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Scientific paper

Synthesis, Crystal Structures and Urease Inhibition of Copper(II) and Cobalt(III) Complexes Derived from (((2-(Pyrrolidin-1-yl)ethyl)imino)methyl)naphthalen-2-ol

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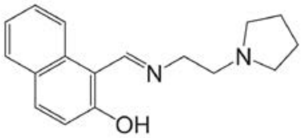
Abstract

Three copper(II) and cobalt(III) complexes, $[CuL(dca)]_n$ (**1**), $[CuL(N_3)]_n$ (**2**) and $[CoL(N_3)_2(DMF)]$ (**3**), where L is the monoanionic form of the Schiff base (((2-(pyrrolidin-1-yl)ethyl)imino)methyl)naphthalen-2-ol (HL), and dca is dicyanamide, have been prepared and characterized by elemental analyses, IR and UV-Vis spectroscopy, as well as single crystal X-ray diffraction. The Cu atoms in complexes **1** and **2** are in square pyramidal coordination, and the Co atom in complex **3** is in octahedral one. Complexes **1** and **2** inhibit the *Jack bean* urease with IC_{50} values of 0.25 ± 0.14 and 0.32 ± 0.15 μmol L^{-1}, respectively. Complex **3** show weak activity on *Jack bean* urease with percentage inhibition of 37%.

Keywords: Schiff base; Copper complex; Cobalt complex; Crystal structure; Urease inhibition

1. Introduction

Urease exists in nature, animals and even our human beings, which efficiently catalyzes the hydrolysis reaction of urea to ammonia. This process has negative effects to soil, plants, animals,[1] and related to many diseases of human beings.[2] It showed a major role in urinary catheter incrustation, peptic ulceration, pyelonephritis, kidney stone, hepatic encephalopathy, urolithiasis, and arthritis.[3] So, it is important to decrease the activity of urease. In the last few years, a number of urease inhibitors have been reported including inorganic metal salts like silver, copper, mercury,[4] and organic compounds like hydroxamic acids, triazoles, semicarbazones, Schiff bases, urea derivatives, oxadiazoles, *etc.*[5] However, most of the above mentioned urease inhibitors are not applicable for their low efficiency and side effect like cytotoxicity.[6] The copper nitrate and copper chloride have effective activities on urease, yet, they are harmful to both soil and living organisms. A search of literature indicated that some Schiff base copper and cobalt complexes have good urease inhibitory activities.[7] Considering that copper and cobalt complexes with Schiff bases have a wide range of biological applications,[8] and their application on urease inhibition is rare, in the present work, three new copper(II) and cobalt(III) complexes, $[CuL(dca)]_n$ (**1**), $[CuL(N_3)]_n$ (**2**) and $[CoL(N_3)_2(DMF)]$ (**3**), where L is the monoanionic form of the Schiff base (((2-(pyrrolidin-1-yl)ethyl)imino)methyl)naphthalen-2-ol (HL, Scheme 1), dca is dicyanamide, and N_3 is azide, are presented.



Scheme 1. The Schiff base HL.

2. Experimental

2. 1. Materials and Measurements

2-Hydroxy-1-naphthaldehyde, *N*-(2-aminoethyl) pyrrolidine, sodium dicyanamide, sodium azide, copper nitrate, cobalt nitrate, and solvents with AR grade were purchased from Xiya Chemicals Co. Ltd. (China). Elemental analyses for C, H and N 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. Electronic spectra were recorded on a Lambda 35 spectrophotometer. Single crystal X-ray diffraction was carried out on a Bruker SMART 1000 CCD diffractometer.

2. 2. Synthesis of (((2-(pyrrolidin-1-yl)ethyl) imino)methyl)naphthalen-2-ol (HL)

2-Hydroxy-1-naphthaldehyde (0.17 g, 1.0 mmol) and *N*-(2-aminoethyl)pyrrolidine (0.11 g, 1.0 mmol) were mixed in 30 mL methanol. The mixture was stirred at ambient temperature for 20 min to give slight yellow solution. The solvent was evaporated to give solid product, which was re-crystallized from methanol. Yield: 0.23 g (85%). Anal. Calc. for $C_{17}H_{20}N_2O$ (%): C, 76.09; H, 7.51; N, 10.44. Found (%): C, 75.87; H, 7.46; N, 10.55. IR data (cm^{-1}): 3412w (OH), 1632s (C=N), 1543m, 1524m, 1492w, 1446w, 1402w, 1356s, 1212m, 1185m, 1141m, 836m, 749m, 640w, 504w. UV-Vis data (methanol, λ/nm (ε/M^{-1} cm^{-1})): 230 (21,530), 305 (4,700), 410 (4,730). ^{1}H NMR (500 MHz, d_6-DMSO) δ 13.91 (s, 1H, OH), 9.07 (s, 1H, CH=N), 8.04 (d, 1H, ArH), 7.69 (d, 1H, ArH), 7.62 (d, 1H, ArH), 7.43 (t, 1H, ArH), 7.17 (t, 1H, ArH), 6.69 (d, 1H, ArH), 3.76 (t, 2H, CH$_2$), 2.73 (t, 2H, CH$_2$), 2.52 (m, 4H, CH$_2$), 1.69 (m, 4H, CH$_2$). ^{13}C NMR (126 MHz, d_6-DMSO) δ 177.88, 158.84, 137.02, 134.42, 128.78, 127.77, 125.83, 124.98, 121.91, 118.22, 105.44, 55.52, 53.51, 49.44, 23.16.

