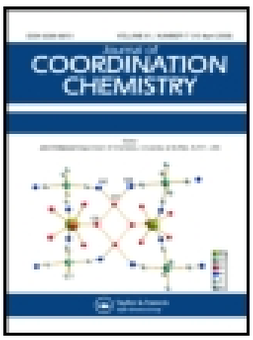

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Synthesis, characterization, DFT calculations and antimicrobial activity of Cd(II) complexes with the condensation product of 2-quinolinecarboxaldehyde and Girard's T reagent

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The chloro (**1**) and isocyanato (**2**) Cd(II) complexes with the condensation product of 2-quinolinecarboxaldehyde and trimethylammonium acetohydrazide chloride (Girard's T reagent) (HLCl) have been synthesized and characterized by elemental analysis, IR and NMR spectroscopy. The crystal structure of chloro Cd(II) complex (**1**) was determined. In **1** and **2**, coordination surrounding of Cd(II) consists of deprotonated hydrazone ligand coordinated through NNO-donor atoms and two monodentates at the rest of the coordination places. Quantum-chemical calculations of the molecular structures and the relative stabilities of linkage isomers of the Cd(II) complex showed that the isomer with N-Cd-N coordination of OCN^- is the most stable. The investigated Cd(II) complexes showed lower activity than standard antimicrobial drugs.

Keywords: Cd(II) Complexes; Hydrazones; Crystal structure; Antimicrobial activity; DFT

1. Introduction

Pseudohalide Cd(II) complexes can exhibit a wide variety of coordination numbers and geometries in their mono-, di- and polynuclear complexes, due to the large radius and d^{10}

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configuration of Cd(II) [1-4]. Not only interesting structures, but also luminescence and fluorescence properties, attracted the attention towards the research of this class of compounds [5-8]. Halides and pseudohalides are versatile building blocks which can bind as monodentate or as bridges between metal centers. Among them, azide is the most used for the synthesis of polynuclear complexes and their supramolecular frameworks due to its versatile bridging coordination modes, single and double: $\mu_{1,3}$-N_3 (end-to-end, EE) and $\mu_{1,1}$-N_3 (end-on, EO), $\mu_{1,1,3}$-N_3, $\mu_{1,1,1}$-N_3, $\mu_{1,1,1,1}$-N_3, $\mu_{1,1,3,3}$-N_3, and $\mu_{1,1,1,3,3,3}$-N_3 [9]. Cyanato ligand can be coordinated as monodentate or bridging ligand (end-on $\mu_{1,1}$-κ_N and $\mu_{1,1}$-κ_O or end-to-end $\mu_{1,3}$) through oxygen or nitrogen donor atoms, although coordination through oxygen is rare [10].

Cadmium was recognized as a human carcinogen by the International Agency for Research on Cancer due to its known toxicity [11]. The toxicity of cadmium depends on the nature of anion in its salts and can be modulated by complexation [12]. Although cadmium is generally known to be extremely toxic to mammals, it is not true that it is not used by nature in any way. A unicellular microalga *Thalassiosira weissflogii* flourishes in environments with high cadmium [13]. If there is not enough zinc in the environment, the diatom uses cadmium instead of zinc as a cofactor of carbonic anhydrase enzyme [14]. Biological activity of Cd(II) complexes was not the subject of intensive research, but some studies which deal with DNA-binding ability, antibacterial and antitumor activity of Cd(II) complexes are reported [11, 12, 15, 16]. One part of our research deals with systematic investigation of coordination chemistry, magnetic properties and biological activity of hydrazone metal complexes with pseudohalide ligands. Recently, we systematically investigated pseudohalide complexes of Ni(II) and Zn(II) with the condensation product of 2-quinolinecarboxaldehyde and trimethylammonium acetohydrazide chloride (Girard's T reagent) (HLCl) [17, 18]. As a continuation of this research, reactions of Cd(II) with HLCl ligand and pseudohalides (azide, cyanate, thiocyanate) were performed in the present study. Mononuclear chloro $[CdLCl_2]\cdot CH_3OH$ (**1**) and isocyanato $[CdL(NCO)_2]$ (**2**) Cd(II) complexes were obtained, structurally characterized and their antimicrobial activity was tested.

