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Microwave Solid Phase Synthesis, Characterization, and Antimicrobial Activity of 3,5-Diiodo-Salicylalidene-Glycine-Cobalt(II)[1]

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Abstract—One mononuclear complex, $C_9H_7I_2NO_4Co(II)$ (**I**) with 3,5-diiodo-salicylalidene, glycine and $Co(CH_3COO)_2 \cdot 4H_2O$ were microwave solid synthesized. The complex was characterized by X-ray crystallography, UV, IR, ESI-MS, and elemental analyses. In addition, further investigation revealed that the central cobalt(II) atom in complex is five-coordinated by one nitrogen atom and four oxygen atoms. The complex was assayed for antibacterial (*B. subtilis*, *S. aureus*, *S. faecalis*, *P. aeruginosa*, *E. coli*, and *E. cloacae*) activities by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl trtrazolium bromide) method. Complex **I** showed favorable antimicrobial activity with MICs of 3.125, 6.25, 6.25, 6.25, 3.125, and 6.25 μg/mL against *B. subtilis*, *S. aureus*, *S. faecalis*, *P. aeruginosa*, *E. coli*, and *E. cloacae*, respectively.

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INTRODUCTION

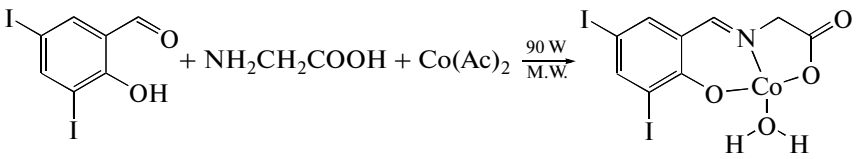
Metal complexes with salicylaldehyde Schiff base ligands posess good antibacterial activity [1–7]. Lots of researchers studied the synthesis, characterization, and structure-activity relationship of Schiff bases [8–10]. It is also reported that salicylaldehyde derivatives, with one or more haloatoms in the aromatic ring, showed variety of biological activities like anti-bacterial and antifungal activities [11, 12]. These investigations lead to the conception that complexes of such Schiff bases would possess potential biological properties. In this paper, one mononuclear complex $C_9H_7I_2NO_4Co(II)$ (**I**) condensated from 3,5-diiodo-salicylaldehyde with glycine and cobalt ion have been designed and synthesized. Complex **I** 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 MTT method. The results of this study may be useful to researchers attempting to gain more understanding of the antimicrobial activity of metal(II) complexes with 3,5-diiodosalicylalidene Schiff bases.

EXPERIMENTAL

Materials and instruments. 3,5-Diiodosalicylalidene was synthesized with salicylaldehyde, KI, and KIO_3 [13]. The other chemicals (reagent grade) used were commercially available. IR spectra were recorded on a Nexus 870 FT-IR. UV spectra were recorded on a U-3000 spectrophotometer. Elemental analyses were performed on a CHN–O-Rapid instrument and were within ±0.4% of the theoretical values. ESI-MS spectra were recorded on a Mariner System 5304 mass spectrometer. Melting points were measured on a Boetius micro melting point apparatus.

Synthesis of complex I. Glycine (0.75 g, 0.01 mol), 3,5-diiodo-salicylalidene (3.74 g, 0.01 mol), and $Co(CH_3COO)_2 \cdot 4H_2O$ (2.49 g, 0.01 mol) were mixed by skived. The mixture was microwave-irradiated (90 W) for 15 min. After filtration, the brown solid was washed with ethanol (20 mL) and water (20 mL), dried, and recrystallized from ethanol–water (1 : 1). The yield was 85%, m.p. >290°C. Synthesis of complex **I** was carried out as it is shown in the following scheme:

[1] The article is published in the original.



(I)

For $C_9H_7NO_4I_2Co$

anal. calcd., %:	C, 21.31;	H, 1.38;	N, 2.76.
Found, %:	C, 21.35;	H, 1.37;	N, 2.72.

UV (λ, nm): 380.0, 256.0. Selected IR data (KBr; ν, cm^{-1}): 3376.4 m, 1647.7 s, 1587.2 s, 1490.8 s, 1439.9 s, 1404.9 m, 1378.1 s, 1291.9 m, 1137.1 s, 1086.2 m, 857.1 m, 739.6 m, 670.4 m. ESI-MS: $C_9H_8I_2NO_4Co^+$, $[M + H]^+$ 506.87.