2. 3. Synthesis of [CuL(dca)]$_n$ (1)

The Schiff base HL (0.027 g, 0.10 mmol), copper nitrate trihydrate (0.024 g, 0.10 mmol) and sodium dicyanamide (0.018 g, 0.20 mmol) were mixed in methanol (30 mL). The mixture was stirred at ambient temperature for 30 min to give brown solution. Half of the solvent was slowly evaporated at room temperature for 5 days to give single crystals. Yield: 0.022 g (55%). Anal. Calc. for $C_{19}H_{19}CuN_5O$ (%): C, 57.49; H, 4.82; N, 17.64. Found (%): C, 57.27; H, 4.91; N, 17.53. IR data (cm^{-1}): 2282s, 2221w, 2152vs (dca), 1621s (C=N), 1542s, 1510 w, 1457m, 1432m, 1417w, 1397w, 1362m, 1347s, 1182m, 1141w, 1041w, 940w, 828m, 743m, 569w, 518w, 483w, 456w. UV-Vis data (methanol, λ/nm (ε/M^{-1} cm^{-1})): 238 (18,310), 250 (16,273), 305 (8,750), 390 (4,135).

2. 4. Synthesis of [CuL(N$_3$)]$_n$ (2)

This complex was prepared by the similar method as described for complex **1**, with sodium dicyanamide

Table 1. Crystal data for the complexes

	1	**2**	**3**
Chemical Formula	$C_{19}H_{19}CuN_5O$	$C_{17}H_{19}CuN_5O$	$C_{20}H_{26}CoN_9O_2$
Fw	396.93	372.91	483.43
T (K)	298(2)	298(2)	298(2)
λ (Mo Kα) (Å)	0.71073	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/c$	Cc	$P2_1/n$
a (Å)	17.4581(15)	9.3323(12)	14.0242(9)
b (Å)	7.5382(11)	23.6903(15)	11.0415(7)
c (Å)	13.5353(13)	7.7450(11)	14.5537(9)
α (°)	90	90	90
β (°)	94.485(2)	108.0630(10)	100.2960(10)
γ (°)	90	90	90
V (Å^3)	1776.0(3)	1627.9(3)	2217.3(2)
Z	4	4	4
μ (Mo Kα) (cm^{-1})	1.248	1.356	0.811
D_c (g cm^{-3})	1.485	1.522	1.448
Reflections	17656	4469	23648
Unique reflections	3304	2813	4131
Observed reflections [$I \geq 2\sigma(I)$]	2929	2606	3410
Parameters	235	218	291
Restraints	0	0	0
Goodness of fit on F^2	1.067	1.028	1.020
R_{int}	0.0273	0.0174	0.0283
R_1 [$I \geq 2\sigma(I)$]	0.0341	0.0278	0.0367
wR_2 [$I \geq 2\sigma(I)$]	0.1097	0.0633	0.0921
R_1 (all data)	0.0390	0.0317	0.0478
wR_2 (all data)	0.1146	0.0649	0.1004
$\Delta\rho_{\max}/\Delta\rho_{\min}$, e Å^{-3}	0.483/–0.393	0.395/–0.324	0.751/–0.275

replaced by sodium azide (0.013 g, 0.20 mmol). Half of the solvent was slowly evaporated at room temperature for 5 days to give single crystals. Yield: 0.024 g (65%). Anal. Calc. for $C_{17}H_{19}CuN_5O$ (%): C, 54.75; H, 5.14; N, 18.78. Found (%): C, 54.54; H, 5.23; N, 18.61. IR data (cm^{-1}): 2051vs (N_3), 1623s (C=N), 1536m, 1506 w, 1457m, 1439m, 1413m, 1385m, 1361m, 1343m, 1181m, 1167w, 1037w, 973w, 827m, 749m, 649w, 518w, 476w, 456w. UV-Vis data (methanol, λ/nm (ε/M^{-1} cm^{-1})): 240 (17,590), 250 (16,132), 261 (12,350), 290 (7,853), 315 (5,430), 385 (4,550).

2. 5. Synthesis of [CoL(N_3)$_2$(DMF)] (3)

The Schiff base HL (0.027 g, 0.10 mmol), cobalt nitrate hexahydrate (0.029 g, 0.10 mmol) and sodium azide (0.013 g, 0.20 mmol) were mixed in methanol (30 mL). The mixture was stirred at ambient temperature for 30 min to give deep brown suspension. Then, 5 mL DMF was added to dissolve the precipitation. Half of the solvent was slowly evaporated at room temperature for 12 days to give single crystals. Yield: 0.031 g (64%). Anal. Calc. for $C_{20}H_{26}CoN_9O_2$ (%): C, 49.69; H, 5.42; N, 26.08. Found (%): C, 49.81; H, 5.50; N, 25.89. IR data (cm^{-1}): 2014vs (N_3), 1640s (C=O), 1620s (C=N), 1538m, 1505w, 1440m, 1414w, 1417w, 1356s, 1287m, 1256w, 1188w, 1120m, 1099w, 1036w, 982w, 929w, 868w, 835m, 761m, 708m, 619w, 593w, 528w, 510w, 454w. UV-Vis data (methanol, λ/nm (ε/M^{-1} cm^{-1})): 230 (16,720), 262 (18,630), 320 (8,317), 400 (3,220).

2. 6. X-ray Diffraction

The diffraction intensities for crystals of the copper and cobalt complexes were collected at room temperature using Bruker SMART 1000 CCD area-detector diffractometer with MoKα radiation (λ = 0.71073 Å). The data were reduced with SAINT program,[9] and multi-scan absorption correction was performed with SADABS program.[10] Structures of the three complexes were solved by direct method and refined against F^2 by full-matrix least-squares method with SHELXL.[11] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed in calculated positions and constrained to ride on their parent atoms. The crystallographic data for the complexes are summarized in Table 1.

