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Synthesis, characterization and antimicrobial activity of pentagonal-bipyramidal isothiocyanato Co(II) and Ni(II) complexes with 2,6-diacetylpyridine bis(trimethylammoniumacetohydrazone)

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Pentagonal-bipyramidal isothiocyanato Co(II) and Ni(II) complexes with condensation product of 2,6-diacetylpyridine and trimethylammoniumacetohydrazide (Girard's T reagent) were synthesized and characterized by elemental analyses, IR and UV-Vis spectra, molar conductivity and magnetic susceptibility. Crystal structures of the Co(II) and Ni(II) complexes were also determined. Antimicrobial activities of the ligand and metal complexes were examined.

Keywords: Co(II) Complexes; Ni(II) Complexes; 2,6-Diacetylpyridine dihydrazone; Crystal structure; Antimicrobial activity

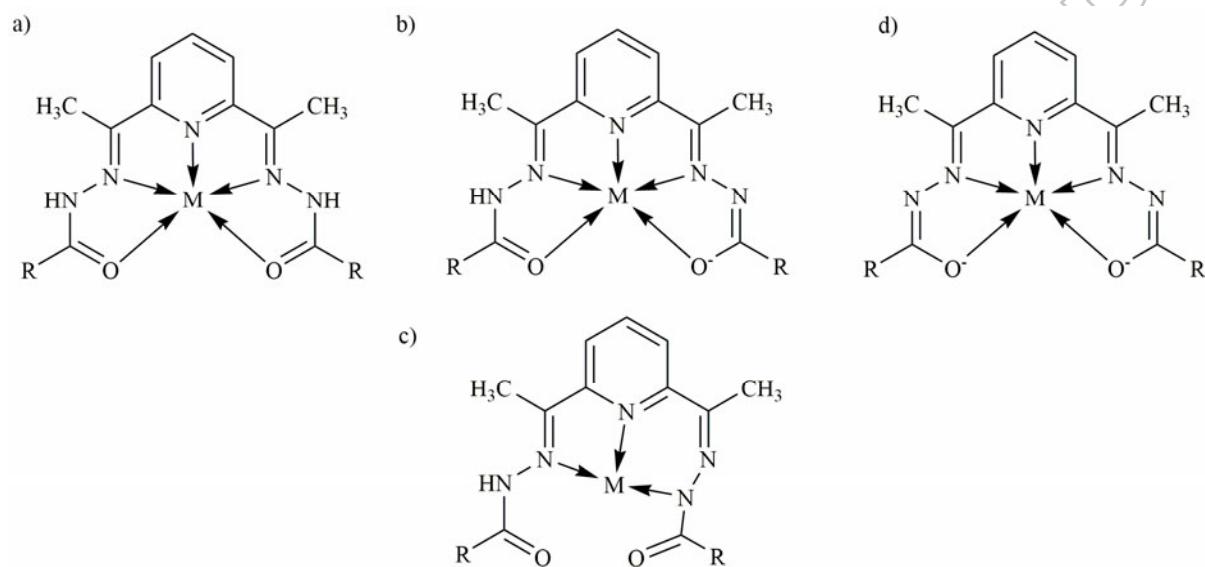
1. Introduction

Schiff bases and their transition metal complexes are studied because of their wide range of possible applications [1-3]. Schiff base ligands with additional donors near the azomethine nitrogen are able to form stable chelates [3]. Conformational flexibility and large number of potential donors of 2,6-diacetylpyridine dihydrazones allow different modes of coordination to

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metal ions. Most obtained complexes have pentagonal-bipyramidal (PBPY-7) geometry with pentadentate coordination of dihydrazone *via* pyridine nitrogen, two azomethine nitrogens and two carbonyl oxygens (N_3O_2) while apical positions are occupied by monodentate ligands [4-9]. Depending on the reaction conditions and nature of the metal, 2,6-diacetylpyridine dihydrazones are able to coordinate in neutral (scheme 1a) [4-9], mono- (schemes 1b and 1c) [10] and double-deprotonated forms (scheme 1d) [11]. Lanthanide complexes with coordination numbers larger than seven were reported [12-17] with one dihydrazone ligand and the remaining coordination sites occupied with monodentate or bidentate ligands [12-17]; however, in isostructural complexes of Pr(III) and Sm(III) two ligands are pentadentate N_3O_2 coordinated to the metal ion [14]. Mono- and binuclear octahedral complexes of Ni(II) with 2,6-diacetylpyridine dihydrazones were reported [18-20]. In the mononuclear Ni(II) complex, two monodeprotonated dihydrazone ligands are NNO tridentate, coordinated through pyridine nitrogen, azomethine nitrogen and carbonyl oxygen [18]. In binuclear Ni(II) complexes, the dihydrazone ligands are coordinated to one Ni(II) center through protonated amide oxygen and azomethine nitrogen, while the pyridine nitrogen is a bridge between two nickel centers [19, 20]. Dinuclear complexes of Zn(II) with octahedral [11] and square-pyramidal geometry [21] around metal centers were reported. Reported complexes of Cu(II) with 2,6-diacetylpyridine dihydrazones possess square-pyramidal geometry with different patterns of dihydrazone ligand coordination [10, 22]. In the case of Cu(II) complex with condensation product of 2,6-diacetylpyridine and semioxamide, the ligand is coordinated through pyridine nitrogen and deprotonated hydrazine nitrogen and the other neutral chain in the coordination includes only azomethine nitrogen (scheme 1c) [10], while in Cu(II) complexes with 2,6-diacetylpyridinebis(benzoic acid hydrazone) the ligand is coordinated as N,N',N'' -tridentate (scheme 1b) [22]. In binuclear Cu(II) complexes with 2,6-diacetylpyridinebis(benzoic acid hydrazone), each Cu(II) binds to three sites of one ligand and two sites of a second ligand [22]. Polynuclear cyanide-bridged compounds consisting of alternating pentagonal-bipyramidal complexes of 2,6-diacetylpyridine dihydrazone and cyanide complexes of Cr(III), Fe(II) or W(V) as building blocks are interesting for structural but magnetic properties [23-25]. Good antimicrobial, genotoxic and SOD activity of 2,6-diacetylpyridine dihydrazone complexes, in some cases similar to the activity of standard drugs, makes them worth investigating because of their potential medicinal use [26-28]. Formation of stable lanthanide complexes with this type of ligand allows them to be used in MRI

