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Syntheses, Crystal Structures, and Antimicrobial Activities of Oxovanadium(V) Complexes with Tridentate Schiff Base Ligand[1]

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Abstract—Two structurally similar new oxovanadium complexes, [VO(L)(L^1)] (**I**) and [VO(L)(L^2)] (**II**), where L is the dianionic form of 3-((3-bromo-2-hydroxyphenyl)-{[1-(3-bromo-2-hydroxyphenyl)methylidene]amino}methyl)pentane-2,4-dione (H_2L), L^1 is the deprotonated form of 8-hydroxyquinoline, L^2 is 2,2'-bipyridine, were prepared and characterized by spectroscopic and single crystal X-ray diffraction (CIF files CCDC nos. 1566824 (**I**), 1566825 (**II**)). Complex **I** crystallizes as the monoclinic space group $P2_1/c$ with unit cell dimensions a = 11.265(1), b = 18.179(2), c = 13.461(2) Å, β = 103.376(3)°, V = 2681.8(5) Å^3, Z = 4, R_1 = 0.0659, wR_2 = 0.1318, GOOF = 1.003. Complex **II** crystallizes as the orthorhombic space group *Pbca* with unit cell dimensions a = 19.958(1), b = 13.600(1), c = 22.8713(2) Å, V = 6192.3(8) Å^3, Z = 8, R_1 = 0.0550, wR_2 = 0.1008, GOOF = 1.074. X-ray analysis indicates that the complexes are mononuclear oxovanadium(V) species with the V atoms in octahedral coordination. The complexes were evaluated for their antibacterial (*Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas fluorescence*) and antifungal (*Candida albicans* and *Aspergillus niger*) activities by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) method. Interestingly, complex **II** has strong activity against *S. aureus*.

Keywords: Schiff base, vanadium complex, mononuclear complex, crystal structure, antimicrobial activity

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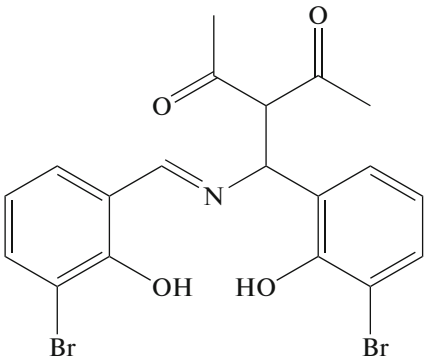
INTRODUCTION

Schiff bases are a kind of biological active compound, which can be prepared by the condensation reaction of carbonyl-containing compounds with primary amines. The compounds have attracted considerable attention for their wide range of biological activities, such as antibacterial [1–3], antifungal [4, 5], and antitumor [6]. It was reported that compounds bearing electron-withdrawing groups can improve their antimicrobial activities [7, 8]. Rai and co-workers reported a series of fluoro, chloro, bromo, and iodo-substituted compounds, and found that they have significant antimicrobial activities [9]. Vanadium complexes with Schiff base ligands have been reported to have interesting biological activities [10–12]. Recently, we have reported the antimicrobial activities of vanadium complexes with hydrazones [13]. As a continuation of work on the exploration of novel complex based antimicrobial agents, in this paper, two new oxovanadium complexes with similar structures, [VO(L)(L^1)] (**I**) and [VO(L)(L^2)] (**II**), where L is the dianionic form of 3-((3-bromo-2-hydroxyphenyl)-{[1-(3-bromo-2-hydroxyphenyl)methylidene]amino}-methyl)pentane-2,4-dione (H_2L), L^1 is the deprotonated form of 8-hydroxyquinoline, L^2 is 2,2'-bipyridine, were prepared and investigated their antimicrobial activities.



(H_2L)

EXPERIMENTAL

Materials and methods. $VO(Acac)_2$ and organic materials were purchased from Sigma-Aldrich and used as received. All other reagents were of analytical reagent grade. Elemental analyses of C, H and N were carried out in a Perkin-Elmer automated model 2400 Series II CHNS/O analyzer. FT-IR spectra were

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obtained on a Perkin-Elmer 377 FT-IR spectrometer with samples prepared as KBr pellets. UV-Vis spectra were obtained on a Lambda 900 spectrometer. X-ray diffraction was carried out on a Bruker APEX II CCD diffractometer. The molar conductivity was performed with a DDS-11A conductor meter.