X-ray structure determinations. The crystal structure of complex **I** was determined using SMART 1000 CCD diffractometer instrument. Single crystal of complex **I** with dimensions 0.43 × 0.35 × 0.28 mm was chosen for X-ray diffraction study. The data were collected with graphite-monochromated MoK_α radiation (λ = 071073 Å) using ω–2θ scan technique. Complex **I** is a green prism crystal. 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 hydrogen atoms were added at calculated positions and refined using a riding model. The structures were refined on F^2 using SHELXTL-97 [14]. The crystal used for the diffraction study showed no decomposition during data collection. The crystal data and refinement data are listed in Table 1. Selected bond lengths and bond angles are given in Table 2. Supplementary material for structure **I** has been deposited with the Cambridge Crystallographic Data Centre (no. 832016; deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

Table 1. Crystallographic data and details of experiment for complex **I**

Parameter	Value
Formula weight	505.89
Crystal system	Orthorhombic
Space group	*Pbca*
a, Å	7.2031(8)
b, Å	15.3073(16)
c, Å	22.5818(2)
V, Å^3	2469.9(4)
Z	8
T, K	298(2)
ρ_{calcd}, g/cm^3	2.699
μ, mm^{-1}	6.338
F(000)	1864
Max and min transmission	0.2699 and 0.1714
Collected reflections	10987
Independent reflectios (R_{int})	2195 (0.0809)
Observed reflections with $I > 2\sigma(I)$	1726
Data/restrains/parameters	2195/0/154
θ Range, deg	2.66–25.02
Index ranges (*h*, *k*, *l*)	$-8 \le h \le 8, -16 \le k \le 18, -20 \le l \le 26$
Reflections collected/unique	10987/2195
R_{int}	0.0809
$R(I > 2\sigma(I))$[a]	0.0456
$wR(I > 2\sigma(I))$[b]	0.1131
$\Delta\rho_{max}/\Delta\rho_{min}$, *e*/Å^3	2.693/–1.366

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

The antibacterial activity of the synthesized complex was tested against *B. subtilis, S. aureus, S. faecalis, P. aeruginosa, E. coli*, and *E. cloacae* using MTT medium. The MICs of the test complex was determined by a colorimetric method using the dye MTT [15]. A stock solution of the synthesized complex (50 μg/mL) in DMSO was prepared and graded quantities of the test complex was incorporated in specified quantity of sterilized liquid medium. A specified quantity of the medium containing complex **I** 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 complex 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, $Na_2HPO_4 \cdot 12H_2O$ 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 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% of M 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 570 nm.

RESULTS AND DISCUSSION

The infrared spectra of complex **I** display an intense absorption band at ~1647.7 cm^{-1} attributable

Table 2. Selected bond lengths (Å) and bond angles (deg) of complex **I***

Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å
Co(1)–O(2)$^{\#1}$	1.999(7)	Co(l)–O(3)	2.000(6)	Co(1)–N(1)	2.016(7)
Co(1)–O(4)	2.082(6)	Co(1)–O(1)	2.148(6)	I(1)–C(6)	2.093(8)
I(2)–C(8)	2.091(9)	N(1)–C(3)	1.266(12)	N(1)–C(2)	1.464(11)
O(1)–C(1)	1.240(10)	O(2)–C(1)	1.272(10)	O(2)–Co(1)$^{\#2}$	1.999(7)
O(3)–C(5)	1.304(11)				
Angle	ω, deg	Angle	ω, deg	Angle	ω, deg
O(2)$^{\#1}$Co(1)O(3)	100.6(3)	O(2)$^{\#1}$Co(1)N(1)	115.8(3)	O(3)Co(1)N(1)	91.5(3)
O(2)$^{\#1}$Co(1)O(4)	95.4(3)	O(3)Co(1)O(4)	91.4(2)	N(1)Co(1)O(4)	147.5(3)
O(2)$^{\#1}$Co(1)O(l)	107.0(3)	O(3)Co(1)O(1)	152.4(3)	N(1)Co(1)O(1)	77.9(3)
O(4)Co(1)O(1)	84.8(2)	C(3)N(1)C(2)	119.2(8)	C(3)N(l)Co(1)	125.9(6)
C(2)N(1)Co(1)	113.5(6)	C(1)O(1)Co(1)	113.8(6)	C(1)O(2)Co(1)$^{\#2}$	124.4(5)
C(5)O(3)Co(1)	127.6(5)	O(1)C(1)O(2)	124.1(9)	O(1)C(1)C(2)	119.7(8)
O(2)C(1)C(2)	116.1(7)	N(1)C(2)C(1)	107.9(7)	N(1)C(3)C(4)	125.1(8)