as contrast agents [12, 13]. Because of interesting structural characteristic of 2,6-diacetylpyridine dihydrazone complexes and opportunities of applications, we have examined the coordination properties of condensation product of 2,6-diacetylpyridine and trimethylammoniumacetohydrazide (Girard's T reagent) and antimicrobial activity of its isothiocyanato Co(II) and Ni(II) complexes.



Scheme 1. Basic coordination modes of 2,6-diacetylpyridine dihydrazone ligands in: a) neutral; b) and c) monodeprotonated; d) double deprotonated form.

2. Experimental

2.1. Materials and methods

2,6-Diacetylpyridine (99%) and Girard's T reagent (99%) were obtained from Aldrich. IR spectra were recorded on a Nicolet 6700 FT-IR spectrometer using the ATR technique from 4000–400 cm^{-1} . Elemental analyses (C, H and N) were performed by standard micro-methods using the ELEMENTARVario ELIII C.H.N.S.O analyzer. Molar conductivities were measured at room temperature (23 °C) on a digital conductivity-meter JENWAY-4009. UV–Vis spectra were recorded on a Shimadzu 1800 UV-Vis spectrometer. Magnetic measurements were performed at 26 °C by Evans' method using an MSB-MK1 balance (Sherwood Scientific Ltd.) with $\text{Hg}[\text{Co}(\text{SCN})_4]$ as calibrant; diamagnetic corrections were calculated from Pascal's constants.

2.2. Synthesis of H_2LCl_2

H_2LCl_2 was obtained by the condensation reaction of 2,6-diacetylpyridine and trimethylammoniumacetohydrazide chloride (Girard's T reagent) using a previously reported method [9]. Yield: 0.23 g (87%). IR: 3394 (s), 3115 (m), 3071 (m), 3020 (m), 2969 (w), 2934 (w), 1709 (vs), 1630 (w), 1568 (w), 1489 (m), 1423 (m), 1366 (w), 1329 (w), 1281 (m), 1228 (m), 1153 (w), 1123 (w), 993 (w), 949 (w), 922 (w), 855 (w), 827 (w), 744 (w), 702 (w) and 663 (w). Anal. Calcd. for $C_{19}H_{41}N_7O_6Cl_2$ (%): C, 42.70; H, 7.73; N, 18.34. Found: C, 42.73; H, 7.69; N, 18.35.

2.3. Synthesis of $Co(H_2L)(NCS)_2(SCN)_2$ and $[Co(H_2L)(NCS)_2][Co(NCS)_4]$

$CoCl_2 \cdot 6H_2O$ (0.04 g, 0.25 mmol) and H_2LCl_2 (0.13 g, 0.25 mmol) were dissolved in methanol (20 mL), then solid NH_4SCN (0.08 g, 1.00 mmol) was added. The reaction mixture was refluxed for 2 h at 65 °C. Slow evaporation of the reaction solution resulted in formation of $[Co(H_2L)(NCS)_2](SCN)_2$ (red crystals) and $[Co(H_2L)(NCS)_2][Co(NCS)_4]$ (green crystals) which can be easily separated by fractional crystallization.

$[Co(H_2L)(NCS)_2](SCN)_2$: Yield: 0.06 g (~33%). IR: 3609 (w), 3379 (w), 3125 (w), 3019 (w), 2966 (w), 2071 (vs), 2034 (vs), 1661 (m), 1634 (w), 1537 (m), 1478 (m), 1440 (w), 1272 (w), 1206 (w), 1169 (w), 1127 (w), 1085 (w), 1022 (w), 968 (w), 922 (w), 812 (w), 740 (w) and 626 (w). Found: C, 38.33; H, 5.14; N, 21.39; S, 17.88. λ_{max} (nm) (1 mM, H_2O): 272, 301, 365. $\mu_{eff} = 4.98$ B.M. Λ_M (1 mM, H_2O): $254 \Omega^{-1} cm^2 mol^{-1}$.

$[Co(H_2L)(NCS)_2][Co(NCS)_4]$: Yield: 0.12 g (~54%). IR: 3410 (w), 3188 (w), 3023 (w), 2918 (w), 2108 (s), 2073 (vs), 1667 (m), 1636 (w), 1551 (w), 1517 (w), 1466 (w), 1263 (w), 1170 (w), 966 (w), 914 (w) and 811 (w). Found: C, 33.49; H, 4.12; N, 20.31; S, 21.47. λ_{max} (nm) (1 mM, H_2O): 270, 300, 358. $\mu_{eff} = 2.65$ B.M. Λ_M (1 mM, H_2O): $241 \Omega^{-1} cm^2 mol^{-1}$.

