonds are shown as dashed lines.

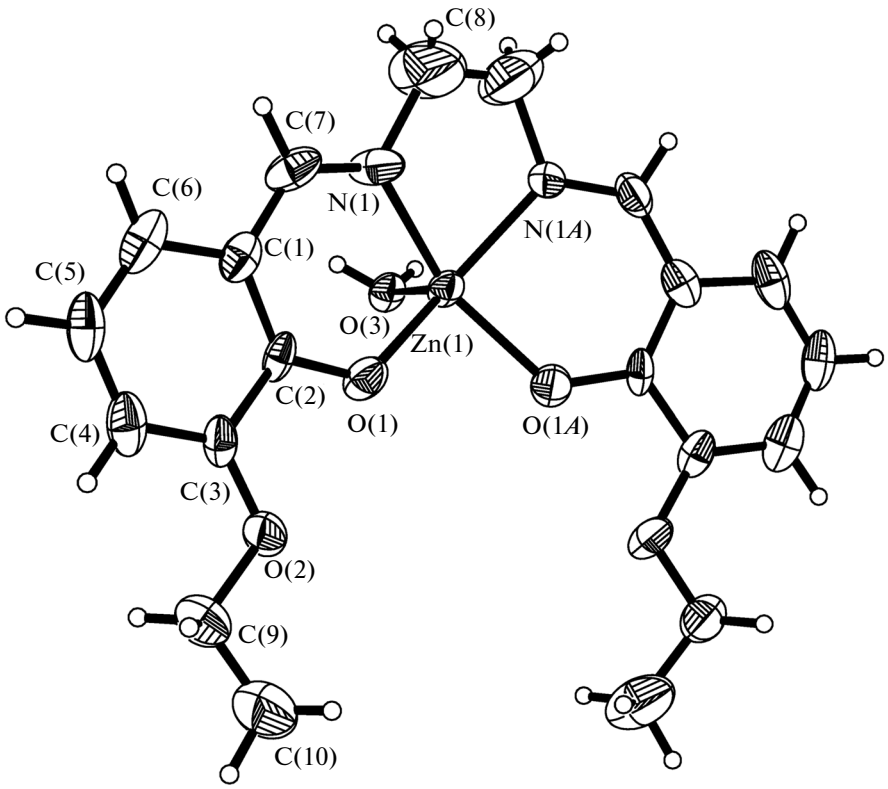

Fig. 2. Structure of complex **II** with the atom labeling scheme. All non-hydrogen atoms are represented at 30% probability thermal ellipsoids. Atoms labeled with the suffix *A* are at the symmetry position: $-1/2 + y$, $1/2 + x$, $-1 + z$.

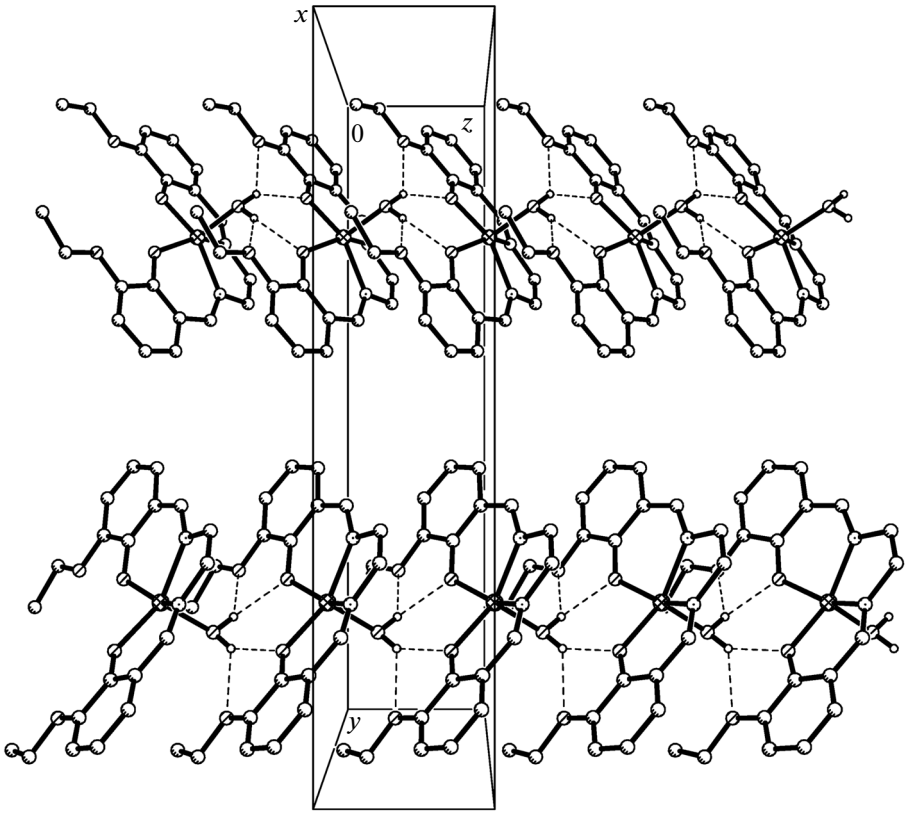

Fig. 3. Hydrogen bond (dashed lines) linked structure of complex **II**, viewed down the *x* axis.

dium activities against the three strains. In general, the complexes have stronger antibacterial activities than the free Schiff base ligand. It is obvious that complex **I** has, to some extent, stronger activities against the bacteria than complex **II** for *B. subtilis* and *S. aureus*, and nearly equal activities against *E. coli*. However, when compared with Penicillin and Kanamycin, the activities of the Schiff base and the complexes are somewhat weak.

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