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Crystal structures and antimicrobial activities of copper(II) complexes of fluorine-containing thioureido ligands ☆

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ABSTRACT

Cu(II) complexes with N-4-fluorobenzoylpiperidine-1-carbothioimidate ($L1^-$), N-2-fluorobenzoylpiperidine-1-carbothioimidate ($L2^-$) and 2-fluorobenzoate ($L3^-$) have been synthesized and characterized by elemental analysis, Fourier Transform infrared (FT-IR), Ultraviolet (UV) and fluorescence spectroscopy methods. The crystal structures of $[Cu(L1)_2]$, $[Cu(L2)_2]$ and $[Cu_2(L3)_4(DMF)_2]$ (DMF: N,N-dimethylformamide) have been determined by X-ray diffraction method. The antimicrobial activities of the complexes against the bacteria (*Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Shewanella* sp.) and the fungi (*Botrytis cinerea*, *Trichoderma* spp., *Myrothecium* and *Verticillium* spp.) have been investigated comparing with the corresponding ligands. The experiments showed that the complexes had the stronger antibacterial and antifungal activities than the corresponding ligands had.

1. Introduction

The heterocyclic compounds containing nitrogen have intense attention due to extensive biological and industrial applications [1–3]. It is known that pyridine and morpholine exhibit broad biological activities, such as antibacterial and antifungal activities [4–7]. And many thiourea derivatives are explored to be pharmacologically active like anticancer [8,9], hypnotic, antifungal [10,11], antibacterial [12], diuretic [13], anti-viral, anti-tubercular, anti-thyroidal, herbicidal and insecticidal activities [14]. Moreover, the biological activity of complexes containing thioureas has also been successful screened for various biological processes [15–19]. Copper complexes have been much explored due to the fact that copper is bio-essential elements responsible for numerous bioactivities in living organism [20]. It is well known that Cu(II) complexation plays an important role in the pharmacological profile of the antimicrobial activities [21–27].

We have investigated the antibacterial activity of N-(piperidylthiocarbonyl) benzamides and N-(morpholinothiocarbonyl) benzamides and their complexes [28,29]. However, the biological activities of metal complexes were different from those of either ligands or the free metal ions. Some complexes such as Co(III) and Ni(II) complexes had the weaker antibacterial activities than the corresponding ligands had [28,29]. But, in many cases, upon the coordination to metal ions, the bioactivity of these complexes increases, suggesting that complexation can be an interesting strategy of dose reduction [30–34]. In consideration of the fact of the good biological effect of copper ion, we have interest in exploring the microbial activities ofcopper complexes. In this paper, we have synthesized two new complexes, $[Cu(L1)_2]$ and $[Cu(L2)_2]$. Moreover, when the complex of $[Cu(L2)_2]$ was heated slightly in DMF, it transformed into a new complex of $[Cu_2(L3)_4(DMF)_2]$. The crystal structures of complexes have been determined successfully by X-ray diffraction. The antimicrobial experiments showed that all of the complexes had stronger controls to the studied fungi and bacteria than their corresponding ligands and free Cu^{2+} had, which indicated the three copper complexes should be the excellent antibacterial reagents to application.

2. Experimental

Melting points are determined on a Kofler melting point apparatus and uncorrected. IR spectra are obtained in KBr discs using a Nicolet 170SX FT-IR spectrometer. Elemental analyses are performed on a Yannaco CHNSO Corder MT-3 analyzer. Absorption and fluorescence spectra were recorded on a CARY50 UV–Vis spectrophotometer and an FLS920 fluorescence spectrophotometer. X-ray diffraction determination is carried out with Rigaku Mercury CCD detector.

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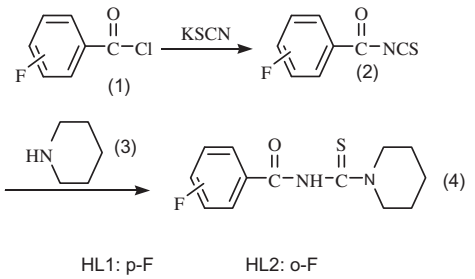


Scheme 1. The synthetic route of HL1 and HL2.

2.1. Synthesis

2.1.1. Synthesis of the ligands

The synthetic route given by the literature [29] of HL1 and HL2 was outlined in Scheme 1. Benzoyl isothiocyanate (2) was obtained by the condensation of fluorobenzoyl chloride (1) with KSCN in acetone solution. Then, the freshly solution was added dropwise to stoichiometric amount of piperidine (3) with stirring and refluxing for 1–2 h. The solids (4) was filtrated, washed with water, and dried to yield.

2.1.2. Synthesis of the complexes

The synthetic reactions of the complexes $[Cu(L1)_2]$ and $[Cu(L2)_2]$ were depicted in Scheme 2. The complexes were obtained by the reaction of $CuCl_2{\cdot}2H_2O$ (0.1 mmol/L, 5.0 mL) with the corresponding ligands (0.1 mmol/L, 10.0 mL) in aqueous solution under the presence of sodium hydroxide (1.0 mmol/L, 1.0 mL). The complexes were isolated as the green solids and then the green solid was washed with water and dried.

