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# Synthesis, Structures, and Antimicrobial Activity of Nickel(II) and Zinc(II) Complexes with Schiff Bases Derived from 3-Bromosalicylaldehyde[1]

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**Abstract**—The Schiff bases 2-bromo-6-[(3-cyclohexylaminopropylimino)methyl]phenol (HCMP) and 2-bromo-6-[(3-dimethylaminopropylimino)methyl]phenol (HDMP) derived from 3-bromosalicylaldehyde with N-cyclohexylpropane-1,3-diamine and N,N-dimethylpropane-1,3-diamine, respectively, and their nickel(II) and zinc(II) complexes $[Ni(CMP)_2]$ (**I**) and $[ZnCl_2(HDMP)]$ (**II**) have been prepared and characterized by elemental analyses, IR, and single crystal X-ray crystallographic determination. The crystal of **I** is monoclinic: space group $P2_1/c$, $a = 12.0304(6)$, $b = 13.1594(6)$, $c = 10.2445(5)$ Å, $\beta = 101.019(1)°$, $V = 1591.9(1)$ Å$^3$, $Z = 2$. The crystal of II is monoclinic: space group $C2/c$, $a = 22.286(5)$, $b = 12.210(3)$, $c = 14.513(3)$ Å, $\beta = 124.118(3)°$, $V = 3269.5(13)$ Å$^3$, $Z = 8$. The Schiff base HCMP coordinates to the Ni atom through the phenolate O, imine N, and amine N atoms, while the Schiff base HDMP coordinates to the Zn atom through the phenolate O and imine N atoms. The effect of these complexes on the antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* were studied.

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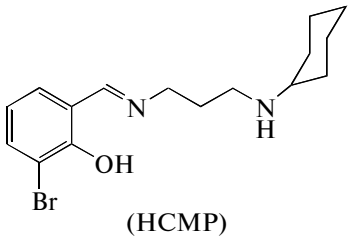
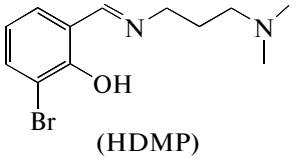
## INTRODUCTION

Schiff bases are a kind of versatile ligands in coordination chemistry [1–3]. In recent years, metal complexes of Schiff bases have attracted considerable attention due to their remarkable biological activity, such as antifungal, antibacterial and antitumor [4–6]. It has been shown that the 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 interesting biological activity [6–10]. To the best of our knowledge, no complexes have been reported with the Schiff bases 2-bromo-6-[(3-cyclohexylaminopropylimino)methyl]phenol (HCMP) and 2-bromo-6-[(3-dimethylaminopropylimino)methyl]phenol (HDMP):




(HCMP)




(HDMP)

In the present paper, the preparation, characterization and antimicrobial activity of new nickel(II) and zinc(II) complexes $[Ni(CMP)_2]$ (**I**) and $[ZnCl_2(HDMP)]$ (**II**) derived from the Schiff bases are reported.

[1] The article is published in the original.

## EXPERIMENTAL

**Material and methods.** 3-Bromosalicylaldehyde, N-cyclohexylpropane-1,3-diamine, and N,N-dimethylpropane-1,3-diamine were purchased from Fluka. Other reagents and solvents were analytical grade and

were used without further purification. Elemental (C, H, and N) analyses were made on a PerkinElmer Model 240B automatic analyser. Nickel and zinc analyses were carried out by EDTA titration. Infrared (IR) spectra were recorded on an IR-408 Shimadzu 568 spectrophotometer. X-ray diffraction was carried out on a Bruker SMART 1000 CCD area diffractometer.

**Synthesis of HCMP**. The Schiff base ligand HCMP was prepared by the condensation of equimolar quantities of 3-bromosalicylaldehyde (0.201 g, 1 mmol) with N-cyclohexylpropane-1,3-diamine (0.156 g, 1 mmol) in methanol (30 mL) at ambient temperature for 1 h. Then the methanol was evaporated by distillation, yielding yellow solid of the Schiff base.

