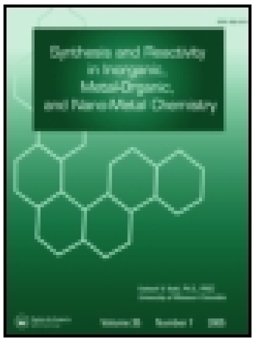

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Copper(II) Complexes with Bis-Schiff Bases: Synthesis, Crystal Structures and Antibacterial Activities

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Abstract

Reaction of copper perchlorate with the tridentate Schiff bases *N,N'*-bis(5-methoxysalicylidene)-1,2-ethanediamine (H_2L^1) and *N,N'*-bis(5-chlorosalicylidene)-1,3-propanediamine (H_2L^2), afforded a dinuclear complex, $[Cu_2(L^1)_2]\cdot 2CH_3OH$ (**1**), and a mononuclear complex, $[CuL^2]$ (**2**). The complexes were characterized by single-crystal X-ray diffraction, FT-IR, and elemental analysis. The Cu atom in complex **1** is in a square pyramidal coordination, with two phenolate O and two imine N atoms of L^1 ligand defining the basal plane, and with one phenolate O atom of another L^1 ligand occupying the apical position. The Cu atom in complex **2** is coordinated by two phenolate O and two imine N atoms of L^2 ligand, forming a tetrahedrally distorted square planar geometry. The free Schiff bases and the complexes were assayed for antibacterial activities. Both complexes are more active against the bacteria than the free Schiff bases. Complex **2** has the MIC value of 0.10 μg mL^{-1} against *Bacillus subtilis*.

Keywords

bis-Schiff base, copper complex, crystal structure, antibacterial activity

Introduction

The chemistry and the biological potential of Schiff base ligands and their metal complexes have been investigated extensively. Schiff bases are reported to possess various biological activities, such as antibacterial[1, 2] and antitumour activities.[3, 4] Metal complexes with Schiff bases as ligands have played important role in the development of coordination chemistry due to their preparative accessibility, structural variety, and biological properties.[5–7] Interest is still high as few have found their way into application as therapeutic drugs, health, skin care products and in paint dye manufacturing.[8] Copper complexes with Schiff bases have interesting biological properties.[9,10] Bis-Schiff bases are readily coordinate to transition metal atoms. We report herein the synthesis and characterization of a new dinuclear complex, $[Cu_2(L^1)_2]\cdot2CH_3OH$ (**1**), and a mononuclear complex, $[CuL^2]$ (**2**), where L^1 and L^2 are the anions of bis-Schiff bases *N,N'*-bis(5-methoxysalicylidene)-1,2-ethanediamine (H_2L^1) and *N,N'*-bis(5-chlorosalicylidene)-1,3-propanediamine (H_2L^2; Scheme 1). Their antibacterial activities against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas fluorescens* were evaluated.

Experimental

Materials and Measurements

5-Methoxysalicylaldehyde, 5-chlorosalicylaldehyde, ethane-1,2-diamine and propane-1,3-diamine were purchased from Sigma-Aldrich. All other chemicals were commercial products and used without further purification. Copper perchlorate were prepared from perchloric acid with copper carbonate in distilled water. C, H and N elemental analysis was performed on a Vario EL-III analyzer. Infrared spectra were recorded as KBr pellet on a Nicolet Avatar 360 spectrophotometer in the range 4000–400 cm^{-1}. Molar conductivity was determined in methanol at room temperature on a DDS-11A conductometer. ^{1}H NMR spectra were recorded on a Bruker spectrometer at 300 MHz.

Synthesis of H_2L^1

5-Methoxysalicylaldehyde (3.04 g, 0.02 mol) dissolved in methanol (30 mL) was added to ethane-1,2-diamine (0.060 g, 0.01 mol) in methanol (30 mL). The reaction mixture was heated under reflux for 1 h and then cooled to room temperature followed by concentrating the resulting mixture to give yellow solid product. Yield 95%. For $C_{18}H_{20}N_2O_4$: Anal. calcd, %: C, 65.84; H, 6.14; N, 8.53. Found, %: C, 65.67; H, 6.73; N, 8.60. ^{1}H NMR (300 MHz, d^6-DMSO): δ 11.32 (s, 2H, O*H*), 8.52 (s, 2H, C*H*=N), 7.37 (s, 2H, Ar*H*), 6.95-6.83 (m, 4H, Ar*H*), 3.79 (s, 6H, CH_3).

