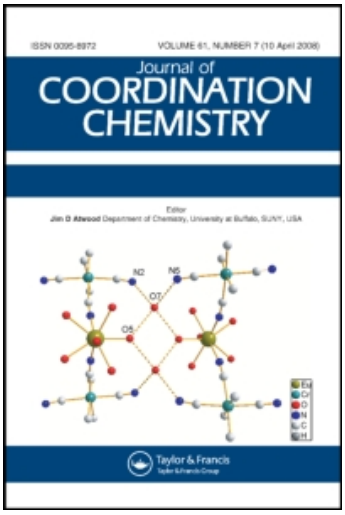


Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455674

Synthesis and antibacterial activities of copper(II) with [(2-hydroxy-3,5-diiodo-benzylidene)-amino]-acetic acid

Suo-Ping Xu[ab]; Lei Shi[b]; Yuan Pei[a]; Ying Yang[b]; Guo Xu[a]; Hai-Liang Zhu[ab]
[a] School of Chemistry and Chemical Engineering, Xuzhou Normal University, Xuzhou 221116, China [b] School of Life Sciences, Nanjing University, Nanjing 210093, China

First published on: 04 September 2010

To cite this Article Xu, Suo-Ping , Shi, Lei , Pei, Yuan , Yang, Ying , Xu, Guo and Zhu, Hai-Liang(2010) 'Synthesis and antibacterial activities of copper(II) with [(2-hydroxy-3,5-diiodo-benzylidene)-amino]-acetic acid', Journal of Coordination Chemistry, 63: 19, 3463 — 3470, First published on: 04 September 2010 (iFirst)
To link to this Article: DOI: 10.1080/00958972.2010.514338
URL: http://dx.doi.org/10.1080/00958972.2010.514338

Journal of Coordination Chemistry
Vol. 63, No. 19, 10 October 2010, 3463–3470

Synthesis and antibacterial activities of copper(II) with [(2-hydroxy-3,5-diiodo-benzylidene)-amino]-acetic acid

SUO-PING XU†‡, LEI SHI‡, YUAN PEI†, YING YANG‡, GUO XU† and HAI-LIANG ZHU*†‡

†School of Chemistry and Chemical Engineering, Xuzhou Normal University, Xuzhou 221116, China
‡School of Life Sciences, Nanjing University, Nanjing 210093, China

(*Received 1 May 2010; in final form 30 June 2010*)

A new tridentate ligand, [(2-hydroxy-3,5-diiodo-benzylidene)-amino]-acetic acid (HDBA), has been synthesized from 3,5-diiodosalicylaldehyde and glycine in ethanol. A 1-D coordination polymer has been synthesized by reaction of HDBA with $Cu(Ac)_2 \cdot H_2O$ in ethanol–water. The complex was characterized by UV, IR, ESI–MS, elemental analyses, and X-ray crystallography. The central copper(II) is five-coordinate by one nitrogen and two oxygens from HDBA, one oxygen from water, and one oxygen from another HDBA. The complex was assayed for antibacterial (*Bacillus subtilis*, *Staphylococcus aureus*, *Streptococcus faecalis*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Enterobacter cloacae*) activities by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide method. Complex **1** showed favorable antimicrobial activity with minimum inhibitory concentrations of 6.25, 6.25, 3.125, 6.25, 6.25, and 3.125 $\mu g\,mL^{-1}$ against *B. subtilis*, *S. aureus*, *S. faecalis*, *P. aeruginosa*, *E. coli*, and *E. cloacae*, respectively.