Synthesis of I. 3-Bromosalicylaldehyde (2.01 g, 0.01 mol) and 2-amino-5-methylpyridine (1.08 g, 0.01 mol) were dissolved in methanol (30 mL). The mixture was stirred at reflux for 30 min. Then, $VO(Acac)_2$ (2.65 g, 0.01 mol), 3-bromosalicylaldehyde (2.01 g, 0.01 mol), and 8-hydroxyquinoline (1.45 g, 0.01 mol) were added. The mixture was further stirred at reflux for 30 min to give a brown solution. Single crystals of the complexes, suitable for X-ray diffraction, were grown from the solution upon slowly evaporation within a few days. The crystals were isolated by filtration, washed with methanol and dried in vacuum containing anhydrous $CaCl_2$. The yield was 37%.

IR (KBr; ν_{max}, cm^{-1}): 1712 m ν(C=O), 1622 s ν(C=N), 952 m ν(V=O). UV-Vis data (MeOH; λ_{max}, nm): 243, 390, 495. Λ_M (10^{-3} M in acetonitrile): 22 Ω^{-1} cm^2 mol^{-1}.

For $C_{28}H_{21}N_2O_6Br_2V$

Anal. calcd., %	C, 48.6	H, 3.1	N, 4.0
Found, %	C, 48.5	H, 3.0	N, 4.1

Synthesis of II. 3-Bromosalicylaldehyde (2.01 g, 0.01 mol) and 2-amino-5-methylpyridine (1.08 g, 0.01 mol) were dissolved in methanol (30 mL). The mixture was stirred at reflux for 30 min. Then, $VO(Acac)_2$ (2.65 g, 0.01 mol), 3-bromosalicylaldehyde (2.01 g, 0.01 mol), and 2,2'-bipyridine (0.01 mol, 1.56 g) were added. The mixture was further stirred at reflux for 30 min to give a brown solution. Single crystals of the complexes, suitable for X-ray diffraction, were grown from the solution upon slowly evaporation within a few days. The crystals were isolated by filtration, washed with methanol and dried in vacuum containing anhydrous $CaCl_2$. The yield was 32%.

IR (KBr; ν_{max}, cm^{-1}): 1725 m ν(C=O), 1608 s ν(C=N), 947 m ν(V=O). UV-Vis data (MeOH; λ_{max}, nm): 235, 270, 330. Λ_M (10^{-3} M in acetonitrile): 27 Ω^{-1} cm^2 mol^{-1}.

For $C_{29}H_{23}N_3O_5Br_2V$

Anal. calcd., %	C, 49.5	H, 3.3	N, 6.0
Found, %	C, 49.3	H, 3.3	N, 5.8

X-ray crystallography. X-ray diffraction was carried out at a Bruker APEX II CCD area diffractometer equipped with MoK_α radiation (λ = 0.71073 Å). The collected data were reduced with SAINT [14], and multi-scan absorption correction was performed using SADABS [15]. The structures of the complexes were solved by direct method, and refined against F^2 by full-matrix least-squares method using SHELXTL [16]. All of the non-hydrogen atoms were refined anisotropically. All hydrogen atoms were placed in calculated positions and constrained to ride on their parent atoms. The crystallographic data and refinement parameters for the compounds are listed in Table 1. Selected bond lengths and angles are listed in Table 2.

Supplementary material for structure **I** and **II** has been deposited with the Cambridge Crystallographic Data Centre (CCDC nos. 1566824 (**I**), 1566825 (**II**); deposit@ccdc.cam.ac.uk or http://www.ccdc. cam.ac.uk).

