

Synthesis, X-Ray Crystal Structures and Urease Inhibitory Activity of 3,5-Dihydroxy-*N'*-(pyridin-2-ylmethylene) benzohydrazide and its Copper(II) and Nickel(II) Complexes

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Abstract

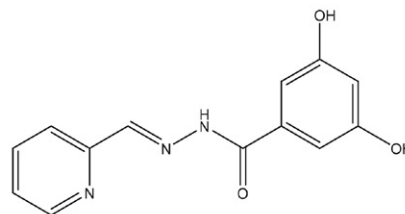
Hydrazone compounds have interesting biological activities. In this work, a new hydrazone compound 3,5-dihydroxy-*N'*-(pyridin-2-ylmethylene)benzohydrazide (HL) was synthesized and characterized by IR, UV-Vis, ¹H and ¹³C NMR spectroscopy. The compound reacts with copper chloride and nickel acetate, respectively, to afford metal complexes [CuCl₂(HL)]·CH₃OH (**1**·CH₃OH) and [NiL₂]·2CH₃OH·2H₂O (**2**·2CH₃OH·2H₂O). The complexes were characterized by elemental analysis, and IR and UV-Vis spectroscopy. Structures of HL and the complexes were further confirmed by single crystal X-ray determination. The hydrazone ligand in complex **1** adopts neutral form and coordinates to Cu ion through pyridine nitrogen, imino nitrogen and carbonyl oxygen atoms. The hydrazone ligands in complex **2** adopt monoanionic form and coordinate to Ni ion through pyridine nitrogen, imino nitrogen and enolate oxygen atoms. The Cu atom in complex **1** is in square pyramidal coordination, and the Ni atom in complex **2** is in octahedral coordination. The compounds were tested for their urease inhibitory activities. Complex **1** has remarkable activity on *Jack bean* urease (IC₅₀ = 0.5 ± 0.1 μmol L⁻¹).

Keywords: Hydrazone; Copper complex; Nickel complex; X-ray crystal structure; Urease inhibition.

1. Introduction

Urease is present in most organisms like bacteria, fungi, algae, plants, and also in soil. *Jack bean* urease is a Ni-containing enzyme. Urea is a widely used fertilizer, which is stable in solution. However, the hydrolysis of urea to ammonia by the catalytic reaction of urease has a rate 10¹⁴ times faster than that without urease. This process causes significant increase of the alkalinity of soil which leads to the damage of plants by depriving them from essential nutrients.¹ In addition, urease plays an important role in many pathogenic processes in human beings and animals. It showed a major role in urinary catheter incrustation, peptic ulceration, pyelonephritis, kidney stone, hepatic encephalopathy, urolithiasis, and arthritis.² Thus, it is necessary to inhibit the activity of urease. A number of urease inhibitors have been described in literature. However, most of them were prevented from being used because of low inhibition efficiency.³

Schiff bases and their metal complexes have displayed interesting structures and significant biological activities.⁴ Recent research indicates that metal complexes with Schiff base ligands have potential urease inhibitory activity.⁵ We have reported a series of Schiff base complexes as urease inhibitors.⁶ Hydrazone is a special kind of Schiff base; its complexes have interesting catalytic and urease inhibitory activities.⁷ Pyridine is a biological active group. A search of literature indicates that urease inhibi-



Scheme 1. The hydrazone compound HL.

tors with pyridinyl derived hydrazone complexes have seldom been studied. To construct new hydrazone complexes, and to explore new urease inhibitors, in this work, a new hydrazone compound 3,5-dihydroxy-*N'*-(pyridin-2-ylmethylene)benzohydrazide (HL; Scheme 1) and two complexes $[\text{CuCl}_2(\text{HL})]\cdot\text{CH}_3\text{OH}$ ($1\cdot\text{CH}_3\text{OH}$) and $[\text{NiL}_2]\cdot 2\text{CH}_3\text{OH}\cdot 2\text{H}_2\text{O}$ ($2\cdot 2\text{CH}_3\text{OH}\cdot 2\text{H}_2\text{O}$) are presented.

2. Experimental

2. 1. Materials and Measurements

2-Pyridinecarboxaldehyde and 3,5-dihydroxybenzohydrazide were purchased from Macklin Chemical Co. Ltd. Copper chloride, nickel acetate and methanol were obtained from Liaodong Chemical Co. Ltd. All solvents and other chemicals used were commercially available and used as received. CHN elemental analyses were performed on a Perkin-Elmer 240C elemental analyzer. IR spectra were recorded on a Nicolet AVATAR 360 spectrophotometer as KBr pellets in the 4000–400 cm^{-1} region. UV-Vis spectra were recorded on a Lambda 35 spectrophotometer. DDS-11A conductivity meter was used to determine molar conductivity values of the complexes. Bruker 500 MHz instrument was used to determine ^1H and ^{13}C NMR spectra of HL. Single crystal structures of HL and the complexes were determined with a Bruker Apex II CCD diffractometer.

