Synthesis, Crystal Structures, and Antimicrobial Activity of Zinc(II) And Manganese(III) Complexes Derived from *N'*-(1-(pyridin-2-yl)ethylidene)isonicotinohydrazide

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Abstract

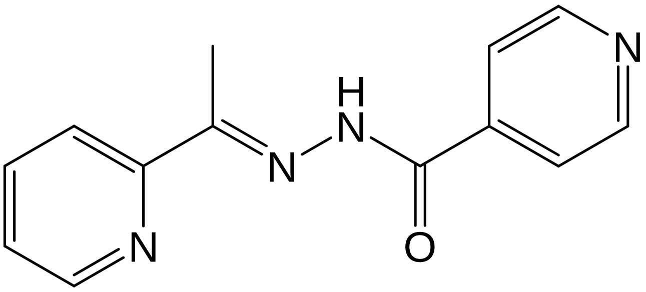
Two mononuclear zinc(II) and manganese(III) compounds, $[ZnL_2]$ (1) and $[MnL_2]\cdot ClO_4$ (2), where L is the monoanionic form of *N'*-(1-(pyridin-2-yl)ethylidene)isonicotinohydrazide (HL), have been prepared and characterized by elemental analyses, IR, UV-Vis, and single crystal X-ray crystallographic determination. The crystal of 1 is orthorhombic: space group *Aba*2 triclinic: space group $P\bar{1}$, a = 12.363(2), b = 20.251(2), c = 9.595(2) Å, V = 2402.2(7) Å^3, Z = 4. The crystal of 2 is monoclinic: space group $P2_1/n$, a = 11.755(2), b = 9.437(2), c = 26.198(2) Å, β = 98.197(2)°, V = 2876.5(8) Å^3, Z = 4. Compound 1 contains a neutral $[ZnL_2]$ complex molecule. Compound 2 contains a $[MnL_2]^+$ complex cation and one perchlorate anion. The metal atoms in the complexes are in octahedral coordination, with the hydrazone ligands coordinate to the metal atoms through the pyridine N, imine N, and enolate O atoms. The effect of the compounds on the antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* was studied.

Keywords: Hydrazone, Zinc complex, Manganese complex, Crystal structure, Antimicrobial activity

1. Introduction

Schiff bases bearing characteristic C=N bonds are a kind of versatile ligands in coordination chemistry.[1] In recent years, metal complexes of Schiff bases have attracted considerable attention due to their interesting biological activity, such as antifungal, antibacterial and antitumor.[2] Schiff base complexes derived from salicylaldehyde and its derivatives with primary amines, bearing the N_2O, N_2S, NO_2 or NSO donor sets, have particular biological activities.[3] Hydrazone is a kind of special Schiff base compound, which possess interesting biological activities.[4] In the present work, a new zinc(II) compound, $[ZnL_2]$ (1), and a new manganese(III) compound, $[MnL_2]\cdot ClO_4$

(2), where L is the monoanionic form of *N'*-(1-(pyridin-2-yl)ethylidene)isonicotinohydrazide (HL), are reported.



2. Experimental

2.1. Material and Methods

2-Acetylpyridine and pyridine-4-carbohydrazide were purchased from Fluka. Other reagents and solvents were analytical grade and used without further purification. Elemental (C, H, and N) analyses were made on a Perkin-Elmer Model 240B automatic analyser. Copper analyses were carried out by EDTA titration. Infrared (IR) spectra were recorded on an IR-408 Shimadzu 568 spectrophotometer. UV-Vis spectra were recorded on a Lambda 35 spectrometer. X-ray diffraction was carried out on a Bruker SMART 1000 CCD area diffractometer.

Caution! Perchlorate salts are potentially explosive. Only a small amount of material should be prepared, and they should be handled with great care.

2.2. Synthesis of HL

The hydrazone compound was prepared by the condensation of equimolar quantities of 2-acetylpyridine (0.121 g, 1.0 mmol) with pyridine-4-carbohydrazide (0.137 g, 1.0 mmol) in methanol (30 mL) at ambient temperature for 1 h. Then the methanol was evaporated by distillation, yielding yellow solid of HL. The solid was recrystallized from methanol to give crystalline product. IR data (KBr, cm^{-1}): 3190 (NH), 1663 (C=O), 1637 (C=N). UV-vis data in methanol [λ_{max} (nm), ε ($L\cdot mol^{-1}\cdot cm^{-1}$)]: 265, 10120; 345, 18270. Anal. Calcd. (%) for $C_{13}H_{12}N_4O$: C, 64.99; H, 5.03; N, 23.32. Found (%): C, 65.17; H, 4.91; N, 23.18.