Synthesis of H_2L^2

5-Chlorosalicylaldehyde (3.12 g, 0.02 mol) dissolved in methanol (30 mL) was added to propane-1,3-diamine (0.074 g, 0.01 mol) in methanol (30 mL). The reaction mixture was heated under reflux for 1 h and then cooled to room temperature followed by concentrating the resulting mixture to give yellow solid product. Yield 97%. For $C_{17}H_{16}Cl_2N_2O_2$: Anal. calcd, %: C, 58.13; H, 4.59; N, 7.98. Found, %: C, 58.27; H, 4.68; N, 7.81. ^{1}H NMR (300 MHz, d^6-DMSO): δ 11.77

(s, 2H, O*H*), 8.53 (s, 2H, C*H*=N), 7.56 (s, 2H, Ar*H*), 7.33 (d, 2H, Ar*H*), 6.98 (d, 2H, Ar*H*), 3.72 (t, 4H, NCH_2), 1.98 (m, 2H, CH_2).

Synthesis of $[Cu_2(L^1)_2]\cdot 2CH_3OH$ (1)

Copper perchlorate (0.37 g, 1 mmol) in methanol (20 mL) was added to H_2L^1 (0.33 g, 1 mmol) in methanol (20 mL), and the resultant blue reaction mixture was stirred at room temperature for 1 h to give a clear solution. Blue single crystals were obtained by slow evaporation of the solution in air. Yield 45%. For $C_{38}H_{44}Cu_2N_4O_{10}$: Anal. calcd, %: C, 54.08; H, 5.26; N, 6.64. Found, %: C, 53.82; H, 5.41; N, 6.55.

Synthesis of $[CuL^2]$ (2)

The blue single crystals of complex **2** were prepared according to a similar procedure as that for **1**, with H_2L^2 (0.35 g, 1 mmol) instead of H_2L^1. Yield 53%. For $C_{17}H_{14}Cl_2CuN_2O_2$: Anal. calcd, %: C, 49.47; H, 3.42; N, 6.79. Found, %: C, 49.62; H, 3.35; N, 6.70.

X-ray Crystallography

Crystal structure determination of the complexes were carried out on a Bruker APEX II CCD area diffractometer equipped with graphite-monochromatized MoKα (λ = 0.71073 Å) radiation. Structures of both complexes were solved by direct methods and refined on F^2 by full-matrix least-squares methods using SHELX-97.[11] All the non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included at geometrically calculated positions and refined using a riding model. The crystal data, experimental details, refinement results and details of structure determinations are listed in Table 1. Selected bond lengths and bond angles are listed in Table 2.

Results and Discussion

The Schiff bases H_2L^1 and H_2L^2 were prepared in quantitative yields in methanol. The compounds are yellow solid product. The elemental analyses are in good agreement with the chemical formulae proposed for the compounds. Complexes **1** and **2** were prepared by the reaction of copper perchlorate with H_2L^1 and H_2L^2, respectively, in methanol (Scheme 2). Both the Schiff bases and the copper complexes are stable in air at room temperature, and soluble in common polar organic solvents, such as DMSO, DMF, methanol, ethanol, and acetonitrile. The molar conductance values of the complexes measured in methanol at concentrations of 10^{-3} mol·L^{-1} at 298 K are 18 and 27 Ω^{-1} cm^2 mol^{-1}, indicating the non-electrolytic nature.[12]

IR Spectra

The IR spectra of the free Schiff bases H_2L^1 and H_2L^2 showed weak bands due to the phenolic groups centered at about 3430 cm^{-1}, which are assigned to the ν_{OH} vibrations. The bands of the phenolic groups are absent in the IR spectra of the copper complexes, indicating the hydroxyl groups are deprotonated during coordination. The intense bands at 1283 cm^{-1} for H_2L^1 and 1287 cm^{-1} for H_2L^2 assigned to phenolic C–O linkage shifting toward to higher wave numbers of 1330 cm^{-1} for **1** and 1337 cm^{-1} for **2**, confirming the involvement of the deprotonated phenolic groups in bond formation with the copper atoms.[13] The strong bands in the free Schiff bases at 1645

cm^{-1} for H_2L^1 and 1651 cm^{-1} for H_2L^2 underwent negative shift of about 10–15 cm^{-1} in the complexes, confirming the coordination of the azomethine N atoms to the copper atoms.[14] The weak absorption bands in the 400–600 cm^{-1} region are assigned to the vibrations of Cu–N and Cu–O coordinate bonds.

