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Microwave Solid Phase Synthesis, Characterization and Antimicrobial Activities of *Bis*(5-chloro-2-hydroxybenzaldehyde)ethane-1,2-diamine-Zinc(II)

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One mononuclear complex (**1**) has been designed and synthesized by *bis*(5-chloro-2-hydroxybenzaldehyde)ethane-1,2-diamine (**L**) with $Zn(CH_3COO)_2{\cdot}2H_2O$ in microwave radiation assistance. The complex was characterized by X-ray crystallography, confirming that the central zinc(II) was coordinated by two oxygen atoms, two nitrogen atoms from **L**. The complex was assayed for *in vitro* antibacterial (*B. subtilis*, *S. aureus, S. faecalis*, *P. aeruginosa, E. coli* and *E. cloacae*) activities and showed better antimicrobial activity against Gram-positive strains than Gram-negative strains.

Keywords: *Bis*(5-chloro-2-hydroxybenzaldehyde)ethane-1,2-diamine, Mononuclear zinc(II) complex, Antibacterial activity.

INTRODUCTION

Salicylaldehyde type's Schiff base and the metal complexes thereof show a wide spectrum of antimicrobial properties [1-7]. A number of researchers studied the synthesis, characterization and structure-activity relationship (SAR) of Schiff bases [5,8-11]. Although these methods synthesize reliable routes for the preparation of Schiff base type's complexes, most of them follow lengthy procedures and time. Therefore, the development of direct and efficient procedures for these classes of compounds from materials has been the target of synthetic organic chemistry. In this paper, one mononuclear complex (**1**) was synthesized by *bis*(5-chloro-2-hydroxybenzaldehyde)-ethane-1,2-diamine (**L**) with $Zn(CH_3COO)_2{\cdot}2H_2O$ in microwave radiation assistance. The 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*) by the 3-(4,5-dimethyl-2-triazyl)-2,5-diphenyl-2*H*-tetrazolium bromide (MTT) method.

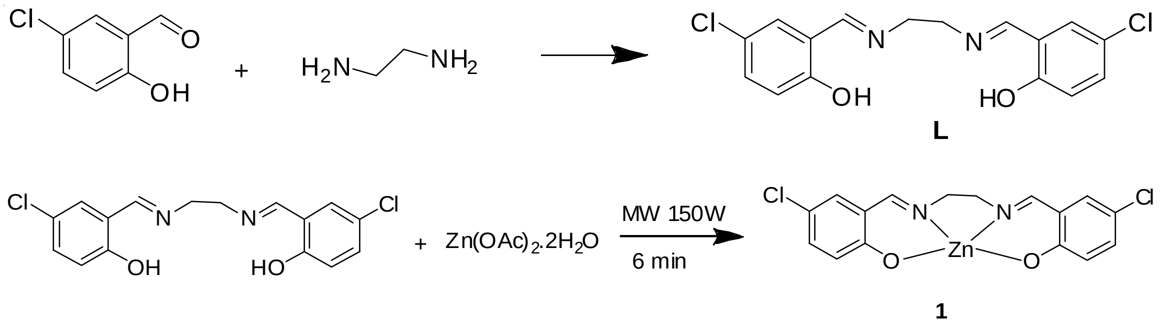
EXPERIMENTAL

All chemicals were of reagent grade and used as received. UV spectra were recorded on a U-3000 spectrophotometer. IR spectra were recorded on a Nexus 870 FT-IR. ^{1}H NMR spectra were recorded on a Bruker DPX 300 model spectrometer (Bruker Bioscience, USA) in $CDCl_3$. Elemental analyses were performed on a CHN-O-Rapid instrument and were within ± 0.4 % of the theoretical values. Melting points were measured a Boetius micro melting point apparatus.

Preparation of 5-chloro-2-hydroxybenzaldehyde and ethane-1,2-diamine in ethanol (L) and its zinc(II) complex (1): Compound **L** was designed and synthesized from 5-chloro-2-hydroxybenzaldehyde and ethane-1,2-diamine in ethanol. The ligand and $Zn(CH_3COO)_2{\cdot}2H_2O$ were mixed together and microwave radiated 6 min in 150 W. The yellow powder was dissolved in ethanol/DMF (1/1) and afforded *bis*(5-chloro-2-hydroxybenzaldehyde)ethane-1,2-diamine-zinc (**1**) (**Scheme-I**).