2.3. Synthesis of compound 1

The hydrazone (48.0 mg, 0.2 mmol) was dissolved by methanol (10 mL), to which was added with stirring a methanol solution (10 mL) of $Zn(ClO_4)\cdot 6H_2O$ (37.2 mg, 0.1 mmol). The mixture was stirred for 1 h at ambient temperature to give a colorless solution. Colorless block-shaped single crystals suitable for X-ray diffraction were formed by slow evaporation of the solution in air for several days. The yield is 45% (based on Zn). IR data (KBr, cm^{-1}): 1595 (C=N). UV-vis data in methanol [λ_{max} (nm), ε ($L\cdot mol^{-1}\cdot cm^{-1}$)]: 277, 6450; 362, 15510. Anal. Calcd. (%) for $C_{26}H_{22}N_8O_2Zn$: C, 57.42; H, 4.08; N, 20.60. Found (%): C, 57.61; H, 4.17; N, 20.45.

2.4. Synthesis of compound 2

The hydrazone (48.0 mg, 0.2 mmol) was dissolved by methanol (10 mL), to which was added with stirring a methanol solution (10 mL) of $Mn(ClO_4)_2 \cdot 6H_2O$ (36.2 mg, 0.1 mmol). The mixture was stirred for 1 h at ambient temperature to give a brown solution. Brown block-shaped single crystals suitable for X-ray diffraction were formed by slow evaporation of the solution in air for several days. The yield is 33% (based on Mn). IR data (KBr, cm^{-1}): 1596 (C=N), 1079 (ClO_4). UV-vis data in methanol [λ_{max} (nm), ε ($L \cdot mol^{-1} \cdot cm^{-1}$)]: 271, 7270; 366, 16480. Anal. Calcd. (%) for $C_{26}H_{22}ClMnN_8O_6$: C, 49.34; H, 3.50; N, 17.70. Found (%): C, 49.16; H, 3.62; N, 17.83.

2.5. X-ray structure determination

Data were collected from selected crystals mounted on glass fibres. The data for the two complexes were processed with SAINT[5] and corrected for absorption using SADABS.[6] Multi-scan absorption corrections were applied with ψ-scans.[7] The structures were solved by direct methods using the program SHELXS-97 and were refined by full-matrix least-squares techniques on F^2 using anisotropic displacement parameters.[8] All hydrogen atoms were placed at the calculated positions. Idealized H atoms were refined with isotropic displacement parameters set to 1.2 (1.5 for methyl groups) times the equivalent isotropic *U* values of the parent atoms. The crystallographic data for the complexes are listed in Table 1, selected bond lengths and bond angles for compounds 1 and 2 are given in Table 2.

Table 1. Crystallographic data and refinement parameters for complexes 1 and 2

Parameters	1	2
Habit, color	Block, colorless	Block, brown
Molecular formula	$C_{26}H_{22}N_8O_2Zn$	$C_{26}H_{22}ClMnN_8O_6$
Formula weight	543.89	632.91
Temperature, K	298(2)	298(2)
Crystal size, mm	0.31 × 0.27 × 0.26	0.27 × 0.27 × 0.23
Radiation (λ, Å)	MoK_α (0.71073)	MoK_α (0.71073)
Crystal system	Orthorhombic	Monoclinic
Space group	*Aba*2	$P2_1/n$
Unit cell dimensions:		
a, Å	12.363(2)	11.755(2)
b, Å	20.251(2)	9.437(2)
c, Å	9.595(2)	26.198(2)
α, °	90	90
β, °	90	98.197(2)
γ, °	90	90

V, Å^3	2402.2(7)	2876.5(8)
Z	4	4
ρ_{calcd}, g cm^{-3}	1.504	1.461
F(000)	1120	1296
Absorption coefficient, mm^{-1}	1.065	0.607
θ Range for data collection, deg	2.01–25.49	1.57–25.50
Index ranges, h, k, l	$-14 \le h \le 14$; $-24 \le k \le 24$; $-11 \le l \le 6$	$-14 \le h \le 14$; $-8 \le k \le 11$; $-31 \le l \le 31$
Reflections collected	6959	16410
Independent reflections	1732	5322
Data/parameters	1353/169	3869/381
Restraints	1	0
Final R indices ($I > 2\sigma(I)$)	$R_1 = 0.0333$, $wR_2 = 0.0634$	$R_1 = 0.0880$, $wR_2 = 0.2438$
R indices (all data)	$R_1 = 0.0538$, $wR_2 = 0.0718$	$R_1 = 0.1133$, $wR_2 = 0.2619$
Goodness-of-fit on F^2	1.020	1.062

