ISSN 1070-3284, Russian Journal of Coordination Chemistry, 2017, Vol. 43, No. 5, pp. 314–319. © Pleiades Publishing, Ltd., 2017.

Synthesis, X-ray Crystal Structures, and Antibacterial Activities of Schiff Base Nickel(II) Complexes with Similar Tetradentate Schiff Bases[1]

Y. Xu[a], L. Xue[a], and Z. G. Wang[b, *]

[a] *Modern Medical Research Center, Third Affiliated Hospital of Soochow University, Changzhou, 213003 P.R. China*
[b] *Department of Respiratory Medicine, Third Affiliated Hospital of Soochow University, Changzhou, 213003 P.R. China*
**e-mail: wangqiangszu@126.com*

Received March 8, 2016

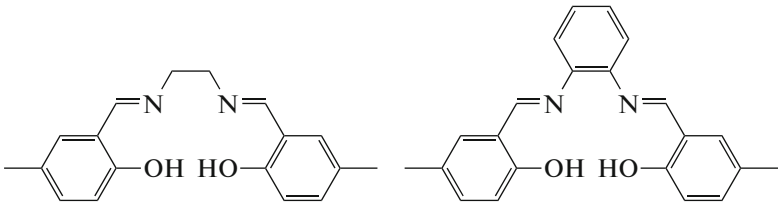
Abstract—Two new mononuclear complexes, $[NiL^1] \cdot CH_3OH$ (**I**) and $[NiL^2]$ (**II**), have been prepared from the tetradentate Schiff bases *N*,*N*'-bis(5-methylsalicylidene)ethylenediamine (H_2L^1) and *N*,*N*'-bis(5-methylsalicylidene)-*o*-phenylenediamine (H_2L^2), respectively. The complexes have been characterized by physico-chemical and spectroscopic methods, as well as single-crystal X-ray determination (CIF files nos. 1428969 (**I**), 1428968 (**II**)). Complex **I** crystallizes in the triclinic space group $P\bar{1}$ with $a = 6.7387(14)$, $b = 10.7010(17)$, $c = 12.681(2)$ Å, $\alpha = 87.059(2)°$, $\beta = 88.828(2)°$, $\gamma = 89.901(2)°$, $V = 913.0(3)$ Å^3, $Z = 2$. Complex **II** crystallizes in the monoclinic space group $P2_1/n$ with $a = 12.1437(11)$, $b = 8.0537(8)$, $c = 18.4545(18)$ Å, $\beta = 105.088(2)°$, $V = 1742.7(3)$ Å^3, $Z = 4$. The nickel atoms in the complexes are coordinated by two phenolate O and two imine N atoms of the tetradentate Schiff base ligands, forming square planar coordination. The complexes and the Schiff base compounds were assayed for antibacterial activities against three Gram-positive bacterial strains (*B. subtilis*, *S. aureus*, and *St. faecalis*) and three Gram-negative bacterial strains (*E. coli*, *P. aeruginosa*, and *E. cloacae*) by MTT method. As a result, the complexes showed effective antimicrobial activity against the microorganisms tested.

Keywords: Schiff base, nickel complex, X-ray diffraction, antibacterial activity

DOI: 10.1134/S1070328417050098

INTRODUCTION

Schiff bases represent one of the most widely utilized classes of ligands in metal coordination chemistry. Metal complexes with Schiff bases as ligands have played important role in the development of coordination chemistry due to their preparative accessibility, structural variety, and biological properties [1–3]. In addition, Schiff bases are reported to possess various biological activities, such as antibacterial [4, 5] and antitumour activities [6, 7]. Interest is still high as few have found their way into application as therapeutic drugs, health, skin care products and in paint dye manufacturing [8]. Nickel complexes with Schiff bases have interesting biological properties [9–12]. We report herein the synthesis and characterization of two new mononuclear nickel(II) complexes, $[NiL^1] \cdot CH_3OH$ (**I**) and $[NiL^2]$ (**II**), where L^1 and L^2 are the dianionic form of *N*,*N*'-bis(5-methylsalicylidene)ethylenediamine (H_2L^1) and *N*,*N*'-bis(5-methylsalicylidene)-*o*-phenylenediamine (H_2L^2), respectively.



