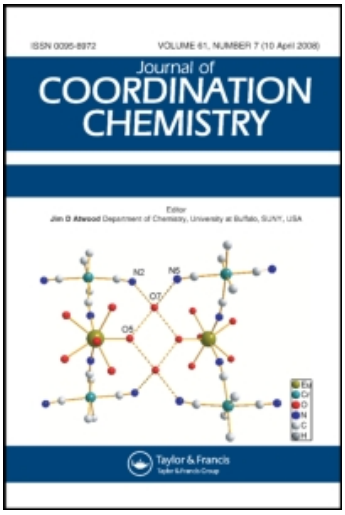

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Syntheses and crystal structures of two Schiff-base copper(II) complexes with urease inhibition

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Syntheses and crystal structures of two Schiff-base copper(II) complexes with urease inhibition

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Two new copper(II) complexes, [CuL1(N_3)] (**1**) and [CuL2(NCS)] (**2**) (HL1 = 4-chloro-2-[(2-piperidin-1-ylethylimino)methyl]phenol, HL2 = 4-chloro-2-[(2-morpholin-4-ylethylimino)-methyl]phenol), were prepared and structurally characterized by elemental analyses, infrared spectroscopy, and single-crystal X-ray diffraction. Complex **1** is an azide coordinated mononuclear complex, while complex **2** is a terminal thiocyanate coordinated mononuclear complex. The coppers in both complexes are four-coordinate, square-planar. Both complexes show potent urease inhibitory properties.

Keywords: Schiff base; copper(ii) complex; synthesis; crystal structure; urease inhibitory property

1. Introduction

Identifying the biological role of copper, primarily through techniques associated with the interface of biology, biochemistry, and coordination chemistry [1–3], shows that it is primarily in redox reactions and as a biological catalyst, although much remains to be understood [4, 5]. An extensive effort has been made to prepare and characterize a variety of copper(II) complexes in an attempt to model the physical and chemical behavior of copper-containing enzymes [6]. The peculiarity of copper lies in its ability to form complexes with coordination numbers four, five, and six [7–9]. Urease (urea amidohydrolase, E.C. 3.5.1.5) is a nickel-containing metalloenzyme that catalyzes the hydrolysis of urea to form ammonia and carbamic acid. The resulting carbamic acid spontaneously decomposes, yielding a second molecule of ammonia and carbon dioxide. High concentrations of ammonia arising from these reactions, as well as the accompanying pH elevation, have important implications in medicine and agriculture [10, 11]. Thus, inhibition of urease is a challenging topic. Recent research indicated that copper(II) complexes with Schiff bases had excellent urease inhibitory activity [12]. Complexes derived from the Schiff bases 4-chloro-2-[(2-piperidin-1-ylethylimino)-methyl]phenol (HL1) and 4-chloro-2-[(2-morpholin-4-ylethylimino)methyl]phenol (HL2) have not been reported. In this article, two new copper(II) complexes,

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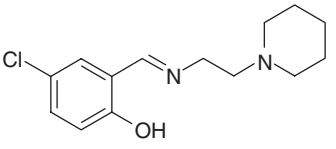
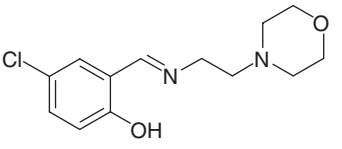
[CuL1(N_3)] (**1**) and [CuL2(NCS)] (**2**), were prepared and structurally characterized. The urease inhibitory properties of these complexes were determined.



HL1



HL2

2. Experimental

2.1. *Materials and methods*

All chemicals (reagent grade) used were commercially available from Lancaster. Elemental analysis for C, H, and N were performed on a Perkin-Elmer 240C elemental analyzer. The infrared spectra were recorded on a Nicolet AVATAR 360 spectrophotometer as KBr pellets in the 4000–400 cm^{-1} region.

2.2. *Synthesis of HL1 and HL2*

The Schiff bases HL1 and HL2 were prepared by condensation of 5-chlorosalicylaldehyde (1.0 mmol, 156.6 mg) with 2-piperidin-1-ylethylamine (1.0 mmol, 128.2 mg) and 2-morpholin-4-ylethylamine (1.0 mmol, 130.2 mg), respectively, in methanol solutions (30 mL) at room temperature. Anal. Calcd for $C_{14}H_{19}ClN_2O$ (HL1,%): C, 63.0; H, 7.2; N, 10.5. Found: C, 62.7; H, 7.3; N, 10.4. Anal. Calcd for $C_{13}H_{17}ClN_2O_2$ (HL2,%): C, 58.1; H, 6.4; N, 10.4. Found: C, 58.3; H, 6.5; N, 10.2.