2. Experimental

2.1. *Materials and methods*

2-Quinolinecarboxaldehyde (97%) Girard's T reagent (99%), $Cd(NO_3)\cdot 4H_2O$ (98%), NH_4SCN (≥97.5%), NaOCN (≥99.5%) and NaN_3 (96%) were obtained from Aldrich. IR spectra were

recorded on a Nicolet 6700 FT-IR spectrometer using the ATR technique from 4000-400 cm^{-1} (vs = very strong, s = strong, m = medium and w = weak). ^{1}H (500 MHz), ^{13}C (125 MHz) and 2-D NMR spectra of HLCl and Cd(II) complexes were recorded on a Bruker Avance 500 spectrometer at room temperature using TMS as internal standard in methanol−d^4 in the case of HLCl and DMSO−d^6 in the case of Cd(II) complexes (see Supporting Information). Chemical shifts (δ) are expressed in ppm and coupling constants (*J*) in Hz. 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 (25 °C) on a digital conductivity-meter JENWAY-4009.

2.2. *Synthesis*

2.2.1. Synthesis of (E)-N,N,N-trimethyl-2-oxo-2-(2-(quinolin-2-ylmethylene)hydrazinyl)-ethan-1-aminium chloride (HLCl). HLCl was synthesized in the reaction of 2-quinolinecarboxaldehyde and Girard's T reagent according to the previously described method [17]. IR (cm^{-1}): 3414(m), 3062(m), 2970(m), 2939(m), 2831(m), 1699(s), 1595(m), 1562(w), 1497(m), 1414(m), 1379(w), 1340(w), 1301(m), 1230(m), 1135(m), 989(w), 950(w), 916(w), 868(w), 832(w), 758(m), 656(w), 633(w), 533(w). ^{1}H NMR (500 MHz, CD_3OD) (numbering of atoms according to scheme 1), δ (ppm): 3.47 (s, 9H, C12-H), 4.94 (s, 2H, C11-H), 8.17 (s, 1H, C9-H), 8.18 (d, 1H, $^{3}J_{C3\text{-}H/C4\text{-}H}$ = 10 Hz, C3-H), 8.36 (d, 1H, $^{3}J_{C3\text{-}H/C4\text{-}H}$ = 10 Hz, C4-H), 7.94 (d, 1H, $^{3}J_{C5\text{-}H/C6\text{-}H}$ = 5 Hz, C5-H), 7.62 (t, 1H, $^{3}J_{C5\text{-}H/C6\text{-}H/C7\text{-}H}$ = 5 Hz, C6-H), 7.78 (t, 1H, $^{3}J_{C6\text{-}H/C7\text{-}H/C8\text{-}H}$ = 5 Hz, C7-H), 8.03 (d, 1H, $^{3}J_{C7\text{-}H/C8\text{-}H}$ = 5 Hz, C8-H). ^{13}C NMR (125 MHz, CD_3OD) (numbering of atoms according to scheme 1), δ (ppm): 55.0 (C12), 64.4 (C11), 146.9 (C9), 154.4 (C2), 119.2 (C3), 138.7 (C4), 130.1 (C4a), 129.3 (C5), 129.0 (C6), 131.7 (C7), 129.7 (C8), 148.9 (C8a), 167.0 (C10).

2.2.2. Synthesis of dichloro (E)-N,N,N-trimethyl-2-oxo-2-(2-(quinolin-2-ylmethylene)hydrazinyl)ethan-1-aminium cadmium(II) complex monomethanole $[CdLCl_2]\cdot CH_3OH$ (1). HLCl (90 mg, 0.30 mmol) was dissolved in methanol (20 mL) and solid $Cd(NO_3)_2\cdot 4H_2O$ (120 mg, 0.30 mmol) was added. After complete dissolution of $Cd(NO_3)_2\cdot 4H_2O$ in the reaction mixture, NaN_3 (40 mg, 0.60 mmol) dissolved in water (10 mL) was added. The yellow reaction solution was stirred at 65 °C for 3 h. After slow evaporation of solvent in a

