Copper(II) and Zinc(II) Complexes Derived from \(N,N'\)-Bis(4-bromosalicylidene)propane-1,3-diamine: Syntheses, Crystal Structures and Antimicrobial Activity

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Abstract

A mononuclear copper(II) complex, [CuL] (1), and a phenolato-bridged trinuclear zinc(II) complex, [Zn\(_3\)Cl\(_2\)L\(_2\)(DMF)\(_2\)] (2), where L is the deprotonated form of \(N,N'\)-bis(4-bromosalicylidene)propane-1,3-diamine (H\(_2\)L), have been prepared and characterized by elemental analyses, IR and UV-Vis spectroscopy, and single crystal X-ray diffraction. The Cu atom in complex 1 is in square planar coordination, while the terminal and central Zn atoms in complex 2 are in square pyramidal and octahedral coordination, respectively. The antibacterial activities of the complexes have been tested on the bacteria Staphylococcus aureus and Escherichia coli, and the yeast Candida parapsilosis.

Keywords: Schiff base; copper complex; zinc complex; crystal structure; antibacterial property

1. Introduction

Schiff bases have been extensively used as multi-dentate ligands to construct metal complexes with versatile structures due to their easy formation and strong metal-binding ability.\(^1\) The increasing interest in the synthesis and structural studies of Schiff bases is due to their bioactivity and coordination properties. Schiff base with donors (N, O, S, etc.) have structure similarities with neutral biological systems. Most of the Schiff bases and their complexes with transition metals have a broad range of applications in biological and pharmaceutical fields.\(^2\) A number of Schiff bases have been reported for their remarkable biological activities, such as antibacterial, antifungal, antimalarial, anti-inflammatory, viral and antipyretic activities.\(^3\) Copper(II) and zinc(II) Schiff base complexes have been studied extensively and are considered as excellent alternatives for classic organic antibacterial agents.\(^4\) Despite the presence of considerable research on the antibacterial properties of such complexes, it is still necessary to search for new complexes to find more effective agents as well as to better understand the mechanism of the action of this class of compounds. With an interest in the chemistry of biologically active Schiff bases and their metal complexes, this study aimed to synthesize copper(II) and zinc(II) complexes. The newly synthesized complexes, [CuL] (1) and [Zn\(_3\)Cl\(_2\)L\(_2\)(DMF)\(_2\)] (2), where L is the deprotonated form of \(N,N'\)-bis(4-bromosalicylidene)propane-1,3-diamine (H\(_2\)L), were structurally characterized, and examined for their antimicrobial activities.

2. Experimental

2.1. Materials and Methods

1,3-Diaminopropane and 4-bromosalicylaldehyde were purchased from TCI. CuCl\(_2\)·2H\(_2\)O and ZnCl\(_2\) were purchased from Aladdin Chemical Reagent Co. Ltd. The solvents methanol and DMF were purchased from Kemiu Chemical Reagent Co. Ltd. Elemental analyses were performed on a Perkin-Elmer 240C elemental analyzer. IR spectra were recorded on a Jasco FT/IR-4000 spectrometer as KBr pellets in the 4000–400 cm\(^{-1}\) region. UV-Vis spectrum was recorded on a Lambda 900 spectrometer. 1H and 13C NMR were determined with a Bruker 500 MHz instrument. Single crystal X-ray diffraction was carried out on a Bruker SMART 1000 CCD diffractometer.

2.2. Synthesis of H\(_2\)L

1,3-Diaminopropane (0.15 g, 2.0 mmol) was diluted by methanol (20 mL). Then, it was added dropwise to the methanol solution (30 mL) of 4-bromosalicylaldehyde.
hyde (0.84 g, 4.0 mmol). The reaction mixture was stirred and heated to reflux for 30 min. The solvent was removed by evaporation under reduced pressure. The yellow solid was recrystallized from ethanol to give yellowish crystalline product. Yield: 0.72 g (82%).

1H NMR (500 MHz, DMSO-d₆; Scheme 1) δ/ppm: 8.58 (s, 2H, CH_d=N), 7.50 (s, 2H, ArHc), 7.33 (t, 2H, ArHa), 7.14 (d, 2H, ArHb), 3.72 (t, 4H, CH_e2), 2.07 (t, 2H, CH_f2). 13C NMR (126 MHz, DMSO-d₆) δ/ppm: 165.12, 153.13, 133.27, 124.54, 123.27, 122.02, 115.57, 54.78, 30.73. IR (KBr, cm⁻¹): 3449, 2980, 2921, 1632, 1471, 1385, 1287, 1231, 1096, 930, 845, 646, 451. UV-Vis λ_max/nm (1.13 × 10⁻⁵ mol L⁻¹, MeOH; ε, L mol⁻¹ cm⁻¹): 230 (27,300), 270 (13,800), 330 (7,120), 420 (4,520). Anal. Calcd. (%) for C_{17}H_{16}Br_{2}N_{2}O_{2}: C, 46.39; H, 3.66; N, 6.36. Found (%): C, 46.22; H, 3.75; N, 6.43.

