# Zinc(II) and Nickel(II) Complexes Derived from 2-Bromo-6-[(2-Isopropylaminoethylimino)methyl]phenol: Synthesis, Structures, and Antimicrobial Activity<sup>1</sup>

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Abstract—The Schiff base 2-bromo-6-[(2-isopropylaminoethylimino)methyl]phenol (HL), derived from 3-bromosalicylaldehyde with *N*-isopropylethane-1,2-diamine, and its zinc(II) and nickel(II) complexes  $[Zn(HL)_2(NCS)_2]$  (I) and  $[Ni(HL)_2(N_3)_2] \cdot 0.25H_2O$  (II) have been prepared and characterized by elemental analyses, IR, and single crystal X-ray crystallographic determination. The crystal of I is orthorhombic: space group *Pbca*, *a* = 13.6928(9), *b* = 9.7203(6), *c* = 22.926(1) Å, *V* = 3051.4(3) Å^3, *Z* = 4. The crystal of II is triclinic: space group *P*T, *a* = 8.0212(7), *b* = 12.744(1), *c* = 15.590(2) Å,  $\alpha = 104.802(3)^{\circ}$ ,  $\beta = 90.561(3)^{\circ}$ ,  $\gamma = 103.130(3)^{\circ}$ , *V* = 1496.6(2) Å^3, *Z* = 1. The zwitterionic Schiff base ligands coordinate to the metal atoms through phenolate O, imine N, and amine N atoms. Each metal atom in the complexes is in octahedral coordination. 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 have long been considered as a kind of interesting ligands in coordination chemistry [1-3]. In recent years, metal complexes of Schiff bases have attracted dramatically attention due to their versatile 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<sub>2</sub>O, N<sub>2</sub>S, NO<sub>2</sub> or NSO donor sets, have interesting biological activity [7–10]. Recent research indicates that the halide-substituent groups in aromatic rings of Schiff bases can severely increase the antimicrobial activity [11]. To the best of our knowledge, no complexes have been reported with the bromo-substituted Schiff base 2-bromo-6-[(2-isopropylaminoethylimino)methyl]phenol (HL):



In the present paper, the preparation, characterization and antimicrobial activity of new zinc(II) and nickel(II) complexes derived from the Schiff base ligand are reported.

## **EXPERIMENTAL**

**Material and methods.** 3-Bromosalicylaldehyde and N-isopropylethane-1,2-diamine 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. Zinc and nickel 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 HL. The Schiff base ligand HL was prepared by the condensation of equimolar quantities of 3-bromosalicylaldehyde (0.201 g, 1 mmol) with N-isopropylethane-1,2-diamine (0.102 g, 1 mmol) in methanol (30 mL) at ambient temperature for 1 h. Then the methanol was evaporated by distillation, yielding yellow gummy product of the Schiff base.

For $C_{12}H_{17}N_2OBr$			
anal. calcd., %:	C, 50.5;	Н, 6.0;	N, 9.8.
Found, %:	C, 50.7;	H, 6.1;	N, 9.7.

Synthesis of the complex  $[Zn(HL)_2(NCS)_2]$  (I). The Schiff base HL (0.285 g, 1.0 mmol) was dissolved by methanol (20 mL), to which was added with stirring a methanol solution (20 mL) of  $Zn(CH_3COO) \cdot 2H_2O$ 

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(0.219 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 38% (based on HL).

For  $C_{26}H_{34}Br_2N_6O_2S_2Zn$ 

anal. calcd., %: C, 41.5; H, 4.6; N, 11.2; Zn, 8.7. Found, %: C, 41.4; H, 4.5; N, 11.0; Zn, 8.9.

Selected IR data (v, cm<sup>-1</sup>): 2062 s, v(NCS), 1622 s v(C=N).

Synthesis of the complex  $[Ni(HL)_2(N_3)_2]$  • 0.25H<sub>2</sub>O (II). The Schiff base HL (0.285 g, 1.0 mmol) was dissolved by methanol (20 mL), to which was added with stirring a methanol solution (20 mL) of Ni(CH<sub>3</sub>COO) • 4H<sub>2</sub>O (0.249 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 53% (based on HL).

For  $C_{48}H_{69}Br_4N_{20}Ni_2O_{4.5}$ anal. calcd., %: C, 40.2; H, 4.8;

anal. calcd., %: C, 40.2; H, 4.8; N, 19.5; Ni, 8.2. Found, %: C, 40.1; H, 4.9; N, 19.6; Zn, 8.3.

Selected IR data (v, cm<sup>-1</sup>): 2040 s v(N<sub>3</sub>), 1630 s v(C=N).