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

1			
Zn(1)–N(3)	2.069(3)	Zn(1)–O(1)	2.149(3)
Zn(1)–N(4)	2.193(4)		
N(3)–Zn(1)–N(3A)	173.3(3)	N(3)–Zn(1)–O(1)A	101.34(13)
N(3)–Zn(1)–O(1)	74.22(13)	O(1)–Zn(1)–O(1)A	100.30(17)
N(3)–Zn(1)–N(4)	75.14(14)	N(3)–Zn(1)–N(4A)	109.70(15)
O(1)–Zn(1)–N(4A)	91.47(13)	O(1)–Zn(1)–N(4)	148.77(11)
N(4)–Zn(1)–N(4A)	93.19(19)		
2			
Mn(1)–O(1)	2.144(4)	Mn(1)–O(2)	2.151(4)
Mn(1)–N(7)	2.191(4)	Mn(1)–N(3)	2.194(4)
Mn(1)–N(4)	2.313(5)	Mn(1)–N(8)	2.325(4)
O(1)–Mn(1)–O(2)	107.36(16)	O(1)–Mn(1)–N(7)	122.03(15)
O(2)–Mn(1)–N(7)	72.28(15)	O(1)–Mn(1)–N(3)	71.99(14)
O(2)–Mn(1)–N(3)	125.52(15)	N(7)–Mn(1)–N(3)	155.58(17)

O(1)–Mn(1)–N(4)	141.99(14)	O(2)–Mn(1)–N(4)	90.09(16)
N(7)–Mn(1)–N(4)	95.17(16)	N(3)–Mn(1)–N(4)	70.42(15)
O(1)–Mn(1)–N(8)	90.69(15)	O(2)–Mn(1)–N(8)	142.59(14)
N(7)–Mn(1)–N(8)	70.38(15)	N(3)–Mn(1)–N(8)	90.87(15)
N(4)–Mn(1)–N(8)	95.31(16)		

Symmetry code for A: $-x, -y, z$.

3. Results and Discussion

3.1. Chemistry

The hydrazone compound HL was prepared by the condensation of equimolar quantities of 2-acetylpyridine with pyridine-4-carbohydrazide in methanol at ambient temperature. The hydrazone compound prepared in this way was formed in nearly quantitative yield and is of high purity. The compounds 1 and 2 were readily synthesized by reaction of the hydrazone compound HL with zinc perchlorate and manganese perchlorate in methanol at ambient temperature. All the compounds are very stable at room temperature in the solid state, and soluble in common organic solvents, such as methanol, ethanol, and acetonitrile. The results of the elemental analyses are in accord with the composition suggested for the hydrazone and the complexes.

3.2. IR and UV-Vis Spectra

For the IR spectra of HL, the strong band observed at 1663 cm^{-1} is assigned to the carbonyl group. The typical band indicative of the azomethine group in HL was observed at 1637 cm^{-1}, while in the complexes, it was observed at 1595 cm^{-1} for compound 1 and 1596 cm^{-1} for compound 2. The strong absorption at 1079 cm^{-1} in the spectrum of compound 2 is assigned to the stretching vibration of the perchlorate anion. The weak and sharp absorption at 3190 cm^{-1} for HL can be attributed to the vibration of N–H group. UV–visible spectra of HL and the complexes were carried out in methanol. In the hydrazone, the band at 345 nm is attributed to the azomethine chromophore π-π* transition. The band at higher energy (265 nm) is associated with the benzene π-π* transition. In the spectra of the complexes, however, the azomethine chromophore π-π* transition is shifted to 362-366 nm, indicating that the imino nitrogen is involved in coordination to the metal ion. The absorption frequencies ascribed to the benzene π-π* transition (271-277 nm) are slightly changed.