2.4. Synthesis of $[Ni(H_2L)(NCS)_2](SCN)_2$

$NiCl_2 \cdot 6H_2O$ (0.06 g, 0.25 mmol) and H_2LCl_2 (0.13 g, 0.25 mmol) were dissolved in acetonitrile (20 mL) and solid NH_4SCN (0.08 g, 1.00 mmol) was added. The reaction mixture was heated for 2 h at 65 °C. After two weeks green crystals precipitated from the solution. Yield: 0.15 g (~83%). IR: 3123 (w), 3019 (w), 2965 (w), 2910 (w), 2805 (w), 2093 (vs), 2046 (vs), 1685 (s),

1626 (w), 1552 (m), 1479 (m), 1441 (w), 1266 (w), 1189 (w), 1122 (w), 968 (w), 918 (w), 818 (w) and 760 (w). Found: C, 38.49; H, 5.12; N, 21.35; S, 17.81. λ_{max} (nm) (1 mM, H₂O): 266, 300, 363. $\mu_{\text{eff}} = 3.94$ B.M. Λ_{M} (1 mM, H₂O): 265 $\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$.

2.5. Synthesis of [Mn(H₂L)(NCS)₂](SCN)₂

[Mn(H₂L)(NCS)₂](SCN)₂ was synthesized according to previously described procedure [9]. Anal. Calcd. for C₂₄H₃₇N₁₁MnO₃S₄ (%): C, 40.55; H, 5.25; N, 21.68; S, 18.04. Found: C, 40.39; H, 5.14; N, 21.45; S, 18.12.

2.6. X-ray structure determination

Crystal data and refinement parameters of [Co(H₂L)(NCS)₂](SCN)₂, [Co(H₂L)(NCS)₂][Co(NCS)₄] and [Ni(H₂L)(NCS)₂](SCN)₂ are listed in table 1. The X-ray intensity data were collected at 150 K with an Agilent SuperNova dual source using an Atlas detector and equipped with mirror-monochromated MoK α radiation ($\lambda = 0.71073 \text{ \AA}$) for [Co(H₂L)(NCS)₂](SCN)₂ and [Ni(H₂L)(NCS)₂](SCN)₂ and CuK α radiation ($\lambda = 1.54184 \text{ \AA}$) for [Co(H₂L)(NCS)₂][Co(NCS)₄]. The data were processed using CRYALIS PRO [29]. The structures were solved using SIR-92 [30] or SHELXS-97 [31] and refined by full-matrix least-squares based on F^2 using SHELXL-97 [31]. All non-hydrogen atoms were refined anisotropically. The N2 and N6 bonded hydrogens in all complexes were located in a difference map and refined with the distance restraints (DFIX) with N-H = 0.88 and $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{N})$. In the final model of refinement some residual density peaks were found in all structures. These peaks are unrefineable and probably an indication of additional solvent molecules. The water molecule in [Co(H₂L)(NCS)₂](SCN)₂ is disordered over a two-fold rotation axis. Water molecules in [Ni(H₂L)(NCS)₂](SCN)₂ were unrefinable and excluded from the model. From the elemental analysis we can conclude the proper formula of [Co(H₂L)(NCS)₂](SCN)₂ and [Ni(H₂L)(NCS)₂](SCN)₂.

CCDC 1429633-1429635 contains the supplementary crystallographic data for [Co(H₂L)(NCS)₂](SCN)₂, [Co(H₂L)(NCS)₂][Co(NCS)₄] and [Ni(H₂L)(NCS)₂](SCN)₂, respectively. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