Table 1. Crystal data for the complexes

	1	2	3
Chemical Formula	$C_{19}H_{19}CuN_5O$	$C_{17}H_{19}CuN_5O$	$C_{20}H_{26}CoN_9O_2$
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R_1 [$I \geq 2\sigma(I)$]	0.0341	0.0278	0.0367
wR_2 [$I \geq 2\sigma(I)$]	0.1097	0.0633	0.0921
R_1 (all data)	0.0390	0.0317	0.0478
wR_2 (all data)	0.1146	0.0649	0.1004
$\Delta\rho_{max}/\Delta\rho_{min}$, e Å–3	0.483/–0.393	0.395/–0.324	0.751/–0.275

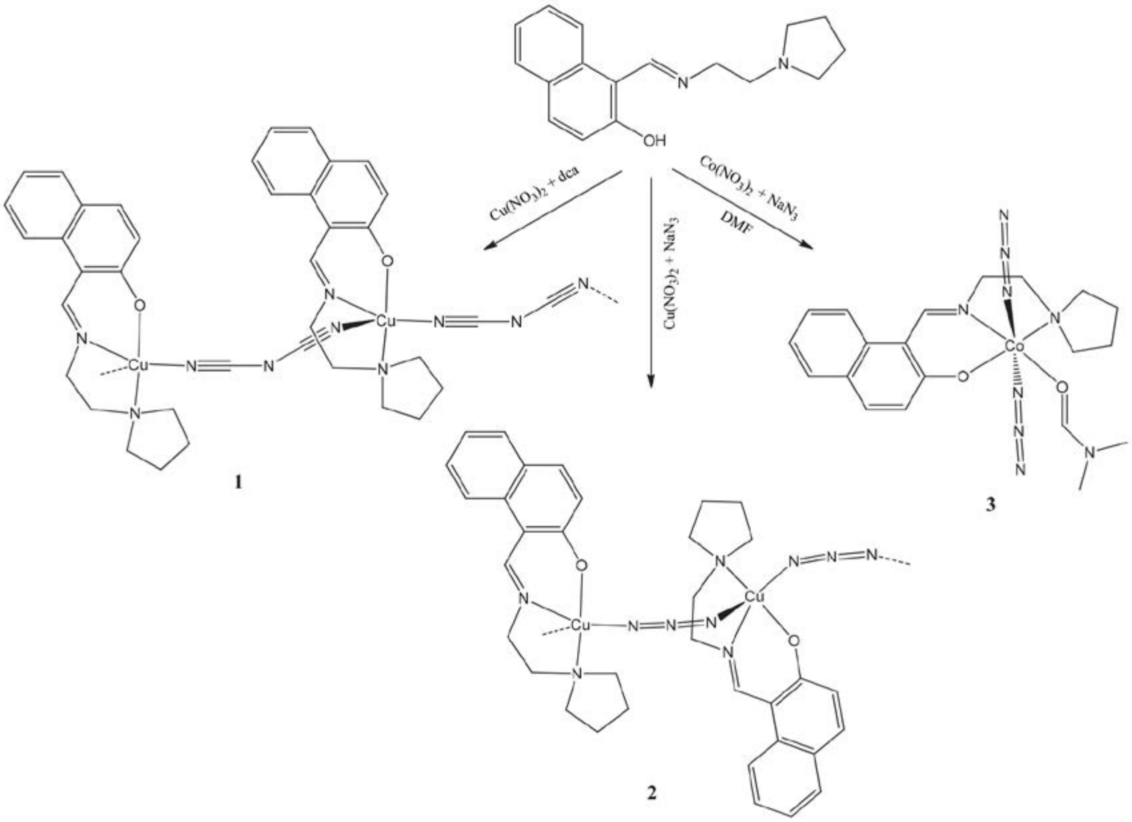
2. 7. Urease Inhibitory Activity Assay

The measurement of urease inhibitory activity was carried out according to the literature method.[12] The assay mixture containing 75 μL of *Jack bean* urease (EC 3.5.1.5, Canavalia ensiformis) and 75 μL of tested compounds with various concentrations (100 μmol L^{-1}, 50 μmol L^{-1}, 25 μmol L^{-1}, 12.5 μmol L^{-1}, 6.25 μmol L^{-1}, 3.12 μmol L^{-1}, 1.56 μmol L^{-1}, 0.78 μmol L^{-1}, 0.39 μmol L^{-1}, 0.20 μmol L^{-1}, 0.10 μmol L^{-1}, 0.05 μmol L^{-1}; dissolved in 1 mL DMSO) was preincubated for 15 min on a 96-well assay plate. Acetohydroxamic acid was used as a reference, and copper nitrate was assayed as comparison. Then 75 μL 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 25 °C. 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 copper complexes were prepared by the reaction of 1:1:2 molar ratio of HL, copper nitrate and sodium dicyanamide or sodium azide in methanol. The cobalt



Scheme 2. The synthetic procedures for the three complexes.

complex was prepared by the reaction of 1:1:2 molar ratio of HL, cobalt nitrate and sodium azide in methanol and DMF (Scheme 2). Single crystals of the complexes were obtained by slow evaporation of the solvents of their synthetic solutions. The crystals are stable in air at room temperature.

3. 2. Structure Description of Complexes 1 and 2

The molecular structures of complexes **1** and **2** are shown in Figs. 1 and 2, respectively. Selected bond lengths and angles are given in Table 2. The Cu atoms in both complexes are five-coordinated in square pyramidal geometry, as evidenced by the *τ* parameters (0.23 for **1**, 0.15 for **2**).[13] The basal plane of the square pyramidal coordination is defined by the phenolate oxygen (O1), imino nitrogen (N1) and pyrrolidine nitrogen (N2) of the Schiff base ligand L and the terminal nitrogen (N3) of the dca ligand for **1** or azide ligand for **2**. The apical position of the square pyramidal coordination is occupied by the other terminal nitrogen (N5) of the second dca or azide ligand. The distortion of the square pyramidal coordination can be observed by the bond angles around the Cu center. The *cis* and *trans* angles in the basal plane are 84.60(9)–92.24(9)° and 158.09(9)–171.97(8)° for **1**, and 84.82(16)–94.42(15)° and 166.3(2)–175.54(14)° for **2**, respectively. The bond angles among the apical and basal donor atoms are 90.08(9)–102.22(9)° for **1** and 86.16(14)–99.7(2)° for **2**. The Cu–O bond lengths are 1.9016(18) Å in **1** and 1.922(3) Å in **2**, which are comparable to each other. The Cu–N bond