2.3. *Synthesis of (1)*

To a methanol solution (10 mL) of HL1 (0.1 mmol, 26.6 mg) was added with stirring a methanol solution (5 mL) of $Cu(CH_3COO)_2{\cdot}H_2O$ (0.1 mmol, 20.0 mg) and an aqueous solution (2 mL) of sodium azide (0.1 mmol, 6.5 mg). The mixture was stirred for 30 min at room temperature and filtered. Upon keeping the filtrate in air for 5 days, blue block-shaped crystals of **1**, suitable for X-ray single-crystal diffraction, formed at the bottom of the vessel. The crystals were collected by filtration, washed three times with cold methanol and dried in a vacuum desiccator containing anhydrous $CaCl_2$. Yield: 51%. Anal. Calcd for $C_{14}H_{18}ClCuN_5O$ (%): C, 45.3; H, 4.9; N, 18.9. Found: C, 45.7; H, 5.2; N, 18.6.

2.4. *Synthesis of (2)*

To a methanol solution (10 mL) of HL2 (0.1 mmol, 26.8 mg) was added with stirring a methanol solution (5 mL) of $Cu(CH_3COO)_2\ H_2O$ (0.1 mmol, 20.0 mg) and an aqueous

solution (2 mL) of ammonium thiocyanate (0.1 mmol, 7.6 mg). The mixture was stirred for 30 min at room temperature and filtered. Upon keeping the filtrate in air for 8 days, blue block-shaped crystals of **2**, suitable for X-ray single-crystal diffraction, formed at the bottom of the vessel. The crystals were collected by filtration, washed three times with cold methanol and dried in a vacuum desiccator containing anhydrous $CaCl_2$. Yield: 73%. Anal. Calcd for $C_{14}H_{16}ClCuN_3O_2S$ (%): C, 43.2; H, 4.1; N, 10.8. Found: C, 42.9; H, 4.3; N, 10.5.

Caution! Although the samples we prepared never exploded during handling, azide metal complexes are potentially explosive; only a small amount of material should be prepared and should be handled with care.

2.5. *X-ray crystallography*

Diffraction data for **1** and **2** were determined at 298(2) K on a Bruker SMART 1000 CCD area-detector diffractometer with Mo-Kα radiation ($\lambda = 0.71073$ Å). The collected data were reduced using SAINT [13] and empirical absorption corrections were performed using SADABS [14]. Both structures were solved by direct methods and refined against F^2 by full-matrix least-squares using the SHELXTL package [15]. All non-hydrogen atoms were refined anisotropically. Hydrogens in the two complexes were generated geometrically. The crystallographic data for the complexes are summarized in table 1. Selected bond lengths and angles are listed in table 2. Crystallographic data for the two complexes have been deposited with the Cambridge Crystallographic Data Centre (CCDC 695553 and 695554).

Table 1. Crystal data for **1** and **2**.

Complex	**1**	**2**
Formula	$C_{14}H_{18}ClCuN_5O$	$C_{14}H_{16}ClCuN_3O_2S$
MW	371.32	389.35
Crystal shape/color	Block/blue	block/blue
Crystal size (mm^3)	$0.32 \times 0.30 \times 0.28$	$0.27 \times 0.25 \times 0.25$
Crystal system	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$	$P2_1/c$
Units of Dimensions (Å, °)		
a	25.907(16)	6.242(4)
b	9.659(6)	17.399(11)
c	6.514(4)	14.055(9)
β		101.392(10)
V (Å^3)	1630.0(17)	1496.3(17)
Z	4	4
λ (Mo-Kα) (Å)	0.71073	0.71073
T (K)	298(2)	298(2)
μ (Mo-Kα) (cm^{-1})	1.512	1.787
T_{min}	0.643	0.644
T_{max}	0.677	0.664
Reflections/parameters	3525/199	3225/199
Goodness of fit on F^2	1.044	1.102
R_1, wR_2 [I 2$\sigma(I)$][a]	0.0449, 0.0862	0.0308, 0.0859
R_1, wR_2 (all data)[a]	0.0701, 0.982	0.0406, 0.0912

[a] $R_1 = \sum||F_o|-|F_c||/\sum|F_o|$, $wR_2 = [\sum w(F_o^2 - F_c^2)^2/\sum w(F_o^2)^2]^{1/2}$.