3.3. Structure Description of Compound 1

The molecular structure of compound 1 is shown in Fig. 1. Selected bond distances and angles are listed in Table 2. The Zn atom is coordinated by two pyridine N, two imine N, and two enolate O atoms from two deprotonated form of hydrazone ligands, forming an octahedral geometry. The hydrazone acts as a tridentate ligand, forming two five-membered chelate rings with the Zn atom. The bond distances subtended at the Zn atom are comparable to those observed in the similar zinc(II) complexes with Schiff bases.[9] The *cis* and *trans* coordinate bond angles are range from 74.22(13) to 109.70(15)º and from 148.77(11) to 173.3(3)º, respectively, indicating the distortion of the octahedral coordination from ideal geometry. In the crystal structure of the compound, the complex molecules are linked through hydrogen bonds (Table 3), to form a three-dimensional network (Fig. 2).

Table 3 Distances (Å) and angles (º) involving hydrogen bonding of the complexes

D–H···*A*	d(*D*–H)	d(H··*A*)	d(*D*···*A*)	Angle(*D*–H···*A*)
1				
C(9)–H(9)···O(1)$^{\#1}$	0.93	2.36(5)	3.180(5)	148(6)
C(10)–H(10)···N(1)$^{\#2}$	0.93	2.54(5)	3.455(5)	170(6)
C(13)–H(13A)···N(2)	0.96	2.43(5)	2.811(5)	103(6)
2				
C(10)–H(10)···O(5)$^{\#3}$	0.93	2.39(3)	3.284(4)	161(7)
C(13)–H(13C)···N(2)	0.96	2.40(3)	2.778(4)	103(5)
C(23)–H(23)···O(6)$^{\#4}$	0.93	2.48(4)	3.258(5)	142(6)
C(26)–H(26A)···N(6)	0.96	2.37(3)	2.788(4)	106(5)

Symmetry codes: #1: 1/2 + *x*, – *y*, –1/2 + *z*; #2: 1/2 – *x*, –1/2 + *y*, –1 + *z*; #3: 1/2 – *x*, 1/2 + *y*, 1/2 – *z*; #4: – *x*, 1 – *y*, – *z*.

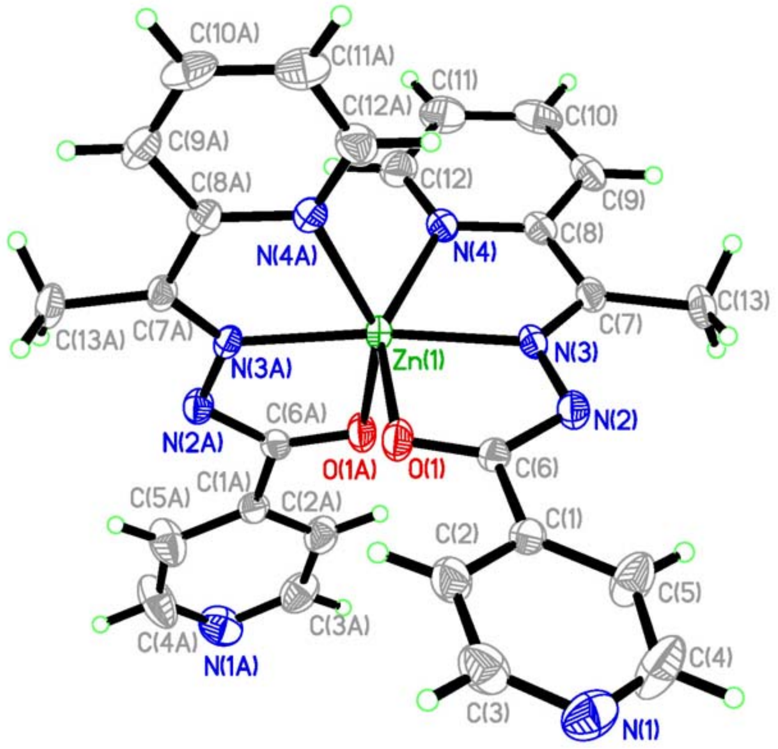


Fig. 1. Perspective view of complex 1 with 30% probability thermal ellipsoids. Atoms labeled with the suffix A are related to the symmetry operation $-x, -y, z$.