Keywords: 3,5-Diiodosalicylaldehyde; Glycine; Copper(II) complex; Structure; Antibacterial

1. Introduction

Salicylaldehyde Schiff bases and their metal complexes have a wide range of antibacterial activities [1–10]. There is much interest shown by researchers in the synthesis, characterization, and structure–activity relationships (SAR) of Schiff bases [11–15]. Salicylaldehyde derivatives, with one or more halogens in the aromatic ring, showed antibacterial and antifungal activities [16]. Recently, Chohan *et al*. [17] reported that some metal complexes of amino acid derived Schiff bases showed favorable antibacterial activities. In this article, a new complex of 3,5-diiodosalicylaldehyde with glycine and copper(II) ions has been synthesized. This copper(II) complex was assayed for antibacterial activities against three Gram-positive bacterial strains (*Bacillus subtilis*, *Staphylococcus aureus*, and *Streptococcus faecalis*) and three Gram-negative bacterial strains (*Escherichia coli*, *Pseudomonas aeruginosa*, and *Enterobacter cloacae*)

*Corresponding author. Email: zhuhl@nju.edu.cn

Journal of Coordination Chemistry
ISSN 0095-8972 print/ISSN 1029-0389 online
DOI: 10.1080/00958972.2010.514338

by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl trtrazolium bromide (MTT) method. This study may be useful to gain in-depth understanding of the antimicrobial activity of metal(II) complexes with 3,5-diiodosalicylalidene Schiff bases.

2. Experimental

2.1. *Physical measurement*

The 3,5-diiodosalicylalidene was synthesized from salicylaldehyde, KI, and KIO_3 [18]. The other chemicals (reagent grade) used were commercially available. UV spectra were recorded on a U-3000 Spectrophotometer. IR spectra were recorded on a Nexus 870 FT-IR. ESI–MS spectra were recorded on a Mariner System 5304 Mass spectrometer. Elemental analyses were performed on a CHN-O-Rapid instrument and the results were within ±0.4% of theoretical values. Melting points were measured on a Boetius micromelting point apparatus.

2.2. *Synthesis of [(2-hydroxy-3,5-diiodo-benzylidene)-amino]-acetic acid*

Equimolar quantities (4 mmol) of 3,5-diiodo-salicylaldehyde and glycine were dissolved in ethanol (10 mL) and stirred at room temperature for 2 h to give yellow Schiff base ([(2-hydroxy-3,5-diiodo-benzylidene)-amino]-acetic acid, HDBA). The precipitates were separated by filtration, washed with ethanol three times, and dried in a vacuum desiccator containing anhydrous $CaCl_2$.

HDBA is a yellow thin prism crystal, yield 90%, m.p.: 268°C. UV (λ nm): 385.0; 256.0. Selected IR data (cm^{-1}, KBr): 3355.2(m); 1629.7(s); 1605.1(s); 1480.4(s); 1423.7(s); 1393.5(s); 1310.4(m); 1278.0(m); 1215.0(s); 1134.8(s); 863.8(m); 759.9(m); 656.6(m). ESI–MS: 431.96 ($C_9H_8I_2NO_3^+$, $[M+H]^+$). Anal. Calcd for $C_9H_7I_2NO_3$: C, 25.08%; H, 1.64%; N, 3.25%. Found: C, 25.13%; H, 1.60%; N, 3.27%.

2.3. *Synthesis of 1*

Equimolar quantities (2 mmol) of HDBA and $Cu(Ac)_2 \cdot H_2O$ were dissolved in ethanol (10 mL) and water (5 mL). The mixture was stirred for 3 h at room temperature and then filtered. Upon keeping the filtrate in air for 5 days, green prism crystals of Cu(II) complex, suitable for X-ray crystal determination, formed at the bottom of vessel on slow evaporation of the solvent. The crystals were isolated, washed three times with ethanol, and dried in a vacuum desiccator containing anhydrous $CaCl_2$.