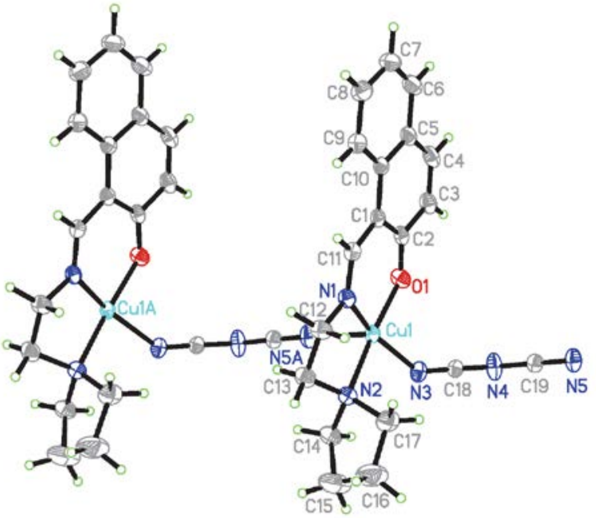


Fig. 1. A perspective view of the molecular structure of complex **1** with the atom labeling scheme. Thermal ellipsoids are drawn at the 30% probability level. Atoms labeled with the suffix A are related to the symmetry operation *x*, –1 + *y*, *z*.

lengths in the basal plane of 1.933(2)–2.065(2) Å in **1** and 1.941(5)–2.077(4) Å in **2** are also comparable to each other. The coordinate bond lengths are within normal values for similar Schiff base copper(II) complexes.[14] The apical bond lengths of Cu1–N5 are longer than the basal bonds, which is not uncommon for such complexes.

In the crystal structure of complex **1**, the [CuL] units are linked by $\mu_{1,5}$-dca ligands, to form one dimensional chain running along the *b* axis (Fig. 3). In the crystal structure of complex **2**, the [CuL] units are linked by $\mu_{1,3}$-N_3 ligands, to form one dimensional chain running along the *a* axis (Fig. 4). In addition, there are π···π interactions among the C1–C10 and C5–C10 planes in complex **1** (Cg···Cg = 3.7–4.4 Å, Table 3).

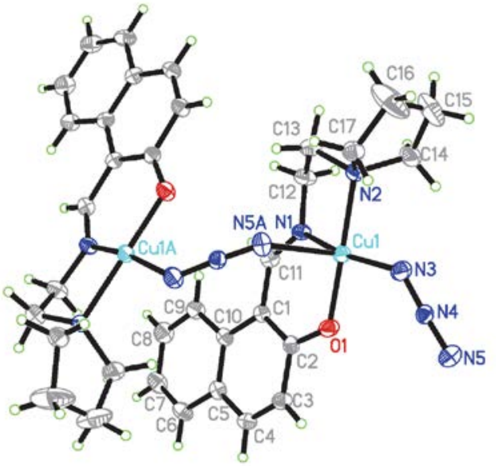


Fig. 2. A perspective view of the molecular structure of complex **2** with the atom labeling scheme. Thermal ellipsoids are drawn at the 30% probability level. Atoms labeled with the suffix A are related to the symmetry operation ½ + *x*, ½ – *y*, ½ + *z*.

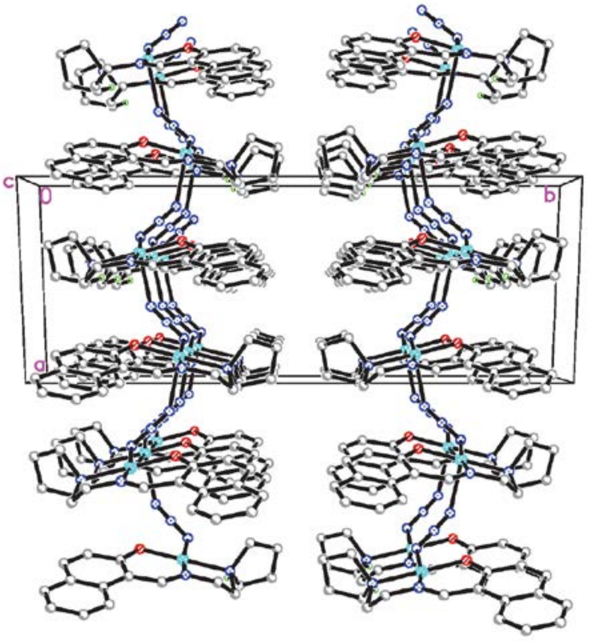


Fig. 4. Molecular packing diagram of complex **2**, viewed along the *c* axis. Hydrogen atoms are omitted for clarity.

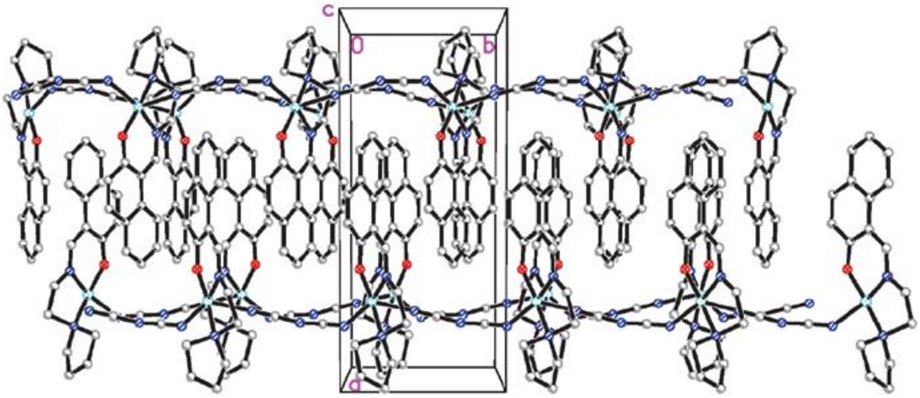


Fig. 3. Molecular packing diagram of complex **1**, viewed along the *c* axis. Hydrogen atoms are omitted for clarity.