refrigerator (~4 °C) for five days, yellow crystals were obtained. Yield: 57 mg (39%). Elemental analysis calcd. for $C_{15}H_{18}N_4OCl_2Cd \cdot CH_3OH$: C 39.57%, H 4.57%, N 11.54%; found: C 39.61%, H 4.65%, N 11.51%. IR (cm^{-1}): 3282(m), 3077(w), 3019(w), 2934(w), 2814(w), 2042(w), 1610(w), 1565(s), 1535(s), 1509(m), 1487(m), 1450(w), 1431(w), 1395(m), 1344(w), 1325(w), 1295(s), 1229(w), 1204(w), 1128(w), 1083(s), 1034(m), 969(w), 919(m), 826(w), 784(w), 760(w). ^{1}H NMR (500 MHz, DMSO-*d*^{6}) (numbering of atoms according to scheme 1), δ (ppm): 3.25 (s, 9H, C12-H), 4.09 (s, 2H, C11-H), 8.60 (s, 1H, C9-H), 7.71 (t, 1H, $^3J_{C3\text{-}H/C4\text{-}H}$ = 10 Hz, C3-H), 8.09 (d, 1H, $^3J_{C3\text{-}H/C4\text{-}H}$ = 10 Hz, C4-H), 8.40 (d, 1H, $^3J_{C5\text{-}H/C6\text{-}H}$ = 10 Hz, C5-H), 7.89 (m, 1H, C6-H), 7.89 (m, 1H, C7-H), 8.67 (d, 1H, $^3J_{C7\text{-}H/C8\text{-}H}$ = 10 Hz, C8-H). ^{13}C NMR (125 MHz, DMSO-*d*^{6}) (numbering of atoms according to scheme 1), δ (ppm): 53.7 (C12), 67.5 (C11), 143.2 (C9), 149.6 (C2), 128.3 (C3), 128.6 (C4), 129.4 (C4a), 128.2 (C5), 123.5 (C6), 131.9 (C7), 140.3 (C8), 146.0 (C8a), 171.9 (C10). Λ_M (1 mM, DMSO): 14.3 Ω^{-1} cm^2 mol^{-1}.

2.2.3. Synthesis of diisocyanato (E)-N,N,N-trimethyl-2-oxo-2-(2-(quinolin-2-ylmethylene)hydrazinyl)ethan-1-aminium cadmium(II) complex [CdL(NCO)$_2$] (2). Into a solution of HLCl (90 mg, 0.30 mmol) in methanol (20 mL), solid $Cd(NO_3)_2 \cdot 4H_2O$ (120 mg, 0.30 mmol) was added. After complete dissolution of Cd(II) salt in reaction solution, NaOCN (80 mg, 1.20 mmol) dissolved in water (10 mL) was added. The reaction mixture was stirred for 3 h at 100 °C. After slow evaporation of solvent in a refrigerator (~4 °C) for ten days yellow crystals were obtained. Yield: 41 mg (29%). Elemental analysis calcd. for $C_{17}H_{18}N_6O_3Cd$: C 43.74%, H 3.89%, N 18.00%; found: C 43.86%, H 3.93%, N 17.98%. IR (cm^{-1}): 3519(w), 3460(w), 2197(vs), 1618(w), 1560(m), 1524(s), 1470(s), 1408(m), 1389(m), 1329(m), 1298(m), 1227(w), 1196(w), 1111(w), 1074(m), 989(w), 970(w), 921(m), 835(w), 810(w), 782(w), 752(m), 624(w). ^{1}H NMR (500 MHz, DMSO-*d*^{6}) (numbering of atoms according to scheme 1), δ (ppm): 3.26 (s, 9H, C12-H), 4.10 (s, 2H, C11-H), 8.62 (s, 1H, C9-H), 7.71 (d, 1H, $^3J_{C3\text{-}H/C4\text{-}H}$ = 10 Hz, C3-H), 8.09 (d, 1H, $^3J_{C3\text{-}H/C4\text{-}H}$ = 10 Hz, C4-H), 8.28 (d, 1H, $^3J_{C5\text{-}H/C6\text{-}H}$ = 10 Hz, C5-H), 7.92 (m, 1H, C6-H), 7.92 (m, 1H, C7-H), 8.68 (d, 1H, $^3J_{C7\text{-}H/C8\text{-}H}$ = 10 Hz, C8-H). ^{13}C NMR (125 MHz, DMSO-*d*^{6}) (numbering of atoms according to scheme 1), δ (ppm): 53.7 (C12), 67.4 (C11), 143.8 (C9), 149.7 (C2), 128.2 (C3), 128.7 (C4), 129.4 (C4a), 127.6 (C5), 123.6 (C6), 132.1 (C7), 140.4 (C8), 146.0 (C8a), 172.0 (C10), 127.8 (OCN^-). Λ_M (1 mM, DMSO): 10.6 Ω^{-1} cm^2 mol^{-1}.