2. 3. Synthesis of [CuL] (1)

H₂L (44 mg, 0.10 mmol) and CuCl₂·2H₂O (34 mg, 0.20 mmol) were mixed in methanol (30 mL). The mixture was stirred at room temperature for 30 min to give a blue solution. Single crystals of the complex, suitable for X-ray diffraction, were obtained after 8 days. Yield: 31 mg (62%). IR data (cm⁻¹): 2925, 2853, 1608, 1514, 1407, 1289, 1192, 1126, 1060, 973, 913, 853, 777, 600, 543, 451. UV-Vis (1.03 × 10⁻⁵ mol L⁻¹, MeOH; ε, L mol⁻¹ cm⁻¹): 230 (23,500), 247 (24,100), 280 (16,320), 355 (7,135). Anal. Calcd. (%) for C_{17}H_{14}Br_{2}CuN_{2}O_{2}: C, 40.70; H, 2.81; N, 5.58. Found (%): C, 40.86; H, 2.92; N, 5.47.

2. 4. Synthesis of [Zn₃Cl₂L₂(DMF)₂] (2)

H₂L (44 mg, 0.10 mmol) and ZnCl₂ (27 mg, 0.20 mmol) were mixed in methanol (30 mL). The mixture was stirred at room temperature for 30 min to give a white precipitate. DMF (5 mL) was added to the mixture until the precipitate dissolved. Single crystals of the complex, suitable for X-ray diffraction, were obtained after 17 days. Yield: 27 mg (42%). IR data (cm⁻¹): 2917, 2849, 1632, 1615, 1581, 1533, 1460, 1390, 1276, 1198, 1112, 1071, 978, 911, 863, 800, 677, 602, 539, 464. UV-Vis (1.30 × 10⁻⁵ mol L⁻¹, MeOH; ε, L mol⁻¹ cm⁻¹): 230 (22,370), 245 (23,920), 272 (12,100), 350 (7,630). Anal. Calcd. (%) for C_{40}H_{42}Br_{4}Cl_{2}N_{6}O_{6}Zn_{3}: C, 37.26; H, 3.28; N, 6.52. Found (%): C, 37.43; H, 3.35; N, 6.44.

2. 5. X-ray Crystallography

Single crystal X-ray data for the complexes were collected on a Bruker SMART 1000 CCD diffractometer using the SMART/SAINT software. Empirical absorption corrections were applied with SADABS. All non-hydrogen atoms were refined with anisotropic displacement coefficients. The hydrogen atoms bonded to carbon were included in geometric positions and given thermal parameters equivalent to 1.2 and 1.5 times those of the atom to which they were attached. The C8-C9-C10 group of the Schiff base ligand in complex 1 is disordered over two sites, with occupancies of 0.5 and 0.5 due to the symmetry. The distances of C8–C9 and C9–C10 are restrained to 1.51(1) Å. The atoms C8, C9 and C10 were refined using ISOR instruction. The thermal factors of atoms C8 and C10 were constrained to be equal. Crystallographic data and refinement parameters are given in Table 1, and important interatomic distances and angles are given in Table 2.

### Table 1. Crystallographic data and refinement parameters for the complexes

|   | Complex 1 | Complex 2 |
|---|-----------|-----------|
| Chemical Formula | C₁₇H₁₄Br₂CuN₂O₂ | C₄₀H₄₂Br₄Cl₂N₆O₆Zn₃ |
| Fw | 501.66 | 1289.45 |
| T (K) | 298(2) | 298(2) |
| Crystal system | Monoclinic | Monoclinic |
| Space group | C2/c | P2/c |
| a (Å) | 23.0385(16) | 11.9976(12) |
| b (Å) | 8.0706(11) | 12.9584(12) |
| c (Å) | 247 (23,500), 247 (16,320), 355 (7,135) | 16847.3(7), 2387.8(4) |
| μ (Mo Kα) (cm⁻¹) | 6.052 | 5.003 |
| Dc (g cm⁻³) | 1.978 | 1.793 |
| μ (Mo Kα) (cm⁻¹) | 1.978 | 1.793 |
| Reflections/parameters | 1543/117 | 4457/278 |
| Unique reflections | 955 | 3272 |
| Restraints | 21 | 0 |
| Goodness of fit on F² | 0.0597 | 0.0360 |
| R₁, wR₂ [I ≥ 2σ(I)] | 0.0617, 0.1442 | 0.0517, 0.1302 |
| R₁, wR₂ (all data) | 0.1064, 0.1641 | 0.0744, 0.1436 |