Complex **1** is a green prism crystal, yield 80%, m.p.: >290°C. UV (λ nm): 376.5; 255.0. Selected IR data (cm^{-1}, KBr): 3370.8(m); 1645.2(s); 1585.1(s); 1490.3(s); 1439.7(s); 1385.3(m); 1369.6(s); 1294.9(m); 1146.0(s); 998.4(m); 869.6(m); 752.1(m); 674.8(m). ESI–MS: 511.49 ($C_9H_8I_2NO_4Cu^+$, $[M+H]^+$). Anal. Calcd for $C_9H_7I_2NO_4Cu$: C, 21.16%; H, 1.37%; N, 2.74%. Found: C, 21.10%; H, 1.39%; N, 2.71%.

2.4. *X-ray crystallography*

The crystal structure of **1** was determined using a SMART 1000 CCD diffractometer. A single crystal of **1** with dimensions $0.30 \times 0.18 \times 0.10\,mm^3$ was chosen for X-ray diffraction study. The data were collected with graphite-monochromated Mo-Kα radiation ($\lambda = 071073$ Å) using ω–2θ scan technique. A total of 10,299 reflections were collected and 2129 were independent ($R_{int} = 0.0735$), of which 1749 were observed reflections with $I > 2\sigma(I)$. The structure was solved using direct methods and refined by full-matrix least-squares techniques. All non-hydrogen atoms were assigned anisotropic displacement parameters in the refinement. All hydrogens were added at calculated positions and refined using a riding model. The structures were refined on F^2 using SHELXTL-97. The crystal used for the diffraction study showed no decomposition during data collection. Crystal data and refinement data are listed in table 1. Selected bond lengths and angles are given in table 2.

2.5. *Antibacterial activity*

Antibacterial activity of the synthesized complex was tested against *B. subtilis*, *S. aureus*, *S. faecalis*, *P. aeruginosa*, *E. coli*, and *E. cloacae* using an MTT medium. The minimum inhibitory concentrations (MICs) were determined by a colorimetric method using the MTT dye [19]. A stock solution of the synthesized complex ($50\,\mu g\,mL^{-1}$) in DMSO was prepared and graded quantities of the test complex were incorporated in a specified quantity of sterilized liquid medium. A specified quantity of the medium

Table 1. Crystallographic and experimental data for **1**.

Empirical formula	$C_9H_7I_2NO_4Cu$
Formula weight	510.50
Temperature (K)	298(2)
Crystal system	Orthorhombic
Space group	*Pbca*
Unit cell dimensions (Å, °)	
a	7.1487(12)
b	7.1487(12)
c	22.760(2)
α	90
β	90
γ	90
Volume (Å^3), Z	2446.9(6), 8
Calculated density ($g\,cm^{-3}$)	2.772
μ (mm^{-1})	6.832
$F(0\,0\,0)$	1880
θ range for data collection (°)	1.79–25.01
Maximum and minimum transmission	0.5482 and 0.2337
Data/restraints/parameters	2129/0/158
Index ranges (h, k, l)	$-8 \le h \le 8$; $-17 \le k \le 10$; $-27 \le l \le 27$
Reflections collected/unique	10,299/2129
R_{int}	0.0735
Final R indices [$I > 2\sigma(I)$]	$R^a = 0.0764$, $wR^b = 0.1849$
$(\Delta\rho)_{max}$, $(\Delta\rho)_{min}$ (e Å^{-3})	5.815 and −1.432

[a] $R = \sum||F_o| - |F_c|/\sum|F_o|$.
[b] $wR = [\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]]^{1/2}$.