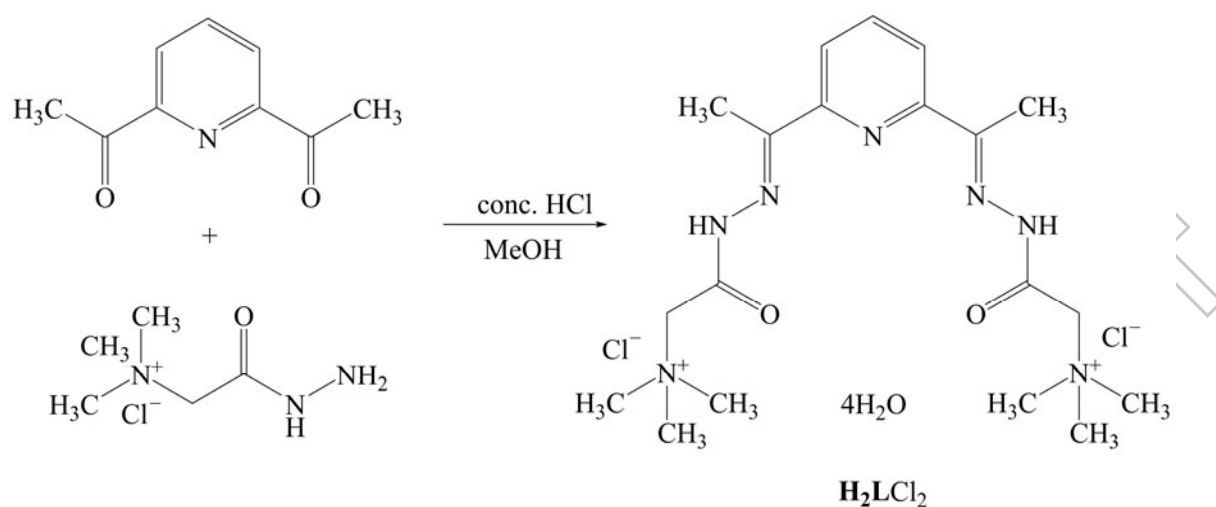
2.7. Antimicrobial activity

Antimicrobial activity was tested against eight laboratory control strains of microorganisms, *i.e.* Gram-positive bacteria: *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Bacillus subtilis*, Gram-negative bacteria: *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Salmonella enterica*, and one strain of yeast *Candida albicans*. Minimum inhibitory concentration (MIC) was determined by broth micro dilution test according to Clinical and Laboratory Standards Institute guidelines [32]. The tested compounds were dissolved in 1% (v/v) DMSO (except ligand which was dissolved in H₂O). Twofold dilutions of compounds and reference drug were prepared. All tests were performed in Müller-Hinton broth for the bacterial strains and Sabouraud dextrose broth for *C. albicans*. All of the MIC determinations were performed in duplicate, and two positive growth controls were included. 2,3,5-Triphenyl-2H-tetrazolium chloride (Sigma-Aldrich) was used in concentration 0.05% as a growth indicator for tested microbial strains (5×10^6 CFU/mL). MICs were determined after incubation for 24 h at 35 °C in aerobic conditions.

3. Results and discussion

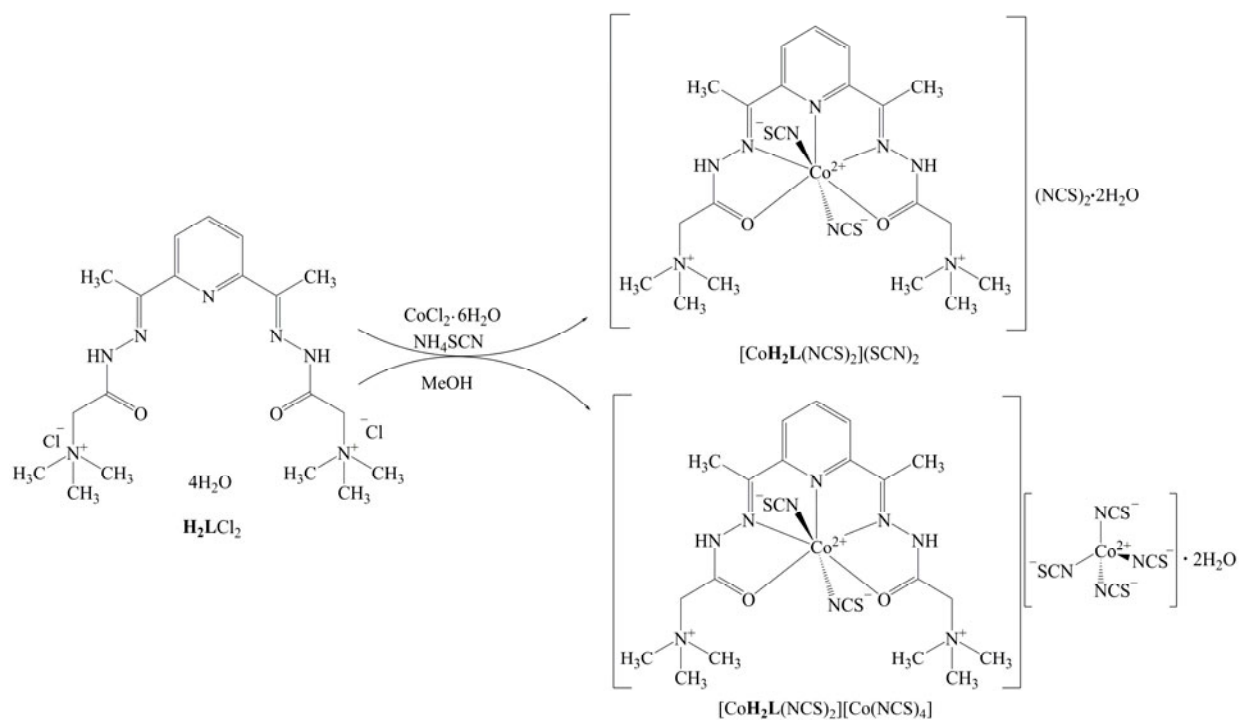
3.1. Chemistry

H₂LC₂ was synthesized from reaction of 2,6-diacetylpyridine and trimethylammoniumacetohydrazide chloride using the previously reported method (scheme 2) [9].



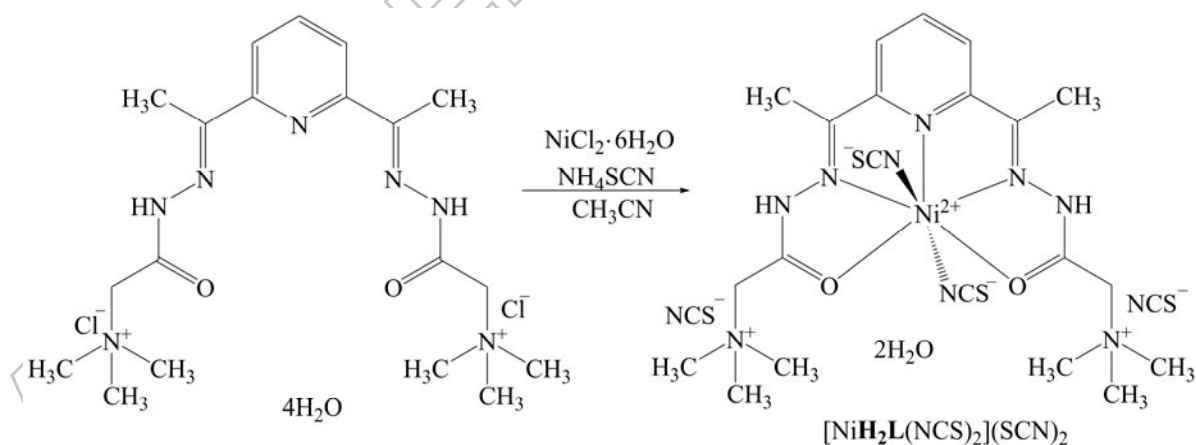
Scheme 2. Synthesis of **H₂LCl₂** from 2,6-diacetylpyridine (top left) and Girard's T reagent (bottom left).