2. 6. Biological Assay

The antibacterial property of the complexes was evaluated by a macro-dilution method using *Staphylococcus aureus*, *Escherichia coli*, and the yeast *Candida parapsi*
lossis. The cultures of bacteria and yeasts were incubated under vigorous shaking. The compounds were dissolved in small amount of DMSO. Concentration of the tested compounds ranging from 0.010 to 2.5 mmol L\(^{-1}\) for the bacteria and yeasts was used in all experiments. The antibacterial activity was characterized by IC\(_{50}\) and MIC values. MIC experiments on subculture dishes were used to assess the minimal microbicidal concentration (MMC). Subcultures were prepared separately in Petri dishes containing competent agar medium and incubated at 30 °C for 48 h. The MMC value was taken as the lowest concentration, which showed no visible growth of microbial colonies in the subculture dishes.

3. Results and Discussion

3.1. Chemistry

The complexes 1 and 2 were facile prepared by the reaction of the Schiff base H\(_2\)L with copper chloride and

![Scheme 2. The synthetic procedure of the complexes](image-url)
zinc chloride, respectively, in methanol (Scheme 2). Single crystals of the complexes were formed by slow evaporation of the solvent at room temperature.

3. 2. Crystal Structure Description

The molecular structure of complex 1 is shown in Fig. 1. The complex is a mononuclear copper(II) species. Molecule of the complex possesses a crystallographic two-fold rotation axis symmetry. The Cu(1) atom is coordinated by the two imine nitrogen and two phenolate oxygen of the Schiff base ligand, forming a tetrahedrally distorted square planar geometry, which is evidenced by the trans bond angles of 154.1(2)° and the cis angles of 87.4(3)–98.6(4)°. The distortion of the square planar coordination results in the deflection of the two benzene rings, which has a dihedral angle of 35.2(3)°. Similarly, the dihedral angle between the two six-membered chelate rings Cu(1)-N(1)-C(7)-C(1)-C(2)-O(1) and Cu(1)-N(1A)-C(7A)-C(1A)-C(2A)-O(1A) is 33.8(3)°. The coordinate bond lengths in the complex are comparable to those observed in the copper(II) complexes with Schiff bases.8 In the crystal structure, the molecules are linked via Br···Br interactions, with a distance of 3.659(4) Å, to form zigzag chains along the x axis (Fig. 2).

The molecular structure of complex 2 is shown in Fig. 3. The complex is a phenolate-bridged trinuclear zinc(II) species, with the two [ZnClL] units connected by the central Zn atom (Zn(2)). Molecule of the complex possesses a crystallographic two-fold rotation axis symmetry. The Zn···Zn distance is 3.227(2) Å. The terminal Zn atom (Zn(1)) shows a distorted square pyramidal coordination geometry, with the two phenolate oxygen atoms (O(1) and O(2)) and the two imine nitrogen atoms (N(1) and N(2)) occupying the basal coordination site, and with a Cl atom occupies the apical position. The Zn(1) atom deviates from the best coordination plane defined by the atoms N(1), N(2), O(1) and O(2) by 0.532(2) Å in direction of the apical Cl atom. The cis and trans bond angles in the basal plane are in the range of 77.24(14)–94.7(2)° and 142.30(17)–155.07(18)°, and those between the apical and basal donor atoms are in the range of 100.25(12)-109.28(14)°. Thus, the coordination is distorted from the ideal geometry of a square pyramid. The bond lengths related to Zn(1) atom

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**Fig. 1.** A perspective view of the molecular structure of complex 1 with the atom labeling scheme. Thermal ellipsoids are drawn at the 30% probability level.

**Fig. 2.** Packing structure for complex 1 viewed along the z axis. Dashed lines represent Br–Br interactions forming zigzag chains along the x axis.

**Fig. 3.** A perspective view of the molecular structure of complex 2 with the atom labeling scheme. Thermal ellipsoids are drawn at the 30% probability level. The carbon hydrogens are omitted for clarity. Atoms labelled with the suffix A or unlabelled are at the symmetry position 1 – x, y, ½ – z.
are 2.06 Å for Zn–O, 2.08 Å for Zn–N and 2.29 Å for Zn–Cl, which are comparable to those observed in Schiff base zinc complexes with square pyramidal coordination. The central Zn atom (Zn(2)), located at the two-fold rotation axis, shows a distorted octahedral coordination geometry. The donor atoms come from two Schiff base ligands (O(1), O(2), O(1A), O(2A)), and two DMF ligands (O(3), O(3A)). The cis and trans bond angles related to Zn(2) are 76.08(14)–96.71(15)° and 169.0(2)–172.65(15)°, respectively. Thus, the coordination is distorted from the ideal geometry of an octahedron. The Zn–O bond lengths related to Zn(2) atom are 2.07–2.11 Å, which are comparable to those observed in Schiff base zinc complexes with octahedral coordination. The [ZnClL] unit is butterfly shaped, with the dihedral angle between the two benzene rings of 33.1(3)°. The bond lengths are also similar to the trinuclear zinc complexes with square pyramidal and octahedral coordination. In the crystal structure, the molecules are linked via Br···Br interactions, with a distance of 3.871(3) Å, to form zigzag chains along the z axis (Fig. 4).