Antibacterial assay. The antibacterial activities of the vanadium complexes were tested against *B. subtilis*, *S. aureus*, *E. coli*, and *P. fluorescence* using MH (Mueller–Hinton) medium. The antifungal activities of the compounds were tested against *C. albicans* and *A. niger* using RPMI-1640 medium. The MIC values of the tested compounds were determined by a colorimetric method using the dye MTT [17]. A stock solution of the compound (150 μg mL^{-1}) in DMSO was prepared and graded quantities (75, 37.5, 18.8, 9.4, 4.7, 2.3, 1.2, 0.59 μg mL^{-1}) were incorporated in specified quantity of the corresponding sterilized liquid medium. A specified quantity of the medium containing the compound was poured into micro-titration plates. Suspension of the microorganism was prepared to contain approximately 1.0×10^5 cfu mL^{-1} and applied to microtitration plates with serially diluted compounds in DMSO to be tested and incubated at 37°C for 24 and 48 h for bacteria and fungi, respectively. Then the MIC values were visually determined on each of the microtitration plates, 50 μL of PBS (phosphate buffered saline 0.01 mol L^{-1}, pH 7.4) containing 2 mg of MTT mL^{-1} 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.

RESULTS AND DISCUSSION

The complexes were readily prepared by the reaction of 3-bromosalicylaldehyde, 2-amino-5-methylpyridine, $VO(Acac)_2$, and bidentate ligands in methanol. Elemental analyses of the complexes are in accordance with the molecular structures proposed by the X-ray analysis. It is interesting that the H_2L ligand can only be formed during the reaction of the complexes. It can't be obtained directly from the reaction of 3-bromosalicylaldehyde and acetylacetone.

In the infrared spectra of the complexes, the medium bands observed at 1710–1730 cm^{-1} are

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

Parameter	Value	
	I	**II**
Mr	692.23	704.26
Crystal color, habit	Brown, block	Brown, block
Crystal size, mm^3	0.27 × 0.27 × 0.26	0.23 × 0.20 × 0.20
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	Cc
a, Å	11.265(1)	18.806(2)
b, Å	18.179(2)	14.960(2)
c, Å	13.461(2)	12.954(2)
β, deg	103.376(3)	123.719(2)
V, $Å^3$	2681.8(5)	3031.5(6)
Z	4	4
ρ_{calcd}, g cm^{-3}	1.714	1.543
μ, mm^{-1}	3.396	3.004
$F(000)$	1376	1404
Number of unique data	4785	5064
Number of observed data ($I > 2\sigma(I)$)	2220	2931
Number of parameters	354	362
Number of restraints	0	2
R_1, wR_2 ($I > 2\sigma(I)$)	0.0659, 0.1318	0.0638, 0.0825
R_1, wR_2 (all data)	0.1766, 0.1779	0.1424, 0.1013
Goodness of fit on F^2	1.003	1.069
Largest peak and deepest hole, e $Å^{-3}$	0.933 and –0.813	0.615 and –0.549

assigned to the vibration of the C=O bonds. The intense bands located at 1622 cm^{-1} for **I** and 1608 cm^{-1} for **II** are assigned to the vibration of the C=N bonds. The medium ν(V=O) bands at about 950 cm^{-1} could be clearly identified for the complexes [18].

Molecular structures of complexes **I** and **II** are shown in Fig. 1. The merely difference is the secondary ligands, viz. 8-hydroxyquinoline (**I**) and 2,2'-bipyridine (**II**). The coordination geometry around the V atoms can be described as distorted octahedral with the ONO donor set of the tridentate Schiff base ligand, NO or NN donor set of the bidentate ligand, and one oxo group. The Schiff base ligand coordinates in a meridional fashion, forming two six-membered chelate rings with bite angles of 83.9(2)° and 82.5(2)° (**I**), 88.1(2)° and 87.2(2)° (**II**). The dihedral angles between the two benzene rings of the Schiff base ligands are 110.3(3)° (**I**), and 107.4(3)° (**II**). The N(2) atoms of the chelating bidentate ligands lie *trans* to the oxo groups. The V(1)–N(2) bonds are elongated with distances of 2.28–2.38 Å, due to the *trans* influence of the oxo groups. The coordinate bond lengths are comparable to each other, and within normal values observed in vanadium complexes with Schiff base ligands [19–22]. In the crystal structure of complex **I**, adjacent two molecules are linked by hydrogen bonds (Table 3) to form a dimer (Fig. 2a). In the crystal structure of complex **II**, the complex molecules are linked by hydrogen bonds (Table 3), to form a 3D network (Fig. 2b).