Isothiocyanato complexes of Co(II) and Ni(II) were synthesized performing direct and template methods of synthesis. Both direct and template synthesis of Co(II) complexes resulted in formation of two complexes with the same complex cation, but different anions, *i.e.* thiocyanate anions in [Co(**H₂L**)(NCS)₂](SCN)₂ and anionic tetrahedral complex [Co(NCS)₄]²⁻ in [Co(**H₂L**)(NCS)₂][Co(NCS)₄] (scheme 3).



Scheme 3. Synthesis of $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$ and $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2][\text{Co}(\text{NCS})_4]$.

$[\text{Ni}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$ was isolated only in direct reaction, while template reaction resulted in decomposition of unstable complex to the starting compounds (scheme 4).



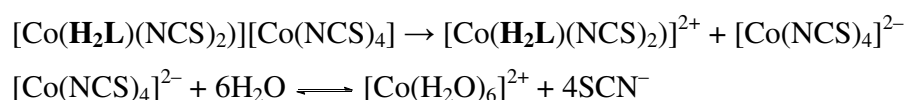
Scheme 4. Synthesis of $[\text{Ni}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$.

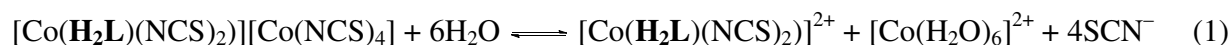
$[\text{Mn}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$ was obtained according to the previously published method [9].

The ligand and the complexes were characterized by elemental analysis, IR and UV-Vis spectroscopy, conductometric and magnetic measurements and X-ray analysis.

Coordination of the carbonyl oxygen in $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$, $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2][\text{Co}(\text{NCS})_4]$ and $[\text{Ni}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$ results in bathochromic shift of the $\nu(\text{C}=\text{O})$ from 1709 cm^{-1} in the spectrum of H_2LCl_2 to 1661 cm^{-1} in the spectrum of $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$, 1667 cm^{-1} in the spectrum of $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2][\text{Co}(\text{NCS})_4]$ and 1685 cm^{-1} in the spectrum of $[\text{Ni}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$ [9]. In IR spectra of complexes $\nu(\text{C}=\text{N})$ bands shift from 1630 cm^{-1} in the spectrum of H_2LCl_2 to 1634 cm^{-1} in $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$, 1636 cm^{-1} in $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2][\text{Co}(\text{NCS})_4]$ and 1626 cm^{-1} in $[\text{Ni}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$ suggesting coordination of the azomethine nitrogen [9]. Two bands in the $\nu(\text{CN})$ vibration range of NCS^- at 2108 cm^{-1} and 2073 cm^{-1} in IR spectrum of $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2][\text{Co}(\text{NCS})_4]$ originate from N coordinated thiocyanato ligands. The band at higher energy corresponds to isothiocyanato ligands from tetrahedral $[\text{Co}(\text{NCS})_4]^{2-}$, while the band at lower energy originates from isothiocyanato ligands in the complex cation. In the spectrum of $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$ the band at 2071 cm^{-1} can be attributed to the SCN^- group coordinated through its nitrogen and the band at lower energy 2034 cm^{-1} originates from non-coordinated SCN^- . Similarly, the band at 2092 cm^{-1} in the spectrum of $[\text{Ni}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$ corresponds to coordinated isothiocyanate, while the band at 2046 cm^{-1} can be assigned to uncoordinated SCN^- [33].

The observed electronic absorption spectra of $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$ and $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2][\text{Co}(\text{NCS})_4]$ indicate the presence of the same pentagonal-bipyramidal complex cation in aqueous solution [34]. In the case of $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2][\text{Co}(\text{NCS})_4]$ transformation presented with equation 1 occurred in aqueous solution. The absence of absorption maximum at 625 nm ($\epsilon = 1800\text{ M}^{-1}\text{ cm}^{-1}$) corresponding to tetrahedral isothiocyanato Co(II) complex is not surprising because of its low stability in water ($K_f = 10^{-3}\text{ M}^{-1}$) [35]. These results are consistent with the observed values of molar conductivity of $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$ and $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2][\text{Co}(\text{NCS})_4]$ corresponding to 1:2 electrolytes [36, 37].





The observed magnetic moment of $[\text{Co}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2](\text{SCN})_2$ ($\mu_{\text{eff}} = 4.98$ B.M.) and $[\text{Ni}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2](\text{SCN})_2$ ($\mu_{\text{eff}} = 3.94$ B.M.) can be attributed to high-spin complexes with three and two unpaired electrons, respectively [38].

3.2. Crystal structures

Crystals suitable for X-ray analysis were obtained by slow evaporation of solvent at room temperature. Selected bond lengths and angles are given in table 2. The structures of all three complexes possess pentadentate 2,6-diacetylpyridine dihydrazone ligand forming four fused five-membered chelate rings. Two additional SCN^- ligands fulfill coordination number seven forming distorted pentagonal-bipyramidal coordination geometries. The coordination geometry of cationic complex in $[\text{Co}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2](\text{SCN})_2$, $[\text{Co}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2][\text{Co}(\text{NCS})_4]$ and $[\text{Ni}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2](\text{SCN})_2$ is close to other pentagonal-bipyramidal complexes with N_3O_2 donor sets [4-9].