(H_2L^1) (H_2L^2)

[1] The article is published in the original.

The antibacterial activity against three Gram-positive bacterial strains (*B. subtilis*, *S. aureus*, and *St. faecalis*) and three Gram-negative bacterial strains (*E. coli*, *P. aeruginosa*, and *E. cloacae*) by MTT method was studied.

EXPERIMENTAL

Materials and physical methods. 5-Methylsalicylaldehyde, ethane-1,2-diamine, and benzene-1,2-diamine were purchased from Aldrich. All other reagents and solvents were purchased from commercial sources and used as received. FT-IR spectra were recorded as KBr pellets on Bruker Tensor-27. Elemental (C, H, and N) analyses were performed on a Perkin-Elmer 2400 II analyzer. Single crystal X-ray diffraction was carried out with a Bruker Apex II CCD diffratometer. Molar conductivity of the complexes in acetonitrile was measured with a DDS-11A molar conductivity meter.

Caution! Perchlorate salts are potentially explosive. Only a small amount of material should be prepared, and it should be handled with care.

Synthesis of H_2L^1. Ethane-1,2-diamine (0.06 g, 0.01 mol) dissolved in methanol (30 mL) was added to 5-methylsalicylaldehyde (2.72 g, 0.02 mol) in methanol (30 mL). The reaction mixture was heated under reflux for 1 h and then cooled to room temperature followed by concentrating the resulting mixture to give a yellow product with quantitative yield.

For $C_{18}H_{20}N_2O_2$			
anal. calcd., %:	C, 72.95;	H, 6.80;	N, 9.45.
Found, %:	C, 72.77;	H, 6.93;	N, 9.37.

Synthesis of H_2L^2. The yellow product of H_2L^2 was synthesized according to a similar procedure as that for H_2L^1 with benzene-1,2-diamine (0.11 g, 0.01 mol) instead of ethane-1,2-diamine.

For $C_{22}H_{20}N_2O_2$			
anal. calcd., %:	C, 76.72;	H, 5.85;	N, 8.13.
Found, %:	C, 76.89;	H, 5.73;	N, 8.18.

Synthesis of I. Nickel perchlorate (0.37 g, 1 mmol) in methanol (20 mL) was added to H_2L^1 (0.30 g, 1 mmol) in methanol (20 mL), and the resultant red reaction mixture was stirred at room temperature for 1 h to give a clear solution. Red single crystals were obtained by slow evaporation of the solution in air. The yield was 0.27 g (71%).

For $C_{19}H_{22}N_2O_3Ni$			
anal. calcd., %:	C, 59.26;	H, 5.76;	N, 7.27.
Found, %:	C, 59.45;	H, 5.91;	N, 7.16.

Synthesis of II. The red single crystals of complex **II** were prepared according to a similar procedure as that for **I**, with H_2L^2 (0.34 g, 1 mmol) instead of H_2L^1. The yield was 0.18 g (45%).

For $C_{22}H_{18}N_2O_2Ni$			
anal. calcd., %:	C, 65.88;	H, 4.52;	N, 6.98.
Found, %:	C, 65.79;	H, 4.71;	N, 7.11.

X-ray structure determination. Intensity data of the complexes were collected at 298(2) K on a Bruker Apex II CCD diffractometer using graphite-monochromated MoK_α radiation ($\lambda = 0.71073$ Å). For data processing and absorption correction the packages SAINT and SADABS were used [13]. The structures were solved by direct and Fourier methods and refined by full-matrix least-squares based on F^2 using SHELXL-97 [14]. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms have been placed at geometrical positions with fixed thermal parameters. Crystallographic data of the complexes are summarized in Table 1. Selected bond lengths and angles are listed in Table 2.