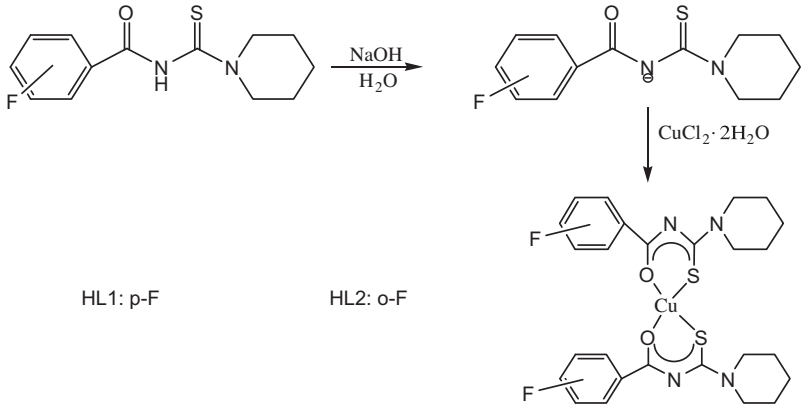
$[Cu(L1)_2]$: Yield: 74%. Green, m.p.:179.3–179.8 °C. Element *Anal.* Calc. for $C_{26}H_{28}CuF_2N_4O_2S_2$ C, 52.51; H, 4.71; N, 9.42; S, 10.77. Found: C, 51.83; H, 4.45; N, 9.82; S, 10.15%. FTIR (cm^{-1}): 3042.6 (w, ν_{ph-H}), 2934.9 (s, ν_{CH2}), 2851.8 (m, ν_{CH2}), 1604.2 (w, $\nu_{C=C(ph)}$), 1588.5(w, $\nu_{C=N}$),1523.7 (s, $\nu_{C=C(ph)}$), 1486.8 (s, $\nu_{C=C(ph)}$), 1423.1 (s, δ_{CH2}), 1341.6 (w, ν_{C-F}), 1211.6 (m, ν_{C-O}), 1197.5 (m, ν_{C-N}), 893.1 (w, ν_{C-S}), 764.5 (w, γ_{ph-H}).

$[Cu(L2)_2]$: Yield: 65%. Green, m.p.:158.5–159.8 °C. Element *Anal.* Calc. for $C_{26}H_{28}CuF_2N_4O_2S_2$: C, 52.51; H, 4.71; N, 9.42; S, 10.77. Found: C, 51.95; H, 4.56; N, 9.65; S, 11.31%. FTIR (cm^{-1}): 3068.9 (w, ν_{ph-H}), 2928.9 (s, ν_{CH2}), 2845.8 (w, ν_{CH2}), 1609.6 (w, $\nu_{C=C(ph)}$), 1584.1(w, $\nu_{C=N}$),1525.8 (m, $\nu_{C=C(ph)}$), 1497.6 (s, $\nu_{C=C(ph)}$), 1423.5 (s, δ_{CH2}), 1357.9 (w, ν_{C-F}), 1259.2 (m, ν_{C-O}), 1126.5 (w, ν_{C-N}), 920.7 (w, ν_{C-S}), 849.1 (w, γ_{ph-H}).

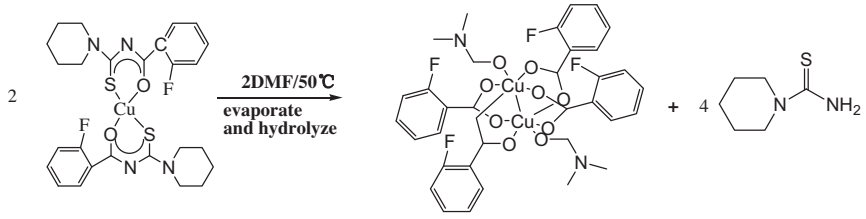
The transform process from $[Cu(L2)_2]$ to $[Cu_2(L3)_4(DMF)_2]$ was shown in Scheme 3. Yield: 87%. m.p.:166.5–167.8 °C, Element *Anal.* Calc. for $C_{34}H_{30}Cu_2F_4N_2O_{10}$: C, 49.04; H, 3.85 N, 3.37. Found: C, 48.83; H, 3.72; N, 3.25%. IR (KBr, cm^{-1}): 3036 (w, ν_{ph-H}), 2850 (w, ν_{CH3}), 1628.7 (s, $\nu_{C=C(ph)}$), 1564.2 (w, $\nu_{C=C(ph)}$), 1485.9 (w, δ_{CH3}), 1445.0 (w, $\nu_{C=C(ph)}$), 1403.4 (s, δ_{CH3}), 1285.4 (w, ν_{C-F}), 1231.9 (w, ν_{C-O}),1181 (m, ν_{C-N}), 760.1 (m, δ_{ph-H}).

2.2. Preparation of microorganism and determination of inhibition zone

The antimicrobial activities were investigated against fungi and bacterium by using agar filter paper diffusion method [35,36]. The cultures of microorganism were grown in autoclaved LB (Luria–Bertani) media (typetone 10 g, yeast extract 5 g, NaCl 10 g, agar 15 g and 1000 mL of distilled water) at 37 °C for 48 h and stored in LB media at 4 °C. The filter paper with thickness of 2.0 mm was made into wafers with diameter of 6 mm by punch. After dry heat sterilization, the wafers were placed on the agar plates which had been cultured with selected fungi and bacteria. The test samples were dissolved in DMSO and confected into the concentration of 500 mg/L. Then, the wafers immerged in test samples for 5 min in advance (the DMSO as reference and the $CuCl_2$ as comparison). The media was inverted in the incubator and cultured for 48 h under 37 °C. The antimicrobial activities were evaluated by



Scheme 2. The synthetic route of [Cu(L1)2] and [Cu(L2)2].