X-ray diffraction. Data were collected from selected crystals mounted on glass fibers. The data for the two complexes were processed with SAINT [12] and corrected for absorption using SADABS [13]. Multiscan absorption corrections were applied with  $\psi$ -scans [14]. The structures were solved by direct methods using the program SHELXS-97 and refined by full-matrix least-squares techniques on  $F^2$  using anisotropic displacement parameters [15]. The amino hydrogen atoms in I were located from a difference Fourier map and refined isotropically, with N-H and H.H distances restrained to 0.90(1) and 1.43(2) Å, respectively. 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 Table 1.

Supplementary material has been deposited with the Cambridge Crystallographic Data Centre (nos. 945894 (I) and 945895 (II); deposit@ ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

#### **RESULTS AND DISCUSSION**

The Schiff base HL was prepared by the condensation of equimolar quantities of 3-bromosalicylaldehyde with *N*-isopropylethane-1,2-diamine in methanol at ambient temperature [10]. The Schiff base prepared in this way is formed in nearly quantitative yield and of high purity. The complexes were readily synthesized by reaction of the Schiff base and metal salts 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, chloroform, and acetonitrile. The results of the elemental analyses are in accord with the composition suggested for the ligand and the complexes.

For the IR spectra of both complexes, the strong bands observed at  $1622 \text{ cm}^{-1}$  for I and  $1630 \text{ cm}^{-1}$  for II are assigned to the azomethine group vibrations. The intense bands at  $2062 \text{ cm}^{-1}$  for I and  $2040 \text{ cm}^{-1}$  for II are assigned to the stretching vibrations of the thiocyanate and azide ligands, respectively.

The molecular structures of complexes I and II are shown in figure. Selected bond distances and angles are listed in Table 2. The complexes are structurally similar centrosymmetric mononuclear compounds, with the metal atoms lying on the inversion centers. Complex I has only one complex molecule, while the asymmetric unit of complex II contains two complex molecules and one quarter disordered water molecule. Each metal atom in the complexes is coordinated by two phenolate O and two imine N atoms from two zwitterionic Schiff base ligands, defining the equatorial plane, and by two N atoms from two pseudohalide ligands (NCS for I and  $N_3$  for II), occupying the two axial positions, generating an octahedral geometry. The Schiff base ligand acts as a zwitterionic tridentate ligand, forming one six-membered chelate ring with the metal center. The amino group of the Schiff base ligand is protonated, which form a hydrogen bond with the phenolate O atom of adjacent Schiff base ligand. The two axial bonds are much longer than the basal bonds, which is caused by the Jahn-Teller effects. The bond distances subtended at the metal atoms are comparable to those observed in similar zinc(II) and nickel(II) complexes with Schiff bases [16-20].

Qualitative determination of antimicrobial activity was done using the disk diffusion method [21, 22]. The results are summarized in Table 3. A comparative study of minimum inhibitory concentration (MIC) values of the Schiff base and the complexes indicate that the two complexes have more effective activity than the free Schiff base. 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 [23]. On chelating, the polarity of the metal atoms will be reduced to a greater extent due to the overlap of the

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Table 1.	Crystallographic	data and	experimental	details for	r I and II
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Paramatar	Value			
Falameter	Ι	II		
Habit; color	Block; colorless	Block; green		
Formula weight	751.9	1435.2		
Temperature, K	298(2)	298(2)		
Crystal size, mm	$0.17 \times 0.17 \times 0.13$	$0.23\times0.23\times0.20$		
Radiation, $\lambda$ , Å	$MoK_{\alpha}$ (0.71073)	$MoK_{\alpha}$ (0.71073)		
Crystal system	Orthorhombic	Triclinic		
Space group	Pbca	$P\overline{1}$		
Unit cell dimensions:				
a, Å	13.6928(9)	8.0212(7)		
b, Å	9.7203(6)	12.744(1)		
c, Å	22.926(1)	15.590(2)		
α, deg	90	104.802(3)		
β, deg	90	90.561(3)		
γ, deg	90	103.130(3)		
$V, Å^3$	3051.4(3)	1496.6(2)		
Ζ	4	1		
$\rho_{calcd}, g \ cm^{-3}$	1.637	1.584		
<i>F</i> (000)	1520	725		
Absorption coefficient, mm <sup>-1</sup>	3.595	3.358		
$\theta$ Range for data collection, deg	2.32-25.75	1.87-25.50		
Index ranges, $h, k, l$	$-16 \le h \le 16, -10 \le k \le 11, -24 \le l \le 27$	$-9 \le h \le 8, -15 \le k \le 14, -18 \le l \le 18$		
Reflections collected	28392	14431		
Independent reflections $(R_{int})$	2920 (0.0521)	5544 (0.0356)		
Reflections with $(I > 2\sigma(I))$	2232	4071		
Data/parameters	2920/186	5544/365		
Restraints	3	6		
Goodness-of-fit on $F^2$	1.035	1.044		
Final <i>R</i> indices, $(I > 2\sigma(I))$	$R_1 = 0.0708, wR_2 = 0.1525$	$R_1 = 0.0448, wR_2 = 0.1149$		
<i>R</i> indices (all data)	$R_1 = 0.0945, wR_2 = 0.1677$	$R_1 = 0.0713, wR_2 = 0.1306$		
Largest difference peak and hole, $e \text{ Å}^{-3}$	1.277, -1.153	1.153, -0.702		