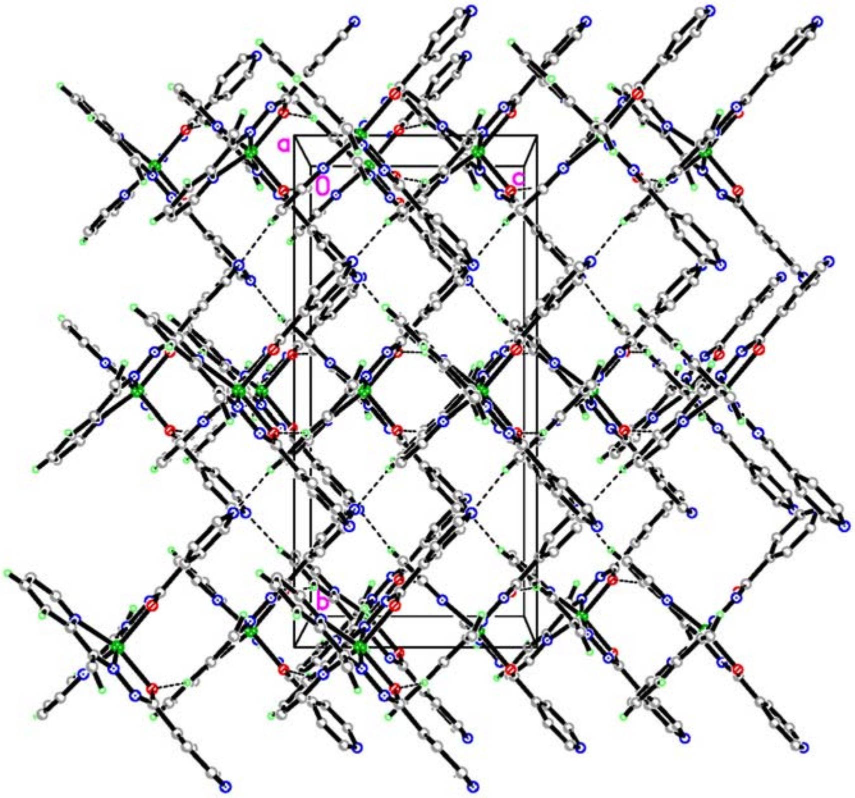


Fig. 2. Molecular packing structure of complex 1, with hydrogen bonds drawn as dashed lines.

3.4. Structure Description of Compound 2

The molecular structure of compound 2 is shown in Fig. 3. Selected bond distances and angles are listed in Table 2. The compound contains a $[MnL_2]^+$ complex cation and a perchlorate anion. The Mn atom in the $[MnL_2]^+$ complex cation is coordinated by two pyridine N, two imine N, and two enolate O atoms from two deprotonated form of hydrazone ligands, forming an octahedral geometry. The hydrazone acts as a tridentate ligand, forming two five-membered chelate rings with the Mn atom. The bond distances subtended at the Mn atom are comparable to those observed in the similar manganese(III) complexes with Schiff bases.[10] The *cis* and *trans* coordinate bond angles are range from 70.38(15) to 125.52(15)° and from 141.99(14) to 155.58(17)°, respectively, indicating the distortion of the octahedral coordination from ideal geometry. In the crystal structure of the compound, the $[MnL_2]^+$ complex cations and the perchlorate anions are linked through hydrogen bonds (Table 3), to form a three-dimensional network (Fig. 4).

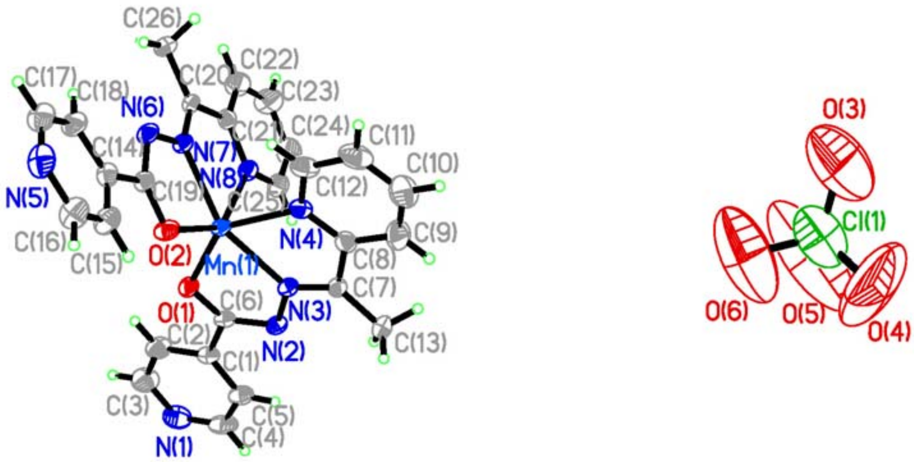


Fig. 3. Perspective view of complex 2 with 30% probability thermal ellipsoids.