3. 3. Structure Description of Complex 3

The molecular structure of complex **3** is shown in Fig. 5. Selected bond lengths and angles are given in Table 2. The Co atom in the complex is six-coordinated in octahedral geometry. The basal plane of the octahedral coordination is defined by the phenolate oxygen (O1), imino nitrogen (N1) and pyrrolidine nitrogen (N2) of the Schiff base ligand L and the carbonyl oxygen (O2) of the DMF ligand. The axial positions of the octahedral coordination are occupied by two terminal nitrogen atoms (N3 and N6) of two azide ligands. The distortion of the octahedral coordination can be observed by the bond angles around the Co center. The *cis* and *trans* angles in the basal plane are 86.79(8)–94.31(8)° and 176.07(8)–177.86(8)°, respectively. The bond angles among the axial and basal donor atoms are 87.11(9)–91.79(9)°. The Co–O and Co–N bond lengths are 1.8726(16)–1.9521(17) Å and 1.8622(19)–2.023(2) Å, respectively, which are within normal values for similar Schiff base cobalt(III) complexes.[15]

In the crystal structure of the complex, the complex molecules are linked through intermolecular non-classical hydrogen bonds of C19–H19C···N5 (C19–H19C = 0.96 Å, H19C···N5 = 2.52 Å, C19···N5 = 3.4454(2) Å, C19–H19C···N5 = 162(3)°, symmetry code for i: ½ – *x*, –½ + *y*, ½ – *z*), to form one dimensional chains running along the *a* axis (Fig. 6). In addition, there are π···π interactions among the C1–C10 and C5–C10 planes in the complex (Cg···Cg = 3.9–4.2 Å, Table 3).

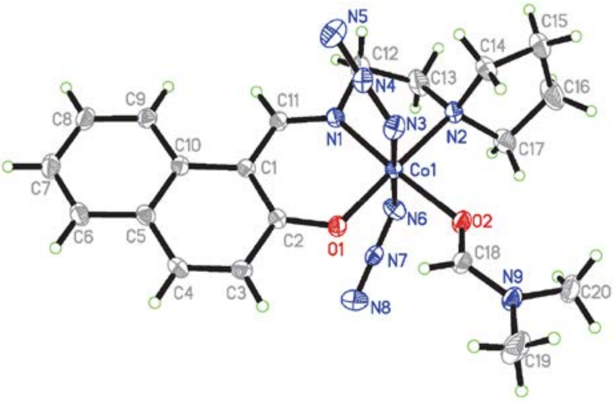


Fig. 5. A perspective view of the molecular structure of complex **3** with the atom labeling scheme. Thermal ellipsoids are drawn at the 30% probability level.

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

	1		
Cu1–O1	1.9016(18)	Cu1–N1	1.933(2)
Cu1–N2	2.065(2)	Cu1–N3	2.026(2)
Cu1–N5A	2.320(2)		
O1–Cu1–N1	92.03(8)	O1–Cu1–N3	88.18(9)
N1–Cu1–N3	158.09(9)	O1–Cu1–N2	171.97(8)
N1–Cu1–N2	84.60(9)	N3–Cu1–N2	92.24(9)
O1–Cu1–N5A	97.77(9)	N1–Cu1–N5A	102.22(9)
N3–Cu1–N5A	99.46(9)	N2–Cu1–N5A	90.08(9)
Symmetry code for A: *x*, –1 + *y*, *z*.			
	2		
Cu1–O1	1.922(3)	Cu1–N1	1.941(5)
Cu1–N2	2.077(4)	Cu1–N3	1.966(5)
Cu1–N5A	2.415(4)		
O1–Cu1–N1	91.06(15)	O1–Cu1–N3	94.42(15)
N1–Cu1–N3	166.3(2)	O1–Cu1–N2	175.54(14)
N1–Cu1–N2	84.82(16)	N3–Cu1–N2	89.23(16)
O1–Cu1–N5A	95.72(14)	N1–Cu1–N5	92.22(18)
N3–Cu1–N5A	99.7(2)	N2–Cu1–N5A	86.16(14)
Symmetry code for A: ½ + *x*, ½ – *y*, ½ + *z*.			
	3		
Co1–O1	1.8726(16)	Co1–O2	1.9521(17)
Co1–N1	1.862(2)	Co1–N2	2.023(2)
Co1–N3	1.976(2)	Co1–N6	1.956(2)
N1–Co1–O1	94.31(8)	N1–Co1–O2	176.07(8)
O1–Co1–O2	89.59(7)	N1–Co1–N6	90.39(10)
O1–Co1–N6	91.04(9)	O2–Co1–N6	89.03(9)
N1–Co1–N3	91.79(9)	O1–Co1–N3	87.85(9)
O2–Co1–N3	88.85(9)	N6–Co1–N3	177.62(10)
N1–Co1–N2	86.79(8)	O1–Co1–N2	177.86(8)
O2–Co1–N2	89.30(8)	N6–Co1–N2	87.11(9)
N3–Co1–N2	93.96(9)		

Table 3. $\pi\cdots\pi$ interactions of the complexes

Cg···*Cg*	distance (Å)	*Cg*···*Cg*	distance (Å)
1			
*Cg*1···*Cg*1^{i}	4.4043(6)	*Cg*1···*Cg*2^{i}	3.7814(6)
3			
*Cg*3···*Cg*4^{ii}	4.1682(3)	*Cg*4···*Cg*4^{ii}	3.9317(3)

Symmetry codes: (i): 1 – *x*, 2 – *y*, –*z*; (ii): –*x*, 1 – *y*, –*z*. *Cg*1 and *Cg*2 are the centroids of C1–C10 and C5–C10 in complex **1**, respectively. *Cg*3 and *Cg*4 are the centroids of C1–C10 and C5–C10 in complex **3**, respectively.