2.3. *X-ray structure determination*

Crystal data and refinement parameters of **1** are listed in table 1. Selected bond distances and angles are listed in table 2. The X-ray intensity data were collected at room temperature with a Nonius Kappa CCD diffractometer equipped with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The data were processed using DENZO [19]. The structure was solved by direct methods implemented in SHELXS-2013 [20] and refined by full-matrix least-squares based on F^2 using SHELXL-2016 [20]. All non-hydrogen atoms were refined anisotropically. The C10- and O2-bound hydrogens were located in a difference map and refined with distance restraints (DFIX) of C-H = 0.98 or O-H = 0.82 Å and with $U_{iso}(H) = 1.2U_{eq}(C)$ or $U_{iso}(H) = 1.5U_{eq}(O)$, respectively. All other hydrogens were included in the model at geometrically calculated positions and refined using a riding model. ORTEP-3 for Windows was used to prepare drawings [21].

CCDC 1562578 contains the supplementary crystallographic data for **1**. These data can be obtained free of charge from the Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/data_request/cif.

2.4. *Antimicrobial activity*

Antimicrobial activity was investigated against seven laboratory control strains of bacteria *i.e.*, gram-positive: *Staphylococcus aureus* (ATCC 6538), *Staphylococcus epidermidis* (ATCC 12228), *Bacillus subtilis* (ATCC 6633); gram-negative: *Escherichia coli* (ATCC 10536), *Klebsiella pneumoniae* (ATCC 13883), *Pseudomonas aeruginosa* (ATCC 9027) and *Salmonella enterica* subsp. *abony* (ATCC 6017) and one strain of yeast *Candida albicans* (ATCC 10231). In order to determine minimum inhibitory concentration (MIC) of tested compounds, a broth microdilution method was used according to Clinical and Laboratory Standards Institute guidelines CLSI (2016) [22] with some modifications. Tests were performed in Müller-Hinton broth for the bacterial strains and in Sabouraud dextrose broth for *Candida albicans*. The tested compounds were dissolved in 1% dimethyl sulfoxide (DMSO) and then diluted to the highest concentration. Twofold serial concentrations of the compounds were prepared in a 96-well microtiter plate (ranging from 62.5-1000 µg/mL) with addition of 0.05% 2,3,5-triphenyl-2*H*-tetrazolium chloride (TTC, Sigma-Aldrich, USA) as a growth indicator. All of the MIC

determinations were performed in duplicate, and two positive growth controls were included (wells containing only the microorganisms in the broth). Each test was repeated three times. Identical MIC values were obtained in all experiments for a particular substance and strain.

3. Results and discussion

3.1. *Synthesis*

The reaction of 2-quinolinecarboxaldehyde and Girard's T reagent was performed according to the previously reported method [17] yielding the ligand *(E)-N,N,N*-trimethyl-2-oxo-2-(2-(quinolin-2-ylmethylene)hydrazinyl)ethan-1-aminium chloride (HLCl), which was used for the synthesis of **1** and **2** (scheme 1). Complex **1** was obtained *via* the reaction of HLCl with $Cd(NO_3)_2 \cdot 4H_2O$ and NaN_3 in molar ratio 1:1:2 in methanol. In this reaction, the source of chloride anions was HLCl ligand itself, while azide anions deprotonated hydrazone ligand. The same reaction performed without NaN_3 was unsuccessful since the products were unstable in reaction solution and decomposed to starting compounds. The synthesis of isothiocyanato/thiocyanato Cd(II) complexes in the reaction of HLCl with $Cd(NO_3)_2 \cdot 4H_2O$ and SCN^- were also unsuccessful regardless of the source of SCN^- (KSCN or NH_4SCN) and molar ratio of the reactants. The reaction of HLCl with $Cd(NO_3)_2 \cdot 4H_2O$ and NaOCN in molar ratio 1:1:4 in methanol results in formation of **2**. The X-ray crystal structure of **1** showed that Cd(II) is five-coordinate with quinoline nitrogen, azomethine nitrogen and carbonyl oxygen atoms from hydrazone ligand and two monodentate chloro ligands. Tridentate NNO-coordination of hydrazone ligand in **2** is proposed from similarity of NMR spectral data for **1** and **2**. The presence of OCN^- in **2** is evidenced from its IR and ^{13}C NMR spectra. The molar conductivity values of **1** and **2** in DMSO are 14.3 Ω^{-1} cm^2 mol^{-1} and 10.6 Ω^{-1} cm^2 mol^{-1}, respectively. These values are lower than 35 Ω^{-1} cm^2 mol^{-1} [23], so **1** and **2** are non-electrolytes and are stable in DMSO. Having all these facts in mind as well as the results of elemental analysis, in **2** coordination environment of Cd(II) consists of quinoline nitrogen, azomethine nitrogen and carbonyl oxygen atoms from hydrazone ligand and two monodentate OCN^- ligands.