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 can be seen that in general the zinc complex I shows greater antibacterial and antifungi activities against *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* when compared to the nickel complex II. And, it is obvious that both complexes have more effective activities than the

free Schiff base HL. For *Staphylococcus aureus* and *Escherichia coli*, the activities of the complexes are somewhat less than the control drug Tetracycline. But for *Candida albicans*, the complexes have stronger activities than Tetracycline. Further work needs to be carried out to investigate the structure-activity relationship.

Thus, a new Schiff base ligand 2-bromo-6-[(2-isopropylaminoethylimino)methyl]phenol and its zinc(II) and nickel(II) complexes were prepared and characterized. The crystal structures of both complexes were confirmed by X-ray single crystal structure determination. The metal atoms in the complexes are in octahedral coordination. The antimicrobial test shows that



Perspective view of the complexes I (a) and II (b) with 30% probability thermal ellipsoids. Hydrogen bonds are drawn as dashed lines.

Bond	d, Å	Bond	<i>d</i> , Å
		I	
Zn(1)–O(1)	2.024(4)	Zn(1)-N(1)	2.071(5)
Zn(1) - N(3)	2.518(10)		
	1	й	•
Ni(1)-O(1)	2.043(3)	Ni(1)-N(1)	2.077(3)
Ni(1)–N(3)	2.131(4)	Ni(2)–O(2)	2.049(3)
Ni(2)-N(6)	2.093(4)	Ni(2)–N(8)	2.151(4)
Angle	ω, deg	Angle	ω, deg
		Ι	
$O(1)Zn(1)O(1)^{#1}$	180	$O(1)Zn(1)N(1)^{#1}$	91.38(18)
O(1)Zn(1)N(1)	88.62(18)	$N(1)Zn(1)N(1)^{#1}$	180
$O(1)Zn(1)N(3)^{\#1}$	89.1(2)	$N(1)Zn(1)N(3)^{#1}$	94.2(2)
O(1)Zn(1)N(3)	90.9(2)	N(1)Zn(1)N(3)	85.8(2)
$N(3)Zn(1)N(3)^{\#1}$	180		
		II	
O(1)Ni(1)O(1) <sup>#2</sup>	180	$O(1)Ni(1)N(1)^{#2}$	92.01(12)
O(1)Ni(1)N(1)	87.99(12)	N(1)Ni(1)N(1) <sup>#2</sup>	180
O(1)Ni(1)N(3) <sup>#2</sup>	89.90(14)	N(1)Ni(1)N(3)	93.05(14)
O(1)Ni(1)N(3)	90.10(14)	N(1)Ni(1)N(3)	86.95(14)
N(3)Ni(1)N(3) <sup>#2</sup>	180	O(2)Ni(2)O(2) <sup>#3</sup>	180
O(2)Ni(2)N(6) <sup>#3</sup>	91.52(13)	O(2)Ni(2)N(6)	88.48(13)
N(6)Ni(2)N(6) <sup>#3</sup>	180	O(2)Ni(2)N(8) <sup>#3</sup>	89.67(16)
N(6)Ni(2)N(8) <sup>#3</sup>	91.42(16)	O(2)Ni(2)N(8)	90.33(16)
N(6)Ni(2)N(8)	88.58(16)	N(8)Ni(2)N(8) <sup>#3</sup>	180

Table 2. Selected bond distances (Å) and angles (deg) for I and  $II^*$ 

\* Symmetry codes:  ${}^{\#1}2 - x, 1 - y, 1 - z; {}^{\#2}-x, 1 - y, 1 - z; {}^{\#3}2 - x, 1 - y, 2 - z.$ 

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Compound	Staphylococcus aureus	Escherichia coli	Candida albicans
HL	64	256	>1024
Ι	2	8	32
II	8	16	64
Tetracycline	0.32	2.12	>1024

**Table 3.** MIC values  $(\mu g/mL)$  for the antimicrobial activities of the tested compounds

both complexes have effective activities against *Sta-phylococcus aureus*, *Escherichia coli*, and *Candida al-bicans*.

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