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Synthesis, Crystal Structure, and Antibacterial Activity of a Manganese(III) Complex Derived from *N*,*N*'-3,4-Chlorophenylene-Bis(5-Methylsalicylaldimine)[1]

L. Xue, D. N. Deng, Y. Xu, and Q. Wang*

Modern Medical Research Center, Third Affiliated Hospital of Soochow University, Changzhou, 213003 P.R. China

**e-mail: wangqiangszu@126.com*

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Abstract—A new mononuclear manganese(III) complex has been synthesized from the Schiff base compound *N*,*N*'-3,4-chlorophenylene-bis(5-methylsalicylaldimine) and manganese perchlorate in the presence of sodium azide. The complex has been characterized by physico-chemical and spectroscopic methods, as well as single crystal X-ray determination (CIF file CCDC no. 1054335). The Mn atom in the complex is six-coordinate by two nitrogen and two oxygen atoms of the Schiff base ligand, one nitrogen atom of an azide ligand, and one oxygen atom of a methanol ligand. Crystal structure of the complex is stabilized by hydrogen bonds and π···π interactions. The complex and the Schiff base compound 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 complex showed effective antimicrobial activity against the microorganisms tested.

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INTRODUCTION

Schiff bases represent one of the most widely utilized classes of ligands in metal coordination chemistry. They offer versatile and flexible ligands capable of binding various metal ions to give complexes with versatile structures and properties [1–5]. Over the past few decades considerable study has been made on the chemistry of manganese(III) complexes derived from Schiff base ligands due to their important role in catalytic, magnetic and biological properties [6–10]. In addition, manganese plays an important role in metalloenzymes such as catalase [11], superoxide dismutase [12, 13], and photosystem II of green plants [14, 15]. An important aspect of Mn(III) salen type complexes is their antibacterial application [16–18]. We report here the synthesis, characterization including single crystal X-ray structure of a new manganese(III) complex, [Mn(L)(N_3)(MeOH)] · MeOH (**I**), where L is the dianionic form of *N*,*N*'-3,4-chlorophenylene-bis(5-methylsalicylaldimine) (H_2L). 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. The Schiff base compound H_2L was prepared by 2 : 1 condensation of 5-methylsalicylaldehyde and 4-chloro-*o*-phenylenediamine in methanol, according to the literature method [19]. All the 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. Magnetic susceptibility measurement was carried out with a Sherwood Scientific Co., UK magnetic susceptibility balance. Electronic spectra were obtained with Lambda 900 spectrophotometer. Molar conductivity of the complex in acetonitrile was measured with a DDS-11A molar conductivity meter.

Caution! Perchlorate and azide complexes of metal ions are potentially explosive. Only a small amount of material should be prepared, and it should be handled with caution.

Synthesis of complex I. To a stirred suspension of H_2L (0.378 g, 1.00 mmol) and sodium azide (0.130 g, 2.00 mmol) in methanol (20 mL) was added dropwise a methanol solution (10 mL) of manganese(II) perchlorate hexahydrate (0.254 g, 1.00 mmol). After a few minutes a brown precipitate started to deposit. This was dissolved by adding the requisite amount of acetonitrile. After one hour stirring, the solution was filtered and the filtrate was kept for slow evaporation. The diffraction quality deep brown single crystals that deposited over a period of a few days were collected by filtra-

[1] The article is published in the original.

Table 1. Crystallographic data and refinement parameters for complex **I**

Parameter	Value
Molecular weight	537.88
Crystal color; habit	Brown; block
Crystal size, mm	0.18 × 0.18 × 0.13
Crystal system	Monoclinic
Space group	$P2_1/n$
Unit cell dimensions:	
a, Å	17.185(2)
b, Å	7.477(1)
c, Å	19.455(3)
β, deg	101.898(2)
V, Å^3	2446.1(6)
Z	4
ρ_{calcd}, g cm^{-3}	1.461
μ, mm^{-1}	0.690
θ Range collected, deg	2.42–25.50
T_{min} and T_{max}	0.886 and 0.916
Reflections collected/unique	21588/4534
Observed reflections ($I \geq 2\sigma(I)$)	3746
Data/restraints/parameters	4534/2/334
R_1, wR_2 ($I \geq 2\sigma(I)$)	0.0375, 0.0956
R_1, wR_2 (all data)	0.0499, 0.1020
GOOF on F^2	1.066
Largest differences in peak/hole, e/Å^3	0.299/–0.267

tion and washed with methanol. The yield was 435 mg (81%).