For $C_{16}H_{23}N_2OBr$

| | | | |
|---|---|---|---|
| anal. calcd., %: | C, 56.6; | H, 6.8; | N, 8.3. |
| Found, %: | C, 56.8; | H, 6.9; | N, 8.2. |

**Synthesis of HDMP**. The Schiff base ligand HDMP was prepared by the condensation of equimolar quantities of 3-bromosalicylaldehyde (0.201 g, 1 mmol) with N,N-dimethylpropane-1,3-diamine (0.285 g, 1 mmol) in methanol (30 mL) at ambient temperature for 1 h. Then the methanol was evaporated by distillation, yielding yellow solid of the Schiff base.

For $C_{12}H_{17}N_2OBr$

| | | | |
|---|---|---|---|
| anal. calcd., %: | C, 50.5; | H, 6.0; | N, 9.8. |
| Found, %: | C, 50.4; | H, 6.1; | N, 9.8. |

**Synthesis of complex I.** The Schiff base HCMP (0.34 g, 1.0 mmol) was dissolved by methanol (20 mL), to which was added with stirring a methanol solution (10 mL) of $Ni(CH_3COO) \cdot 4H_2O$ (0.25 g, 1.0 mmol). The mixture was stirred for 1 h at ambient temperature to give a green solution. Green block-shaped single crystals suitable for X-ray diffraction were formed by slow evaporation of the solution in air for several days. The yield was 49% (based on HCMP). IR data ($\nu$, $cm^{-1}$): 3272 w, 1625 s, 1539 s, 1475 m, 1438 m, 1423 w, 1387 m, 1254 s, 1225 m, 1113 m, 1083 m, 967 m, 831 m, 733 m, 573 w, 539 w, 462 w.

For $C_{32}H_{44}N_4O_2Br_2Ni$

| | | | | |
|---|---|---|---|---|
| anal. calcd., %: | C, 52.3; | H, 6.0; | N, 7.6; | Ni, 8.0. |
| Found, %: | C, 52.1; | H, 6.1; | N, 7.7; | Ni, 8.2. |

**Synthesis of complex II.** The Schiff base HDMP (0.28 g, 1.0 mmol) was dissolved by methanol (20 mL), to which was added with stirring a methanol solution (10 mL) of $ZnCl_2$ (0.14 g, 1.0 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 was 63% (based on HDMP). IR data ($\nu$, $cm^{-1}$): 3251 w, 1626 s, 1603 s, 1536 s, 1485 w, 1437 m, 1422 w, 1396 m, 1351 w, 1297 m, 1223 s, 1120 m, 973 w, 837 m, 735 w, 654 w, 628 w, 572 w, 543 w, 455 w.

For $C_{12}H_{17}N_2OCl_2BrZn$

| | | | | |
|---|---|---|---|---|
| anal. calcd., %: | C, 34.2; | H, 4.1; | N, 6.6; | Zn, 15.5. |
| Found, %: | C, 34.3; | H, 4.0; | N, 6.7; | Zn, 15.7. |

**X-ray structure determination**. Data were collected from selected crystals mounted on glass fibres. The data for the two complexes were processed with SAINT [11] and corrected for absorption using SADABS [12]. Multi-scan absorption corrections were applied with $\psi$-scans [13]. 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 [14]. The amino hydrogen atoms were located from difference Fourier map and refined isotropically with N–H distances restrained to 0.90(1) Å. The remaining 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 carbon and nitrogen atoms. The crystallographic data for the complexes are listed in Table 1, selected bond lengths and bond angles for **I** and **II** are given in Table 2.