2. 2. Synthesis of HL

2-Pyridinecarboxaldehyde (1.07 g, 0.010 mol) and 3,5-dihydroxybenzohydrazide (1.68 g, 0.010 mol) were dissolved in 50 mL methanol. The reaction mixture was refluxed for 20 min, and with the solvent removed by distillation under reduced pressure. The white powder was re-crystallized from methanol to give crystalline product. Yield: 2.38 g (93%). $\text{C}_{13}\text{H}_{11}\text{N}_3\text{O}_3$: calcd.: C 60.70; H 4.31; N 16.33%; found: C 60.53; H 4.37; N 16.20%. Characteristic IR: $\bar{\nu} = 3402 \text{ } \nu(\text{OH})$, $3330 \text{ } \nu(\text{NH})$, $1653 \text{ } \nu(\text{C}=\text{O})$, $1611 \text{ } \nu(\text{C}=\text{N}) \text{ cm}^{-1}$. UV-Vis data (λ_{max} , ϵ): 213 nm, $16,350 \text{ L mol}^{-1} \text{ cm}^{-1}$; 300 nm, $18,720 \text{ L mol}^{-1} \text{ cm}^{-1}$. ^1H NMR (500 MHz, d_6 -DMSO): δ 11.88 (s, 1H, NH), 9.59 (t, 2H, OH), 9.45 (s, 1H, OH), 8.61 (d, 1H, PyH), 8.46 (s, 1H, CH=N), 7.96 (d, 1H, PyH), 7.87 (t, 1H, PyH), 7.39 (t, 1H, PyH), 6.77 (s, 1H, ArH), 6.76 (s, 1H, ArH), 6.45 (s, 1H, ArH). ^{13}C NMR (126 MHz, d_6 -DMSO): δ 166.19, 163.52, 158.39, 153.33, 149.41, 147.71, 136.76, 135.43, 124.24, 119.77, 105.79. Colorless block like single crystals were obtained by slow evaporation of methanolic solution of the compound.

2. 3. Synthesis of the Complexes

2. 3. 1. $[\text{CuCl}_2(\text{HL})]\cdot\text{CH}_3\text{OH}$ ($1\cdot\text{CH}_3\text{OH}$)

HL (26 mg, 0.10 mmol) was dissolved in 30 mL methanol. Then, copper chloride dihydrate (17 mg, 0.10 mmol) was added to the solution. The reaction mixture

was stirred for 30 min at room temperature to afford a clear bluish green solution. The solution was allowed to slowly evaporate at ambient condition for 3 days to form single crystals, which were collected by filtration and dried in air. Yield: 18 g (43%). $\text{C}_{14}\text{H}_{15}\text{Cl}_2\text{CuN}_3\text{O}_4$: calcd.: C 39.68; H 3.57; N 9.92%; found: C 39.83; H 3.66; N 9.82%. Characteristic IR: $\bar{\nu} = 3425 \text{ } \nu(\text{OH})$, $3186 \text{ } \nu(\text{NH})$, $1628 \text{ } \nu(\text{C}=\text{O})$, $1613 \text{ } \nu(\text{C}=\text{N}) \text{ cm}^{-1}$. UV-Vis data (λ_{max} , ϵ): 226 nm, $16,720 \text{ L mol}^{-1} \text{ cm}^{-1}$; 245 nm, $16,385 \text{ L mol}^{-1} \text{ cm}^{-1}$; 330 nm, $10,317 \text{ L mol}^{-1} \text{ cm}^{-1}$; 383 nm, $\text{L mol}^{-1} \text{ cm}^{-1}$.

2. 3. 2. $[\text{NiL}_2]\cdot 2\text{CH}_3\text{OH}\cdot 2\text{H}_2\text{O}$ ($2\cdot 2\text{CH}_3\text{OH}\cdot 2\text{H}_2\text{O}$)