Scheme 3. The transform route from [Cu(L2)2] to [Cu2(L3)4(DMF)2].

Table 1
Summary data of X-ray diffraction.

Molecules	$[Cu(L1)_2]$	$[Cu(L2)_2]$	$[Cu_2(L3)_2(DMF)_2]$
Empirical formula	$C_{26}H_{28}CuF_2N_4O_2S_2$	$C_{26}H_{28}CuF_2N_4O_2S_2$	$C_{34}H_{30}Cu_2F_4N_2O_{10}$
Formula weight	594.18	594.18	829.68
Crystal system	Tetragonal	Triclinic	Monoclinic
Space group	$I\,4_1/a$	$P\bar{1}$	$P\,2_1/n$
a (Å)	19.894(3)	8.346(8)	10.575(3)
b (Å)	19.894(3)	8.575(7)	10.434(3)
c (Å)	13.562(2)	10.271(9)	16.122(4)
α (°)	90	100.237(7)	90
β (°)	90	107.28(3)	93.338(6)
γ (°)	90	106.761(13)	90
Z	8	1	2
D_{calc} (g/cm^3)	1.471	1.533	1.552
Radiation (Mo Kα) (Å)	0.71070	0.71070	0.71070
μ (Mo Kα) (mm^{-1})	1.014	1.058	1.277
θ (°)	3.33–24.49	3.01–24.50	3.07–24.50
Reflections collected	21012	5226	13064
Independent reflections	2187	2039	2895
R_{int}	0.0842	0.0915	0.0662
Data	2187	2039	2895
Restraints	0	0	0
Parameters	178	179	238
Goodness-of-fit GOF on F^2	1.004	0.917	1.000
$R_1[I > 2\sigma(I)]$	0.0764	0.0698	0.0708
wR_2 $[I > 2\sigma(I)]$	0.1448	0.1194	0.1356
R_1(all data)	0.1062	0.1375	0.0995
wR_2 (all data)	0.1601	0.1606	0.1515
Largest difference peak (e A^{-3})	0.221 and −0.335	0.634 and −0.725	0.440 and −0.389

measuring the breadth of the inhibition zones, Δr, which was determined by the following equation:

$$\Delta r = \frac{(d_1 - d_2)}{2}$$

where d_1 was the diameter of the inhibition zones and d_2 was the diameter of the wafer. The tests were performed three times for each sample. Differences between the experimental group and the control group were analyzed by LSD (Least Significant Difference) t-test. $P < 0.05$ was considered to indicate a statistically significant difference. In this paper, all results of experiments were measured up to $P < 0.05$.

2.3. X-ray determination

The single crystals of $[Cu(L1)_2]$ and $[Cu(L2)_2]$ were grown by diffusion method. 2 mL ethanol solution of the complex (0.1 mmol/L) was added in a glass tube, and then 8 mL diethyl ether was added. Finally, the glass tube was sealed and stood. After 15 days, the green single crystals suitable for X-ray diffraction analysis were observed. The single crystal of $[Cu_2(L3)_4(DMF)_2]$ was grown by solvent evaporation method at constant temperature. The powder of the pure $[Cu(L2)_2]$ was dissolved in DMF. A blue-green block-shaped crystal of $[Cu_2(L3)_4(DMF)_2]$ was obtained at the temperature of 50 °C after 14 days. X-ray diffraction experiments were carried out on a Rigaku Mercury CCD X-ray diffractometer by using graphite monochromated Mo Kα radiation (λ = 0.71070 Å). Single crystals were mounted with grease at the top of a glass fiber. Cell parameters were refined on all observed reflections by using the program of CrystalClear (Rigaku and MSC, Ver. 1.3, 2001). The collected data were reduced by the program of CrystalClear and an absorption correction (multiscan) was applied.

The reflection data of crystals were corrected based on Lorentz and polarization effects. The crystal structures were solved by the direct methods and refined on F^2 by the full-matrix least-squares methods using the software package of SHELXTL [37,38]. All of the non-hydrogen atoms were refined anisotropically. The hydrogen atoms were placed at the calculated positions. The structure of $[Cu(L1)_2]$ involved a orientation disorder of atom S. The molecule was refined in two positions with the main position of the atom S1A (61%) and the secondary position of the atom S1B (39%). In $[Cu(L2)_2]$, the atom F1 was disordered by bonding to C7 (69.8%) and C3 (30.2%). A summary of the key crystallographic information, the selected bond lengths and the bond angles of three crystals were listed in Tables 1 and 2. The other information of the crystals, such as the final fractional coordinates, the temperature parameters, the bond distances and the bond angles have been deposited

Table 2
Some structure parameters of three complexes.