A full detail of data collections and structure determinations has been deposited with the Cambridge Crystallographic Data Centre (nos. 885818 (**I**), 885819 (**II**); deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

## RESULTS AND DISCUSSION

The Schiff bases HCMP and HDMP were prepared by the condensation of equimolar quantities of 3-bromosalicylaldehyde with N-cyclohexylpropane-1,3-diamine and N,N-dimethylpropane-1,3-diamine, respectively, in methanol at ambient temperature [10]. The Schiff bases prepared in this way are formed in nearly quantitative yields and are of high purity. The complexes were readily synthesized by reaction of the corresponding Schiff base and metal salt in methanol at ambient temperature. All the compounds are very stable at room temperature in the solid state, and are soluble in common organic solvents, such as methanol, ethanol, chloroform, and acetonitrile. The results of the elemental analyses are in accord with the composition suggested for the ligands and the complexes.

**Table 1.** Crystallographic data and refinement parameters for structures **I** and **II**

| Parameter | Value | |
|---|---|---|
| | **I** | **II** |
| Habit, color | Block, green | Block, colorless |
| Formula weight | 735.2 | 421.5 |
| Temperature, K | 298(2) | 298(2) |
| Crystal size, mm | 0.18 × 0.17 × 0.17 | 0.23 × 0.18 × 0.17 |
| Radiation (λ, Å) | Mo$K_\alpha$ (0.71073) | Mo$K_\alpha$ (0.71073) |
| Crystal system | Monoclinic | Monoclinic |
| Space group | $P2_1/c$ | $C2/c$ |
| Unit cell dimensions: | | |
| $a$, Å | 12.0304(6) | 22.286(5) |
| $b$, Å | 13.1594(6) | 12.210(3) |
| $c$, Å | 10.2445(5) | 14.513(3) |
| β, deg | 101.019(1) | 124.118(3) |
| $V$, Å$^3$ | 1591.9(1) | 3269.5(13) |
| $Z$ | 2 | 8 |
| $\rho_{calcd}$, g cm$^{-3}$ | 1.534 | 1.712 |
| $F$(000) | 756 | 1680 |
| Absorption coefficient, mm$^{-1}$ | 3.155 | 4.266 |
| θ Range for data collection, deg | 2.5–27.6 | 2.2–25.0 |
| Index ranges, $h$, $k$, $l$ | $-12 \le h \le 14$; $-9 \le k \le 15$; $-12 \le l \le 12$ | $-26 \le h \le 20$; $-13 \le k \le 14$; $-16 \le l \le 17$ |
| Reflections collected | 8294 | 8294 |
| Independent reflections | 2964 | 3000 |
| Data/parameters | 2476/190 | 2104/177 |
| Final $R$ indices ($I > 2\sigma(I)$) | $R_1 = 0.0265$, $wR_2 = 0.0608$ | $R_1 = 0.0344$, $wR_2 = 0.0714$ |
| $R$ indices (all data) | $R_1 = 0.0353$, $wR_2 = 0.0647$ | $R_1 = 0.0612$, $wR_2 = 0.0810$ |
| Goodness-of-fit on $F^2$ | 1.044 | 1.034 |
| $\Delta\rho_{max}/\Delta\rho_{min}$, $e$ Å$^{-3}$ | 0.349/–0.478 | 0.430/–0.500 |

**Table 2.** Selected bond lengths (Å) and bond angles (deg) for compounds for **I** and **II**

| Bond | $d$, Å | Bond | $d$, Å |
|---|---|---|---|
| | **I** | | |
| Ni(1)–O(1) | 2.0245(13) | Ni(1)–N(1) | 2.0500(16) |
| Ni(1)–N(2) | 2.2527(17) | | |
| | **II** | | |
| Zn(1)–O(1) | 1.939(3) | Zn(1)–N(1) | 2.025(3) |
| Zn(1)–Cl(1) | 2.2502(10) | Zn(1)–Cl(2) | 2.2101(12) |
| Angle | ω, deg | Angle | ω, deg |
| | **I** | | |
| O(1)Ni(1)N(2) | 93.63(6) | O(1)Ni(1)N(1) | 87.15(6) |
| N(1)Ni(1)N(2) | 84.08(6) | | |
| | **II** | | |
| O(1)Zn(1)N(1) | 95.64(12) | O(1)Zn(1)Cl(2) | 110.63(8) |
| O(1)Zn(1)Cl(1) | 109.99(8) | N(1)Zn(1)Cl(2) | 117.37(9) |
| N(1)Zn(1)Cl(1) | 106.44(8) | Cl(2)Zn(1)Cl(1) | 115.02(5) |

For the IR spectra of both complexes, the strong bands observed at 1625 cm$^{-1}$ for **I** and 1626 cm$^{-1}$ for **II** are assigned to the azomethine group vibration.