For $C_{24}H_{25}N_5O_4ClMn$			
anal. calcd., %:	C, 53.59;	H, 4.68;	N, 13.02.
Found, %:	C, 53.45;	H, 4.77;	N, 13.15.

Crystal structure determination. Intensity data of complex **I** were collected at 298(2) K on a Bruker Apex II CCD diffractometer using graphite-monochromated MoK_α radiation (λ = 0.71073 Å). For data processing and absorption correction the packages SAINT and SADABS [20] were used. The structure was solved by direct and Fourier methods and refined by full-matrix least-squares based on F^2 using SHELXL-97 [21] package. The non-hydrogen atoms were refined anisotropically. The remaining hydrogen atoms have been placed at geometrical positions with fixed thermal parameters. The Cl atom is disordered over two sites and modeled accordingly, with occupancies of 0.89(1) and 0.11(1). Crystallographic data are summarized in Table 1. Selected bond lengths and angles are listed in Table 2.

Supplementary material for structure **I** has been deposited with the Cambridge Crystallographic Data Centre (no. 1054335; deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

Antibacterial activity. Antibacterial activity of the complex 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 complex were determined by a colorimetric method using MTT dye [22]. A stock solution of the complex (50 μg mL^{-1}) in DMSO was prepared and quantities of the complex were incorporated in specified quantity of sterilized liquid medium. A specified quantity of the medium containing the com-

Table 2. Selected bond distances (Å) and angles (deg) for complex **I**

Bond	d, Å	Bond	d, Å
Mn(1)–O(1)	1.8651(15)	Mn(1)–O(2)	1.8766(15)
Mn(1)–N(1)	1.9930(17)	Mn(1)–N(2)	1.9868(17)
Mn(1)–O(3)	2.4548(18)	Mn(1)–N(3)	2.229(2)
Angle	**ω, deg**	**Angle**	**ω, deg**
O(1)Mn(1)O(2)	90.51(7)	O(1)Mn(1)N(2)	172.88(7)
O(2)Mn(1)N(2)	93.40(7)	O(1)Mn(1)N(1)	93.19(7)
O(2)Mn(1)N(1)	173.53(7)	N(2)Mn(1)N(1)	82.39(7)
O(1)Mn(1)N(3)	99.33(8)	O(2)Mn(1)N(3)	96.36(8)
N(2)Mn(1)N(3)	86.15(8)	N(1)Mn(1)N(3)	88.28(7)
O(1)Mn(1)O(3)	90.43(7)	O(2)Mn(1)O(3)	88.47(7)
N(2)Mn(1)O(3)	83.73(7)	N(1)Mn(1)O(3)	86.20(7)
N(3)Mn(1)O(3)	169.04(7)		