	$[Cu(L1)_2]$	$[Cu(L2]_2]$	$[Cu_2(L3)_4(DMF)_2]$	
Bonds	(Å)	(Å)	Bonds	(Å)
Cu–O1	1.918(4)	1.896(5)	Cu1–O1	1.948(4)
Cu–O1 #1	1.918(4)	1.896(5)	Cu1–O4#1	1.958(4)
Cu–S1	2.193(17)	2.249(3)	Cu1–O2#1	1.959(4)
Cu–S1#1	2.193(17)	2.249(3)	Cu1–O3	1.972(4)
S1–C8	1.683(13)	1.745(7)	Cu1–O5	2.142(4)
O1–C1	1.273(6)	1.274(8)	Cu1–Cu1#1	2.633(14)
N1–C1	1.320(7)	1.326(8)	O1–C1	1.268(7)
N1–C8	1.340(7)	1.324(8)	O2–C1	1.252(7)
N2–C8	1.342(7)	1.332(8)	O3–C8	1.245(7)
			O4–C8	1.257(7)
			O5–C15	1.215(7)
Angles	(°)	(°)	Angles	(°)
O1–Cu–O1 #1	90.7(2)	180.0 (2)	O1–Cu1–O3	90.64(19)
O1–Cu–S1 #1	154.3(5)	86.18(16)	O1–Cu1–O5	95.23(17)
O1–Cu–S1	92.2(4)	93.82(16)	O3–Cu1–O5	91.07(17)
O1#1–Cu–S1	154.3(5)	86.18(16)	O1–Cu1–O4#1	88.79(19)
O1#1–Cu–S1#1	92.2(4)	93.82(16)	O1–Cu1–O2#1	168.72(17)
S1–Cu–S1#1	98.0(6)	180.00(11)	O4#1–Cu1–O3	167.96(17)
			O2#1–Cu1–O3	88.08(19)
			O4#1–Cu1–O5	100.96(17)
			O2#1–Cu1–O5	96.00(16)
Dihedral angles	(°)	(°)	Dihedral angles	(°)
S1–C8–N1–C1	−12.1(13)	−6.2(12)	O3–Cu1–O1–C1	82.5(5)
			O5–Cu1–O1–C1	173.6(5)
			O1–Cu1–O3–C8	−83.8(5)
			O5–Cu1–O3–C8	−179.1(5)
			O1–Cu1–O5–C15	−122.0(5)

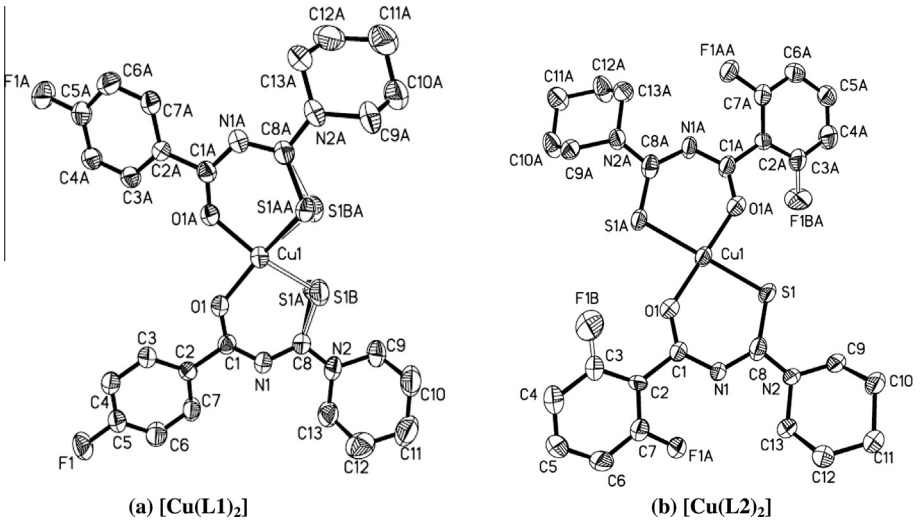


Fig. 1. Crystal structures of the complexes $[Cu(L1)_2]$ (a) and $[Cu(L2)_2]$ (b).

Table 3
The intramolecular interactions of $[Cu(L1)_2]$.

D–H···A	*d*(D–H)	*d*(H···A)	*d*(D···A)	∠(DHA)
C3–H3···O1	0.93	2.416	2.735(7)	99.69°
C7–H7···N1	0.93	2.445	2.764(7)	99.80°
C13–H13···N1	0.97	2.311	2.739(8)	106.05°

in the Cambridge Crystallographic Data Centre as CCDC 912040 ($[Cu(L1)_2]$), 912039 ($[Cu(L2)_2]$) and 882187 ($[Cu_2(L3)_4(DMF)_2]$).

3. Results and discussion

3.1. Structure characteristic

The crystal structures of two fluorobenzoylthiourato complexes were presented in Fig. 1. $[Cu(L1)_2]$ presented a symmetric *cis*-tetra-coordinate planar square structure in a relatively distorted manner, which was similar to the *cis*-bis (N,N-diethyl -N′-pivaloyl-thioureato) copper(II) [39], *cis*-bis [N,N-diethyl-N-(p-nitrobenzoyl) thioureato] copper(II) [40], *cis*-bis [*N*-(4-morpholinothiocarbonyl)-N-1-naphthylbenzamidin] copper(II) [41] and *cis*-bis [1,1-bis(2-hydroxyethyl)-3-benzoylthioureato] copper(II) [42]. The Cu–O bonds (average length, 1.918 Å) were obviously shorter than the Cu–S bonds (average length, 2.193 Å). The divergent geometry of the two arms benefited to allow the sulfur atom to approach the metal atom within a reasonable bonding distance. The angles of O–Cu–O and S–Cu–S were 90.7° and 98.0° while the bond angles of O1–Cu–S1 and O1#1–Cu–S1 were 92.2° and 154.3°, which resulted in slightly distorted quadrangle geometry. The intramolecular interactions of $[Cu(L1)_2]$ were C3–H3···O1, C7–H7···N1 and C13–H13B···N1 and their main information were listed in Table 3. Moreover, a pair of intermolecular interactions were C3–H3···O1# and O1···H3#–C3#, symm., $(3/4 - y, -1/4 + x, -1/4 - z)$, the distance of H3#···O1, 2.591 Å. The complex was self-assembled by intermolecular interactions mainly.