The cationic part of $[\text{Co}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2](\text{SCN})_2$ is depicted in figure 1. Two uncoordinated SCN^- ligands are connected via two $\text{N}-\text{H}\cdots\text{N}$ hydrogen bonds (figure S1, table S1).

In $[\text{Co}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2][\text{Co}(\text{NCS})_4]$, the counter ion of cationic cobalt-ligand complex is anionic tetrahedral $[\text{Co}(\text{NCS})_4]^{2-}$ instead of two SCN^- ligands (figure 2). In the solid state of $[\text{Co}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2][\text{Co}(\text{NCS})_4]$, the cations are connected by $\text{N}-\text{H}\cdots\text{S}$ hydrogen bonds into infinite chains. Additional $\text{N}-\text{H}\cdots\text{O}$ and $\text{O}-\text{H}\cdots\text{O}$ hydrogen bonds exist between complex cation and uncoordinated water (figure S2, table S1).

The crystal structure of $[\text{Ni}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2](\text{SCN})_2$ (figure 3) is isomorphous with the structure of $[\text{Co}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2](\text{SCN})_2$. The crystal space group and cell dimensions are almost identical regardless of nickel as the central ion. The hydrogen bonding topology in $[\text{Ni}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2](\text{SCN})_2$ (identical to $[\text{Co}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2](\text{SCN})_2$) is depicted in figure S3 (table S1). In the crystals of isostructural complex cations $[\text{M}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2]^{2+}$ ($\text{M} = \text{Co}(\text{II})$ and $\text{Ni}(\text{II})$) form dimers through the $\text{C}-\text{H}\cdots\pi$ interactions ($\text{H14B}\cdots\text{Cg}$ distance is 2.90 \AA , where Cg is the center of gravity of the pyridine ring). Dimers are illustrated in the Supplementary Material (figure S4). In $[\text{Mn}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2](\text{SCN})_2$, the complex cations $[\text{Mn}(\mathbf{H}_2\mathbf{L})(\text{NCS})_2]^{2+}$ also form dimers, but through $\pi\cdots\pi$ interactions between pyridine rings [9].

3.3. Antimicrobial activity

The antimicrobial activities of H_2LCl_2 , $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2][\text{Co}(\text{NCS})_4]$, $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$ and $[\text{Ni}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$, as well as previously synthesized $[\text{Mn}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$, were examined against Gram-positive bacteria: *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Bacillus subtilis*, Gram-negative bacteria: *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Salmonella enterica*, and one strain of yeast *Candida albicans* using a micro broth dilution assay. The observed MIC values for the complexes were much higher than that for gentamicin, ceftriaxone and amphotericin B (table 3). The ligand and corresponding salts ($\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$, $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$, $\text{MnCl}_2 \cdot 2\text{H}_2\text{O}$ and NH_4SCN) were inactive. All the complexes showed the most pronounced activity against Gram positive bacteria *S. aureus* and *S. epidermidis*. Among the Co(II) complexes better activity was observed for $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$. The low stability of $[\text{Co}(\text{NCS})_4]^{2-}$ in water solution (equation 1) makes it clear that the presence of pentagonal-bipyramidal complex cation is crucial for antimicrobial activity of Co(II) complexes. Coordination of metal ions to 2,6-diacetylpyridine dihydrazone results in increased activity of the corresponding complexes, which can be explained on the basis of chelation theory [39-41]. Metal ion chelates are more capable to penetrate through cell membrane of microorganism due to electron delocalization over the whole chelate ring and sharing of positive charge of metal ions with donor atoms of ligands [41]. The central metal in pentagonal-bipyramidal complex has influence on antimicrobial activity of compounds. Among the investigated complexes the best activity was observed for Mn(II) complex.

4. Conclusion

The synthesized high-spin pentagonal-bipyramidal isothiocyanato complexes of Co(II) and Ni(II) with pentadentate 2,6-diacetylpyridine bis(trimethylammoniumacetohydrazone) ligand coordinated in equatorial plane *via* N_3O_2 donor set and two additional SCN^- ligands in apical positions. Coordination of 2,6-diacetylpyridine bis(trimethylammoniumacetohydrazone) leads to the improved activity against Gram positive bacteria, but the observed MIC values are higher than those of standard antibacterial and antifungal drugs. Schiff base ligand containing trimethylammoniumacetohydrazone and metal complexes showing stronger activity than

[Co(H₂L)(NCS)₂][Co(NCS)₄], [Co(H₂L)(NCS)₂](SCN)₂, [Ni(H₂L)(NCS)₂](SCN)₂ and [Mn(H₂L)(NCS)₂](SCN)₂ are reported. The presence of quaternary ammonium salt improves solubility of complexes in water, while the nature of metal ion and donors from hydrazone and monodentate ligands dictate their geometry [42-46]. Further systematic research of coordination and pharmacological properties of Schiff base ligands containing trimethylammoniumaceto-hydrazone are necessary to elucidate the structure-activity relationship.

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Table 1. Crystal data and structure refinement details for [Co(H₂L)(NCS)₂](SCN)₂, [Co(H₂L)(NCS)₂][Co(NCS)₄] and [Ni(H₂L)(NCS)₂](SCN)₂.