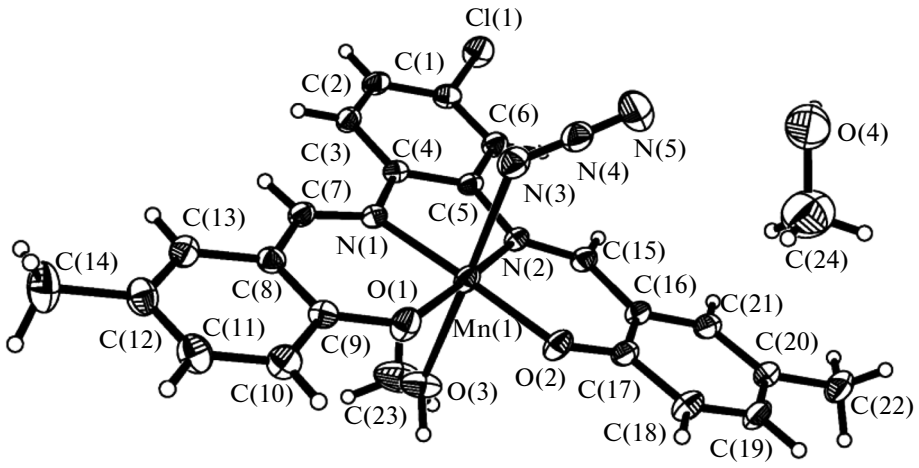

Fig. 1. Molecular structure of complex **I** with 30% thermal ellipsoids.

plex 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 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.

RESULTS AND DISCUSSION

Reaction of manganese(II) perchlorate and H_2L in the presence of sodium azide produces the mononuclear manganese(III) complex **I**. Clearly, aerial oxidation of manganese(II) to manganese(III) and metal assisted deprotonation of the phenolic moieties take place during the formation of the complex. The poor conductivity of the complex (15 Ω^{-1} cm^2 mol^{-1}) indicates that azide ion is coordinated to the metal center and is not dissociated by acetonitrile molecule in solution. The characteristic imine stretching of the complex is observed at 1605 cm^{-1} as a strong signal. Appearance of intense band at 2037 cm^{-1} indicates the presence of azide ligand. The IR spectrum of the complex exhibits one broad and weak absorption centered at 3432 cm^{-1} due to the vibration of the hydroxyl groups of the methanol molecules. UV-Vis spectrum of the complex exhibits two typical bands centered at 415 and 312 nm which can be assigned to phenolate → manganese(III) charge transfer and manganese(III) → imine ($d \rightarrow \pi^*$) metal to ligand charge transfer transitions, respectively. The observed magnetic moment at 300 K of the complex is 4.70 B. M., indicating that the manganese(III) center in the complex exists in high spin state.

The components and crystal structure of the complex are shown in Fig. 1. The asymmetric unit of complex **I** contain a mononuclear [Mn(L)(N_3)(MeOH)] molecule and a methanol molecule of crystallization. The structure shows that the complex having the metal center in the salen-type cavity of L^{2-}. The Mn atom is six-coordinated, with two oxygen and two nitrogen atoms of the Schiff base ligand in the equatoiral plane, and with one azido nitrogen and one methanol oxygen atoms defining the axial positions. The coordination environment of the metal ion is slightly distorted octahedral. The average deviation (0.0053 Å) of the equatorial donor atoms and the displacement (0.0914 Å) of the metal center from the least-squares plane O(1)–O(2)–N(1)–N(2) indicates that the N_2O_2 cavity affords an almost perfect plane to the metal center. In the equatorial plane, the metal–ligand bond distances involving the imine nitrogens (Mn(1)–N(1) 1.993(2), Mn(1)–N(2) 1.987(2) Å) are slightly longer than the bond lengths involving phenolate oxygens (Mn(1)–O(1) 1.865(2), Mn(1)–O(2) 1.877(2) Å). As expected due to Jahn–Teller distortion of high spin manganese(III), the bond distances involving the axial methanol and azide donor atoms (Mn(1)–O(3) 2.455(2), Mn(1)–N(3) 2.229(2) Å) significantly longer than the bond lengths involving the equatorial atoms. The transoid angles (172.88(7)°, 173.53(7)°, and 169.04(7)°) and the cisoid angles (82.39(7)°–99.33(8)°) deviate slightly from the ideal values. The coordinate bond values are comparable to those in manganese(III) complexes with Schiff bases [23–25]. The Schiff base ligand is approximate planar with dihedral angel between the two methyl-substituted benzene rings of 9.6(2)°.