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

Bond	Distance	Bond	Distance	Bond	Distance
Cu(1)–N(1)	1.926(11)	Cu(1)–O(3)	1.928(9)	Cu(1)–O(1)	1.973(10)
Cu(1)–O(4)	1.982(9)	Cu(1)–O(2)$^{\#1}$	2.288(11)	I(1)–C(6)	2.102(15)
I(2)–C(8)	2.092(14)	N(1)–C(3)	1.233(18)	N(1)–C(2)	1.482(16)
O(1)–C(1)	1.251(17)	O(2)–C(1)	1.248(16)	O(2)–Cu(1)$^{\#2}$	2.288(11)
O(3)–C(5)	1.303(17)				
Angle	(°)	Angle	(°)	Angle	(°)
N(1)–Cu(1)–O(3)	93.1(4)	N(1)–Cu(1)–O(1)	83.3(4)	O(3)–Cu(1)–O(1)	168.8(5)
N(1)–Cu(1)–O(4)	164.5(5)	O(3)–Cu(1)–O(4)	92.1(4)	O(1)–Cu(1)–O(4)	88.7(4)
N(1)–Cu(1)–O(2)$^{\#1}$	103.8(4)	C(3)–N(1)–C(2)	121.1(12)	C(3)–N(1)–Cu(1)	126.8(9)
O(3)–Cu(1)–O(2)$^{\#1}$	90.1(4)	C(2)–N(1)–Cu(1)	111.2(9)	C(1)–O(1)–Cu(1)	116.0(10)
O(1)–Cu(1)–O(2)$^{\#1}$	101.1(5)	C(5)–O(3)–Cu(1)	123.1(8)	O(2)–C(1)–O(1)	125.8(15)
O(4)–Cu(1)–O(2)$^{\#1}$	90.7(4)	O(2)–C(1)–C(2)	117.7(12)	O(1)–C(1)–C(2)	116.3(12)
C(1)–O(2)–Cu(1)$^{\#2}$	127.3(10)	N(1)–C(2)–C(1)	108.4(11)	N(1)–C(3)–C(4)	125.5(12)

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

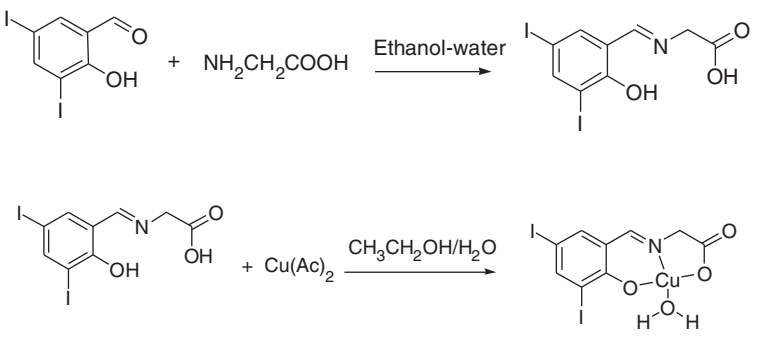
Table 3. MICs of **1**.

	Microorganisms MICs ($\mu g\,mL^{-1}$)					
	Gram-positive			Gram-negative		
Compound	*B. subtilis*	*S. aureus*	*S. faecalis*	*P. aeruginosa*	*E. coli*	*E. cloacae*
1	6.25	6.25	3.125	6.25	6.25	3.125
HDBA	6.25	12.5	6.25	12.5	12.5	6.25
$Cu(Ac)_2 \cdot H_2O$	12.5	25	25	12.5	25	25
Penicillin	1.562	1.562	1.562	6.25	6.25	3.125
Kanamycin	0.39	1.562	3.125	3.125	3.125	1.562

containing the complex 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 complex 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 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 mol L^{-1} HCl was added to extract the dye. After 12 h of incubation at room temperature, the optical density (OD) was measured with a microplate reader at 570 nm. The observed MICs are given in table 3.

3. Results and discussion

The HDBA was synthesized with 3,5-diiodosalicylaldehyde and glycine. The reaction of the Schiff base with $Cu(Ac)_2 \cdot H_2O$ in ethanol–water led to the formation of a new 1-D



Scheme 1. Synthesis of **1**.

coordination polymer (scheme 1). The complex gave satisfactory results for chemical analyses (±0.4%) and UV, IR, and ESI–MS spectra were consistent with the assigned structure.