	[Co(H ₂ L)(NCS) ₂](SCN) ₂	[Co(H ₂ L)(NCS) ₂][Co(NCS) ₄]	[Ni(H ₂ L)(NCS) ₂](SCN) ₂
Formula	C ₂₃ H ₃₇ CoN ₁₁ O ₄ S ₄	C ₂₅ H ₃₇ Co ₂ N ₁₃ O ₄ S ₆	C ₂₃ H ₃₇ N ₁₁ NiO ₄ S ₄
Fw (g mol ⁻¹)	718.81	893.90	718.59
Crystal size (mm)	0.50 × 0.40 × 0.30	0.30 × 0.20 × 0.02	0.50 × 0.30 × 0.10
Crystal color	Red	Green	Green
Radiation, wavelength (Å)	MoKα, 0.71073	CuKα, 1.54184	MoKα, 0.71073
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	<i>I</i> 2/ <i>a</i>	<i>P</i> 2 ₁ / <i>n</i>	<i>I</i> 2/ <i>a</i>
<i>a</i> (Å)	18.0935(6)	20.9201(7)	18.0808(6)
<i>b</i> (Å)	13.1154(4)	9.0845(2)	13.2134(4)
<i>c</i> (Å)	27.6303(9)	21.0055(6)	27.5013(10)
β (°)	104.165(3)	91.356(3)	104.270(4)
<i>V</i> (Å ³)	6357.4(4)	3991.0(2)	6367.6(4)
<i>Z</i>	8	4	8
Calcd density (g cm ⁻³)	1.502	1.488	1.499
<i>F</i> (000)	3000	1840	3008
Collected reflns.	19566	14377	20299
Independent reflns.	7285	7722	7299
<i>R</i> _{int}	0.0283	0.0721	0.0295
Reflns. observed	5986	5044	6134
Parameters	399	477	384
<i>R</i> [<i>I</i> > 2σ(<i>I</i>)] ^a	0.0718	0.0702	0.0550
<i>wR</i> ₂ (all data) ^b	0.2123	0.1966	0.1741
<i>Goof</i> , <i>S</i> ^c	1.028	1.030	1.031
Maximum/minimum residual electron density (e Å ⁻³)	+2.28/-1.82	+1.67/-0.74	+3.06/-0.98

^a $R = \frac{\sum ||F_o| - |F_c||}{\sum |F_o|}$; ^b $wR_2 = \left\{ \frac{\sum [w(F_o^2 - F_c^2)^2]}{\sum [w(F_o^2)^2]} \right\}^{1/2}$.

^c $S = \left\{ \frac{\sum [w(F_o^2 - F_c^2)^2]}{n/p} \right\}^{1/2}$ where *n* is the number of reflections and *p* is the total

Table 2. Selected bond lengths (Å) and angles (°) of [Co(H₂L)(NCS)₂](SCN)₂, [Co(H₂L)(NCS)₂][Co(NCS)₄] and [Ni(H₂L)(NCS)₂](SCN)₂.*

	[Co(H ₂ L)(NCS) ₂](SCN) ₂	[Co(H ₂ L)(NCS) ₂][Co(NCS) ₄]	[Ni(H ₂ L)(NCS) ₂](SCN) ₂
M–N3	2.191(3)	2.171(4)	2.157(3)
M–N4	2.188(3)	2.180(4)	2.015(3)
M–N5	2.207(3)	2.194(5)	2.139(3)
M–N8	2.048(3)	2.097(5)	1.997(3)
M–N9	2.094(4)	2.087(5)	1.989(3)
M–O1	2.290(3)	2.192(4)	2.573(3)
M–O2	2.291(3)	2.219(4)	2.544(2)
O1–M–N3	70.69(10)	71.77(15)	67.99(10)
O1–M–N4	140.36(12)	142.57(16)	143.26(10)
O1–M–N5	148.95(13)	147.30(15)	141.75(9)
O1–M–N8	88.36(12)	86.63(17)	81.60(11)
O1–M–N9	82.85(13)	88.79(17)	82.05(10)
O1–M–O2	78.41(10)	76.99(15)	73.82(7)

*M = Co ([CoH₂L(NCS)₂](SCN)₂, [CoH₂L(NCS)₂][Co(NCS)₄]; Ni [NiH₂L(NCS)₂](SCN)₂.

Table 3. Minimum inhibitory concentration of investigated compounds (values in µg/mL).

Microorganism	[Co(H ₂ L)(NCS) ₂](SCN) ₂	[Co(H ₂ L)(NCS) ₂][Co(NCS) ₄]	[Ni(H ₂ L)(NCS) ₂](SCN) ₂	[Mn(H ₂ L)(NCS) ₂](SCN) ₂	gentamicin	ceftriaxone	amphotericin B
<i>S. aureus</i> ATCC 6538	1000.0	1000.0	500.0	500.0	0.5	0.5	n.t.
<i>S. epidermidis</i> ATCC 12228	125.0	1000.0	500.0	125.0	0.5	0.5	n.t.
<i>B. subtilis</i> ATCC 6633	1000.0	>1000.0	1000.0	1000.0	0.5	1.0	n.t.
<i>E. coli</i> ATCC 10536	1000.0	>1000.0	1000.0	>1000.0	1.0	2.0	n.t.
<i>K. pneumoniae</i> ATCC 13883	1000.0	1000.0	1000.0	>1000.0	1.0	2.0	n.t.
<i>P. aeruginosa</i> ATCC 9027	1000.0	>1000.0	1000.0	>1000.0	3.5	>4.0	n.t.
<i>S. enterica</i> NCTC 6017	1000.0	>1000.0	1000.0	>1000.0	2.0	2.0	n.t.
<i>C. albicans</i> ATCC 10231	1000.0	1000.0	1000.0	<1000.0	n.t.	n.t.	1.0