3.2. *Spectroscopy*

3.2.1. IR spectra. On the basis of IR spectroscopy results, coordination of HLCl ligand in deprotonated α-oxyazine form in **1** and **2** was confirmed. The new band at 1535 cm^{-1} in the

spectrum of **1** and at 1524 cm^{-1} in the spectrum of **2** corresponding to ν($^{-}$O–C=N) vibration of deprotonated hydrazine moiety appeared instead of the band of carbonyl group of non-coordinated hydrazonic form of HLCl at 1699 cm^{-1}. In the IR spectrum of **2** a strong band at 2197 cm^{-1} can be attributed to vibration of coordinated cyanate ions [24].

3.2.2. NMR spectra. The signal of hydrazide NH is absent in the ^{1}H NMR spectra of **1** and **2**, indicating that the ligand is coordinated in deprotonated zwitterionic form. Coordination of azomethine nitrogen in **1** and **2** can be confirmed from downfield shift of C9-H from 8.17 ppm in the spectrum of HLCl to 8.60 ppm and 8.62 ppm in spectra of **1** and **2**, respectively. Due to coordination of carbonyl oxygen atom, signal of the carbonyl carbon (C10) is shifted downfield from 167.0 ppm in the spectrum of HLCl to 171.9 ppm and 172.0 ppm in the spectra of **1** and **2**, respectively. Upfield shift of azomethine carbon atom (C9) signal from 146.9 ppm in the spectrum of HLCl to 143.2 ppm in the spectrum of **1** and 143.8 in the spectrum of **2** indicates coordination of azomethine nitrogen. Coordination of quinoline nitrogen atom caused upfield shift of C2 atom signal from 154.4 ppm in the spectrum of HLCl to 149.6 ppm and 149.7 ppm in the spectra of **1** and **2**, respectively. In the ^{13}C NMR spectrum of **2** the signal of coordinated OCN^{-} ion was observed at 127.8 ppm.

3.3. *Description of the crystal structure*

The molecular structure (ORTEP) of **1** is depicted in figure 1. In **1**, Cd1 has fivefold coordination with tridentate ligand L and two Cl^{-} ligands (Cl1 and Cl2). L is coordinated to Cd1 in the zwitterionic form through NNO-set of donor atoms forming two fused five-membered chelate rings. The dihedral angle of nearly 11.1° between two five-membered chelate rings fused along Cd1-N2 junction during complexation shows the non-coplanar nature of metal-ligand system. The coordination polyhedron formed around Cd1 is irregular in shape with very bent *trans* bond angles of 138.03(7)° and 135.68(7)° for N2-Cd1-Cl1 and N1-Cd1-O1, respectively. The out-of-plane *cis* bond angles span the range from 97.40(7) to 116.85(3)° and the in-plane *cis* bond angles are 67.46(7) to 106.32(6)°. The smallest values of 67.46(7)° and 70.31(8)° have been observed for bite angles N2-Cd1-O1 and N1-Cd1-N2, respectively. Solvent molecule serving as H-bond donor is involved in discrete intermolecular hydrogen bond with deprotonated amide nitrogen which functions as an acceptor (figure 1, table S1, see Supporting Information).

The distortion in the five coordinated systems is described by the trigonallity index, $\tau = (\beta-\alpha)/60$, where β is the greatest basal angle and α is the second greatest angle [25]. The parameter τ is 0 for regular square based pyramidal forms and 1 for trigonal bipyramidal forms. The τ value of 0.04 in **1** indicates that the irregular coordination geometry about Cd1 is 4.0% trigonally distorted square-based pyramidal. The Cd1 is lifted out of the plane of the four in-plane ligand atoms (N1, N2, O1 and Cl1) by a distance ρ of 0.7024(2) Å. The axial Cd1-Cl2 bond is slightly longer than the equatorial Cd1-Cl1 bond (2.466(1) *versus* 2.424(2) Å). The other metal-ligand bond distances are in the order Cd-$N_{heteroaromatic}$ (2.408(2) Å) > Cd-O_{amide} (2.375(2) Å) > Cd-N_{imine} (2.278(2) Å). The angular structural parameter (τ) of **1** has been compared with those of structurally related five-coordinate Cd(II) complexes with hydrazone ligands (table 3).