As shown in Fig. 2, methanol molecules are linked to the mononuclear manganese complex molecules via intermolecular O(3)–H(3*A*)···O(2)[i] hydrogen bonds (O(3)–H(3*A*) 0.88(1), H(3*A*)···O(2)[i] 2.35(2), O(3)···O(2)[i] 3.033(2) Å, O(3)–H(3*A*)···O(2)[i] = 135(3)°, symmetry code: [i] $1-x, -1-y, -z$), as well as π···π interactions (Cg(1)···Cg(2)[ii] 4.313(2), Cg(2)···Cg(3)[ii] 3.762(2), Cg(3)···Cg(4)[iii] 4.792(2), Cg(4)···Cg(3)[iii] 4.866(2) Å, symmetry codes: [ii] $-x, -y, 1-z$; [iii] $1/2-x, 1/2+y, 3/2-z$; Cg(1), Cg(2), Cg(3), and Cg(4) are the centroids of Mn(1)–O(1)–C(9)–C(8)–C(7)–N(1), C(1)–C(2)–C(3)–C(4)–C(5)–C(6), C(8)–C(9)–C(10)–C(11)–C(12)–C(13), and C(16)–C(17)–C(18)–C(19)–C(20)–C(21), respectively).

Complex **I** and H_2L were screened 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. The MICs of the complexes against the bacteria are presented in Table 3. Penicillin and kanamycin were tested as reference compounds. The antibacterial activities of the complex are obvious higher than H_2L, except for *St. faecalis*. The free Schiff base is inactive against the Gram-positive bacterial strains while shows weak activities against the Gram-negative bacterial strains. The complex exhibited significant activities against *B. subtilis*, *S. aureus* and *E. coli*, and medium activity against *P. aeruginosa* and *E. cloacae*. Such an enhanced activity of the complex can be explained on the basis of Overtone's concept and Tweedy's chelation theory [26]. 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 complex 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.

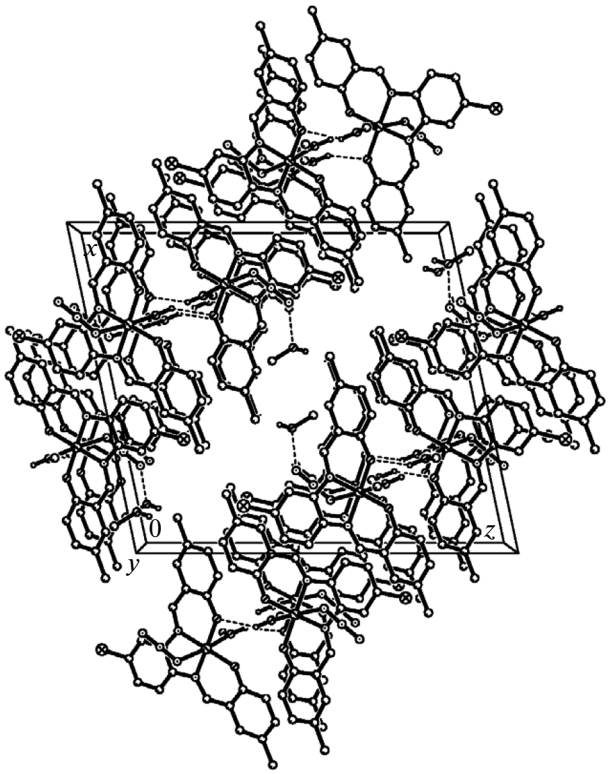

Fig. 2. Molecular packing diagram of complex **I**, viewed along the *y* axis direction. Hydrogen bonds are drawn as dotted lines.