Table 2. Selected bond lengths (Å) and angles (°) for **1** and **2**.

1			
Cu1–O1	1.923(3)	Cu1–N1	1.947(4)
Cu1–N2	2.082(3)	Cu1–N3	1.980(4)
Cu1···N5^{i}	2.451(4)		
O1–Cu1–N1	93.0(1)	O1–Cu1–N3	91.5(1)
N1–Cu1–N3	161.3(1)	O1–Cu1–N2	175.9(1)
N1–Cu1–N2	83.71(1)	N3–Cu1–N2	90.8(1)
O1–Cu1···N5^{i}	93.18(1)	N1–Cu1···N5^{i}	91.8(1)
N3–Cu1···N5^{i}	106.1(2)	N2–Cu1···N5^{i}	89.4(1)
2			
Cu1–O1	1.880(2)	Cu1–N1	1.897(2)
Cu1–N2	2.078(2)	Cu1–N3	1.927(2)
Cu1···S1^{ii}	2.969(2)		
O1–Cu1–N1	92.4(1)	O1–Cu1–N3	90.0(1)
N1–Cu1–N3	170.0(1)	O1–Cu1–N2	175.7(1)
N1–Cu1–N2	84.7(1)	N3–Cu1–N2	92.3(1)
O1–Cu1···S1^{ii}	92.6(1)	N1–Cu1···S1^{ii}	84.5(1)
N2–Cu1···S1^{ii}	90.3(1)	N3–Cu1···S1^{ii}	105.1(1)

Symmetry codes: (i)–x, $1/2+y$, $5/2-z$; (ii)–$1+x$, y, z.

Table 3. Inhibitory properties against urease.

Tested materials	IC_{50} (μM)
1	37.2 ± 0.5
2	41.1 ± 0.7
HL1	>100
HL2	>100
Copper acetate	18.5 ± 0.2
Acetohydroxamic acid	45.4 ± 0.3

2.6. *Urease inhibitory tests*

The measurement of urease inhibitory properties was carried out according to the literature [16]. The assay mixture, containing 25 μL of *jack bean* urease (10 kU L^{-1}) and 25 μL of the test materials of various concentrations (dissolved in DMSO : H_2O = 1:1 (v/v)), was preincubated for 1 h at 37°C in a 96-well assay plate. Then 0.2 mL of 100 mM Hepes (*N*-[2-hydroxyethyl]piperazine-*N*′-[2-ethanesulfonic acid]) buffer at pH 6.8 containing 500 mM 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 Hepes buffer from 6.8 to 7.7, was measured by micro-plate reader (570 nm) with the end-point being determined by the color of the phenol red indicator. The results are listed in table 3.

3. Results and discussion

Both air-stable Schiff bases are orange oils, soluble in polar organic solvents such as DMF, DMSO, methanol, ethanol, and acetonitrile. The elemental analyses are in good

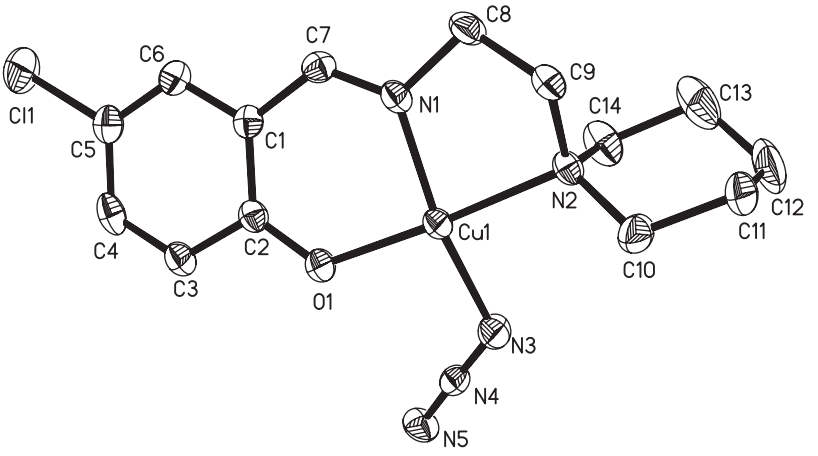


Figure 1. The structure of **1**, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level. Hydrogen atoms have been omitted for clarity.