Complex **1** ($C_9H_7I_2NO_4Cu$) was prepared from HDBA and $Cu(Ac)_2 \cdot H_2O$ in ethanol–water, as described in section 2. Infrared spectra of the complex (KBr pellets) display an intense absorption band at 1645 cm^{-1} attributable to the $\nu_{(C=N)imine}$. This band shifts by 15 cm^{-1} to higher wavenumbers compared to 1630 cm^{-1}, which is attributable to $\nu_{(C=N)imine}$ of HDBA. The 1605 cm^{-1} is attributable to $\nu_{(C=O)carbonyl}$. This band is shifted 20 cm^{-1} to lower wavenumbers compared to 1585 cm^{-1}, which is attributable to $\nu_{(C=O)carbonyl}$ of HDBA. The absorption at 3355 cm^{-1} attributed to $\nu_{(-OH)carbonyl}$ of the ligand disappeared in 1. The absorption at 3371 cm^{-1} is attributed to $\nu_{(-OH)water}$ of 1. UV spectra of the complex display an intense absorption at 255 nm ($\pi \rightarrow \pi^*$) and 376 nm ($n \rightarrow \pi^*$).

The molecular structure of **1** crystallizes in orthorhombic with space group *Pbca*. A perspective view of the crystal structure and packing diagram is shown in figure 1. The Cu(II) adopts a distorted pyramidal geometry coordinated by one nitrogen and two oxygens from HDBA, and one water and one oxygen from another HDBA. The Cu(1)–N(1), Cu(1)–O(3), Cu(1)–O(1), Cu(1)–O(4), and Cu(1)–O(2A) bond lengths are 1.926(1), 1.928(9), 1.973(1), 1.982(9), and 2.288(1) Å, respectively. The dihedral angle between phenyl ring plane A (C4–C9) and plane B (N1/Cu1/O3/C5/C4/C3) is 8.3°. The dihedral angle between B (N1/Cu1/O3/C5/C4/C3) and C (N1/C2/C1/O1/Cu1) planes is 16.3°. Some important torsion angles of **1** are: O(1)–C(1)–C(2)–N(1) = 18°, O(2)–C(1)–C(2)–N(1) = −157.0°, O(3)–Cu(1)–N(1)–C(3) = 18.2°, O(1)–Cu(1)–N(1)–C(3) = −151.1°, O(3)–Cu(1)–O(1)–C(1) = −80°, and O(4)–Cu(1)–O(1)–C(1) = −174.9°. The bond angles of *trans* O(3)–Cu(1)–O(1) and N(1)–Cu(1)–O(4) are 168.8(5) and 164.5(5)°, respectively, while bond angles of *cis* N(1)–Cu(1)–O(3), O(3)–Cu(1)–O(2A), O(1)–Cu(1)–O(2A), and O(4)–Cu(1)–O(2A) are in the range 90.1(4)–101.1(5)°. A 1-D chain structure is formed by the Cu–O coordination bond (figure 2). These chains are stacked to furnish a 3-D supramolecular network (figure 3). There are three intramolecular hydrogen bonds in **1** (table 4).