Supplementary material for structures has been deposited with the Cambridge Crystallographic Data Centre (CCDC nos. 1428969 for **I** and 1428968 for **II**; deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk/conts/retrieving.html).

Antibacterial activity. Antibacterial activity of the complexes was tested against *B. subtilis*, *S. aureus*, *St. faecalis*, *P. aeruginosa*, *E. coli*, and *E. cloacae* using MTT medium. The minimum inhibitory concentrations (MICs) of the complexes were determined by a colorimetric method using MTT dye [15]. A stock solution of the complexes (50 μg mL^{-1}) in DMSO was prepared and quantities of the complexes were incorporated in specified quantity of sterilized liquid medium. A specified quantity of the medium containing the complexes was poured into microtitration plates. Suspension of the microorganism was prepared to contain approximately 10^5 cfu mL^{-1} and applied to microtitration plates with serially diluted complexes in DMSO to be tested, and incubated at 37°C for 24 h for bacteria. After the MICs were visually determined on each microtitration plates, 50 μL of phosphate buffered saline (PBS 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 mL^{-1} of MTT 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 M HCl was added to extract the dye. After 12 h of incubation at room tempera-

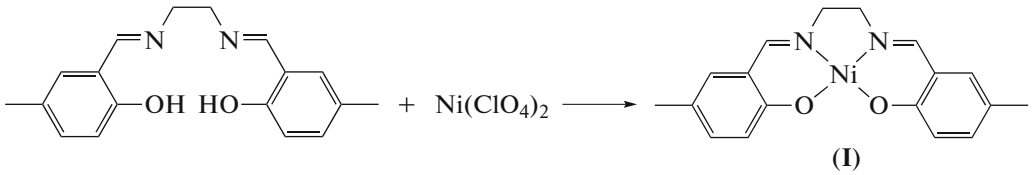
Table 1. Crystallographic data and structure refinement for complexes **I** and **II**

Parameter	Value	
	I	**II**
Formula weight	385.10	401.09
Crystal system	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P2_1/n$
Unit cell dimensions:		
a, Å	6.7387(14)	12.1437(11)
b, Å	10.7010(17)	8.0537(8)
c, Å	12.681(2)	18.4545(18)
α, deg	87.059(2)	90
β, deg	88.828(2)	105.088(2)
γ, deg	89.901(2)	90
V, Å^3	913.0(3)	1742.7(3)
Z	2	4
ρ_{calcd}, g cm^{-3}	1.401	1.529
μ, mm^{-1}	1.082	1.134
F(000)	404	832
Crystal size, mm	0.30 × 0.27 × 0.26	0.23 × 0.20 × 0.20
θ Range for data collection, deg	1.61–25.49	1.81–24.52
Index range hkl	$-8 \le h \le 8$, $-12 \le k \le 12$, $-15 \le l \le 11$	$-11 \le h \le 14$, $-9 \le k \le 9$, $-21 \le l \le 21$
Reflections collected	4739	8080
Observed reflections ($I > 2\sigma(I)$)	2626	2107
Max and min transmission	0.7373 and 0.7662	0.7805 and 0.8050
Data/restraints/parameters	3358/0/230	2895/0/244
Goodness-of-fit on F^2	1.052	1.031
Final R_1, wR_2 indices ($I > 2\sigma(I)$)	0.0496, 0.1154	0.0379, 0.0748
R_1, wR_2 indices (all data)	0.0698, 0.1262	0.0655, 0.0843
Largest difference peak and hole, e Å^{-3}	0.365, –0.362	0.558, –0.433