HL (26 mg, 0.10 mmol) was dissolved in 30 mL methanol. Then, nickel acetate tetrahydrate (25 mg, 0.10 mmol) was added to the solution. The reaction mixture was stirred for 30 min at room temperature to afford a clear green solution. The solution was allowed to slowly evaporate at ambient condition for 6 days to form single crystals, which were collected by filtration and dried in air. Yield: 21 g (66%). $\text{C}_{27}\text{H}_{28}\text{N}_6\text{NiO}_9$: calcd.: C 50.73; H 4.41; N 13.15%; found: C 50.61; H 4.37; N 13.26%. Characteristic IR: $\bar{\nu} = 3430 \text{ } \nu(\text{OH})$, $1608 \text{ } \nu(\text{C}=\text{N}) \text{ cm}^{-1}$. UV-Vis data (λ_{max} , ϵ): 218 nm, $15,370 \text{ L mol}^{-1} \text{ cm}^{-1}$; 286 nm, $5,750 \text{ L mol}^{-1} \text{ cm}^{-1}$; 373 nm, $8,235 \text{ L mol}^{-1} \text{ cm}^{-1}$.

2. 4. Crystal Structure Determination

Selected crystals of HL and the complexes were mounted on a Bruker Apex II CCD area diffractometer equipped with Mo K α radiation ($\lambda = 0.71073 \text{ \AA}$). Crystal data were collected at room temperature and corrected for Lorentz polarization effects and for linear decay. Multi-scan absorption correction based on ω -scans was applied. Data refinement was carried out with SMART and reduction with SAINT.⁸ Structures of the complexes were solved by direct method using SHELXS and refined with SHELXL.⁹ All non-hydrogen atoms were refined anisotropically. The H atoms attached to O and N in HL and the two complexes were located from difference Fourier maps and refined isotropically, with N...H and O...H distances restrained to 0.90(1) and 0.85(1) $\text{\AA}$, respectively. The remaining H atoms were fixed geometrically and refined using riding model. Atoms O7, O8, O9, O10, C27 and C28 in complex **1** were restrained as isotropic behavior with ISOR instruction. Crystallographic data and structure refinement parameters are listed in Table 1.

2. 5. Urease Inhibitory Activity Assay

The measurement of urease inhibitory activity was carried out according to the literature method.¹⁰ The assay mixture containing 75 μL of *Jack bean* urease and 75 μL of tested compounds with various concentrations (dissolved in DMSO) was preincubated for 15 min on a 96-well assay plate. Acetohydroxamic acid was used as a reference. Then

Table 1. Crystallographic and experimental data for HL·2MeOH and the complexes

Compound	HL·2MeOH	1·CH ₃ OH	2·2CH ₃ OH·2H ₂ O
Formula	C ₁₅ H ₁₉ N ₃ O ₅	C ₁₄ H ₁₅ Cl ₂ CuN ₃ O ₄	C ₂₇ H ₂₈ N ₆ NiO ₉
Formula Weight	321.33	423.73	639.26
Crystal system	Monoclinic	Orthorhombic	Monoclinic
Space group	Cc	P2 ₁ 2 ₁ 2 ₁	P2 ₁ /n
<i>a</i> / Å	25.6823(18)	7.3472(6)	10.7185(12)
<i>b</i> / Å	4.6954(11)	12.7614(11)	15.6995(13)
<i>c</i> / Å	17.5556(15)	17.7045(16)	19.5232(15)
α / °	90	90	90
β / °	128.8130(10)	90	95.5220(10)
γ / °	90	90	90
<i>V</i> / Å ³	1649.6(4)	1660.0(2)	3270.0(5)
<i>Z</i>	4	4	4
<i>D_c</i> / (g·cm ⁻³)	1.294	1.695	1.298
μ / mm ⁻¹	0.098	1.662	0.649
<i>F</i> (000)	680	860	1328
Reflections/parameters	5959/225	8932/230	18979/422
Unique reflections	2809	3087	6012
Observed reflections (<i>I</i> ≥ 2σ(<i>I</i>))	2470	2868	4806
Restraints	7	4	48
Goodness-of-fit on <i>F</i> ²	1.023	0.990	1.042
<i>R</i> ₁ , <i>wR</i> ₂ [<i>I</i> ≥ 2σ(<i>I</i>)] ^{a)}	0.0320, 0.0786	0.0237, 0.0508	0.0566, 0.1558
<i>R</i> ₁ , <i>wR</i> ₂ (all data)	0.0389, 0.0829	0.0266, 0.0520	0.0704, 0.1689

75 μ L of phosphate buffer at pH 6.8 containing phenol red (0.18 mmol L⁻¹) and urea (400 mmol L⁻¹) were added and incubated at room temperature. The reaction time required for enough ammonium carbonate to form to raise the pH of the phosphate buffer from 6.8 to 7.7 was measured by a micro-plate reader (560 nm) with the end-point being determined by the color change of phenol-red indicator.