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

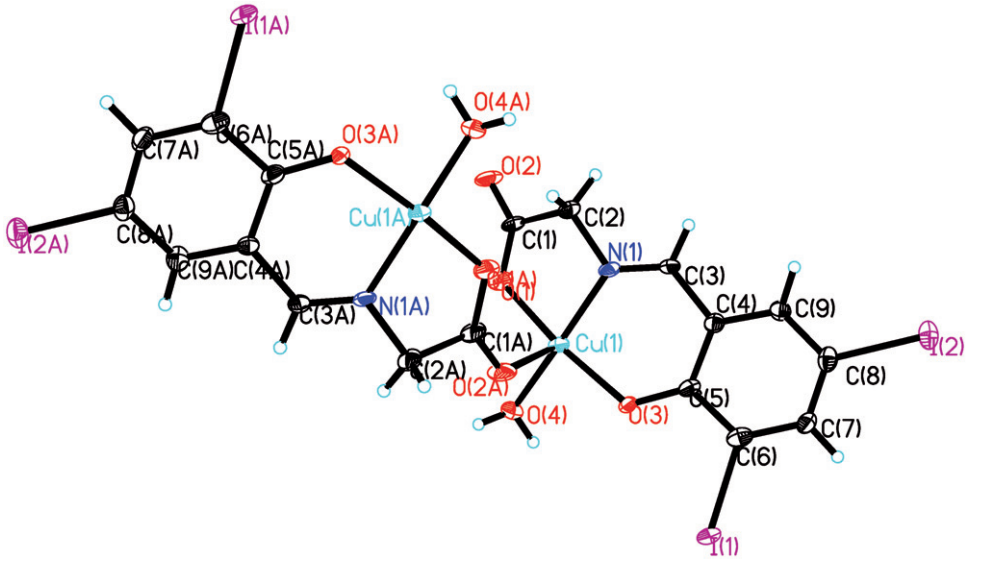


Figure 1. Crystal structure of **1** showing 30% probability displacement ellipsoids (arbitrary spheres for hydrogens).

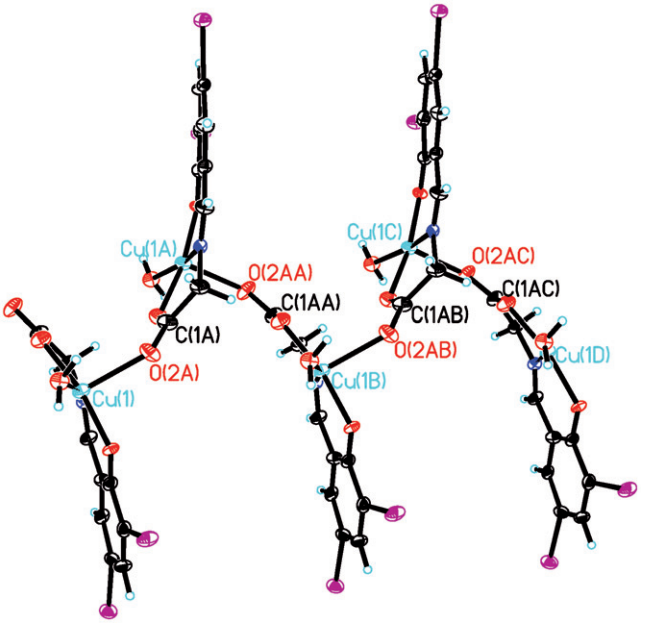


Figure 2. The 1-D chain structure of **1**.

of the complex against the bacteria are shown in table 3. Also included was the activity of reference compounds, penicillin (North China Pharmaceutical Co. Ltd, D0211107, Hebei 050015, China) and kanamycin (Nanjing Zhuyan Biotechnology Co. Ltd, Amresco 060D0504, Nanjing 210002, China). Compared with other copper complexes