Crystal Structure Description of Complex 1

The structure of complex **1** is shown in Figure 1. The compound contains a crystallographic inversion center symmetry. The independent component of the compound contains a dinuclear complex molecule and two methanol molecules of crystallization. The Cu atom is in a square pyramidal coordination, with two phenolate O and two imine N atoms of a Schiff base ligand L^1 defining the basal plane, and with one phenolate O atom occupying the apical position. The Cu-N and Cu-O bonds in the complex are within normal values as compared with other similar copper complexes with Schiff base ligands.[15–17] The *cis* and *trans* angles subtended at the Cu atom in the basal plane of the complex are in the range 84.8(1)–93.1(1)º and 175.8(1)–177.0(1)º, respectively. The coordinate bond angles among the apical and basal donor atoms are in the range 85.2(1)–98.2(1)º. Thus, the square pyramidal coordination in the complex is distorted. The dihedral angle between the two benzene rings of the Schiff base ligand is 3.7(3)º. In the crystal structure of the complex, the methanol molecules are linked to the complex molecules through $O5–H5\cdots O1^i$ hydrogen bonds [$O5–H5 = 0.82$ Å, $H5\cdots O1^i = 1.95$ Å, $O5\cdots O1^i = 2.765(4)$ Å, $O5–H5\cdots O1^i = 174$º; symmetry code for i: 1 + *x*, *y*, *z*] (Figure 2).

Crystal Structure Description of Complex 2

The structure of complex **2** is shown in Figure 3. The Cu atom is coordinated in a square planar geometry, with two phenolate O and two imine N atoms of a Schiff base ligand. The Cu-N and Cu-O bonds in the complex are comparable to those of complex **1** and also within normal values as compared with other similar copper complexes with Schiff bases.[15–17] The *cis* and *trans* angles subtended at the Cu atom are in the range 87.5(1)–97.7(1)º and 153.0(2)–154.1(2)º, respectively. Thus, the square pyramidal coordination in the complex is tetrahedrally distorted. In the crystal structure of the complex, the complex molecules are stack along the *b* axis through $\pi\cdots\pi$ interactions [$Cg1\cdots Cg1^{ii}$ = 4.738(3) Å, $Cg1\cdots Cg2^{ii}$ = 4.998(3) Å, $Cg1\cdots Cg3^{iii}$ = 4.313(3) Å, $Cg2\cdots Cg3^{iv}$ = 4.534(3) Å; Cg1, Cg2, Cg3 are the centroids of Cu(1)-O(2)-C(13)-C(12)-C(11)-N(2), C(1)-C(2)-C(3)-C(4)-C(5)-C(6), and C(12)-C(13)-C(14)-C(15)-C(16)-C(17), respectively. Symmetry codes: ii: x, $-y$, $-1/2 + z$; iii: x, $-y$, $1/2 + z$; iv: $1/2 + x$, $1/2 - y$, $1/2 + z$] (Figure 4).

Antibacterial Activity

The free Schiff bases and the two complexes were screened for antibacterial activity against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas fluorescens* by the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) method. The minimum inhibitory concentrations (MICs) of the compounds against the bacteria are presented in Table 3. Penicillin was used as a reference. The results revealed that the free Schiff base H_2L^1 showed weak activity against *Bacillus subtilis*, *Staphylococcus aureus* and *Escherichia coli*, and no activity against *Pseudomonas fluorescens*. The free Schiff base H_2L^2 showed medium activity against *Bacillus subtilis* and *Staphylococcus aureus*, and weak activity against *Escherichia coli* and *Pseudomonas fluorescens*. It is clear that the activities of the two complexes are much effective than the free Schiff bases. Complexes **1** and **2** have strong activities against *Bacillus subtilis*, *Staphylococcus aureus* and *Escherichia coli*, and weak activity against *Pseudomonas fluorescens*. It should be noted that complex **2** has the MIC value of 0.10 $\mu g\ mL^{-1}$ against *Bacillus subtilis*, which is much lower than the reference drug. This phenomenon is in accordance with the conclusion that compounds bearing halide groups have more potent antibacterial activities.[18]

Conclusion

In the present work, a dinuclear copper(II) complex and a mononuclear copper(II) complex were prepared and characterized by single-crystal X-ray diffraction. The biological assay revealed that both complexes are more active against the bacteria than the free Schiff bases. The mononuclear copper(II) complex with the bis-Schiff base *N*,*N'*-bis(5-chlorosalicylidene)-1,3-propanediamine has the MIC value of 0.10 $\mu g\ mL^{-1}$ against *Bacillus subtilis*.