3. 4. IR Spectra

In the infrared spectra of the complexes, there are no typical bands at 3200–3500 cm^{-1}, indicating the coordination of the Schiff bases through deprotonated form. The strong bands at 1621 cm^{-1} for **1**, 1623 cm^{-1} for **2**, and 1620 cm^{-1} for **3** are due to the azomethine groups, μ(C=N).[16] The strong band for the C=O group of the DMF ligand is observed at 1640 cm^{-1} for **3**. The typical absorptions for the dicyanamide ligand in complex **1** are observed at 2282, 2221 and 2152 cm^{-1}.[17] The intense absorptions for the azide ligands in complexes **2** and **3** are observed at 2051 and 2014 cm^{-1}, respectively.[18]

3. 5. Urease Inhibitory Activity

The two copper complexes **1** and **2** have effective inhibitory activity on *Jack bean* urease, with IC$_{50}$ values of 0.43 ± 0.26 and 0.34 ± 0.15 μmol L^{-1}, respectively, whereas the free Schiff base HL and the cobalt complex **3** have weak activity (> 50 μmol L^{-1}). The reported copper complexes have shown better activity than the reference drug acetohydroxamic acid (IC$_{50}$ = 28.5 ± 2.7 μmol L^{-1}) and the copper nitrate (IC$_{50}$ = 8.6 ± 1.5 μmol L^{-1}). The two copper complexes have better activity against urease than the copper(II) complex with the Schiff base ligand *N,N'*-bis(4-fluorosalicylidene)-1,2-diaminopropane (IC$_{50}$ = 2.1–3.4 μmol L^{-1}),[19] and the copper(II) complex with the reduced Schiff base ligand 2,2'-((propane-1,3-diylbis(azanediyl))bis(methylene)diphenol (IC$_{50}$ = 1.6 μmol L^{-1}),[20] and have similar activity when compared with the copper complexes derived from *N'*-(pyridin-2-ylmethylene)picolinohydrazide and 4-methyl-2-(((pyridin-2-ylmethyl)imino)methyl)phenol.[21] The cobalt complex has weaker activities than the cobalt complexes with the Schiff

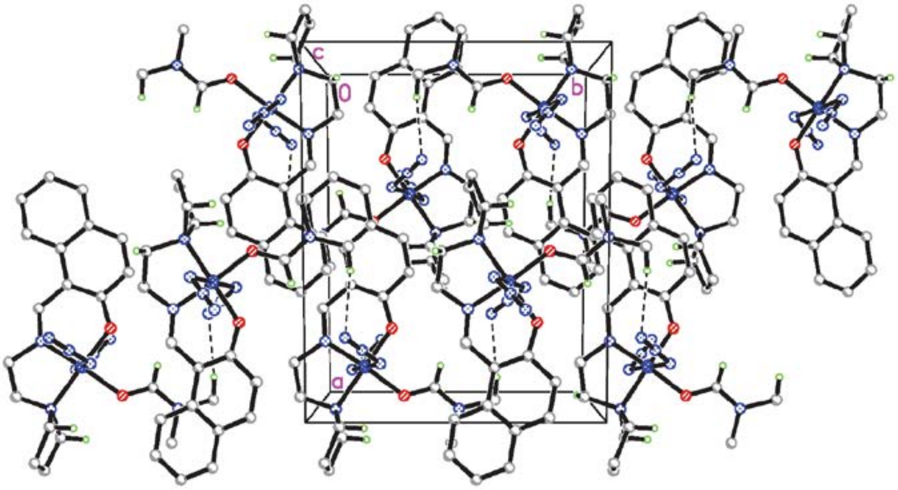


Fig. 6. Molecular packing diagram of complex **3**, viewed along the *c* axis. Hydrogen atoms are omitted for clarity.

base ligands 5-((benzylamino)methylene)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (IC_{50} = 16 μmol L^{-1}),[22] *N,N'*-bis(5-chlorosalicylidene)-1,3-propanediamine (IC_{50} = 45 μmol L^{-1}),[23] *N'*-(2-hydroxy-5-methoxybenzylidene)-3-methylbenzohydrazide and 2-[(2-dimethylaminoethylimino)methyl]-4-methylphenol (IC_{50} = 0.3-4.3 μmol L^{-1}).[24]

4. Conclusion

The present paper intends to report the syntheses, crystal structures and urease inhibition activity of three copper(II) and cobalt(III) complexes with the tridentate Schiff base ligand (((2-(pyrrolidin-1-yl)ethyl)imino)methyl)naphthalen-2-ol. The dicyanamide ligand in **1** and the azide ligand in **2** act as bridging groups, while the azide ligands in **3** act as terminal ligands. The two copper complexes have remarkable inhibitory activity on *Jack bean* urease, with IC_{50} values lower than 1.0 μmol L^{-1}.

Appendix A. Supplementary material

CCDC 2266362 (**1**), 2266363 (**2**) and 2266364 (**3**) contain the supplementary crystallographic data for this article. 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 (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44(0)1223-336033 or E-mail: deposit@ccdc.cam.ac.uk.