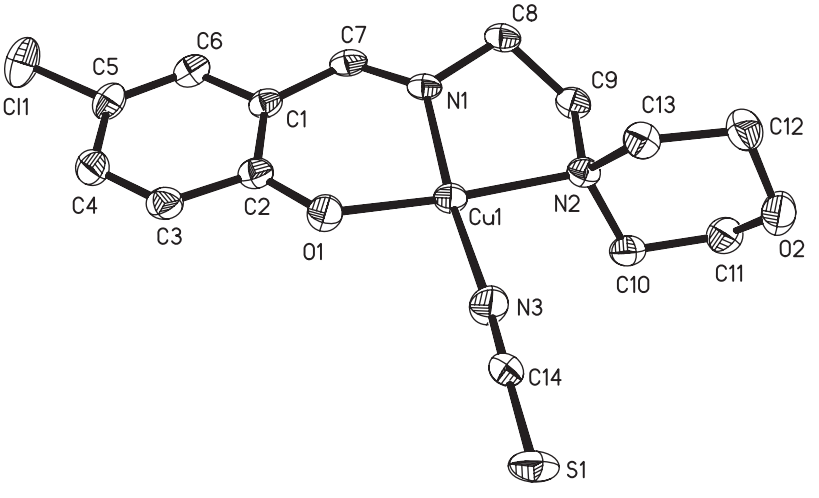


Figure 2. The structure of **2**, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level. Hydrogen atoms have been omitted for clarity.

agreement with the chemical formula proposed for the compounds. Both complexes are stable in air at room temperature and soluble in DMF, DMSO, methanol, ethanol, and acetonitrile.

3.1. *Structure description of (1) and (2)*

Figures 1 and 2 give perspective views of **1** and **2**, respectively. Complex **1** is an azide coordinated mononuclear copper(II) compound, while complex **2** is a thiocyanate coordinated mononuclear copper(II) compound.

In both complexes, each Cu is four-coordinate, square-planar, with one phenolic O, one imine N, one amine N of a Schiff-base ligand, and one N of a terminal-coordinated

ligand (azide for **1** and thiocyanate for **2**). Considering the weakly coordinated $N5^{i}$ and $S1^{ii}$ atoms (table 2) at apical positions, the coordination of each Cu atom may be described as square pyramidal geometry (figures 3 and 4).

As expected, each piperidine ring in **1** or morpholine ring in **2** is in a chair conformation. Azide or thiocyanate is nearly linear and shows bent coordination with the copper [in **1**, N3–N4–N5/Cu1–N3–N4 = 178.1(4)°/123.3(3)°; in **2**, N3–C14–S1/Cu1–N3–C14 = 179.3(3)°/173.0(2)°]. The coordinate bond lengths of **1** and **2** are similar to each other and comparable with the values observed in similar copper(II) complexes [17–19].

In the crystal structure of **1**, molecules are weakly linked through the end-to-end azide ligands, forming chains running along the *b* axis (figure 3). In the crystal structure of **2**, molecules are weakly linked through the thiocyanate ligands, forming chains running along the *a* axis (figure 4).