$[Cu(L2)_2]$ presented a symmetric *trans*-tetra-coordinate planar square structure, which was similar to *trans*-bis [N,N-diethyl-N-(p-nitrobenzoyl) thioureato] copper(II) [39], *trans*-[Cu(SON$(CNiPr_2)_2)_2$] [43] and *trans*-$[Cu(3\text{-}OHFT)_2]$ [44]. The bond lengths of Cu–O (1.896 Å) and Cu–S (2.249 Å) were shorter than that of Cu–O (1.918 Å) and longer than Cu–S (2.193 Å) in $[Cu(L1)_2]$, which were consisted with those of in *trans*-bis [N, N-diethyl-N-(p-nitrobenzoyl) thioureato] copper (II) [39]. As the Jahn–Teller's effect shown [45], the bond lengths were longer than those of in $Ni(MTCB)_2$ [46]. The other bond lengths and angles were in agreement with the reported structures. As shown in the crystal structures, the metal ion was located in the basal plane. The bond angles of both O–Cu–O and S–Cu–S in the equatorial plane were 180°. The bond angles of the O–Cu–S were 93.82° and 86.18°, leading to slightly distorted quadrangle geometry. Neither intermolecular hydrogen bond nor short contact interaction was observed in the crystal. It indicated that the complex was self-assembled only by Van der Waals's interactions.

According to Congdon's suggestion for hydrolyzation of benzoylthioureas in sulfuric acid [47], the complex of $[Cu_2(L3)_4(DMF)_2)]$ might derive from the decomposition of $[Cu(L2)_2]$ in DMF (Scheme 3). The crystal data and parameters of $[Cu_2(L3)_4(DMF)_2]$ were given in Table 1 and the selected bond lengths and angles were collected in Table 2. The molecular structure of crystal was shown in Fig. 2. The structure consisted of a quadruply bridged neutral molecule lying on a crystallographic mirror. Similar to binuclear copper(II) complexes of tolfenamic, four carboxylato groups from four ligands were in the familiar bidentate syn., $\eta^1{:}\eta^1{:}\mu^2$ bridging mode [48], two Cu atoms were linked by four benzoate groups. Each DMF molecule was bound to the Cu–Cu vector on each of Cu atom. The complex had a Jahn–Teller distorted and an octahedral geometry with four short Cu–O (fluorobenzoate) bonds (1.948–1.972 Å) and a long Cu–O (DMF) bond (2.142 Å). The distance of two copper atoms in a same dimer was 2.633 Å, which was longer than that found in $[Cu(CH_3COO)\ 2H_2O]_2$ (2.608 Å) [49]. There was an obviously movement of copper atom out of the basal plane of its square pyramidal coordination polyhedron. The Cu-basal plane distance, 0.401 Å, was longer than that of in [Cu(diclofenac)$_2$(DMF)]$_2$ (0.203 Å) [50] and $[Cu(CF_3COO)_2$quinoline$]_2$ (0.32 Å) [51]. The carboxylato portion of each ligand was not co-planar enough to decrease the intensity of F···O interactions. The dihedral angle between the aromatic ring of fluorobenzoate and the carboxylato portion was 39.6°.

A C–H···π interaction was found in $[Cu_2(L3)_4{\cdot}(DMF)_2]$. C11–H11 was directed towards the symmetry related $(-1/2 - x, -1/2 + y, 1/2 - z)$ aromatic ring containing the C2–C7 atoms. A couple of intermolecular hydrogen bondings were C4–H4···O5 (#), symm., $(1/2 - x, -1/2 + y, 1/2 - z)$ and O5···C4–H4, symm., $(1/2 - x, 1/2 + y, 1/2 - z)$. The short contact of H14···H14 (#), symm., $(-x, 2 - y, -z)$ was 2.369 Å.