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

Bond	*d*, Å	Bond	*d*, Å
		I	
V(1)–O(1)	1.884(5)	V(1)–O(6)	1.586(5)
V(1)–O(2)	1.861(5)	V(1)–N(1)	2.121(6)
V(1)–O(5)	1.852(5)	V(1)–N(2)	2.375(7)
		II	
V(1)–O(1)	1.953(4)	V(1)–N(1)	2.075(6)
V(1)–O(2)	1.964(5)	V(1)–N(2)	2.287(6)
V(1)–O(5)	1.598(4)	V(1)–N(3)	2.152(6)
Angle	ω, deg	Angle	ω, deg
		I	
O(6)V(1)O(5)	97.1(2)	O(2)V(1)N(1)	82.5(2)
O(6)V(1)O(2)	98.5(3)	O(1)V(1)N(1)	83.9(2)
O(5)V(1)O(2)	97.3(2)	O(6)V(1)N(2)	172.6(3)
O(6)V(1)O(1)	98.0(3)	O(5)V(1)N(2)	75.7(2)
O(5)V(1)O(1)	91.2(2)	O(2)V(1)N(2)	84.0(2)
O(2)V(1)O(1)	160.3(2)	O(1)V(1)N(2)	80.9(2)
O(6)V(1)N(1)	100.7(2)	N(1)V(1)N(2)	86.4(2)
O(5)V(1)N(1)	162.0(2)		
		II	
O(5)V(1)O(2)	100.4(2)	O(1)V(1)N(2)	80.9(2)
O(5)V(1)O(1)	102.2(2)	N(1)V(1)N(2)	96.0(2)
O(2)V(1)O(1)	157.4(2)	O(5)V(1)N(3)	91.6(3)
O(5)V(1)N(1)	100.1(2)	O(1)V(1)N(3)	86.4(2)
O(2)V(1)N(1)	88.1(2)	O(2)V(1)N(3)	93.8(2)
O(1)V(1)N(1)	87.2(2)	N(1)V(1)N(3)	167.6(3)
O(5)V(1)N(2)	163.7(2)	N(3)V(1)N(2)	72.5(3)
O(2)V(1)N(2)	77.7(2)		