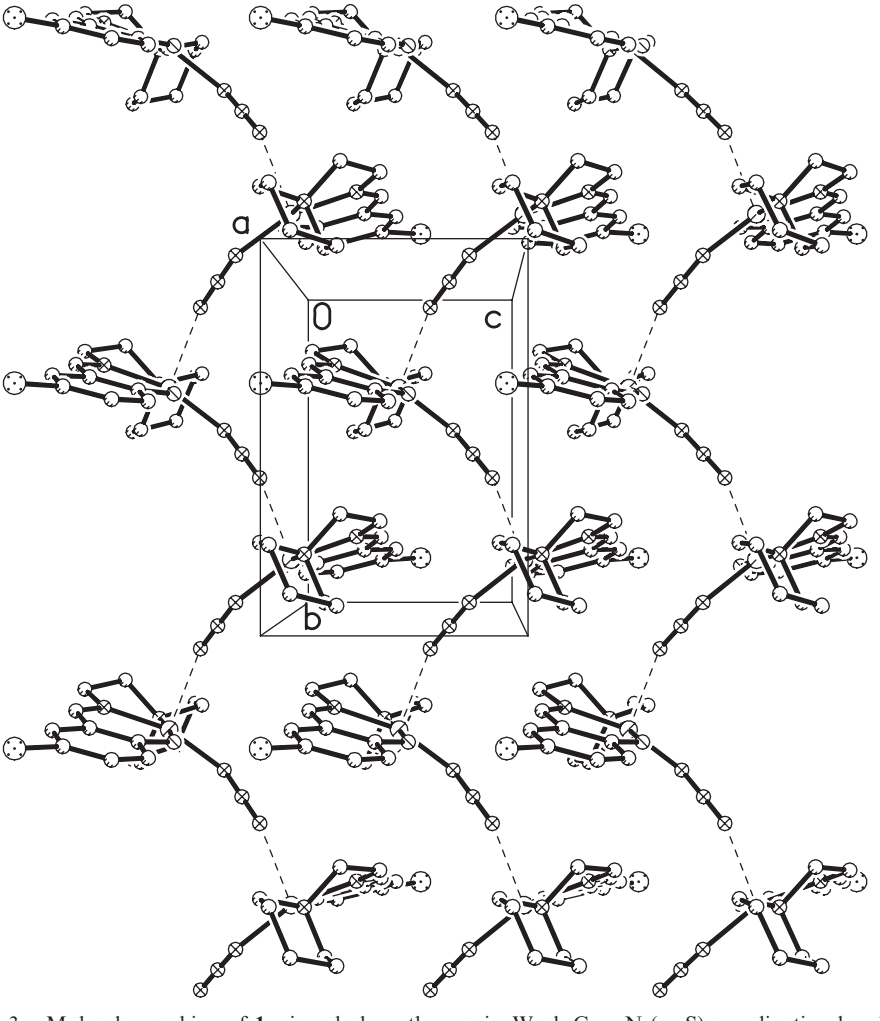


Figure 3. Molecular packing of **1**, viewed along the *a* axis. Weak Cu···N (or S) coordination bonds are shown as dashed lines.

3.2. *IR spectra of (1) and (2)*

The infrared spectra of the Schiff bases and the two complexes provide information about the metal–ligand bonding. The weak and broad absorption bands, observed for the Schiff bases in the 3250–3320 cm^{-1} region, are assigned to stretching of O–H, which are absent in the complexes. The strong absorption bands at 1637 cm^{-1} for HL1 and 1635 cm^{-1} for HL2 are assigned to the azomethine groups, $\nu(C=N)$ [20], which are shifted to lower frequencies in the complexes (1622 cm^{-1} for **1** and 1618 cm^{-1} for **2**). The spectral difference between the Schiff bases and the complexes indicates coordination of the imine N and phenolic O to copper. The strong absorption at 2043 cm^{-1} for **1** is assigned to the terminal coordinated azide and the strong absorption band at 2109 cm^{-1} for **2** is assigned to the vibration of the terminal coordinated thiocyanate ligand. The results of the infrared spectra of the complexes agree with the X-ray analysis.

3.3. *Urease inhibitory properties*

From table 3, both complexes show potent urease inhibition with the IC_{50} values being slightly lower than that of the acetohydroxamic acid coassayed as a standard reference against urease. Both complexes possess stronger urease inhibitory properties than the corresponding Schiff bases, but weaker than that of copper(II) acetate. The results