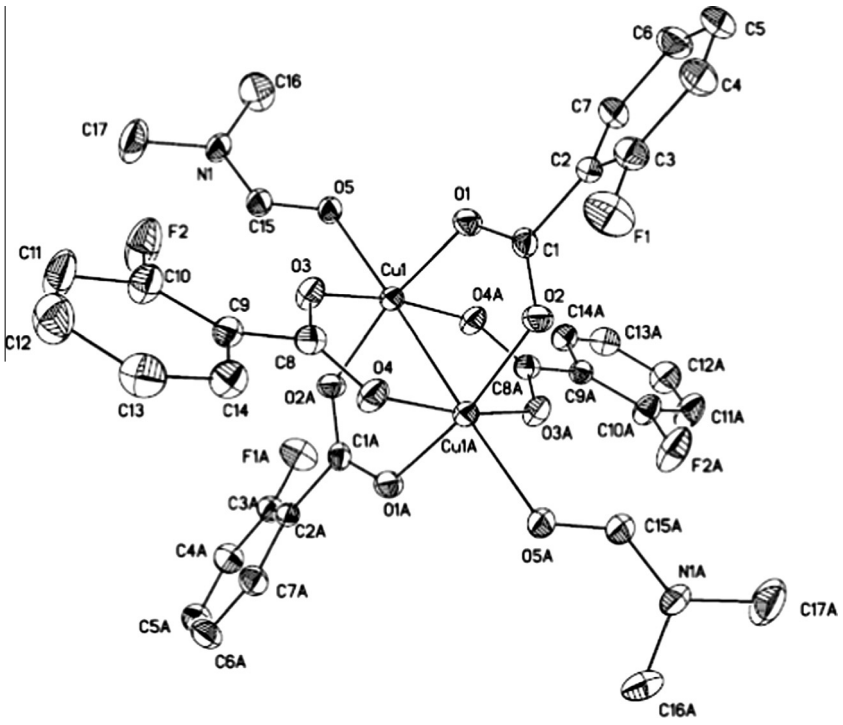


Fig. 2. Crystal structure of the complex $[Cu_2(L3)_4(DMF)_2]$.

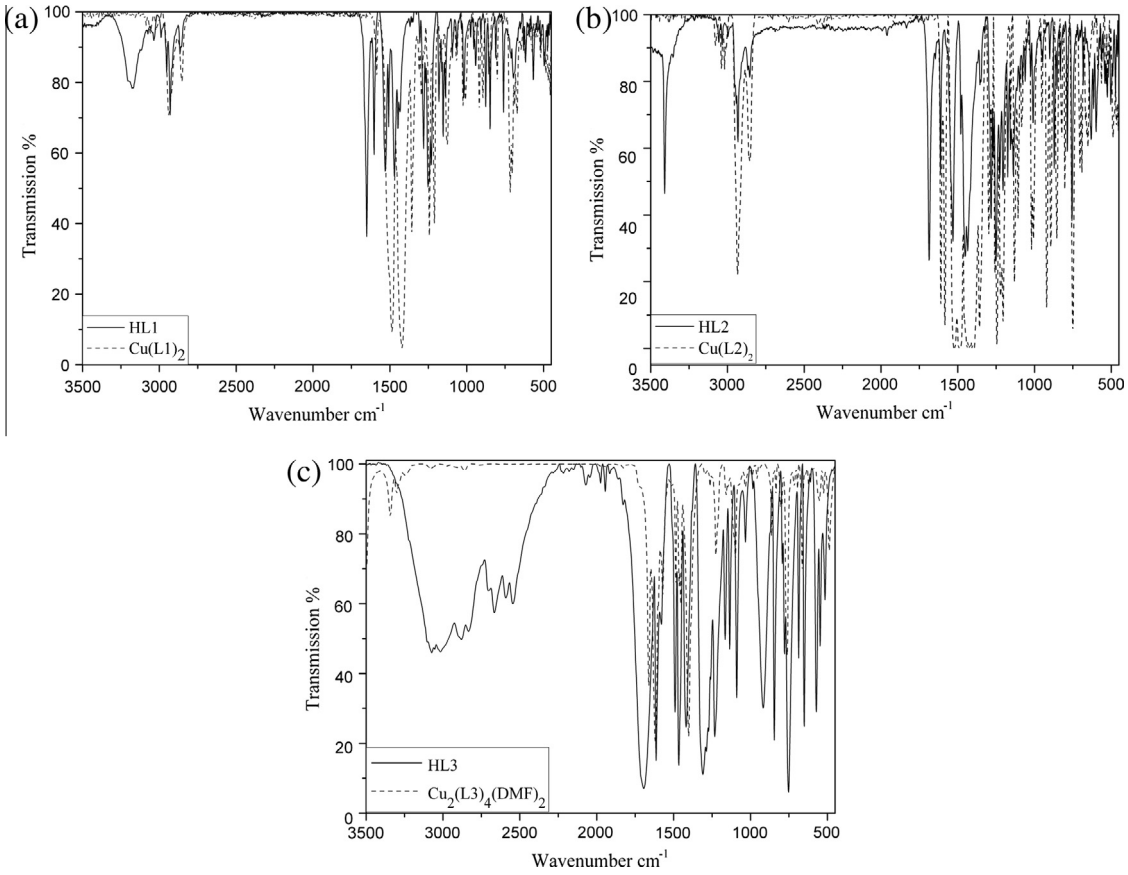


Fig. 3. IR spectra of the ligands and the complexes (a) HL1 and $[Cu(L1)_2]$, (b) HL2 and $[Cu(L2)_2]$, (c) HL3 and $[Cu_2(L3)_4(DMF)_2]$.