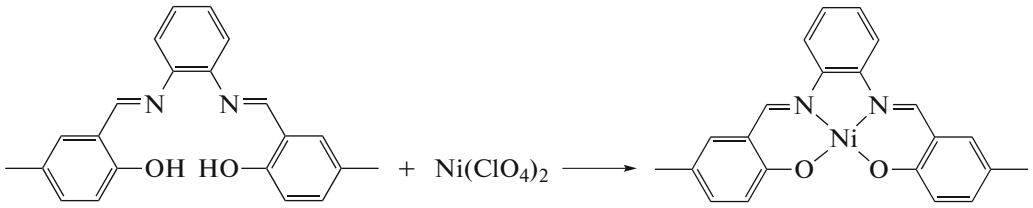
ture, the optical density (OD) was measured with a microplate reader at 570 nm.

RESULTS AND DISCUSSION

The Schiff bases H_2L^1 and H_2L^2 were prepared in quantitative yields in methanol. The compounds are yellow solid product. The elemental analyses are in good agreement with the chemical formulae proposed for the compounds. Complexes were prepared by the reaction of the Schiff bases with nickel perchlorate in methanol acording to Scheme:



(I)



(II)

Both the Schiff bases and the complexes are stable in air at room temperature, and soluble in common polar organic solvents, such as DMSO, DMF, methanol, ethanol, and acetonitrile. The molar conductance values of the complexes measured in methanol at concentrations of 10^{-3} mol L^{-1} at 298 K are 20 and 25 Ω^{-1} cm^2 mol^{-1}, indicating the non-electrolytic nature [16].

The IR spectra of the free Schiff bases showed weak bands due to the phenolic groups in the region 3350–3500 cm^{-1}, which are assigned to the ν(OH) vibrations. The bands of the phenolic group are absent in the IR spectra of the nickel complexes, indicating the deprotonation of the phenolic groups. The intense bands at about 1287 cm^{-1} assigned to phenolic C–O linkage shifting towards to higher wave numbers of 1315 cm^{-1} for **I** and **II**, confirming the involvement of the deprotonated phenolic groups in bond formation with the metal atoms [17]. The strong bands in the Schiff bases at 1641 cm^{-1} for H_2L^1 and 1645 cm^{-1} for H_2L^2 underwent a negative shift of about 15 cm^{-1} in the complexes, confirming the coordination of the azomethine N atoms to the nickel atoms [18]. The weak absorption bands in the 400–600 cm^{-1} region are assigned to the vibrations of Ni–N and Ni–O coordinate bonds.

In the free Schiff bases, the bonds at about 340 nm are attributed to the azomethine chromophore π–π* transition. The bands at higher energies (280 nm) are associated with the benzene π–π* transitions. In the spectra of the complexes, however, the azomethine chromophore π–π* transition is shifted to 300 nm, indicating that the imino nitrogen is involved in coordination to the nickel atoms. The absorption frequencies ascribed to the benzene π–π* transition (270 nm) are slightly changed, representing an influence on the benzene ring due to the coordination interaction. The bands at 400 nm in the spectra of both complexes can be assigned to the LMCT transitions.

The structures of the nickel complexes **I** and **II** are similar (Fig. 1). Both of the complexes are mononuclear species. Complex **I** contains a methanol molecule, which link to the complex molecule via intramolecular hydrogen bond O(3)–H(3)···O(2) (O(3)–H(3) 0.82, H(3)···O(2) 2.07, O(3)···O(2) 2.882(5) Å, O(3)–H(3)···O(2) 174°). The Ni atom in each of the com-