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Table 1. Crystallographic data and structure refinement for the complexes **1** and **2**.

Complex	**1**	**2**
Empirical formula	$C_{38}H_{44}Cu_2N_4O_{10}$	$C_{17}H_{14}Cl_2CuN_2O_2$
Formula weight	843.85	412.74
Temperature	298(2) K	298(2) K
Wavelength	0.71073 Å	0.71073 Å
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	*Cc*
Unit cell dimensions		
a (Å)	11.1108(9)	21.007(2)
b (Å)	7.5550(6)	8.111(2)
c (Å)	23.964(2)	9.399(2)
β (°)	114.814(2)	94.230(2)
V (Å^3)	1825.8(2)	1597.1(6)
Z	2	4
ρ (calcd.) (g cm^{-3})	1.535	1.717
μ (mm^{-1})	1.230	1.714
F(000)	876	836
Crystal size (mm^3)	0.27 × 0.26 × 0.23	0.19 × 0.18 × 0.18

θ range for data collection (°)	2.85 – 25.50	1.94 – 25.50
$h/k/l$ (max, min)	-13, 13/-8, 9/-29,25	-24, 25/-6, 9/-11, 11
Reflections collected	15966	3970
Observed reflections [$I > 2\sigma(I)$]	2931	2563
Max. and min. transmission	0.7324 and 0.7651	0.7365 and 0.7478
Data/restraints/parameters	3392/0/248	2681/2/217
Goodness-of-fit on F^2	1.046	1.222
Final R_1, wR_2 indices [$I > 2\sigma(I)$]	0.0406, 0.1066	0.0378, 0.1014
R_1, wR_2 indices (all data)	0.0490, 0.1133	0.0396, 0.1045

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

1			
Cu1-O1	1.898(2)	Cu1-O2	1.904(2)
Cu1-N1	1.943(2)	Cu1-N2	1.939(2)
Cu1-O2A	2.832(3)		
O1-Cu1-O2	89.4(1)	O1-Cu1-N2	175.8(1)
O2-Cu1-N2	92.5(1)	O1-Cu1-N1	93.1(1)
O2-Cu1-N1	177.0(1)	N2-Cu1-N1	84.8(1)
N1-Cu1-O2A	86.6(1)	N2-Cu1-O2A	85.2(1)
O1-Cu1-O2A	98.2(1)	O2-Cu1-O2A	94.7(1)
Symmetry operation for generating atoms with the suffix A: $-x, -y, -z$.			
2			
Cu1-O1	1.906(5)	Cu1-O2	1.898(5)
Cu1-N1	1.949(6)	Cu1-N2	1.971(6)
O2-Cu1-O1	87.47(9)	O2-Cu1-N1	154.1(2)
O1-Cu1-N1	92.6(2)	O2-Cu1-N2	93.7(2)
O1-Cu1-N2	153.0(2)	N1-Cu1-N2	97.7(1)

Table 3. Antibacterial activity of the tested material (MIC, μg mL^{-1}).

Compound	*Bacillus subtilis*	*Staphylococcus aureus*	*Escherichia coli*	*Pseudomonas fluorescens*
H_2L^1	12.5	12.5	25	> 100
H_2L^2	3.12	6.25	25	50
1	0.78	3.12	6.25	25
2	0.10	1.56	6.25	25
Penicillin	0.78	3.13	> 100	> 100