Preparation of L: A mixture of 5-chloro-2-hydroxybenzaldehyde (20 mmol) and ethane-1,2-diamine (10 mmol) in 20 mL ethanol was refluxed for 1 h. After filtration, the yellow solid was washed with ethanol and water, dried and recrystallized from ethanol. Yield: 76 %, m.p.: 125-128 °C. UV (λ nm): 375; 253. Selected IR data (KBr, ν_{max}, cm^{-1}): 2960(m), 1638(s), 1595(m), 1524(s), 1455(s), 1378(s), 1332(m), 1309(s), 1241(m), 1175(s), 1138(m), 1089(s), 1052(m), 970(s), 834(m), 706(m); ^{1}H NMR ($CDCl_3$) δ ppm: 11.65 (s, 2H), 8.24 (s, 2H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.20 (d, *J* = 5.4 Hz, 2H), 6.82 (m, *J* = 12.6 Hz, 2H), 4.06 (s, 4H). Anal. Calcd. for $C_{16}H_{14}N_2Cl_2O_2$ (%): C, 56.99; H, 4.18; N, 8.31. Found (%): C, 57.06; H, 4.21; N, 8.27.

Complex 1: Compound **L** (10 mmol) and $Zn(CH_3COO)_2{\cdot}2H_2O$ (10 mmol) were mixed together and microwave radiated 6 min in 150 W. The yellow powder was dissolved in ethanol/DMF (1/1). After standing for 7 days, the single crystals of **1** were



Scheme-I: Synthesis of ligand and compound **1**

obtained, separated by filtration, washed with ethanol thrice and dried. Yield: 80 %, m.p.: > 300 °C. UV (λ nm): 386; 253. Selected IR data (KBr, ν_{max}, cm^{-1}): 1618(s), 1596(m), 1524(s), 1455(s), 1378(m), 1309(s), 1241(m), 1175(m), 1139(s), 1089(m), 1052(s), 970(m), 835(m), 792(m), 743(m), 707(s). Anal. calcd. for $C_{16}H_{12}N_2O_2ZnCl_2$ (%): C, 47.98; H, 3.02; N, 6.99. Found (%): C, 47.76; H, 3.05; N, 7.03.

Crystal structure determinations and refinements: The crystallographic date for **1** was collected on a Bruker Smart 1000 CCD area detector diffractometer equipped with MoK_α (λ = 0.71073 Å) radiation using ω-scan mode. Empirical absorption correction was applied to the data. Unit cell dimensions were obtained with least-squares refinements and all structures were solved by direct methods with SHELXL-97. All non-hydrogen atoms were located from the trial structure and then refined anisotropically. All hydrogens were generated in idealized positions. All calculations were performed with SHELXL-97 programs [12]. Other relevant parameters of the crystal structure are listed in Table-1.

TABLE-1
CRYSTALLOGRAPHIC AND EXPERIMENTAL DATA FOR COMPOUND **1**

Empirical formula	$C_{16}H_{12}N_2O_2ZnCl_2$
Formula weight	400.55
Crystal system	Triclinic
Space group	P-1
a (Å)	4.7669(9)
b (Å)	12.690(4)
c (Å)	27.505(5)
α (°)	90.211(11)
β (°)	92.277(6)
γ (°)	90.095(5)
V (Å^3)	1662.5(7)
Z	4
T (K)	296(2)
Density (g/cm^3)	1.600
μ (mm^{-1})	1.807
F(000)	808
Data/restrains/parameters	7683 / 0 / 415
θ range (°)	1.48 to 28.50
Reflections collected/ unique	21608 / 7683
R_{int}	0.0393
Final R indices [I > 2σ(I)]	R_1 =0.0408, wR_2 = 0.1089
$(\Delta\rho)_{max}$, $(\Delta\rho)_{min}$ (e/Å^3)	0.624 and -0.198