5. References

1. (a) A. M. Duff, P. Forrestal, I. Ikoyi, F. Brennan, *Soil Biol. Biochem.* **2022**, *170*, 108709; **DOI:**10.1016/j.soilbio.2022.108709
   (b) T. Lan, Y. X. Huang, X. Song, O. P. Deng, W. Zhou, L. Luo, X. Y. Tang, J. Zeng, G. D. Chen, X. S. Gao, *Environ. Pollut.* **2021**, *293*, 118499; **DOI:**10.1016/j.envpol.2021.118499
   (c) M. P. Byrne, J. T. Tobin, P. J. Forrestal, M. Danaher, C. G. Nkwonta, K. Richards, E. Cummins, S. A. Hogan, T. F. O'Callaghan, *Sustainability* **2020**, *12*, 6018. **DOI:**10.3390/su12156018
2. (a) A. T. Fiori-Duarte, R. P. Rodrigues, R. R. Kitagawa, D. F. Kawano, *Curr. Med. Chem.* **2020**, *27*, 3967–3982; **DOI:**10.2174/0929867326666190301143549
   (b) M. Taha, N. H. Ismail, S. Imran, A. Wadood, F. Rahim, M. Riaz, *J. Bioorg. Med. Chem.* **2015**, *23*, 7211–7218. **DOI:**10.1016/j.bmc.2015.10.017
3. (a) C. Montecucco, R. Rappuoli, *Nat. Rev. Mol. Cell Biol.* **2001**, *2*, 457–466; **DOI:**10.1038/35073084
   (b) H. Mobley, R. P. Hausinger, *Microbiol. Rev.* **1989**, *53*, 85–108. **DOI:**10.1128/mr.53.1.85-108.1989
4. G. I. Perez-Perez, C. B. Gower, M. J. Blaser, *Infect. Immun.* **1994**, *62*, 299–302. **DOI:**10.1128/iai.62.1.299-302.1994
5. (a) W. Q. Song, M. L. Liu, L. C. Yuan, S. Y. Li, Y. N. Wang, Z. P. Xiao, H. L. Zhu, *Bioorg. Med. Chem. Lett.* **2022**, *78*, 129043; **DOI:**10.1016/j.bmcl.2022.129043
   (b) S. Iqbal, A. Khan, R. Nazir, S. Kiran, S. Perveen, K. M. Khan, M. I. Choudhary, *Med. Chem.* **2020**, *16*, 244–255; **DOI:**10.2174/1573406415666190415163309
   (c) S. Daud, O. U. R. Abid, A. Sardar, B. A. Shah, M. Rafiq, A. Wadood, M. Ghufran, W. Rehman, Zain-ul-Wahab, F. Iftikhar, R. Sultana, H. Daud, B. Niaz, *Med. Chem. Res.* **2022**, *31*, 316–336; **DOI:**10.1007/s00044-021-02814-6
   (d) M. Talebi, E. Hamidian, F. Niasari-Naslaji, S. Rahmani, F. S. Hosseini, S. Boumi, M. N. Montazer, M. Asadi, M. Amanlou, *Med. Chem. Res.* **2021**, *30*, 1220–1229; **DOI:**10.1007/s00044-021-02727-4
   (e) M. A. S. Aslam, S. Mahmood, M. Shahid, A. Saeed, J. Iqbal, *Eur. J. Med. Chem.* **2011**, *46*, 5473–5479; **DOI:**10.1016/j.ejmech.2011.09.009
   (f) E. Menteşe, M. Emirik, B. B. Sökmen, *Bioorg. Chem.* **2019**, *86*, 151–158. **DOI:**10.1016/j.bioorg.2019.01.061