For the complexes listed, the value τ varies from 0.03 to 0.12, indicating that these structures span the range of trigonally distorted square-pyramidal configurations. The Cd(II) ions of these complexes are displaced by distance ρ (ρ = 0.0359(4)-0.8459(3) Å) from the equatorial plane towards corresponding apical ligands. The angular structural parameter τ of previously analyzed five-coordinate Zn(II) complexes with hydrazone ligands comprises the range from 0.13 to 0.40 [18], indicating that these complexes also span the range of trigonally distorted square-pyramidal configurations. However, Zn(II) complexes show greater trigonal distortion of square-based pyramidal configuration than Cd(II) complexes analyzed here, as indicated by the values τ listed in table 3 and those reported earlier [18].

In the crystals of **1**, the complex molecules are linked along the *b*-axis through π···π interactions between neighboring quinoline rings (figure 2, table 4).

3.4. *Computational studies*

The molecular structures of [CdL$(NCO)_2$] (Cd-1), [CdL$(OCN)_2$] (Cd-2) and [CdL(OCN)(NCO)] (Cd-3) have been optimized and analyzed by DFT computations. The initial geometries of investigated Cd(II) complexes were generated with completely linear OCN^- and NCO^- ligands. XRD structure of [$CdLCl_2$]·CH_3OH was used as reference for typical five-coordinate Cd(II) complexes. Optimizations were carried out within DFT/B3LYP/3-21G approach in gas-phase, without any restrictions. Optimized geometries are shown in figure 3. The preference for N-binding over O is found by comparing relative energies of Cd complexes: N-Cd-N

coordination of OCN^- is the most stable, the next in stability is N-Cd-O isomer (ΔE = 8.37 kcal/mol) and the most destabilized is O-Cd-O isomer (ΔE = 14.55 kcal/mol). Selected bond lengths and angles of optimized structures are given in table 5.

Analysis of Cd(II) complexes containing two NCO^- ligands in the Cambridge Structure Database [31] showed that, in majority of complexes, metal centers are bridged with NCO^- ligands (9 out of 16). Only six mononuclear Cd(II) complexes containing two monodentate NCO^- ligands were found. In all of them, NCO^- ligands are coordinated through nitrogen atom.

HOMO and LUMO orbitals of Cd(II) complexes are shown in figure 4. The HOMOs of all complexes are delocalized mainly at the linear group and metal center, whereas the LUMOs are delocalized on the planar ring of Schiff base. The preference for N-binding over O is found in the investigated isostructural Cd(II) complexes. The frontier molecular orbitals of OCN^- and NCO^-, specifically the π (HOMO), both have primarily N-character in all complexes (figure 4), which explains large isomerism energy.

Influences of NCO^- and OCN^- ligands on LUMO and HOMO are estimated by comparing energies of frontier molecular orbitals (E_{LUMO}, E_{HOMO}) and their energy gap (E_{gap}). Substitution of NCO^- with OCN^- ligand has the same influence on HOMO and LUMO energy levels (table S2). Energies of HOMO and LUMO orbitals are the highest for Cd-2 complex but the E_{gap} does not differ much from E_{gap} in Cd-1 complex.

3.5. *Antimicrobial activity*

Complexes **1** and **2** showed lower activity than the standard antimicrobial drugs (meropenem and amphotericin, table 6). Isocyanato **2** exhibited better activity than chloro **1** against all tested microbial strains. These results indicate that antimicrobial activity of the investigated Cd(II) complexes depends on the nature of monodentate ligands. Complex **2** possesses better activity than Cd(II) salt against *S. aureus*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. enterica* and *S. epidermidis*, but the activity of Cd(II) salt was better in the case of *C. albicans* and *B. subtilis* strains. HLCl showed lower activity than **2** against all examined microbial strains.