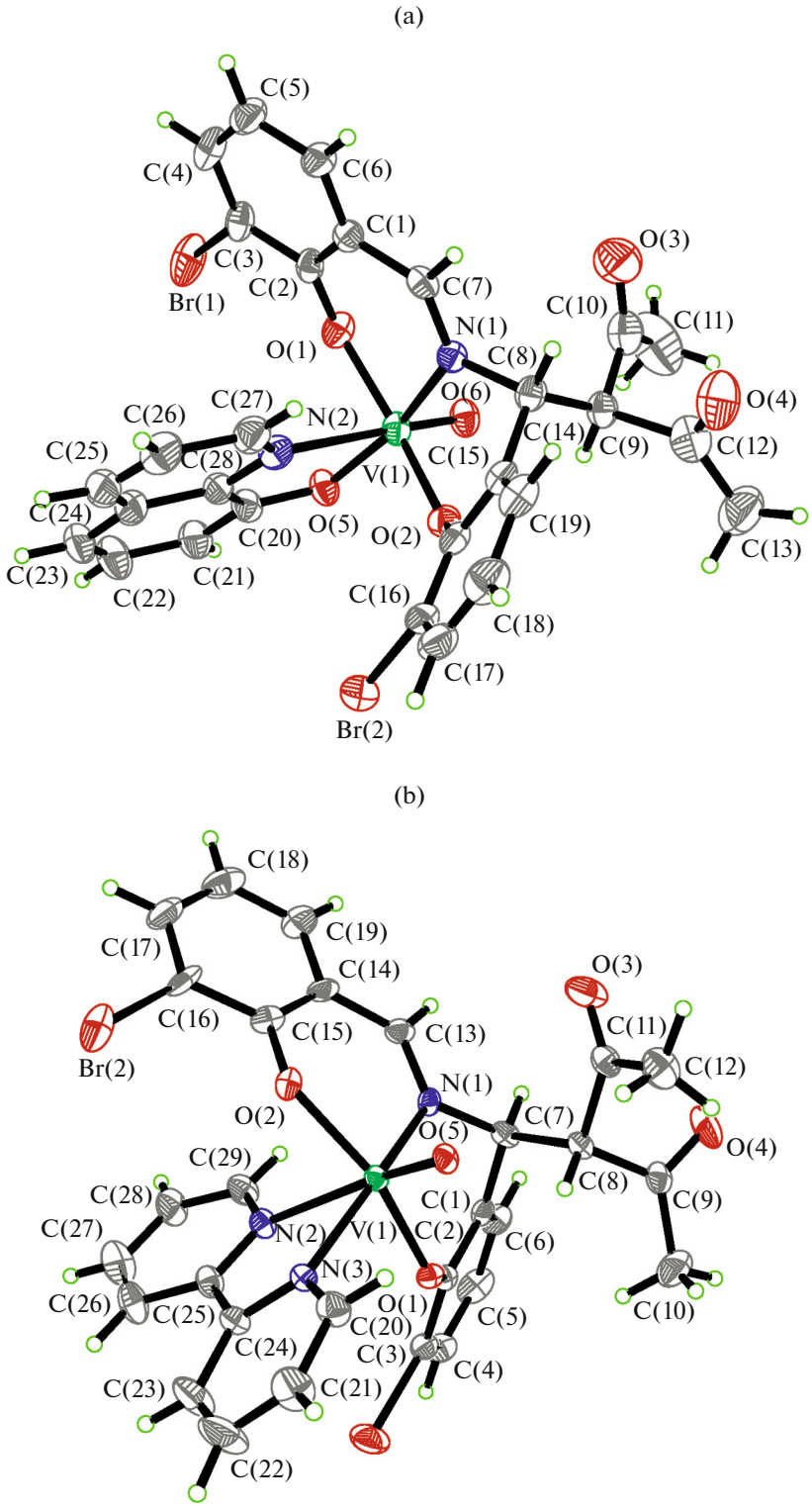

Fig. 1. A perspective view of complexes **I** (a) and **II** (b) with the atom labeling scheme. Thermal ellipsoids are drawn at the 30% probability level.

The complexes were screened for antibacterial activities against two Gram (+) bacterial strains (*Bacillus subtilis* and *Staphylococcus aureus*) and two Gram (–) bacterial strains (*Escherichia coli* and *Pseudomonas fluorescence*) by MTT method. The MIC (minimum inhibitory concentration, μg mL^{-1}) values

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		
C(7)–H(7)···O(5)^{i}	0.93	2.35	3.275(6)	173
C(9)–H(9)···O(2)	0.98	2.43	3.027(6)	119
C(21)–H(21)···O(3)^{ii}	0.93	2.55	3.432(6)	158
		II		
C(7)–H(7)···O(5)^{iii}	0.98	2.55	3.484(5)	160
C(8)–H(8)···O(1)	0.98	2.51	3.112(5)	120
C(8)–H(8)···O(5)	0.98	2.52	3.163(5)	123
C(12)–H(12*C*)···O(4)^{iv}	0.96	2.45	3.275(5)	143
C(20)–H(20)···O(5)	0.93	2.44	2.918(4)	112
C(20)–H(20)···O(3)^{iv}	0.93	2.60	3.283(5)	131
C(23)–H(23)···O(4)^{v}	0.93	2.44	3.348(4)	167
C(27)–H(27)···O(1)^{vi}	0.93	2.32	3.130(4)	145
C(27)–H(27)···O(5)^{vi}	0.93	2.59	3.362(5)	141

* Symmetry codes: ^{i} x, $1/2 - y$, $1/2 + z$; ^{ii} x, $1/2 - y$, $-1/2 + z$; ^{iii} x, $1 - y$, $1/2 + z$; ^{iv} x, $1 - y$, $-1/2 + z$; ^{v} $1/2 + x$, $-1/2 + y$, z; ^{vi} $1/2 + x$, $1/2 - y$, $1/2 + z$.