6. (a) Z.-J. Chen, Y.-N. Chen, C.-N. Xu, S.-S. Zhao, Q.-Y. Cao, S.-S. Qian, J. Qin, H.-L. Zhu, *J. Mol. Struct.* **2016**, *1117*, 293–299; **DOI:**10.1016/j.molstruc.2016.03.084
(b) Z.-P. Xiao, Z.-Y. Peng, J.-J. Dong, R.-C. Deng, X.-D. Wang, H. Ouyang, P. Yang, J. He, Y.-F. Wang, M. Zhu, X.-C. Peng, W.-X. Peng, H.-L. Zhu, *Eur. J. Med. Chem.* **2013**, *68*, 212–221. **DOI:**10.1016/j.ejmech.2013.07.047
7. (a) W. Yang, Z. Y. Peng, G. C. Wang, *J. Enzyme Inhib. Med. Chem.* **2023**, *38*, 361–375; **DOI:**10.1080/14756366.2022.2150182
(b) A. Barakat, S. M. Soliman, M. Ali, A. Elmarghany, A. M. Al-Majid, S. Yousuf, Z. Ul-Haq, M. I. Choudhary, A. El-Faham, *Inorg. Chim. Acta* **2020**, *503*, 119405; **DOI:**10.1016/j.ica.2019.119405
(c) H. Y. Yu, S. H. Guo, J. Y. Cheng, G. F. Jiang, Z. W. Li, W. Q. Zhai, A. Li, Y. M. Jiang, Z. L. You, *J. Coord. Chem.* **2018**, *71*, 4164–4179; **DOI:**10.1080/00958972.2018.1533959
(d) C. L. Jing, C. F. Wang, K. Yan, K. D. Zhao, G. H. Sheng, D. Qu, F. Niu, H. L. Zhu, Z. L. You, *Bioorg. Med. Chem.* **2016**, *24*, 270–276; **DOI:**10.1016/j.bmc.2015.12.013
(e) L. Habala, A. Roller, M. Matuska, J. Valentova, A. Rompel, F. Devinsky, *Inorg. Chim. Acta* **2014**, *421*, 423–426. **DOI:**10.1016/j.ica.2014.06.035
8. (a) S. Dasgupta, K. Kar, A. Barua, D. Ghosh, B. Kabi, K. Dewan, A. Chandra, *Life Sci.* **2022**, *308*, 120963; **DOI:**10.1016/j.lfs.2022.120963
(b) H. Pervez, N. Khan, J. Iqbal, S. Zaib, M. Yaqub, M. M. Naseer, *Acta Chim. Slov.* **2018**, *65*, 108–118; **DOI:**10.17344/acsi.2017.3649
(c) H. Zhao, X.-R. Liu, X. Wang, J. Hu, Y.-J. Cai, Q.-A. Peng, *Acta Chim. Slov.* **2021**, *68*, 804–810; **DOI:**10.17344/acsi.2021.6781
(d) M. Wozniczka, M. Lichawska, M. Sutradhar, M. Chmiela, W. Gonciarz, M. Pajak, *Pharmaceuticals* **2021**, *14*, 1254. **DOI:**10.3390/ph14121254
9. Bruker, SMART and SAINT, Bruker AXS Inc., Madison, **2002**.
10. G. M. Sheldrick. SADABS, University of Göttingen, Germany, **1996**.
11. G. M. Sheldrick, *Acta Crystallogr.* **2015**, *C71*, 3–8.
12. W.-J. Mao, P.-C. Lv, L. Shi, H.-Q. Li, H.-L. Zhu, *Bioorg. Med. Chem.* **2009**, *17*, 7531–7536. **DOI:**10.1016/j.bmc.2009.09.018
13. A. W. Addison, T. N. Rao, J. Reedijk, J. van Rijn, G. C. Verschoor, *J. Chem. Soc., Dalton Trans.* **1984**, 1349–1356. **DOI:**10.1039/DT9840001349
14. (a) S.-F. Yu, X.-Y. Qiu, S.-J. Liu, *Acta Chim. Slov.* **2020**, *67*, 1301–1308; **DOI:**10.17344/acsi.2020.6321
(b) J. Q. Wang, Y. Y. Luo, Y. X. Zhang, Y. Chen, F. Gao, Y. Ma, D. M. Xian, Z. L. You, *J. Coord. Chem.* **2021**, *74*, 1028–1038. **DOI:**10.1080/00958972.2020.1861603
15. (a) D. Bandyopadhyay, M. Layek, M. Fleck, R. Saha, C. Rizzoli, *Inorg. Chim. Acta* **2017**, *461*, 174–182; **DOI:**10.1016/j.ica.2017.02.018
(b) X. Q. Luo, Q. R. Liu, Y. J. Han, L. W. Xue, *Acta Chim. Slov.* **2020**, *67*, 159–166; **DOI:**10.17344/acsi.2019.5303
(c) H. Y. Qian, *Acta Chim. Slov.* **2021**, *68*, 700–708. **DOI:**10.17344/acsi.2021.6721
16. (a) Y. Y. Luo, J. Q. Wang, B. T. Zhang, Y. X. Guan, T. Yang, X. Y. Li, L. Y. Xu, J. Wang, Z. L. You, *J. Coord. Chem.* **2020**, *73*, 1765–1777; **DOI:**10.1080/00958972.2020.1795645
(b) M. M. Duan, Y. M. Li, L. Y. Xu, H. L. Yang, F. W. Luo, Y. X. Guan, B. T. Zhang, C. L. Jing, Z. L. You, *Inorg. Chem. Commun.* **2019**, *100*, 27–31. **DOI:**10.1016/j.inoche.2018.12.009
17. (a) A. Ray, G. Pilet, C. J. Gomez-Garcia, S. Mitra, *Polyhedron* **2009**, *28*, 511–520; **DOI:**10.1016/j.poly.2008.11.054
(b) P. Talukder, S. Shit, A. Sasmal, S. R. Batten, B. Moubaraki, K. S. Murray, S. Mitra, *Polyhedron* **2011**, *30*, 1767–1773. **DOI:**10.1016/j.poly.2011.03.049
18. (a) S.-F. Yu, X.-Y. Qiu, S.-J. Liu, *Acta Chim. Slov.* **2020**, *67*, 1301–1308; **DOI:**10.17344/acsi.2020.6321
(b) G.-P. Cheng, L.-W. Xue, C.-X. Zhang, *Acta Chim. Slov.* **2017**, *64*, 261–265. **DOI:**10.17344/acsi.2016.3036
19. Y. Y. Luo, J. Q. Wang, B. T. Zhang, Y. X. Guan, T. Yang, X. Y. Li, L. Y. Xu, J. Wang, Z. L. You, *J. Coord. Chem.* **2020**, *73*, 1765–1777. **DOI:**10.1080/00958972.2020.1795645
20. M. M. Duan, Y. M. Li, L. Y. Xu, H. L. Yang, F. W. Luo, Y. X. Guan, B. T. Zhang, C. L. Jing, Z. L. You, *Inorg. Chem. Commun.* **2019**, *100*, 27–31. **DOI:**10.1016/j.inoche.2018.12.009
21. J. Jiang, P. Liang, H. Yu, Z. You, *Acta Chim. Slov.* **2022**, *69*, 629–637. **DOI:**10.17344/acsi.2022.7513
22. A. Barakat, S. M. Soliman, M. Ali, A. Elmarghany, A. Mohammed Al-Majid, S. Yousuf, Z. Ul-Haq, M.I. Choudhary, A. El-Faham, *Acta Chim. Slov.* **2022**, *69*, 629–637.
23. Z.-L. You, P. Zhou, *Inorg. Chem. Commun.* **2007**, *10*, 1273–1275. **DOI:**10.1016/j.inoche.2007.08.007
24. C. Jing, C. Wang, K. Yan, K. Zhao, G. Sheng, D. Qu, F. Niu, H. Zhu, Z. You, *Bioorg. Med. Chem.* **2016**, *24*, 270–276. **DOI:**10.1016/j.bmc.2015.12.013

Povzetek

Sintetizirali smo tri bakrove(II) in kobaltove(III) komplekse $[CuL(dca)]_n$ (**1**), $[CuL(N_3)]_n$ (**2**) in $[CoL(N_3)_2(DMF)]$ (**3**), kjer je L monoanionska oblika Schiffove baze (((2-(pirolidin-1-il)etil)imino)metil)naftalen-2-ol (HL) in dca je dicianamid, ter jih okarakterizirali z elementno analizo, IR in UV-Vis spektroskopijo ter monokristalno rentgensko difrakcijo. Cu atomi v kompleksih **1** in **2** so v kvadratno piramidalni koordinaciji, Co atom v kompleksu **3** pa v oktaedrični. Kompleksa **1** in **2** zavirata ureazo stročnice *Canavalia ensiformis* z vrednostmi IC_{50} 0,25 ± 0,14 oziroma 0,32 ± 0,15 μmol L^{-1}. Kompleks **3** ima šibko delovanje na ureazo stročnice *Canavalia ensiformis* s 37 % inhibicije.