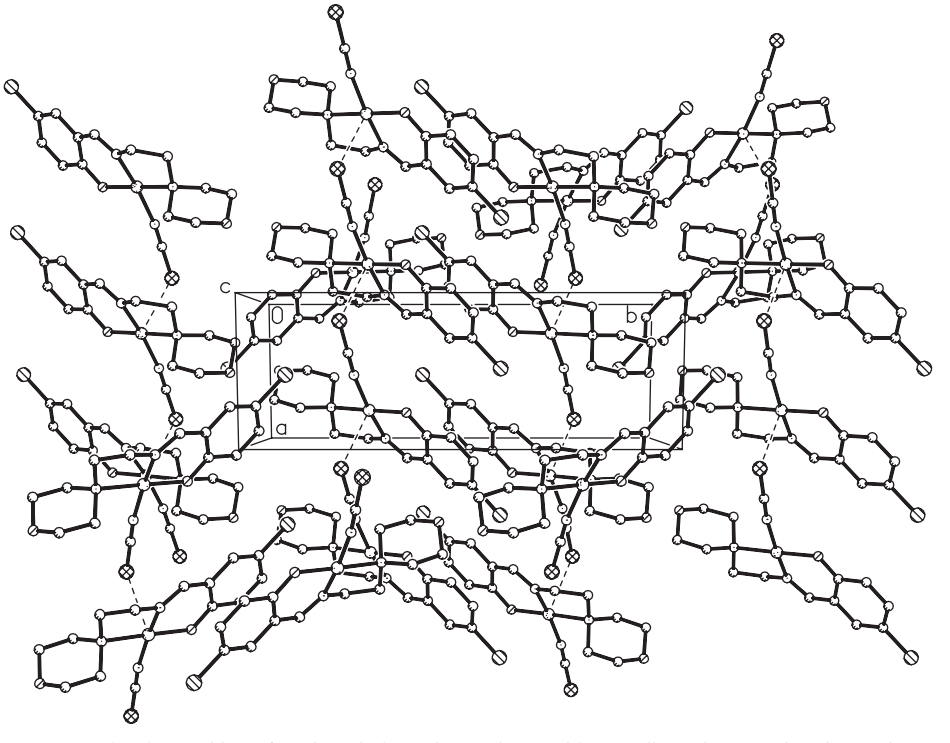


Figure 4. Molecular packing of **2**, viewed along the *c* axis. Weakly coordinated Cu···S bonds are shown as dashed lines.

agree with those reported previously [21], but are much weaker than the IC_{50} value (1.06 μM) of the mononuclear copper(II) complex with 12,24-dihydroxy-1,6-dioxo-2,5,14,17-tetraaza[6*6]metacyclophane-13,17-diene [12].

4. Conclusion

Two Schiff-base copper(II) complexes with azide or thiocyanate co-ligand have been synthesized and their structures were characterized by X-ray crystallography. Both complexes showed urease inhibitory properties.

Acknowledgments

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References

[1] S.R. Collinson, D.E. Fenton. *Coord. Chem. Rev.*, **148**, 19 (1996).
[2] M.E. Hossain, M.N. Alam, J. Begum, M.A. Ali, M. Nazimuddin, F.E. Smith, R.C. Hynes. *Inorg. Chim. Acta*, **249**, 207 (1996).
[3] M.T.H. Tarafder, K.T. Jin, K.A. Crouse, A.M. Ali, B.M. Yamin, H.-K. Fun. *Polyhedron*, **21**, 2547 (2002).
[4] Á. García-Raso, J.J. Fiol, A. López-Zafra, J.A. Castro, A. Cabrero, I. Mata, E. Molins. *Polyhedron*, **22**, 403 (2003).
[5] G.T. Musie, X. Li, D.R. Powell. *Inorg. Chim. Acta*, **348**, 69 (2003).
[6] P.A.N. Reddy, R. Datta, A.R. Chakravarty. *Inorg. Chem. Commun.*, **3**, 322 (2000).
[7] P.J. Arnold, S.C. Davies, M.C. Durrant, D.V. Griffiths, D.L. Hughes, P.C. Sharpe. *Inorg. Chim. Acta*, **348**, 143 (2003).
[8] C.P. Raptopoulou, A.N. Papadopoulos, D.A. Malamatari, E. Ioannidis, G. Moisidis, A. Terzis, D.P. Kessissoglou. *Inorg. Chim. Acta*, **272**, 283 (1998).
[9] M.S. Ray, R.B. Bhattacharya, S. Chaudhuri, L. Righi, G. Bocelli, G. Mukhopadhyay, A. Ghosh. *Polyhedron*, **22**, 617 (2003).
[10] M.J. Todd, R.P. Hausinger. *Biochem.*, **39**, 5389 (2000).
[11] M.A. Pearson, L.O. Michel, R.P. Hausinger, P.A. Karplus. *Biochemistry*, **36**, 8164 (1997).
[12] K. Cheng, Z.-L. You, H.-L. Zhu. *Aust. J. Chem.*, **60**, 375 (2007).
[13] Bruker. *SMART and SAINT*, Bruker AXS Inc., Madison, WI, USA (2002).
[14] G.M. Sheldrick. *SADABS Program for Empirical Absorption Correction of Area Detector*, University of Göttingen, Germany (1996).
[15] G.M. Sheldrick. *SHELXTL V5.1 Software Reference Manual*, Bruker AXS, Inc., Madison, WI, USA (1997).
[16] T. Tanaka, M. Kawase, S. Tani. *Life Sci.*, **73**, 2985 (2003).
[17] C.-Y. Wang. *Acta Crystallogr.*, **E63**, m489 (2007).
[18] M. Zbiri, S. Saha, C. Adhikary, S. Chaudhuri, C. Daul, S. Koner. *Inorg. Chim. Acta*, **359**, 1193 (2006).
[19] A.K. Sah, T. Tanase, M. Mikuriya. *Inorg. Chem.*, **45**, 2083 (2006).
[20] J.E. Kovacic. *Spectrochim. Acta*, **A23**, 183 (1963).
[21] D.-H. Shi, Z.-L. You, C. Xu, Q. Zhang, H.-L. Zhu. *Inorg. Chem. Commun.*, **10**, 404 (2007).