3. Results and Discussion

3.1. Chemistry

The hydrazone(HL) was easily prepared by reaction of 2-pyridinecarboxaldehyde and 3,5-dihydroxybenzohydrazide in 1:1 molar ratio in MeOH. Synthetic procedures for HL and the complexes are shown in Scheme 2. Complexes **1** and **2** were prepared by reaction of HL with copper chloride and nickel acetate, respectively in MeOH. Interestingly, the hydrazone ligand in complex **1** adopts neutral form, while those in complex **2** adopt monoanionic form. Chloride anion coordinates to the Cu ion of complex **1**, while acetate anion is absent in complex **2**. The elemental analyses of HL and the twocomplexes agree well with the formulae proposed by single crystal X-ray determination. In 10⁻³ mol L⁻¹ solution, complexes **1** and **2** behave as non-electrolytes as evidenced by molar conductivity values of 32 and 25 Ω^{-1} cm² mol⁻¹.¹¹

3.2. IR and UV-Vis Spectra

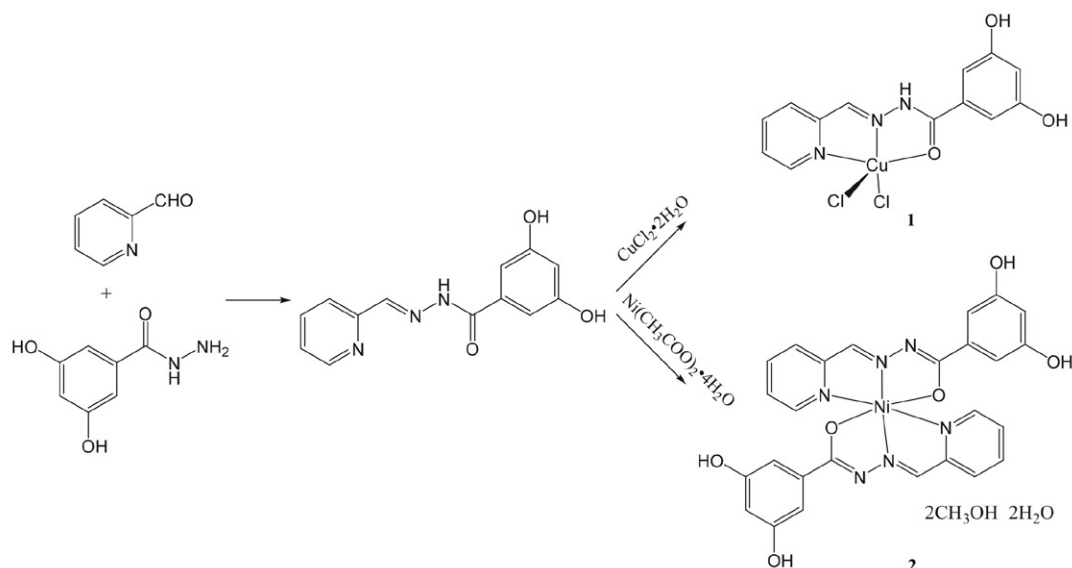
IR data of HL and the complexes agree well with their X-ray structures. The weak absorptions centered at

about 3400 cm⁻¹ can be assigned to ν (O-H), and those at 3330 cm⁻¹ for HL and 3186 cm⁻¹ for complex **1** are caused by ν (N-H). The spectrum of HL featurestypical peaks at 1653 and 1611 cm⁻¹, which are attributed to the stretching vibrations of the carbonyl [ν (C=O)] and azomethine [ν (C=N)] groups.¹² In the IR spectra of both complexes, the stretching vibrations of the C=N groups shift to lower frequencies as compared to HL, indicating that hydrazone ligands coordinate to metal ions *via* azomethine nitrogen. In the spectrum of complex **1**, strong peak at 1628 cm⁻¹ is ν (C=O), which shift to lower frequency as compared to HL, indicating it coordinates through carbonyl form. This peak is absent in the spectrum of complex **2**, because the ligands in this complex adopt enolate form.

The UV-Vis spectra of HL and the complexes have been recorded in methanol solutions. In the free ligand, the band at 300 nm is attributed to the azomethine chromophore $n\text{-}\pi^*$ transition, and that at higher energy (213 nm) is associated with the benzene $\pi\text{-}\pi^*$ transition. In the spectra of the complexes, the bands at 245–286 nm can be assigned to $\pi\text{-}\pi^*$ transition of the ligands. The bands at 330–383 nm are attributed to ligand to metal charge transfer (LMCT) transition.