The molecular structure of complex **I** is shown in Fig. 1a. The complex is a centrosymmetric mononuclear nickel(II) compound. The Ni atom is coordinated by two phenolate O, two imine N, and two amine N atoms from two CMP ligands, forming an octahedral geometry. The Schiff base ligand CMP acts as a tridentate ligand, forming two six-membered chelate rings with the Ni atom. The two axial bonds (Ni(1)–N(2) and Ni(1)–N(2$A$), symmetry code for $A$: $1 - x, -y, 2 - z$) are much longer than the basal bonds, which is caused by the Jahn–Teller effects. The bond distances subtended at the Ni atom are comparable to those observed in the similar nickel(II) complexes with Schiff bases [15–17].

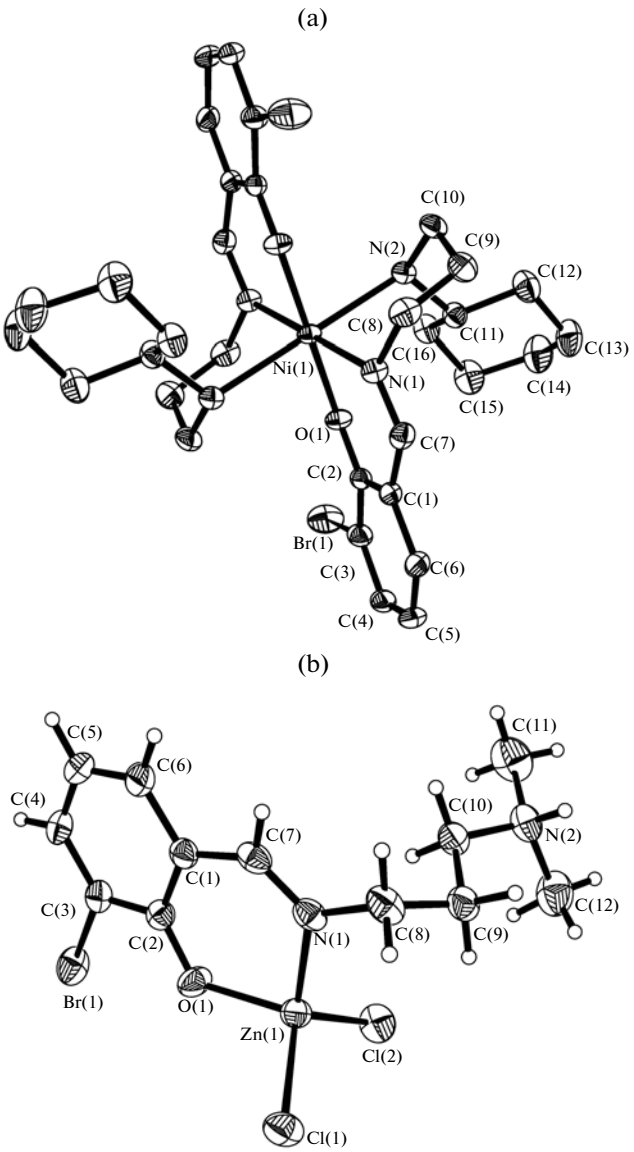



**Fig. 1.** Perspective view of the complex **I** (a) and **II** (b) with 30% probability thermal ellipsoids.

**Table 3.** MIC values (μg/mL) for the antimicrobial activities of the tested compounds

| Compounds | *Staphylococcus aureus* | *Escherichia coli* | *Candida albicans* |
|---|---|---|---|
| HCMP | 256 | 256 | >512 |
| HDMP | 256 | 128 | >512 |
| **I** | 16 | 32 | 128 |
| **II** | 4 | 8 | 64 |
| Tetracycline | 0.32 | 2.12 | >1024 |