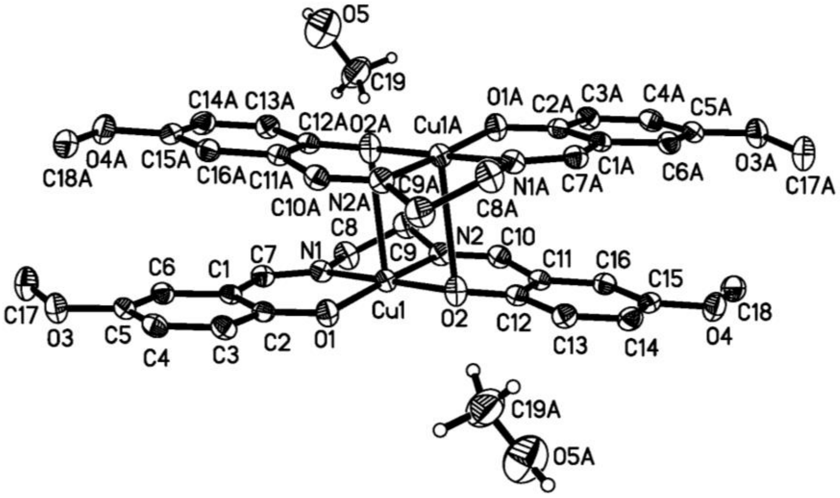


Fig. 1. ORTEP plots (30% probability level) and numbering scheme for **1**. Symmetry operation for generating atoms with the suffix A: – *x*, – *y*, – *z*.

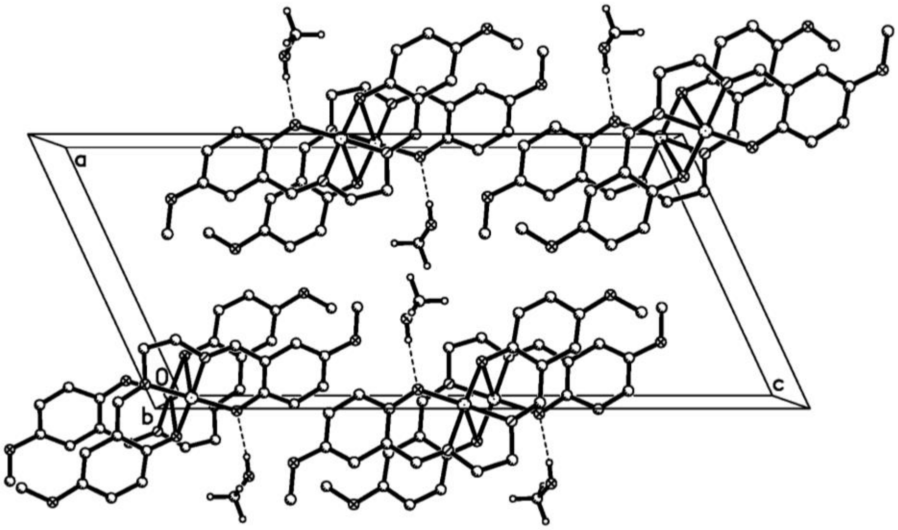


Fig. 2. Molecular packing structure of **2**. Hydrogen bonds are drawn as thin dashed lines.

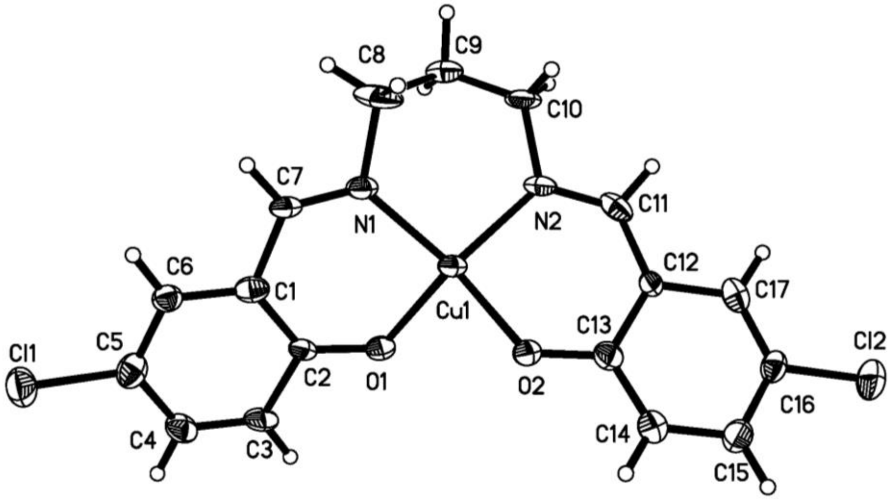


Fig. 3. ORTEP plots (30% probability level) and numbering scheme for **2**.