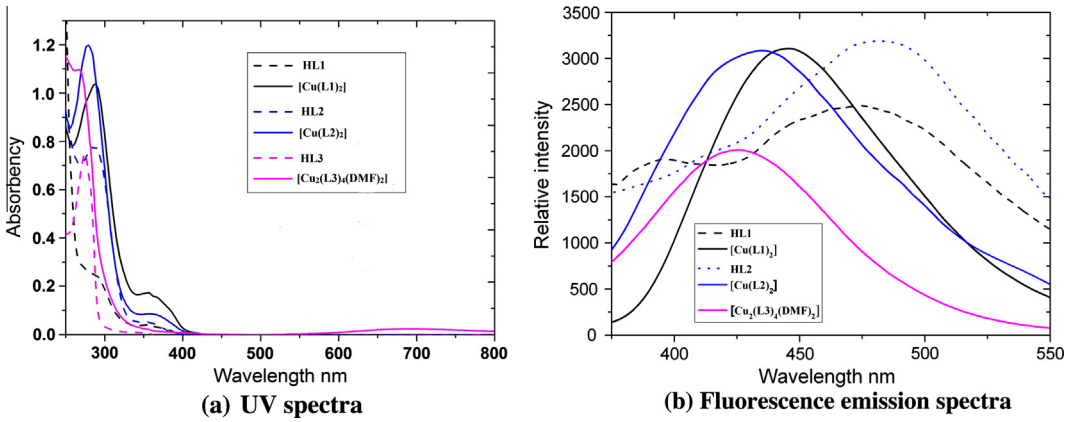


Fig. 4. UV spectra (a) and fluorescence emission spectra (b) in THF solutions for three complexes and their corresponding ligands.

Fungi	$CuCl_2$	HL1	$[Cu(L1)_2]$	HL2	$[Cu(L2)_2]$	HL3	$[Cu_2(L3)_4(DMF)_2]$
Botrytis cinerea							
Trichoderma spp.							
Myrothecium							
Verticillium.spp							
Bacteria							
Shewanella							
Pseudomonas aeruginosa							
E. coli							
Staphylococcus aureus							
Bacillus subtilis							

Fig. 5. The photos of the complexes against the studied fungal and bacteria strains corresponding to the ligands and $CuCl_2$.

Table 4
Average values of the breadth of inhibition zones ($\triangle r$) of the ligands and the complexes against the studied fungi and bacteria (the concentration of test sample is 500 mg/L).

$\triangle r$ (mm)	$CuCl_2$	HL1	$[Cu(L1)_2]$	HL2	$[Cu(L2)_2]$	HL3	$[Cu_2(L3)_4(DMF)_2]$
Fungi							
Botrytis cinerea	0.9	1.2	2.6	1.5	2.8	0.0	7.5
Trichoderma spp.	0.4	1.5	3.5	1.1	3.5	1.5	8.0
Myrothecium	1.0	1.7	2.4	0.6	3.5	0.8	6.0
Verticillium.spp	1.3	2.3	3.0	1.6	3.0	0.2	2.1
Bacteria							
Shewanella	0.9	1.7	1.0	1.6	1.1	0.1	1.5
Pseudomonas aeruginosa	1.0	3.6	1.2	1.8	2.6	1.0	2.4
E. coli	1.1	2.8	3.2	1.7	2.8	0.9	4.1
Staphylococcus aureus	2.3	2.1	3.5	1.5	4.0	2.6	3.7
Bacillus subtilis	0.5	1.8	1.6	1.7	3.0	0.4	2.3

3.2. Electronic spectra

3.2.1. FI-IR spectra

The products were stable in air at room temperature, insoluble in water and soluble in organic solvents such as alcohol, DMF and DMSO (dimethylsulfoxide). The FT-IR spectra of two ligands, HL1 and HL2, together with their copper complexes were shown in Fig. 3(a)–(b). In the IR spectra of $[Cu(L1)_2]$ and $[Cu(L2)_2]$, the stretching vibrations of N–H (3200–3400 cm^{-1}) existed in the ligands disappeared, which indicated that the ligands participated in the coordination reaction as the enamine anion. The stretching vibrations of C=O at 1650.9 cm^{-1}, 1680.4 cm^{-1} and the stretching vibrations C=S at 1156.7 cm^{-1}, 1170.7 cm^{-1} in HL1 and HL2 shifted to the smaller value and appeared at 1211.6, 1259.2 cm^{-1} and 893.1, 920.7 cm^{-1} in $[Cu(L1)_2]$ and $[Cu(L2)_2$ respectively. It indicated that the C=O bond and C=S bond transformed to the C–O bond and C–S bond upon the coordination reaction. Moreover, the C=S and C=O bond coordinating to Cu^{2+} enhanced the resonance delocalization of nitrogen atom lone pair electrons, provided more double bond character for C–N–C. Thus, both symmetric and asymmetric C–N–C stretching was shifted to higher values. The vibrational bands at about 1585 cm^{-1} are attributed to C=N double bonded in both complexes. The IR spectra of $[Cu_2(L3)_4(DMF)_2]$ was exhibited in Fig. 3(c). The stretching vibrations of C=C (-ph) appeared at about 1609.6, 1525.8 and 1497.6 cm^{-1}. The band at 1695.7 cm^{-1}($\nu_{C=O}$) of ligand shifted to 1231.9 cm^{-1} (ν_{C-O}) in the complex, which showed that the ligand was coordinated by the O atoms of C=O.

3.2.2. UV–Vis spectra

UV–visible spectra of the ligands and the complexes were shown in Fig. 4(a). In ligands of HL1 and HL2, the weak absorption band at about 350 nm resulted from the charge transfer transition and a strong absorption band at about 285 nm was assigned to $\pi \rightarrow \pi^*$ transitions. Because of d–d transition of Cu(II), the absorption bands at about 350 nm shifted red to 364 nm in complexes, and accompanied with the absorption bands broadening and increasing. The absorption bands at about 285 nm shifted blue slightly in complexes and the absorptions intensity increase comparing with that of the ligands. The absorption of $[Cu_2(L3)_4(DMF)_2]$ was observed as a new broad band centered at about 690 nm, which was attributed to the d–d transition of Cu(II). The strong absorption band of HL3 at about 266 nm shifted blue to 248 nm in $[Cu_2(L3)_4(DMF)_2]$, which was assigned to $\pi \rightarrow \pi^*$ transitions. The blue shift of the bands in the complexes indicated that the coordination reaction decreased the delocalization of π electrons and resulted in the increase of the energy of $\pi \rightarrow \pi^*$ transition.