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

Bond	*d*, Å	Bond	*d*, Å
	I		
Ni(1)–O(1)	1.845(3)	Ni(1)–O(2)	1.855(3)
Ni(1)–N(1)	1.845(3)	Ni(1)–N(2)	1.845(3)
	II		
Ni(1)–O(1)	1.840(2)	Ni(1)–O(2)	1.844(2)
Ni(1)–N(1)	1.862(2)	Ni(1)–N(2)	1.857(2)
Angle	ω, deg	Angle	ω, deg
	I		
O(1)Ni(1)N(2)	178.52(13)	O(1)Ni(1)N(1)	95.05(13)
N(2)Ni(1)N(1)	86.21(13)	O(1)Ni(1)O(2)	83.85(11)
N(2)Ni(1)O(2)	94.89(13)	N(1)Ni(1)O(2)	178.91(12)
	II		
O(1)Ni(1)O(2)	84.20(9)	O(1)Ni(1)N(2)	179.26(11)
O(2)Ni(1)N(2)	95.08(10)	O(1)Ni(1)N(1)	94.87(10)
O(2)Ni(1)N(1)	178.78(10)	N(2)Ni(1)N(1)	85.85(11)

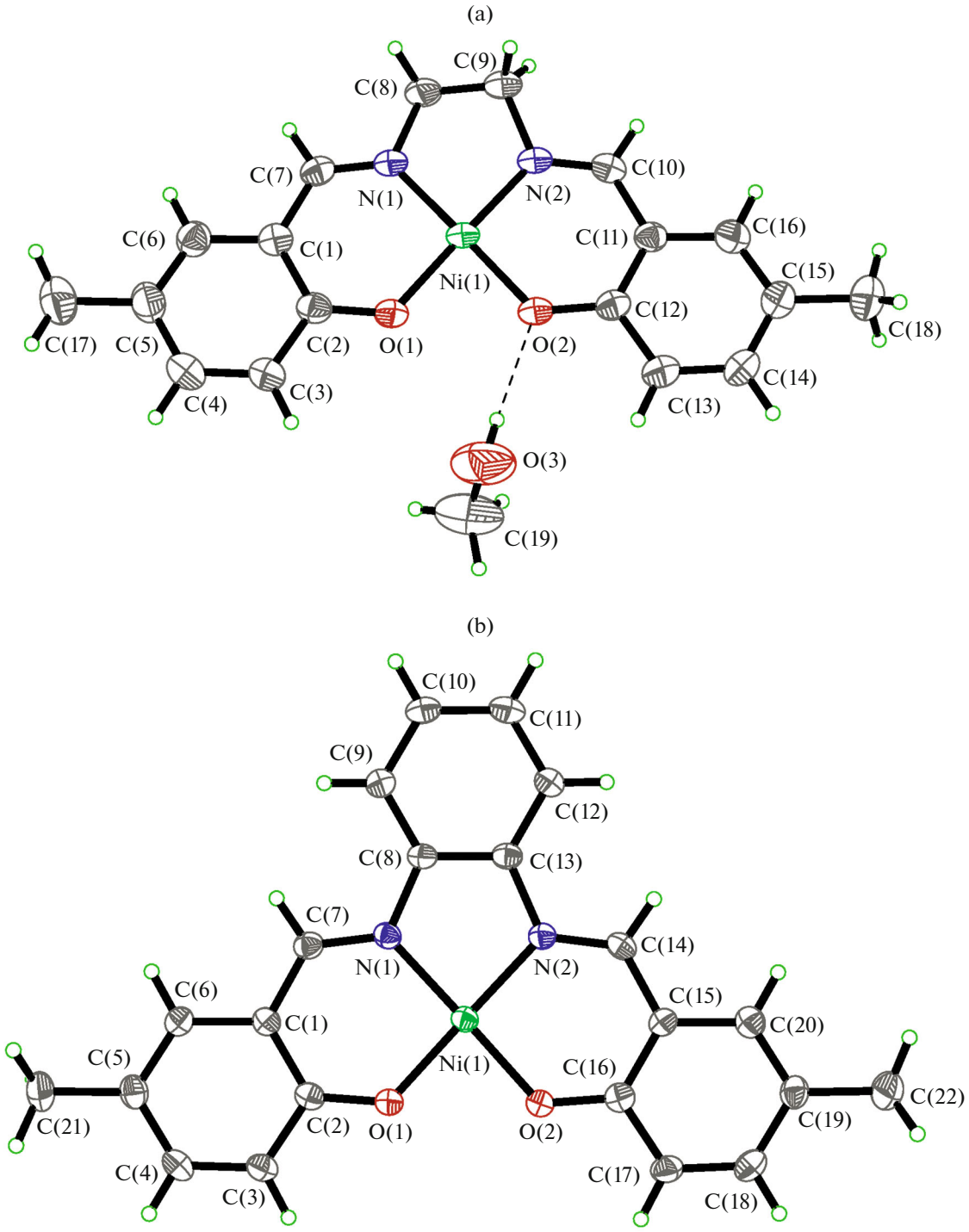


Fig. 1. ORTEP plots (30% probability level) and numbering scheme for **I** (a)and **II** (b). Hydrogen bond is shown as a dotted line.

plexes is coordinated by two phenolate O and two imine N atoms from two Schiff base ligands, forming square planar coordination. The Ni–N and Ni–O bonds in the complexes are comparable to each other, and within normal values as compared with other similar nickel complexes with Schiff bases [19–22]. The *cis* and *trans* angles subtended at the Ni atoms in the complexes are in the ranges 83.85(11)°–95.05(13)° and 178.52(13)°–178.91(12)° for **I**, and 84.20(9)°–95.08(10)° and 178.78(10)°–179.26(11)° for **II**. Thus, the square planar coordination in both complexes are distorted. The dihedral angles between the two benzene rings are 0.6(3)° for **I** and 1.9(5)° for **II**.

The complexes and the Schiff bases were screened for antibacterial activities against three Gram-positive bacterial strains (*B. subtilis*, *S. aureus*, and *St. faecalis*)

Table 3. MICs (μg mL^{-1}) of complexes **I** and **II** and related material

Tested material	Gram positive			Gram negative		
	B. subtilis	*S. aureus*	*St. faecalis*	*P. aeruginosa*	*E. coli*	*E. cloacae*
I	3.12	6.25	12.5	12.5	12.5	6.25
II	3.12	6.25	12.5	>50	12.5	25
H_2L^1	12.5	25	>50	>50	>50	>50
H_2L^2	12.5	50	>50	>50	>50	>50