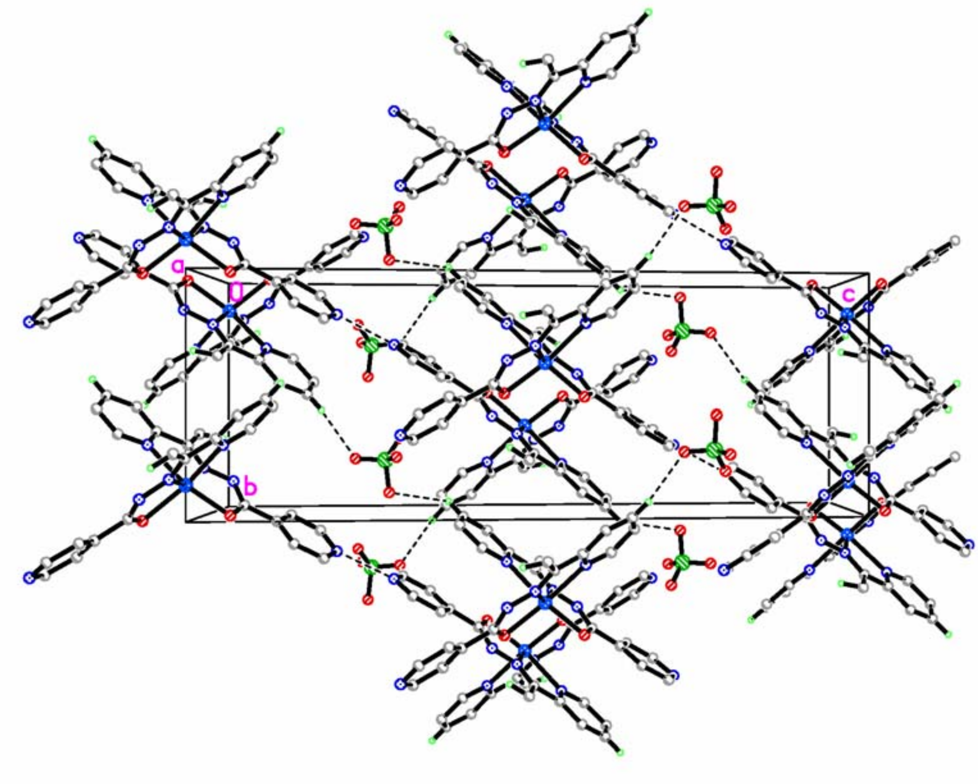


Fig. 4. Molecular packing structure of complex 2, with hydrogen bonds drawn as dashed lines.

3.5. Antimicrobial Activity

Qualitative determination of antimicrobial activity was done using the disk diffusion method.[11] The results are summarized in Table 4. A comparative study of minimum inhibitory concentration (MIC) values of the hydrazone and the metal complexes indicates that the complexes have better activity than the free hydrazone. Generally, this is caused by the greater lipophilic nature of the complexes than the ligand. Such increased activity of the metal chelates can be explained on the basis of chelating theory.[12] On chelating, the polarity of the metal atoms will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of positive charge of the metal atoms with donor atoms. Further, it increases the delocalization of *p*-electrons over the whole chelate ring and enhances the lipophilicity of the complexes. This increased lipophilicity enhances the penetration of the complexes into lipid membrane and blocks the metal binding sites on enzymes of micro-organisms.

From Table 4, it is obvious that the two complexes have higher antibacterial and antifungi activities against *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* when compared to the free hydrazone. Complex 1 has strong activity against *Escherichia coli*, with MIC value of 0.20 μg/mL, which is comparable to Tetracycline. Complex 1 has medium activity against *Staphylococcus aureus* and weak activity against *Candida albicans*. Complex 2 has effective activity against *Escherichia coli*, and weak activity against *Staphylococcus aureus* and *Candida albicans*.

Table 4. MIC values (μg/mL) for the antimicrobial activities of the tested compounds

Compounds	*Staphylococcus aureus*	*Escherichia coli*	*Candida albicans*
The hydrazone	64	32	> 512
1	8.0	2.0	64
2	16.0	8.0	128
Tetracycline	0.32	2.12	> 1024

4. Supplementary mateiral

CCDC 1871743 for 1, and 1871744 for 2 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at http://www.ccdc.cam.ac.uk/const/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033 or email: deposit@ccdc.cam.ac.uk.

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