3.3. Structure Description of HL·2MeOH

The perspective view of HL·2MeOH is shown in Figure 1. The compound contains a hydrazone molecule (HL) and two methanol solvate molecules. The methanol molecules are linked to HL through hydrogen bonds (Table 3). The hydrazone molecule adopts *E* configuration with respect to the methylidene unit. The pyridine and benzene



Scheme 2. Synthetic procedures for HL and the two complexes.

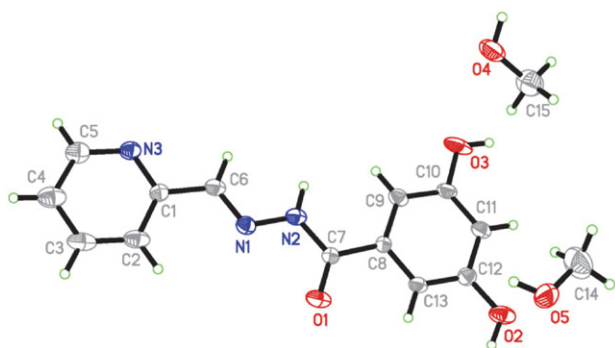


Figure 1. Crystal structure of HL·2MeOH. Displacement ellipsoids for non-hydrogen atoms are drawn at the 30% probability level.

rings form a dihedral angle of $3.3(2)^\circ$. The distance of the methyldene bond ($C6-N1 = 1.272(3) \text{ \AA}$) confirms it as a typical double bond. The shorter distance of $C7-N2(1.363(3) \text{ \AA})$ bond and the longer distance of $C7=O1(1.224(3) \text{ \AA})$ bond than usual, suggest the presence of conjugation effect in the hydrazone molecule. All the bond lengths in the compound are within normal values.¹³ Crystal of the compound is stabilized by hydrogen bonds of types $O-H\cdots N$, $N-H\cdots O$ and $O-H\cdots O$ (Table 3), to form one-dimensional chains along a axis (Figure 2).

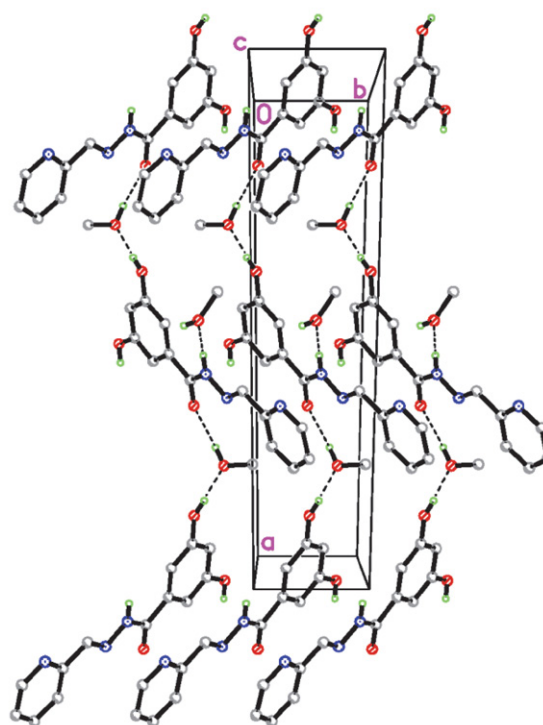


Figure 2. Molecular packing of HL·2MeOH, viewed along c axis. Hydrogen bonds are shown as dashed lines.

3. 4. Structure Description of the Complexes

Selected bond lengths and angles are given in Table 2.

3. 4. 1. Complex 1

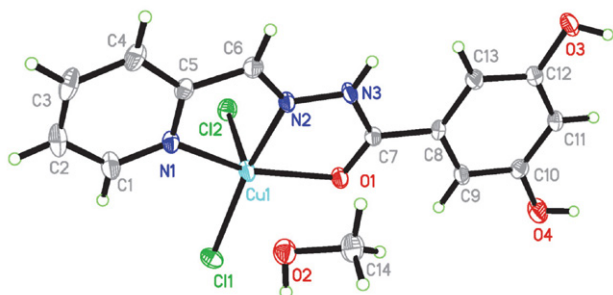
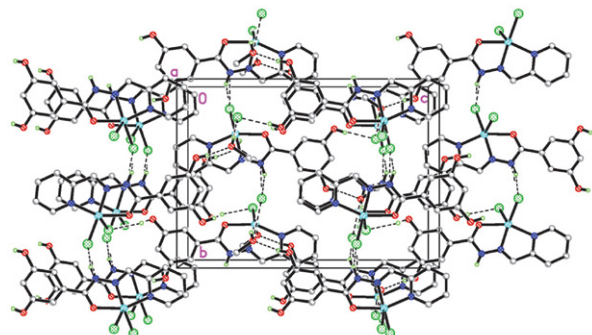
The perspective view of complex 1 is shown in Figure 3. The compound is a mononuclear copper complex. The Cu ion is coordinated in a square pyramidal geometry, with the basal plane defined by the pyridine nitrogen N1,