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

Antimicrobial activity: The antibacterial activity of **L** and **1** was tested against *B. subtilis*, *S. aureus, S. faecalis*, *P. aeruginosa, E. coli* and *E. cloacae* using MTT medium. The MICs of the test complexes were determined by a colorimetric method using the dye MTT [13]. A stock solution of the synthesized complex (50 µg/mL) in DMSO was prepared and graded quantities of the test complexes were incorporated in specified quantity of sterilized liquid medium. A specified quantity of the medium containing the complex was poured into microtitration plates. Suspension of the microorganism was prepared to contain approximately 10^5 cfu/mL and applied to microtitration plates with serially diluted complexes in DMSO to be tested and incubated at 37 °C for 24 h for bacterial. After the MICs were visually determined on each of the microtitration plates, 50 µL of PBS (phosphate buffered saline 0.01 mol/L, pH 7.4: $Na_2HPO_4\cdot12H_2O$ 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 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 HCl was added to extract the dye. After 12h of incubation at room temperature, the optical density (OD) was measured with a microplate reader at 570 nm. The observed MICs were presented in Table-2.

RESULTS AND DISCUSSION

The complex of the formula $C_{16}H_{12}N_2O_2ZnCl_2$ was prepared in moderate yield (80 %). IR spectra of **L** show four bands in 2960 cm^{-1} and 1638 cm^{-1} region, characteristic of the mixed modes of vibrations arising from normal coordinates having contributions from ν(OH) and ν(C=N) [14]. The infrared spectra of complex **1** (KBr pellets) display an intense absorption band at about 1618 cm^{-1} attributable to the ν(C=N) shifted about 20 cm^{-1} lower wave-number compared with 1638 cm^{-1} of **L**. The UV spectra of the complex display an intense absorption peak at 253 nm ($\pi\rightarrow\pi^*$) and 386 nm ($n\rightarrow\pi^*$). The structure of complex **1** was confirmed by a single-crystal X-ray diffraction and shown in Figs. 1 and 2. The crystal structure consists of mononuclear complex. The molecular structure of complex **1** crystallize in triclinic with space group P-1; bond distances and angles are provided in Table-3. The complex **1** is electronically neutral mononuclear compound. The central metal (Zn), on an inversion center, are in octahedral coordination geometry with oxygen and nitrogen donors from **L**. The general Zn-O and Zn-N bond lengths are in the range 1.963(14)-2.006(13) Å and 2.121(19)-2.123(15) Å, unexceptional and similar to the corresponding bonds in other manganese Schiff base complexes [15].

TABLE-2
MINIMUM INHIBITORY CONCENTRATIONS (MICs) OF THE SYNTHETIC COMPOUNDS

Compound	Microorganisms MICs (μg/mL)					
	Gram-positive			Gram-negative		
	B. subtilis	*S. aureus*	*S. faecalis*	*P. aeruginosa*	*E. coli*	*E. cloacae*
1	3.125	6.25	6.25	6.25	12.5	12.5
L	25	12.5	12.5	25	25	12.5
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