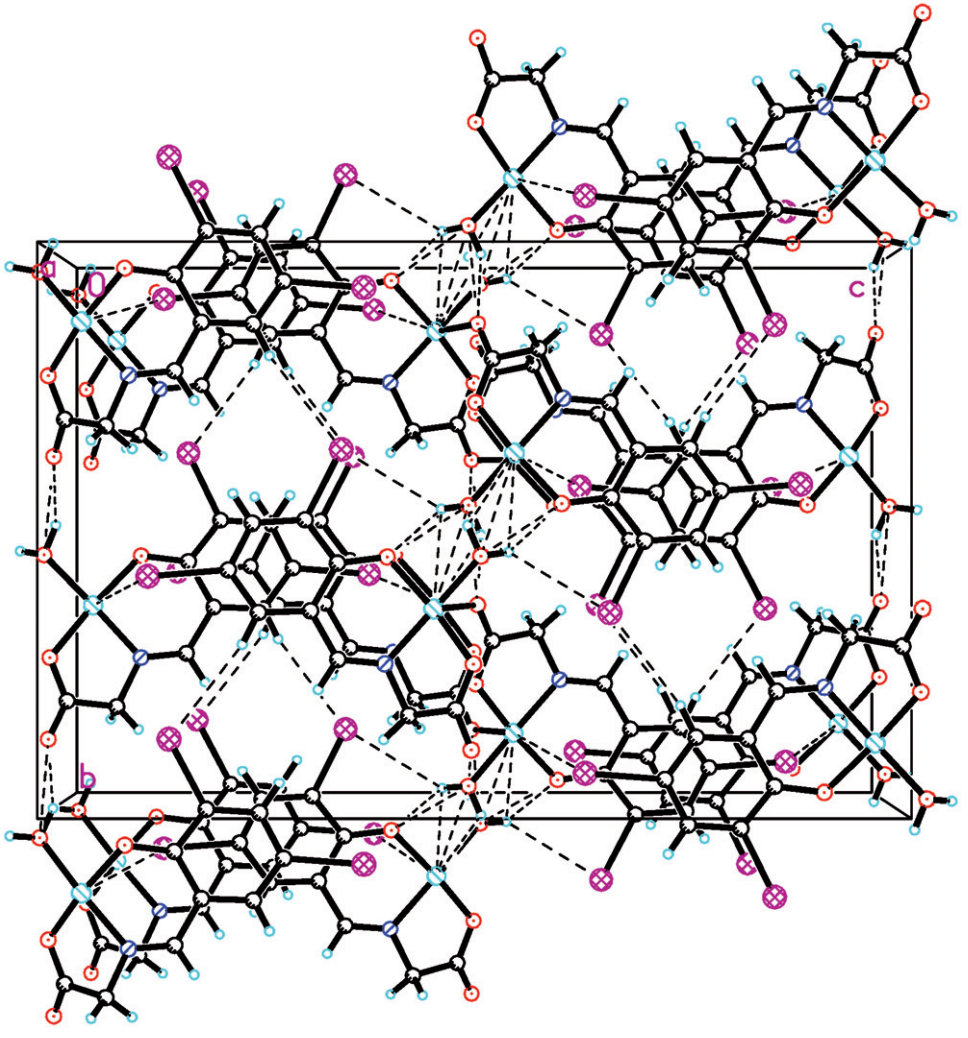


Figure 3. The packing structure of **1** along the *a*-axis.

Table 4. Hydrogen bonds for **1** [(Å) and (°)].

D–H···A	*d*(D–H)	*d*(H···A)	*d*(D···A)	∠(DHA)
O(4)–H(4C)···O(2)	0.85	1.87	2.64(3)	150
O(4)–H(4D)···O(3)	0.85	2.12	2.88(7)	150
C(2)–H(2B)···O(1)	0.97	2.52	3.19(6)	126

recently reported [20–23], **1** showed higher activity against *S. faecalis* and *E. cloacae* (MICs: 3.125 μg mL^{-1}) than against *B. subtilis*, *S. aureus*, *P. aeruginosa*, and *E. coli* (MICs: 6.25 μg mL^{-1}). HDBA showed high antimicrobial activity against *B. subtilis*, *S. faecalis*, *P. aeruginosa*, *E. coli*, and *E. cloacae* (MICs: 6.25–12.5 μg mL^{-1}).

Supplementary material

Crystallographic data for **1** have been deposited with the Cambridge Crystallographic Data Centre (CCDC 779843).

Acknowledgments

This study was co-financed by grants (Projects 30772627) from National Natural Science Foundation of China and (Projects 09KJD150005) from Province Natural Science Foundation of Jiang Su.