imino nitrogen N2 and carbonyl oxygen O1 atoms of HL, and one chloride ligand Cl1. The apical position is occupied by the other chloride ligand Cl2. The Cu atom deviated from the least squares plane defined by the basal donor atoms by $0.220(2) \text{ \AA}$. The Cu–O and Cu–N bond lengths are comparable to the copper complexes with hydrazone ligands.¹⁴ The deviation of square pyramidal coordination arises mainly from the strain created by the five-membered chelate rings $Cu1-N1-C5-C6-N2$ and $Cu1-N2-N3-C7-O1$. The *cis* and *trans* bond angles in the basal

Table 2. Selected bond lengths/Å and angles/° for the complexes

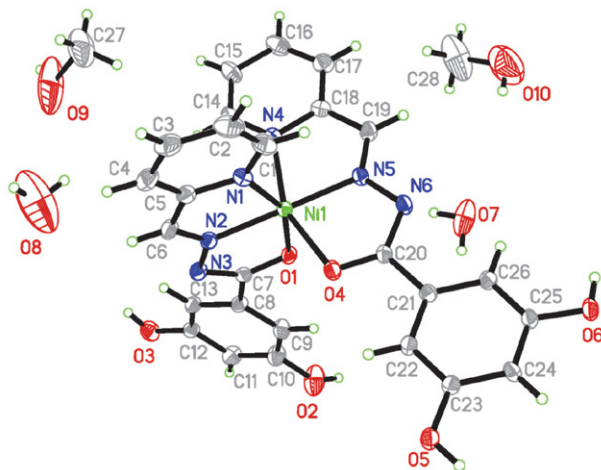
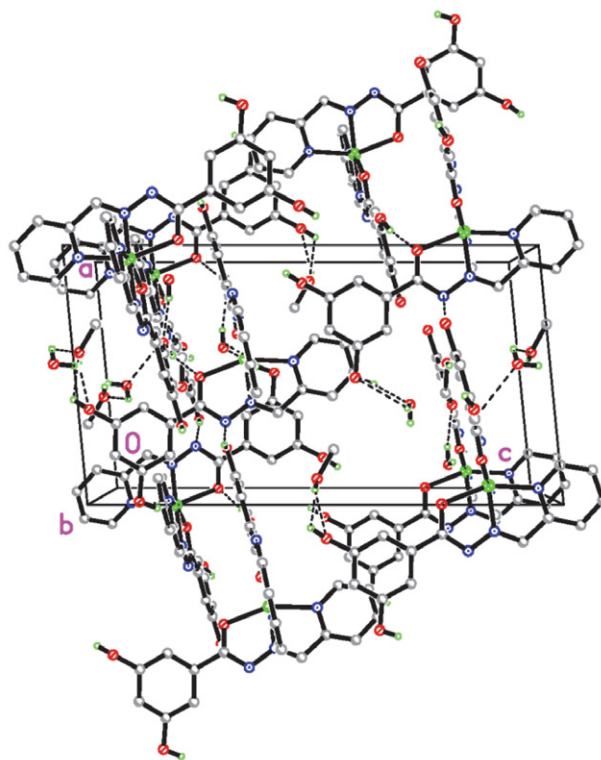
1			
Cu1–N1	2.036(3)	Cu1–N2	1.940(3)
Cu1–O1	2.109(2)	Cu1–Cl1	2.2008(9)
Cu1–Cl2	2.5817(10)		
N2–Cu1–N1	79.38(11)	N2–Cu1–O1	77.31(10)
N1–Cu1–O1	155.51(10)	N2–Cu1–Cl1	165.95(8)
N1–Cu1–Cl1	100.23(8)	O1–Cu1–Cl1	100.55(7)
N2–Cu1–Cl2	96.45(8)	N1–Cu1–Cl2	100.33(8)
O1–Cu1–Cl2	89.69(6)	Cl1–Cu1–Cl2	97.44(3)
2			
Ni1–N1	2.101(3)	Ni1–N2	1.979(3)
Ni1–N5	1.979(3)	Ni1–O4	2.102(2)
Ni1–O1	2.107(2)	Ni1–N4	2.116(3)
N2–Ni1–N5	176.38(11)	N2–Ni1–N1	78.37(11)
N5–Ni1–N1	104.38(11)	N2–Ni1–O4	106.29(10)
N5–Ni1–O4	76.07(10)	N1–Ni1–O4	93.10(10)
N2–Ni1–O1	76.09(10)	N5–Ni1–O1	101.23(10)
N1–Ni1–O1	154.36(11)	O4–Ni1–O1	91.95(9)
N2–Ni1–N4	98.62(11)	N5–Ni1–N4	78.92(11)
N1–Ni1–N4	94.44(11)	O4–Ni1–N4	154.95(10)
O1–Ni1–N4	91.51(9)		