3. 3. IR and UV-Vis Spectra

The medium and broad absorption centered at 3449 cm⁻¹ in the spectrum of H₂L substantiates the presence of O–H groups. The intense band indicative of the C=O groups of the DMF ligands of complex 2 are observed at 1632 cm⁻¹. The strong absorption at 1632 cm⁻¹ for H₂L is assigned to the azomethine groups, ν(C=N), which is shifted to lower wave numbers 1608 cm⁻¹ for complexes 1 and 1615 cm⁻¹ for complex 2. The weak bands in the low wave numbers 450–550 cm⁻¹ are due to the vibration of the Cu–O and Cu–N bonds.

In the electronic spectra of complexes 1 and 2 measured in methanol, the intense bands observed at about 230–280 nm for the complexes are assigned to intra-ligand π–π* transitions. The complexes displayed bands centered at 270–280 nm, which can be assigned to the n–π* transition. The charge transfer LMCT bands are located in the range of 350 nm.

3. 4. Antibacterial Activity

The antibacterial results are summarized in Table 3. The Schiff base H₂L showed activity against E. coli, while no activity on S. aureus and C. parapsilosis. Both the copper and the zinc complexes have higher activities than the free Schiff base. The copper complex showed strong activity against S. aureus and E. coli, and weak activity against C. parapsilosis. The zinc complex showed medium activity against S. aureus, and weak activities against E. coli and C. parapsilosis. Obviously, the copper complex is more effective than the zinc complex. The copper complex has the most activity against S. aureus, with IC₅₀ and MIC values of 0.16 and 0.27 mmol L⁻¹, which deserves further study. As a comparison, the copper complex has similar antibacterial activities against S. aureus and E. coli to the Schiff base manganese(III) complex and the Schiff base copper(II) complexes. However, it has weaker activity against the yeast C. para-

Table 3. Antibacterial property of the Schiff base and the complexes

| Compound | S. aureus | E. coli | C. parapsilosis |
|----------|-----------|---------|----------------|
|          | IC₅₀      | MIC     | IC₅₀ | MIC | IC₅₀ | MIC |
| H₂L      | >2.50     | >2.50   | 1.63 | 2.50 | >2.50 | >2.50 |
| 1        | 0.27      | 0.16    | 0.56 | 0.32 | 2.17 | 1.25 |
| 2        | 1.15      | 0.62    | 1.83 | 1.25 | 3.39 | 2.50 |

H₂L = mmol L⁻¹
psilosis when compared with the manganese and copper complexes.

4. Conclusion

In summary, with the bis-Schiff base \( N,N'-\text{bis}(4\text{-bromosalicylidene})\text{propane}-1,3\text{-diamine} \) a mononuclear copper(II) complex and a phenolato-bridged trinuclear zinc(II) complex were synthesized. The complexes were characterized by physical-chemical methods, and their structures were confirmed by single crystal X-ray determination. The Schiff base ligand coordinates to the metal atoms through the phenolate oxygen and imine nitrogen. The complexes have significant antibacterial activities on the bacteria \( Staphylococcus aureus \) and \( Escherichia coli \), and the yeast \( Candida parapsilosis \).

Supplementary Material

CCDC 2007656 (1) and 2007657 (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.

5. References

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Sintetizirali smo enojedrni bakrov(II) kompleks [CuL] (1) in trijedrni cinkov(II) kompleks s fenolatnim mostom [Zn₃Cl₂L₂(DMF)₂] (2), kjer je L deprotonirana oblika N,N'-bis(4-bromosaliciliden)propan-1,3-diamina (H₂L), ter ju okarakterizirali z elementno analizo, IR in UV-Vis spektroskopijo in rentgensko monokristalno analizo. Cu atom v kompleksu 1 ima kvadratno planarno koordinacijo, medtem ko imata terminalna Zn atoma v kompleksu 2 kvadratno piramidalno koordinacijo in centralni Zn atom oktaedrično koordinacijo. Protimikrobno aktivnost kompleksov smo testirali na bakterijah Staphylococcus aureus in Escherichia coli ter na glivi Candida parapsilosis.