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

to the $\nu(C{=}N)_{imine}$ stretching vibrations. The ~1605.1 cm^{-1} attributable to the $\nu(C{=}O)_{carbonyl}$ stretching vibrations. The ~3376.4 cm^{-1} attributable to the $\nu(OH)_{water}$ stretching fibrations of complex **I**. The UV spectrum of complex **I** display an intense absorption peak at 256.0 ($\pi \longrightarrow \pi^*$) and 380.0 nm ($n \longrightarrow \pi^*$).

A perspective view of the crystal structure and packing diagram of complex **I** is shown in Fig. 1. As shown in Fig. 1, complex is five-coordinated. The Co(II) center adopts a distorted tetragonal pyramidal geometry coordinated by one nitrogen atom and two oxygen atoms from ligand, one water molecule, and one oxygen atom from other ligand. The Co(1)–N(1), Co(1)–O(3), Co(1)–O(1), Co(1)–O(4), and Co(1)–O(2)$^{\#1}$ ($^{\#1}$ $x - 1/2, -y + 3/2, -z$) bond lengths are 2.016(7), 2.000(6), 2.148(6), 1.082(6), and 1.999(7) Å, respectively. The dihedral angle between the atoms of phenyl ring plane (C(4)–C(9)) and plane (N(1)/C(3)/C(4)/C(5)/O(3)/Co(1)) planes is 4.5°. The dihedral angle between N(1)/Co(1)/O(3)/C(5)/C(4)/C(3)), and (N(1)/C(2)/C(1)/O(1)/Co(1)) planes is 28.6°. As indicated by the torsion angles separately being O(1)–C(1)–C(2)–N(1) 19.3°, O(2)–C(1)–C(2)–N(1) –157.0°, O(3)–Co(1)–N(1)–C(3) 18.2°, O(1)–

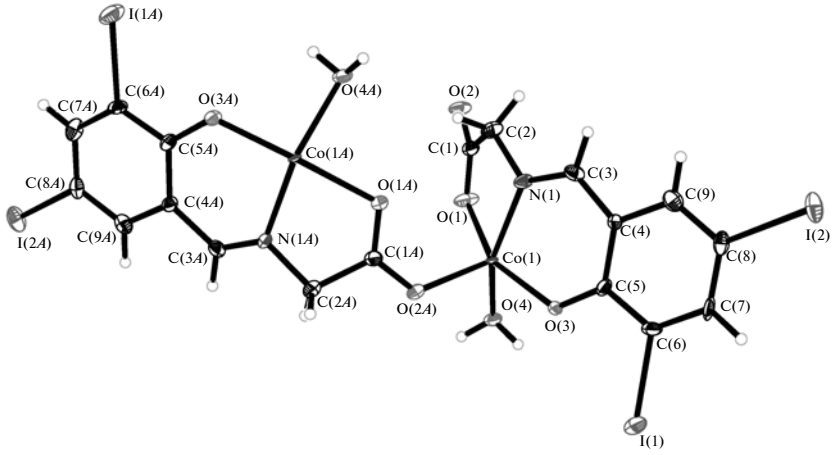


Fig. 1. Crystal structure of complex **I**, showing 30% probability displacement ellipsoids (arbitrary spheres for the H atoms).

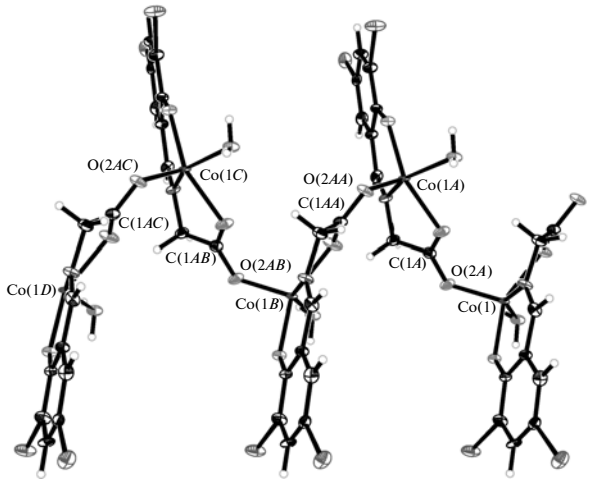


Fig. 2. One-dimensional chain structure of complex **I**.