TABLE-3
SELECTED BOND LENGTHS (Å) AND BOND ANGLES (°) OF COMPLEX **1**

Bond	Distance	Bond	Distance	Bond	Distance
Zn(1)-O(1)	2.006(13)	Zn(1)-O(2)	1.963(14)	Zn(1)-N(1)	2.123(15)
Zn(1)-N(2)	2.121(19)	Cl(1)-C(35)	1.67(3)	O(1)-C(19)	1.30(2)
O(2)-C(33)	1.31(2)	N(1)-C(28)	1.25(3)	N(1)-C(9)	1.46(3)
Cl(2)-C(48)	1.75(3)	N(2)-C(37)	1.26(3)	N(2)-C(47)	1.42(2)
Angle	(°)	Angle	(°)	Angle	(°)
O(2)-Zn(1)-O(1)	96.9(5)	O(2)-Zn(1)-N(2)	87.0(6)	O(1)-Zn(1)-N(2)	154.5(6)
O(2)-Zn(1)-N(1)	150.4(7)	O(1)-Zn(1)-N(1)	86.5(7)	N(2)-Zn(1)-N(1)	78.3(7)
C(19)-O(1)-Zn(1)	123.1(12)	C(33)-O(2)-Zn(1)	132.3(11)	C(28)-N(1)-C(9)	122.9(18)
C(9)-N(1)-Zn(1)	114.0(15)	O(1)-C(19)-C(24)	127.3(19)	O(1)-C(19)-C(32)	121.5(18)
C(37)-N(2)-C(47)	124(2)	C(37)-N(2)-Zn(1)	125.1(14)	C(47)-N(2)-Zn(1)	111.1(15)
N(1)-C(28)-C(24)	130.7(19)	O(2)-C(33)-C(22)	124.3(17)	O(2)-C(33)-C(40)	116.6(17)
N(2)-C(37)-C(22)	128(2)	N(2)-C(47)-C(9)	112(2)	C(20)-C(35)-Cl(1)	125(2)
C(45)-C(35)-Cl(1)	119.8(19)	C(39)-C(48)-Cl(2)	125(3)	C(10)-C(48)-Cl(2)	114(2)

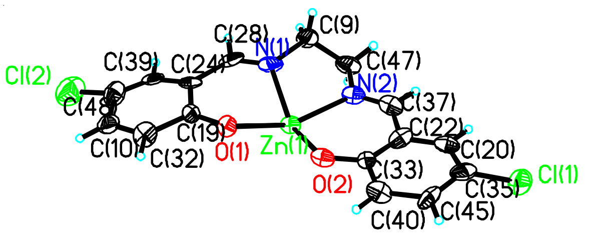


Fig. 1. Crystal structure of complex **1**, showing 30 % probability displacement ellipsoids (arbitrary spheres for the H atoms)

From MIC values (Table-2), the complex was more toxic towards Gram-positive strains than Gram-negative strains when compared to the positive controls penicillin and kanamycin, respectively. The reason may be the difference in the structures of the cell walls. The walls of the Gram-negative cells are more complex than those of Gram-positive cells. Lipopolysaccharides form an outer lipid membrane and contribute to the complex antigenic specificity of Gram-negative cells. Antimicrobial activity of complexes is due to either killing the