Penicillin G	1.56	1.56	1.56	6.25	6.25	3.12

and three Gram-negative bacterial strains (*E. coli*, *P. aeruginosa*, and *E. cloacae*) by MTT method. The MICs of the compounds against the bacteria are presented in Table 3. Penicillin G was tested as a reference drug. The results revealed that the free Schiff bases H_2L^1 and H_2L^2 showed no activity against *St. faecalis*, *P. aeruginosa*, *E. coli*, and *E. cloacae*, and weak activity against *B. subtilis* and *S. aureus*. In general, the activities of the two complexes are much effective than the free Schiff bases. The only exception is complex **II**, which show no activity against *P. aeruginosa*. Complexes **I** and **II** have similar activities against all the bacteria, indicating the central benzene ring of the Schiff base ligand is not an essential factor in the antibacterial processes. Such an enhanced activity of the complexes than the free Schiff base can be explained on the basis of Overtone's concept and Tweedy's chelation theory [23]. According to Overtone's concept of cell permeability, the lipid membrane that surrounds the cell favors the passage of only lipid soluble materials due to which liposolubility is an important factor that controls antimicrobial activity. On chelation, the polarity of the metal ion is reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalisation of π-electrons over the whole chelate ring and enhances the lipophilicity of the complexes. This increased lipophilicity enhances the penetration of the complexes into lipid membranes and blocking of metal binding sites on the enzymes of the microorganisms. The complexes also disturb the respiration process of the cell and thus block the synthesis of the proteins that restricts further growth of the organism. The variation in the effectiveness of the different compounds against different organisms depends on the impermeability of the cells of microbes or difference in ribosome of the microbial cells.