Co(1)–N(1)–C(3) –159.5°, O(3)–Co(1)–O(1)–C(1) –81.8°, O(4)–Co(1)–O(1)–C(1) –164.9°. One-dimensional chain structure is shown by Co–O coordination bond (Fig. 2). These discrete mononuclear clusters in complex **I** are stacked to furnish a 3D supramolecular network (Fig. 3). There are three intramolecular hydrogen bonds in complex **I** (Table 3).

Structural analysis of the complex may provide some explanation for the structure-activity relation-

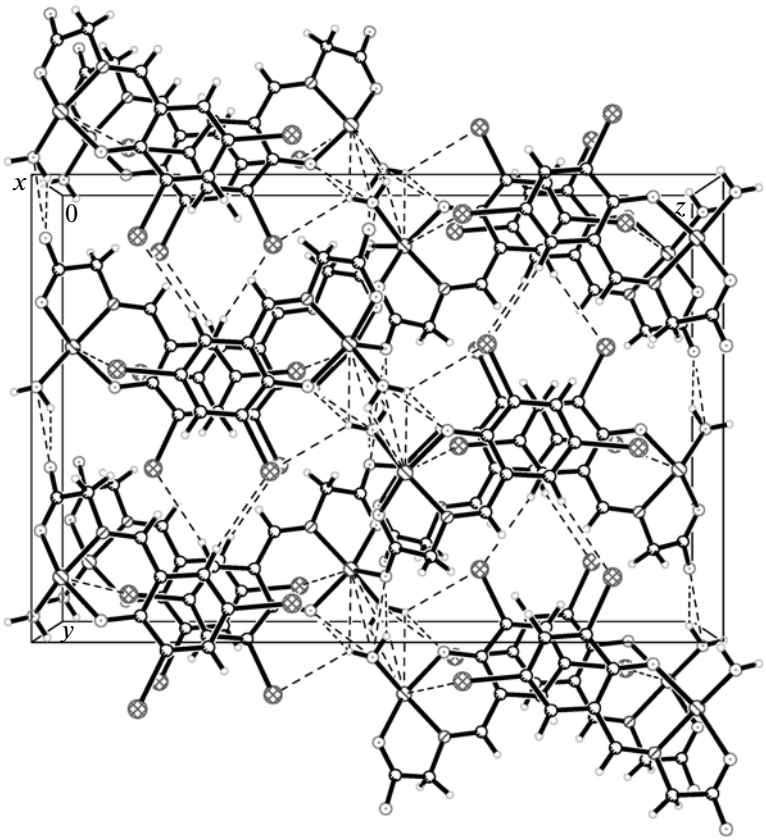


Fig. 3. The packing structure of complex **I** along the *x* axis.

Table 3. Geometric parameters of hydrogen bonds for complex **I***

Contact D–H···A	Distance, Å			Angle DHA, deg
	D–H	H···A	D···A	
O(4)–H(4*A*)···O(2)$^{\#3}$	0.85	2.01	2.75(7)	146
O(4)–H(4*B*)···*I*(1)$^{\#4}$	0.85	3.05	3.71(6)	137
O(4)–H(4*B*)···O(3)$^{\#4}$	0.85	2.14	2.90(6)	149

* Symmetry codes: $^{\#3}$ $3/2 - x, 1/2 + y, z$; $^{\#4}$ $1 - x, 1 - y, z$.

ships. Such an analysis might be helpful in the design of better inhibitors. The biological activity of a particular substance depends on a complex sum of individual properties including complex structure, affinity for the target site, and survival in the medium of application, survival within the biological system, transport properties, and state of the target organism [16]. In this study, we focused our attention on the structure-activity relationships.

The synthesized complex was screened for antibacterial activity against three Gram (+) bacterial strains (*B. subtilis, S. aureus, and S. faecalis*) and three Gram (–) bacterial strains (*E. coli, P. aeruginosa* and *E. cloacae*) by MTT method. The MICs (minimum inhibitory concentrations) of the complex against 6 bacteria were presented in Table 4. 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). Complex **I** showed higher activity against *B. subtilis* and *E. coli* (MICs: 3.125 μg/mL) than against, *S. faecalis, S. aureus, P. aeruginosa*, and *E. cloacae* (MICs: 6.25 μg/mL).

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Table 4. MICs (minimum inhibitory concentrations) of complex **I**

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