References

[1] S.-P. Xu, L. Shi, P.-C. Lv, R.-Q. Fang, H.-L. Zhu. *J. Coord. Chem.*, **62**, 2048 (2009).
[2] S.-P. Xu, P.-C. Lv, L. Shi, X.-L. Li, H.-L. Zhu. *J. Coord. Chem.*, **62**, 3198 (2009).
[3] L. Shi, H.-M. Ge, S.-H. Tan, H.-Q. Li, Y.-C. Song, H.-L. Zhu, R.-X. Tan. *Eur. J. Med. Chem.*, **42**, 558 (2007).
[4] A. Roth, E.T. Spielberg, W. Plass. *Inorg. Chem.*, **46**, 4362 (2007).
[5] L.-M. Wu, H.-B. Teng, X.-C. Feng, X.-B. Ke, Q.-F. Zhu, J.-T. Su, W.-J. Xu, X.-M. Hu. *Cryst. Growth Des.*, **7**, 1337 (2007).
[6] J.D. Ranford, J.J. Vittal, Y.M. Wang. *Inorg. Chem.*, **37**, 1226 (1998).
[7] S.-P. Xu, P.-C. Lv, R.-Q. Fang, L. Shi, H.-L. Zhu. *J. Chem. Cryst.*, **39**, 931 (2009).
[8] M. Chauhan, K. Banerjee, F. Arjmand. *Inorg. Chem.*, **46**, 3072 (2007).
[9] C.T. Yang, B. Moubaraki, K.S. Murray, J.J. Vittal. *Dalton Trans.*, 880 (2003).
[10] O. Yamauchi, A. Odani, M. Takani. *J. Chem. Soc., Dalton Trans.*, **18**, 3411 (2002).
[11] E.F. Elslager, J. Battaglia, A.A. Phillips, L.M. Werbel. *J. Med. Chem.*, **13**, 587 (1970).
[12] S. Ren, R. Wang, K. Komatsu, P.B. Krause, Y. Zyrianov, C.E. McKenna, C. Csipke, Z.A. Tokes, E.J. Lien. *J. Med. Chem.*, **45**, 410 (2002).
[13] P. Prusis, M. Dambrova, V. Andrianov, E. Rozhkov, V. Semenikhina, I. Piskunova, E. Ongwae, T. Lundstedt, I. Kalvinsh, J.E.S. Wikberg. *J. Med. Chem.*, **47**, 3105 (2004).
[14] S. Ren, R. Wang, K. Komatsu, P.B. Krause, Y. Zyrianov, C.E. McKenna, C. Csipke, Z.A. Tokes, E.J. Lien. *J. Med. Chem.*, **45**, 410 (2002).
[15] P.H. Wang, J.G. Keck, E.J. Lien, M.M.C. Lai. *J. Med. Chem.*, **33**, 608 (1990).
[16] L.C. Felton, J.H. Brewer. *Science*, **105**, 409 (1947).
[17] Z.H. Chohan, M. Arif, M. Sarfraz. *Appl. Organomet. Chem.*, **21**, 294 (2007).
[18] S.-P. Xu, G.-Z. Zhu, R.-Q. Fang, X.-L. Li, H.-L. Zhu. *Chin. J. Struct. Chem.*, **28**, 87 (2009).
[19] E.M. Kosower, T. Miyadera. *J. Med. Chem.*, **15**, 307 (1972).
[20] N. Nishat, M. Zulfequar, S.H. Asma. *J. Coord. Chem.*, **63**, 1273 (2010).
[21] N.E.A. El-Gamel. *J. Coord. Chem.*, **63**, 534 (2010).
[22] M. Rajasekar, S. Sreedaran, R. Prabu, V. Narayanan, R. Jegadeesh, N. Raaman, A. Kalilur. *J. Coord. Chem.*, **63**, 136 (2010).
[23] S. Budagumpi, U.N. Shetti, N.V. Kulkarni, V.K. Revankar. *J. Coord. Chem.*, **62**, 3961 (2009).