n.t. – not tested

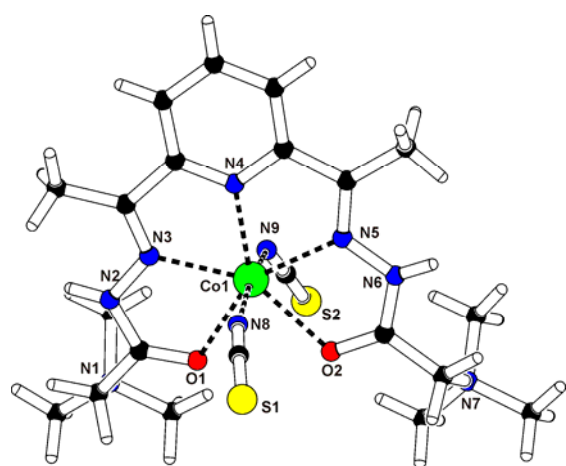
Figure captions

Figure 1. Graphical representation of $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$. Non-coordinated SCN^- ions and solvate water molecules are omitted for clarity.

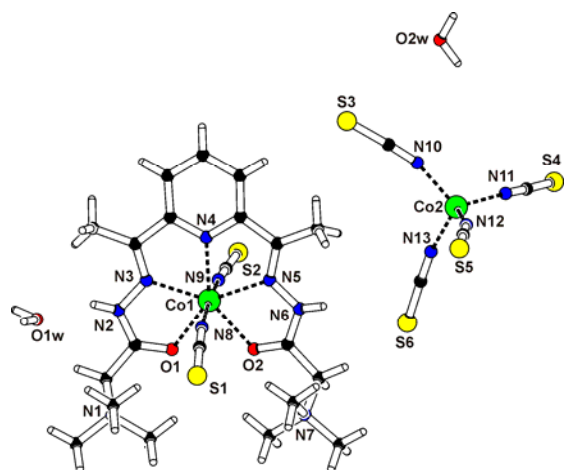
Figure 2. Graphical representation of $[\text{Co}(\text{H}_2\text{L})(\text{NCS})_2][\text{Co}(\text{NCS})_4]$.

Figure 3. Graphical representation of $[\text{Ni}(\text{H}_2\text{L})(\text{NCS})_2](\text{SCN})_2$. Solvate water molecules are not included in the refinement model because of poor quality data.

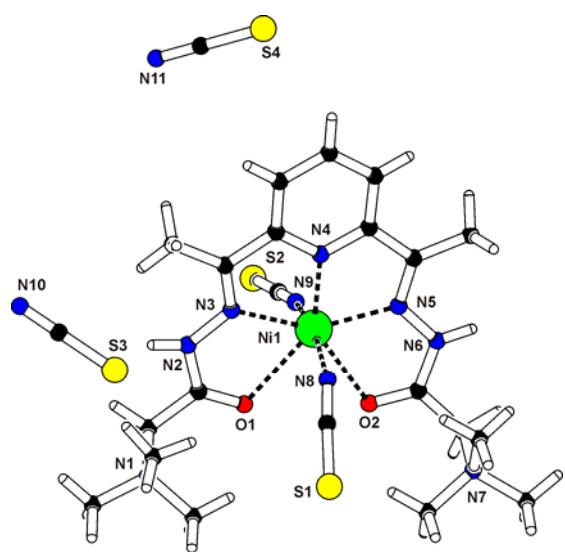
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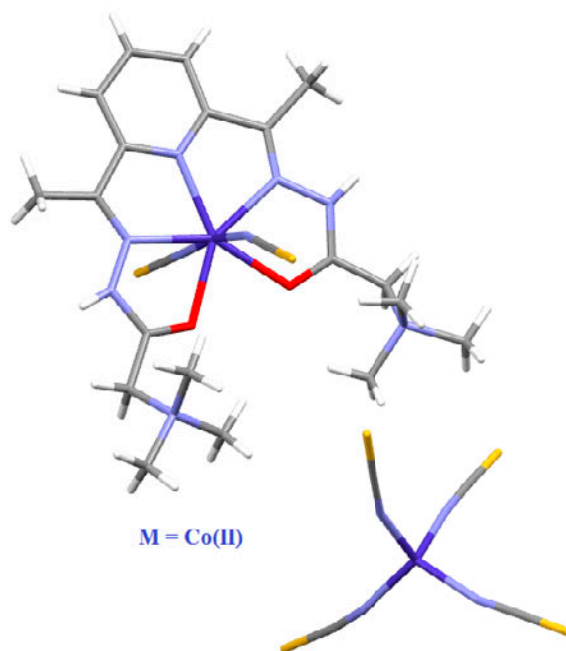
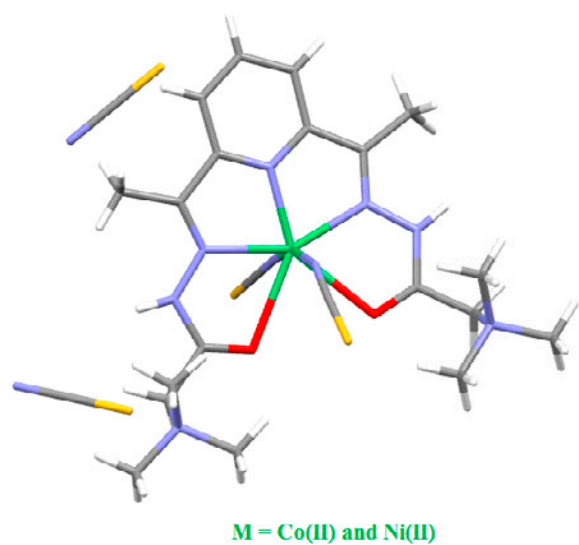
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