plane are 77.31(10)–100.55(7)° and 155.51(10)–165.95(8)°, respectively. The angles among the apical and basal donor atoms are 89.69(6)–100.33(8)°. The pyridine and benzene rings form a dihedral angle of 9.3(3)°. Crystal of the complex is stabilized by intermolecular hydrogen bonds of types O–H...Cl, N–H...Cl and O–H...O (Table 3), to form three-dimensional network (Figure 4).

**Figure 3.** Crystal structure of 1-CH₃OH. Displacement ellipsoids for non-hydrogen atoms are drawn at the 30% probability level.**Figure 4.** Molecular packing in 1-CH₃OH viewed along *a* axis. Hydrogen bonds are shown as dashed lines.

3. 4. 2. Complex 2

The perspective view of complex **2** is shown in Figure 5. The compound is a mononuclear nickel complex. The Ni ion is coordinated by two pyridine nitrogens (N1, N4), two imino nitrogens (N2, N5) and two enolate oxygens (O1, O4) atoms from two hydrazone ligands, to form an octahedral coordination. The Ni–O and Ni–N bond lengths are comparable to the nickel complexes with hydrazone ligands.¹⁵ The deviation of octahedral coordination arises mainly from the strain created by the five-membered che-

**Figure 5.** Crystal structure of 2-2CH₃OH-2H₂O. Displacement ellipsoids for non-hydrogen atoms are drawn at the 30% probability level.**Figure 6.** Molecular packing in 2-2CH₃OH-2H₂O viewed along *b* axis. Hydrogen bonds are shown as dashed lines.

late rings Ni1–N1–C5–C6–N2, Ni1–N5–N6–C20–O4, Ni1–N2–N3–C7–O1, and Ni1–N4–C18–C19–N5. The *cis* and *trans* bond angles are 76.07(10)–106.29(10)° and 154.36(11)–176.38(11)°, respectively. The pyridine and benzene rings form dihedral angles of 32.4(5)° for one ligand and 3.6(5)° for the other one. Crystal of the complex is stabilized by intermolecular hydrogen bonds of types O–H...N and O–H...O (Table 3), to form three-dimensional network (Figure 6).

Table 3. Hydrogen bond distances (Å) and bond angles (°) for the compounds.

<i>D</i> – <i>H</i> ... <i>A</i>	<i>d</i> (<i>D</i> – <i>H</i>)	<i>d</i> (<i>H</i> ... <i>A</i>)	<i>d</i> (<i>D</i> ... <i>A</i>)	Angle (<i>D</i> – <i>H</i> ... <i>A</i>)
HL				
O5–H5...O2 ⁱ	0.85(1)	1.94(2)	2.770(3)	166(4)
O2–H2...N3 ⁱⁱ	0.85(1)	1.85(2)	2.707(3)	175(4)
O4–H4...O1 ⁱⁱⁱ	0.85(1)	1.98(2)	2.789(3)	160(4)
O3–H3...O4 ^{iv}	0.85(1)	1.80(2)	2.653(3)	172(4)
N2–H2A...O5 ^v	0.90(1)	2.10(2)	2.977(3)	163(3)
1				
O2–H2...Cl2 ^{vi}	0.85(1)	2.38(2)	3.227(3)	170(5)
O4–H4...Cl2 ^{vii}	0.83(1)	2.30(2)	3.114(3)	165(5)
O3–H3...O2	0.85(1)	1.90(2)	2.714(4)	162(5)
2				
O6–H6...N3 ^{viii}	0.85(1)	1.94(2)	2.735(4)	155(5)
O5–H5...O1 ^{ix}	0.85(1)	1.82(2)	2.661(3)	168(5)
O3–H3...O7 ^x	0.85(1)	1.82(2)	2.664(5)	170(5)
O7–H7A...O5 ^{xi}	0.85(1)	1.99(2)	2.826(4)	166(5)

Symmetry codes: (i) $x, 1 + y, z$; (ii) $x, 1 - y, -\frac{1}{2} + z$; (iii) $-\frac{1}{2} + x, -\frac{1}{2} - y, \frac{3}{2} + z$; (iv) $x, -1 + y, z$; (v) $x, 1 - y, \frac{1}{2} + z$; (vi) $1 - x, 1 - y, -z$; (vii) $-\frac{1}{2} + x, \frac{1}{2} - y, 1 - z$; (viii) $1 + x, y, z$; (ix) $\frac{3}{2} - x, -\frac{1}{2} + y, \frac{1}{2} - z$; (x) $-1 + x, y, z$; (xi) $\frac{3}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z$.