The molecular structure of complex **II** is shown in Fig. 1b. The Zn atom in the mononuclear complex is coordinated by one phenolate O and one imine N atoms of a HDMP ligand and by two chloride atoms, forming a tetrahedral geometry. The Schiff base ligand HDMP acts as a bidentate ligand, forming a six-membered chelate ring with the Zn atom. The coordinate bond angles are in the range 95.6(1)°–117.4(1)°, as well as the coordinate bond distances are typical and comparable with those observed in the similar zinc(II) complexes with Schiff bases [18, 19], suggesting a slightly distorted tetrahedral coordination of the Zn atom. In the crystal structure of **II**, molecules are linked through intermolecular N(2)–H(2)···Cl(1) hydrogen bonds (N(2)···Cl(1)$^{i}$ 3.093(4), H(2)···Cl(1)$^{i}$ 2.21(1) Å, angle N(2)H(2)··Cl(1)$^{i}$ 169(4)° ($^{i}x$, $2 - y$, $1/2 + z$)), forming chains running along the $z$ axis, as shown by Fig. 2.

Qualitative determination of antimicrobial activity was done using the disk diffusion method [20, 21]. The results are summarized in Table 3. A comparative study of minimum inhibitory concentration (MIC) values of the Schiff bases and the two complexes indicate that the two complexes have better activity than the free Schiff bases. 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 [22]. 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 microorganisms.

From Table 3, it is obvious that the zinc complex **II** shows greater antibacterial and antifungi activities against *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* when compared to the Schiff bases and the nickel complex **I**. For *Staphylococcus aureus* and *Escherichia coli*, even though the activity of the zinc complex is stronger than the other tested materials, it is still much less than the control drug Tetracycline. But for *Candida albicans*, both complexes show stronger activity than the Schiff bases and Tetracycline. Further work needs to be carried out to investigate the structure-activity relationship.

## ACKNOWLEDGMENTS

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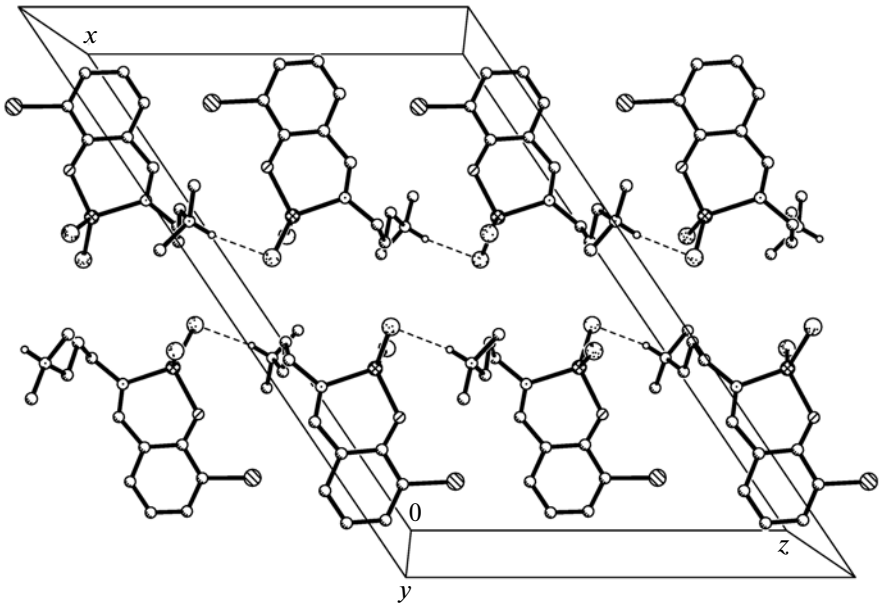


**Fig. 2.** Molecular packing of the complex **II** viewed along the *z* axis.

20877036) and Top-class foundation of Pingdingshan University (no. 2008010).

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