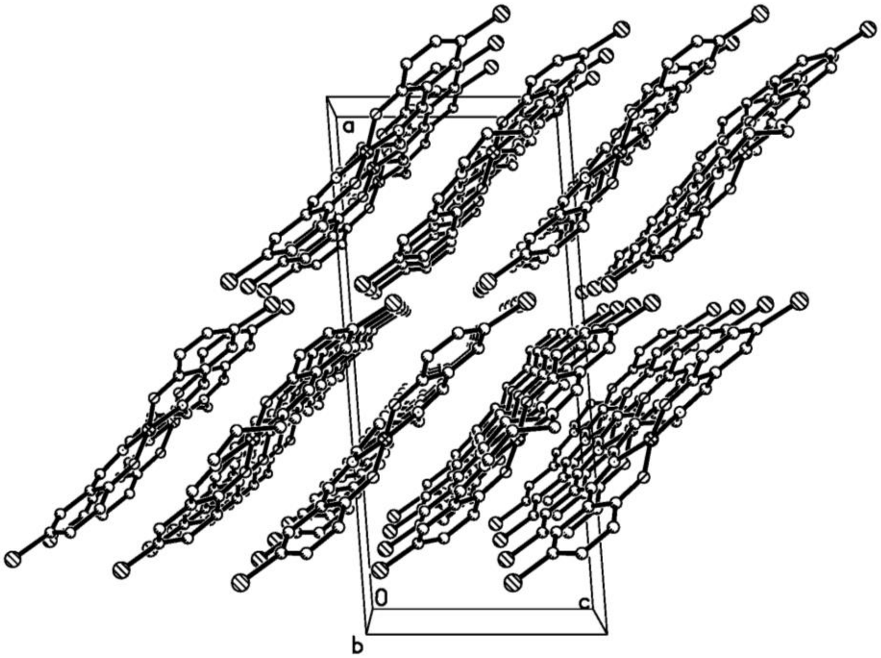
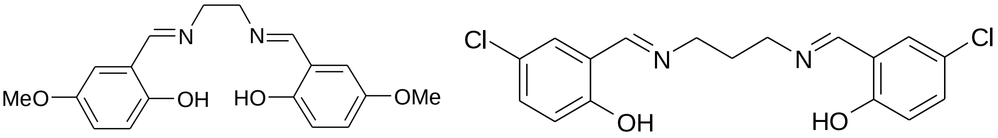
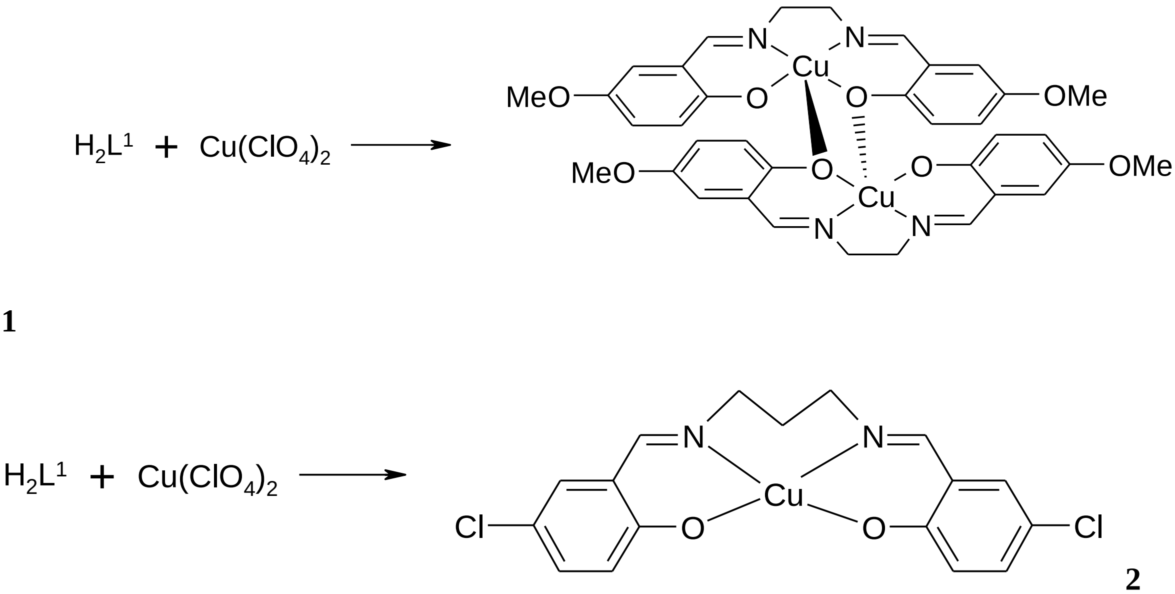


Fig. 4. Molecular packing structure of **2**.



Scheme 1. H_2L^1 and H_2L^2.



1

2

Scheme 2. The synthetic procedure of the complexes.