3. 5. Urease Inhibitory Activity

The hydrazone has medium activity on urease. The copper complex has excellent inhibitory activity on *Jack bean* urease, with IC₅₀ value of 0.49 ± 0.13 μmol L⁻¹. However, the nickel complex has lower activity as compared with HL. Acetohydroxamic acid and copper chloride were used as references. The copper complex has better activity against urease than the copper(II) complexes with the Schiff base ligand *N,N'*-bis(4-fluorosalicylidene)-1,2-diaminopropane (IC₅₀ = 2.1–3.4 μmol L⁻¹),¹⁶ the reduced Schiff base ligand 2,2'-((propane-1,3-diylbis(azanediyl)) bis(methylene)diphenol (IC₅₀ = 1.6 μmol L⁻¹),¹⁷ the Schiff base ligands derived from tyrosine and 3,5-dibromosalicylaldehyde, 5-chlorosalicylaldehyde or 2-hydroxy-1-naphthaldehyde (IC₅₀ = 2.15–32.12 μmol L⁻¹).¹⁸ Thus, the present copper complex may be used as a urease inhibitor, which deserves further study.

Table 4. Urease inhibition of the compounds

Tested materials	Percentage Inhibition ^a	IC ₅₀ (μmol L ⁻¹)
HL	43 ± 1.5	–
1	97 ± 1.8	0.49 ± 0.13
2	21 ± 1.2	–
CuCl ₂	85 ± 1.8	8.3 ± 0.5
Ni(CH ₃ COO) ₂	41 ± 0.8	–
Acetohydroxamic acid	86 ± 1.7	24 ± 1.1

^a The concentration of the tested material is 100 μmol L⁻¹. – means no activity or IC₅₀ > 100 μmol L⁻¹.

4. Conclusion

A new pyridinyl hydrazone compound 3,5-dihydroxy-*N'*-(pyridin-2-ylmethylene)benzohydrazidewas prepared and utilized to synthesize two copper and nickel complexes. The hydrazone coordinates to Cu ion through phenolate oxygen, imino nitrogen, and carbonyl oxygen atoms, and coordinates to Ni ion through phenolate oxygen, imino nitrogen, and enolate oxygen atoms. The copper complex has excellent inhibitory activity against *Jack bean* urease, which may be used as a precursor for the design of new urease inhibitors.

Supplementary Data

CCDC 2487326 (HL), 2487327 (**1**) and 2487328 (**2**) contain supplementary crystallographic data for the complexes. These data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html>, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44)1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

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Povzetek

Hidrazoni imajo zanimive biološke lastnosti. V tej raziskavi je bil sintetiziran nov hidrazon 3,5-dihidroksi-*N'*-(piridin-2-ilmetilen)benzohidrazid (HL), ki je bil okarakteriziran z IR, UV-Vis, ^1H in ^{13}C NMR spektroskopijo. Spojina reagira z bakrovim kloridom in nikljevimi acetatom, pri čemer sta nastala kovinska kompleksa $[\text{CuCl}_2(\text{HL})]\cdot\text{CH}_3\text{OH}$ (**1**·CH₃OH) in $[\text{NiL}_2]\cdot 2\text{CH}_3\text{OH}\cdot 2\text{H}_2\text{O}$ (**2**·2CH₃OH·2H₂O). Kompleksa sta bila okarakterizirani z elementarno analizo ter IR in UV-Vis spektroskopijo. Strukture HL in kompleksov so bile dodatno potrjene z monokristalno rentgensko analizo. Hidrazon v kompleksu **1** je v nevtralni obliki in se veže na Cu ion preko piridinskega in iminskega dušikovega atoma ter karbonilnega kisikovega atoma. Hidrazon v kompleksu **2** je v monoanionski obliki in se veže na Ni ion preko piridinskega in iminskega dušikovega atoma ter preko enolatnega kisikovega atoma. Cu atom v kompleksu **1** je v kvadratno piramidalni koordinaciji, Ni atom v kompleksu **2** pa v oktaedrični koordinaciji. Snovi so bile testirane na njihovo zaviralno delovanje na ureazo. Kompleks **1** izkazuje izjemno aktivnost na ureazo ($\text{IC}_{50} = 0.5 \pm 0.1 \mu\text{mol L}^{-1}$).



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