Table 4. Antimicrobial activities of the compounds

Tested material	Minimum inhibitory concentrations, μg mL^{-1}		
	B. subtilis	*S. aureus*	*E. coli*
I	18.8	4.7	75
II	9.4	2.3	18.8
$VO(Acac)_2$	37.5	18.8	75
Penicillin G	2.3	4.7	>150

of the compounds against four bacteria are listed in Table 4. Penicillin G was used as the standard drug. The complexes have from medium to strong activities against *B. subtilis*, *S. aureus*, and *E. coli*. And, apparently, complex **II** is more active than complex **I**, and even better than Penicillin G. The two complexes are also superior to the vanadium complexes we reported recently as for *S. aureus* [13]. As for comparison, the present results are better than those reported for two oxovanadium(IV) complexes with tridentate Schiff base ligands [23] or with hydroxamate ligands [24]. When compared to the oxovanadium(IV) complexes with triazole Schiff base ligands [25], the complexes are better than the chloro-substituted species and worse than the nitro-substituted one for *B. subtilis* and *E. coli*. As for *S. aureus*, the two complexes are weaker than the reported values in the literature. So, they deserve further study to explore therapeutic drugs based on vanadium species. However, it is not optimistic that the complexes have no activity against *P. fluorescence* and two fungal strains (*Candida albicans* and *Aspergillus niger*). As comparison, the ligands 8-hydroxyquinoline, 2,2'-bipyridine and 1,10-phenanthroline have no activity on the bacteria and fungi.

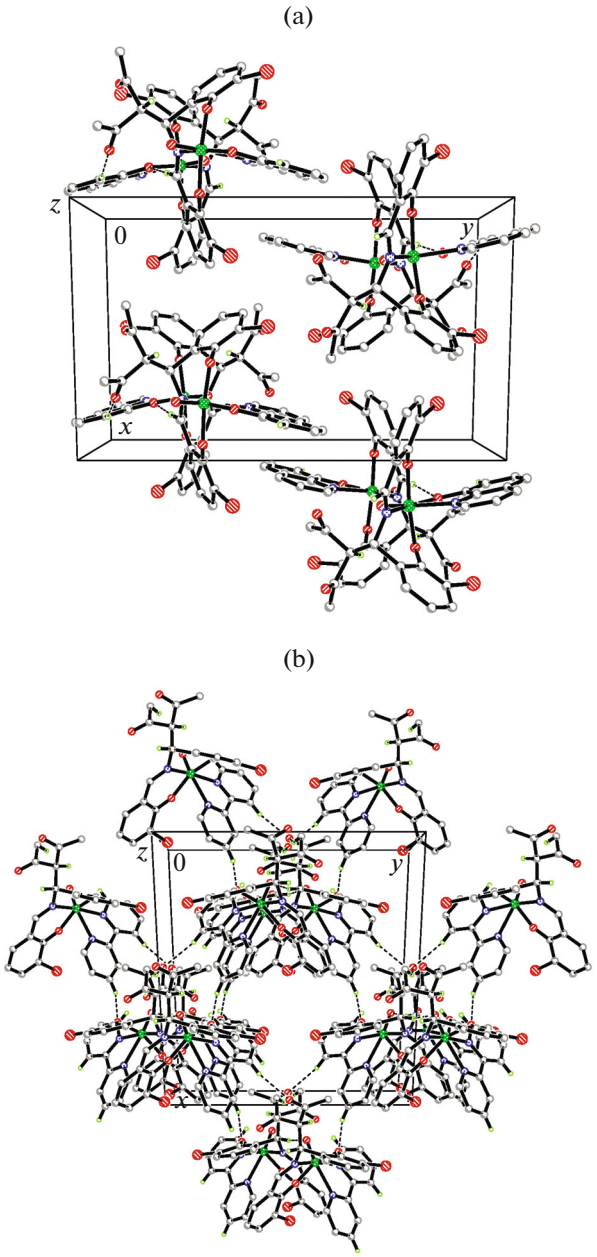

Fig. 2. Molecular packing diagram of complexes **I** (a) and **II** (b), viewed along the *z* axis direction. Hydrogen bonds are drawn as dashed lines.

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