ACKNOWLEDGMENTS

Financial support from the Third Affiliated Hospital of Soochow University is gratefully acknowledged.

REFERENCES

1. Zhang, J.-C., Li, Y.-N., Huang, D., et al., *Chin. J. Inorg. Chem.*, 2014, vol. 30, no. 2, p. 425.
2. Niu, F., Yan, K.-X., Pang, L.H., et al., *Inorg. Chim. Acta*, 2015, vol. 435, p. 299.
3. Mohamed, R.G., Elantabli, F.M., Helal, N.H., et al., *Synth. React. Inorg. Met.-Org. Nano-Met. Chem.*, 2015, vol. 45, no. 12, p. 1839.
4. Matin, S.J. and Khojasteh, R.R., *Russ. J. Coord. Chem.*, 2015, vol. 85, no. 7, p. 1763.
5. Li, W., Ding, B.-W., Sun, H., et al., *Synth. React. Inorg. Met.-Org. Nano-Met. Chem.*, 2012, vol. 42, no. 5, p. 666.
6. Hazari, P.P., Pandey, A.K., Chaturvedi, S., et al., *Chem. Biol. Drug Des.*, 2012, vol. 79, no. 2, p. 223.
7. Ramadan, R.M., Abu Al-Nasr, A.K., and Noureldeen, A.F.H., *Spectrochim. Acta, A*, 2014, vol. 132, p. 417.
8. Khoo, T.-J., Bin Break, M.K., Crouse, K.A., et al., *Inorg. Chim. Acta*, 2014, vol. 413, p. 68.
9. Mukherjee, T., Pessoa, J.C., Kumar, A., et al., *Dalton Trans.*, 2013, vol. 42, no. 7, p. 2594.
10. Maurya, R.C., Malik, B.A., Mir, J.M., et al., *J. Coord. Chem.*, 2015, vol. 68, no. 16, p. 2902.
11. Lu, Y., Shi, D.-H., You, Z.-L., et al., *J. Coord. Chem.*, 2012, vol. 65, no. 2, p. 339.
12. Zhou, X.-S., Cheng, X.-S., Li, Y.-N., et al., *Chin. J. Inorg. Chem.*, 2013, vol. 29, no. 2, p. 397.
13. Sheldrick, G.M., *SAINT (version 6.02), SADABS (version 2.03)*, Madison: Bruker AXS lnc., 2002.
14. Sheldrick, G.M., *SHELXL-97, Program for Crystal Structure Solution*, Göttingen: Univ. of Göttingen, 1997.
15. Meletiadis, J., Meis, J.F., Mouton, J.W., et al., *J. Clin. Microbiol.*, 2000, vol. 38, no. 8, p. 2949.
16. Geary, W.J., *Coord. Chem. Rev.*, 1971, vol. 7, no. 1, p. 81.
17. Lal, R.A., Choudhury, S., Ahmed, A., et al., *J. Coord. Chem.*, 2009, vol. 62, no. 23, p. 3864.
18. Surati, K. and Thaker, B.T., *Spectrochim. Acta, A*, 2010, vol. 75, no. 1, p. 235.
19. Jana, A., Majumder, S., Carrella, L., et al., *Inorg. Chem.*, 2010, vol. 49, no. 19, p. 9012.
20. Rusere, L.N., Shalumova, T., Tanski, J.M., et al., *Polyhedron*, 2009, vol. 28, no. 17, p. 3804.
21. Prabhakar, M., Zacharias, P.S., and Das, S.K., *Inorg. Chem. Commun.*, 2006, vol. 9, no. 9, p. 899.
22. Abe, Y., Akao, H., Yoshida, Y., et al., *Inorg. Chim. Acta*, 2006, vol. 359, no. 10, p. 3147.
23. Taherlo, R. and Salehi, M., *Inorg. Chim. Acta*, 2014, vol. 418, p. 180.