3.2.3. Fluorescence spectra

HL1 and HL2 exhibited the weakly fluorescnece emissions in THF. As shown in Fig. 4(b), selecting 285 nm as the excitation wavelength, HL1 emitted double fluorescence bands with the maxima emissions at 394 nm and 475 nm. Both bands were attributed to the normal fluorescence ($\pi^* \rightarrow \pi$) and charge transfer fluorescence, which were consistent of that of the UV absorptions. HL2 emitted a charge transfer fluorescence band with the maximum emission at 481 nm. The normal fluorescence bands wasn't observed due to the intramolecular hydrogen bond interaction F···H–N. The maxima fluorescence emission wavelength were located at 445 and 434 nm for $[Cu(L1)_2]$ and $[Cu(L2)_2]$ respectively. Because the coordination reaction decreased the delocalization of π electrons, the fluorescence bands of $[Cu(L1)_2]$ and $[Cu(L2)_2]$ shifted blue, which corresponded to that of UV absorption. HL3 didn't emitted fluorescence. However, a strong fluorescence emission band was detedcted with the maximum emission wavelength of 424 nm in $[Cu_2(L3)_4(DMF)_2]$. It may be a new fluorescence method to determine Cu^{2+} by o-fluorobenzoic acid.

3.3. Antimicrobial activities

The photos and the diameter of inhibition zones against the bacteria and the fungal strains were depicted in Fig. 5 and Table. 4. The three complexes showed stronger inhibiting fungi abilities than the corresponding ligands and $CuCl_2$. As we known, $CuCl_2$ also exhibited the considerable inhibition activities against the studied fungi and bacteria. The breadth of the inhibition zones (Δr, mm) is 0.9 (*Botrytis cinerea*), 0.4 (*Trichoderma spp.*), 1.0 (*Myrothecium)*, 1.3 (*Verticillium* spp.), 0.9 (*Shewanella*), 1.0 (*Pseudomonas aeruginosa*), 1.1 (*Escherichia coli*), 2.3 (*Staphylococcus aureus*) and 0.5 (*Bacillus subtilis*). The antibacterial and antifungal activities of $[Cu(L1)_2]$ were superior to that of the ligand and free Cu^{2+}. For example, the Δr of $[Cu(L1)_2]$, 2.6 mm and 3.5 mm were larger than those of HL1, 1.2 mm and 2.1 mm against *B. cinerea* and *S. aureus*. The antibacterial and antifungal activities of $[Cu(L2)_2]$ were similar to $[Cu(L1)_2]$. It suggested that the substituted positions of fluorine did not affect antibacterial and antifungal activities. The Δr of $[Cu_2(L3)_4(DMF)_2]$ was 7.5, 8.0, 6.0 and 2.1 mm, respectively, larger than the Δr of HL3, 0.0, 1.5, 0.8, 0.2 mm against *Botrytis cinerea, Trichoderma* spp., *Myrothecum* and *Verticillium* spp. respectively. For the bacteria, the Δr of $[Cu_2(L3)_4(DMF)_2]$, 1.5 mm (*Shewanella*), 2.4 mm (*P. aeruginosa*), 4.1 mm (*E. coli*), 3.7 mm (*S. aureus*) and 2.3 mm (*B. subtilis*) also larger than that of HL3, 0.1 mm (*Shewanella*), 1.0 mm (*P. aeruginosa*), 0.9 mm (*E. coli*), 2.6 mm (*S. aureus*) and 0.4 mm (*B. subtilis*) respectively. It indicated that both antifungal and antibacterial abilities of the $[Cu_2(L3)_4(DMF)_2]$ were stronger than that of HL3. For bacteria, *Shewanella* and *P. aeruginosa*, the antibacterial abilities of complexes were weak, the Δr were close to the ligands and $CuCl_2$. Anyway, three complexes with Cu^{2+} exhibited stronger antifungal abilities than the ligands and $CuCl_2$. It pronounced the increasing of activity may be attributed to the formation of chelate, a less polar form of the metalloelement, which increases the lipophilic character. The increased lipophilic

character of chelate was benefit for the interaction of the complexes with the cell constituents, resulting in interference with the normal cell processes [52,53].

4. Conclusion

Two fluorine-containing thioureido complexes of ([$Cu(L1)_2$] and [$Cu(L2)_2$]), have been synthesized successfully. The binuclear complex of [$Cu_2(L3)_4(DMF)_2$] were obtained by the transformation of [$Cu(L2)_2$] under slightly heated in DMF. The crystal structures of three complexes have been determined by X-ray diffraction. Both [$Cu(L1)_2$] and [$Cu(L2)_2$] presented tetra-coordinate planar square structures. The structure of [$Cu_2(L3)_4(DMF)_2$] consisted of a quadruply bridged neutral molecule lying on a crystallographic mirror. All of complexes had stronger antifungal ability than the corresponding ligands had. It might be attributed to that the formation of chelate reduced the polar form of the metal ions and increased the lipophilic character, which made for the interaction of the complexes with cell constituents.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ica.2013.06.029.

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