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

Tested material	Gram positive			Gram negative		
	B. subtilis	*S. aureus*	*St. faecalis*	*P. aeruginosa*	*E. coli*	*E. cloacae*
Complex I	3.12	6.25	>50	12.5	6.25	12.5
H_2L	>50	>50	>50	50	25	25
Penicillin	1.56	1.56	1.56	6.25	6.25	3.12
Kanamycin	0.39	1.56	3.12	3.12	3.12	1.56

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REFERENCES

1. Zangrando, E., Islam, M.T., Islam, M.A.A.A., et al., *Inorg. Chim. Acta*, 2015, vol. 427, p. 278.
2. Ghorbani-Choghamarani, A., Ghasemi, B., Safari, Z., et al., *Catal. Commun.*, 2015, vol. 60, p. 70.
3. Davis, K.J., Richardson, C., Beck, J.L., et al., *Dalton Trans.,* 2015, vol. 44, no. 7, p. 3136.
4. Judy-Azar, A.R. and Mohebbi, S., *J. Mol. Catal. A*, 2015, vol. 397, p. 158.
5. Li, H.-H., Zhou, X.-X., and You, Z.-L., *Chin. J. Inorg. Chem.*, 2013, vol. 29, no. 3, p. 649.
6. Sakiyan, I., Ozdemir, R., and Ogutcu, H., *Synth. React. Inorg. Met.-Org. Nano-Met. Chem.*, 2014, vol. 44, no. 3, p. 417.
7. Choubey, S., Roy, S., Bhar, K., et al., *Polyhedron*, 2014, vol. 74, p. 134.
8. Maiti, M., Sadhukhan, D., Thakurta, S., et al., *Polyhedron,* 2014, vol. 75, p. 40.
9. Erdem, O. and Guzel, B., *Inorg. Chim. Acta*, 2014, vol. 418, p. 153.
10. You, Z.-L., Liu, T., Zhang, N., et al., *Inorg. Chem. Commun.,* 2012, no. 19, p. 47.
11. Kar, P., Drew, M.G.B., and Ghosh, A., *Inorg. Chim. Acta,* 2013, vol. 405, p. 349.
12. Grau, M., Rigodanza, F., White, A.J.P., et al., *Chem. Commun.,* 2014, vol. 50, no. 35, p. 4607.
13. Lieb, D., Kenkell, I., Miljkovic, J.L., et al., *Inorg. Chem.,* 2014, vol. 53, no. 2, p. 1009.
14. Liao, R.-Z., Karkas, M.D., Lee, B.-L., et al., *Inorg. Chem.*, 2015, vol. 54, no. 1, p. 342.
15. Hirahara, M., Shoji, A., and Yagi, M., *Eur. J. Inorg. Chem.*, 2014, no. 4, p. 595.
16. Hao, Y.M., *Russ. J. Coord. Chem.*, 2015, vol. 41, no. 1, p. 25.
17. Hassan, K., Mozhdeh, L.-D., Majid, R., et al., *Chin. J. Inorg. Chem.*, 2014, vol. 30, no. 7, p. 1733.
18. Sang, Y.-L., Li, X.-C., and Xiao, W.-M., *J. Coord. Chem.*, 2013, vol. 66, no. 22, p. 4015.
19. Mederos, A., Medina, A., Gili, P., et al., *Anales de Quimica, B*, 1986, vol. 82, no. 3, p. 338.
20. Sheldrick, G.M., *SAINT* (*version 6.02*), *SADABS* (*Version 2.03*), Madison (WI, USA): Bruker AXS Inc., 2002.
21. Sheldrick, G.M., *SHELXL-97, a Program for Crystal Structure Solution*, Göttingen (Germany): Univ. of Göttingen, 1997.
22. Meletiadis, J., Meis, J.F., Mouton, J.W., et al., *J. Clin. Microbiol.*, 2000, vol. 38, no. 8, p. 2949.
23. Yuan, M., Zhao, F., Zhang, W., et al., *Inorg. Chem.*, 2007, vol. 46, no. 26, p. 11235.
24. Zhang, N., Huang, C.-Y., Shi, D.-H., et al., *Inorg. Chem. Commun.*, 2011, vol. 14, no. 10, p. 1636.
25. You, Z.-L., Zhang, M., Xian, D.-M., et al., *Transition Met. Chem.*, 2012, vol. 37, no. 3, p. 279.
26. Raman, N., Kulandaisamy, A., Thangaraja, C., et al., *Transition Met. Chem.*, 2004, vol. 29, no. 2, p. 129.