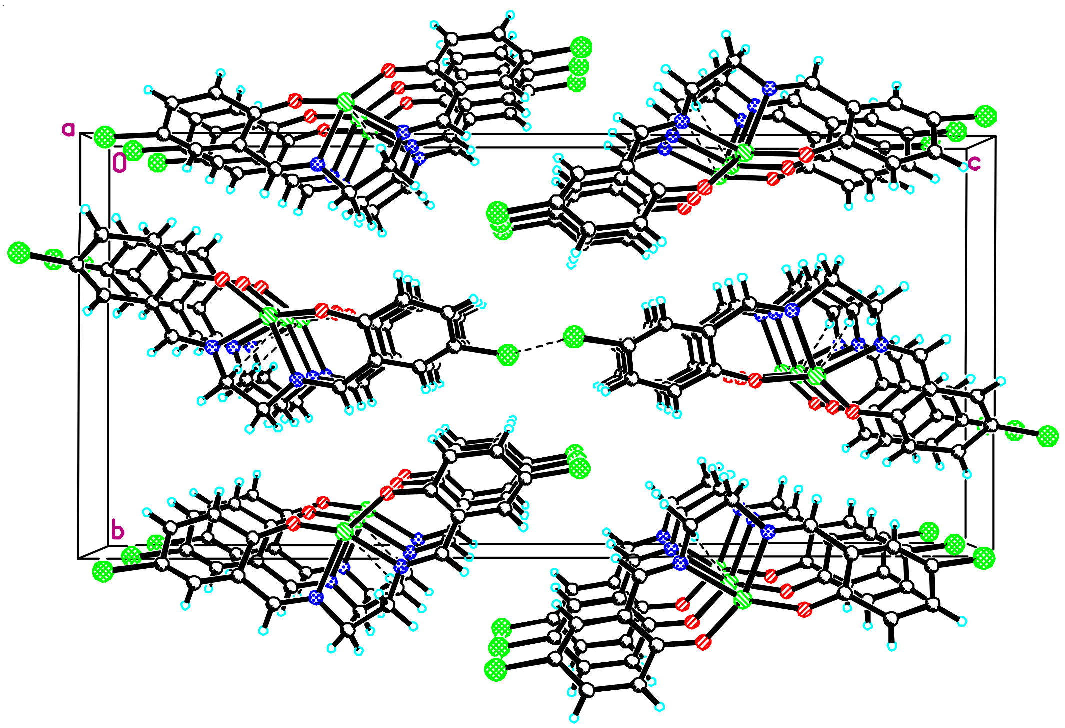


Fig. 2. Packing structure of complex **1**

microbes or inhibiting their multiplication by blocking their active sites [16]. Since the molecular structure is quite similar, the antibacterial activity of **1** is also quite similar.

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REFERENCES

1. S.-P. Xu, L. Shi, P.-C. Lv, R.-Q. Fang and H.-L. Zhu, *J. Coord. Chem.*, **62**, 2048 (2009).
2. L. Shi, H.-M. Ge, S.-H. Tan, H.-Q. Li, Y.-C. Song, H.-L. Zhu and R.-X. Tan, *Eur. J. Med. Chem.*, **42**, 558 (2007).
3. A. Roth, E.T. Spielberg and W. Plass, *Inorg. Chem.*, **46**, 4362 (2007).
4. J.D. Ranford, J.J. Vittal and Y.M. Wang, *Inorg. Chem.*, **37**, 1226 (1998).
5. S.-P. Xu, Y. Pei, G. Xu, W.-X. Su and J.-X. Shu, *J. Xuzhou Norm. Univ. Nat. Sci. Ed.*, **28**, 57 (2010).
6. L.-M. Wu, H.-B. Teng, X.-C. Feng, X.-B. Ke, Q.-F. Zhu, J.-T. Su, W.-J. Xu and X.-M. Hu, *Cryst. Growth Des.*, **7**, 1337 (2007).
7. S.-P. Xu, P.-C. Lv, L. Shi and H.-L. Zhu, *Arch. Pharm. Chem. Life Sci.*, **343**, 282 (2010).
8. P. Prusis, M. Dambrova, V. Andrianov, E. Rozhkov, V. Semenikhina, I. Piskunova, E. Ongwae, T. Lundstedt, I. Kalvinsh and J.E.S. Wikberg, *J. Med. Chem.*, **47**, 3105 (2004).
9. S. Ren, R. Wang, K. Komatsu, P. Bonaz-Krause, Y. Zyrianov, C.E. McKenna, C. Csipke, Z.A. Tokes and E.J. Lien, *J. Med. Chem.*, **45**, 410 (2002).
10. P.H. Wang, J.G. Keck, E.J. Lien and M.M.C. Lai, *J. Med. Chem.*, **33**, 608 (1990).
11. S.-P. Xu, B.-F. Ruan, Q.-Y. Pan and R.-T. Hu, *J. Coord. Chem.*, **64**, 2489 (2011).
12. G.M. Sheldrick, SHELXL V5.1 Software Reference Manual, Bruker AXS, Inc., Madison, WI, USA (1997).
13. J. Meletiadis, J.F. Meis, J.W. Mouton, J.P. Donnelly and P.E. Verweij, *J. Clin. Microbiol.*, **38**, 2949 (2000).
14. K. Nakamato, Infrared Spectra of Inorganic and Coordination Compounds, Wiley, New York (1994).
15. J.-M. Li, J.-Z. Li, H.-Q. Zhang and L.-Y. Xu, *Inorg. Chem. Commun.*, **13**, 573 (2010).
16. M. Nath, S. Pokharia, X. Song, G. Eng, M. Gielen, M. Kemmer, M. Biesemans, R. Willem and D. De Vos, *Appl. Organomet. Chem.*, **17**, 305 (2003).