4. Conclusion

The reaction of HLCl with $Cd(NO_3)_2 \cdot 4H_2O$ and NaN_3 in molar ratio 1:1:2 in methanol results in formation of chloro Cd(II) complex (**1**). The presence of excess of basic N_3^- caused

deprotonation of HLCl, while Cl^- originating from HLCl coordinates to Cd(II). In the case of reaction of HLCl with $Cd(NO_3)_2 \cdot 4H_2O$ and NaOCN in molar ratio 1:1:4 in methanol basic OCN^- facilitate deprotonation of HLCl and coordinates to Cd(II) resulting in formation of **2**. In both **1** and **2**, coordination surrounding of Cd(II) consists of deprotonated hydrazone ligand coordinated through NNO-set of donor atoms and two monodentates at the remaining coordination places. Since the X-ray determined structure of **2** was not obtained, DFT calculations were performed to give theoretical evidence about the coordination of OCN^- ligand. The results showed that N-Cd-N coordination of OCN^- is the most stable, the next in stability is N-Cd-O isomer (ΔE = 8.37 kcal/mol) and the most destabilized is O-Cd-O isomer (ΔE = 14.55 kcal/mol). The obtained MIC values for **1** and **2** are higher than the values for standard antimicrobial drugs. Antimicrobial activity of the investigated Cd(II) complexes depends on the nature of monodentate ligand, since isocyanato Cd(II) complex (**2**) showed better activity than chloro Cd(II) complex (**1**) against all tested microbial strains. Complexation of Cd(II) with NCO^- and L generally results in improvement of its antimicrobial activity. This effect can be attributed to sharing of positive charge of cadmium(II) ion with donor atoms of ligands which improved its lipophilicity and penetration through cell membranes of microorganism.

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Table 1. Crystal data and structure refinement details for **1**.

Formula	$C_{16}H_{22}CdCl_2N_4O_2$
Fw (g mol^{-1})	485.67
Crystal size (mm)	0.15×0.13×0.10
Crystal color	Yellow
Crystal system	Triclinic
Space group	$P\,\bar{1}$
a (Å)	8.348(5)
b (Å)	8.698(5)
c (Å)	13.748(5)
α (°)	90.069(5)
β (°)	98.922(5)
γ (°)	98.376(5)
V (Å^3)	975.4(9)
Z	2
Calcd density (g cm^{-3})	1.654
F(000)	488
No. of collected reflns.	5896
No. of independent reflns.	4403
R_{int}	0.0163
No. of reflns. observed	3769
No. parameters	236
R [I> 2σ (I)][a]	0.0311
wR_2 (all data)[b]	0.0689
Goof, S[c]	1.063
Maximum / minimum residual electron density (e Å^{-3})	+0.56 / -0.61

[a] $R = \sum||F_o|-|F_c||/\sum|F_o|$. [b] $wR_2 = \{\sum[w(F_o^2-F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$.
[c] $S = \{\sum[(F_o^2-F_c^2)^2]/(n/p)\}^{1/2}$ where n is the number of reflections and p is the total number of parameters refined.

Table 2. Selected bond lengths (Å) and angles (°) for **1**.

Bond	Distance (Å)	Angle	(°)
Cd1-N1	2.408(2)	N1-Cd1-N2	70.31(8)
Cd1-N2	2.278(2)	N1-Cd1-O1	135.68(7)
Cd1-O1	2.375(2)	N1-Cd1-Cl1	106.32(6)
Cd1-Cl1	2.4238(15)	N1-Cd1-Cl2	105.13(6)
Cd1-Cl2	2.4662(12)	N2-Cd1-Cl1	138.03(7)
N2-N3	1.375(3)	N2-Cd1-Cl2	103.85(7)
N2-C10	1.275(3)	Cl1-Cd1-Cl2	116.85(3)

Table 3. Structural parameters correlating coordination geometry of structurally related five-coordinated Cd(II) complexes.

Complex	β (°)	α (°)	τ	ρ (Å)	References
$[CdLCl_2]\cdot CH_3OH$ (**1**)	138.03(7)	135.68(7)	0.04	0.7024(2)	This work
$[Cd(L^2)I_2]$[a] (**2**)	134.17(11)	132.24(8)	0.03	0.7701(3)	[26]
$[Cd(L^3)Cl_2]$[b] (**3**)	133.61(10)	130.69(9)	0.05	0.7684(3)	[27]
$[Cd(L^4)Br_2]$[c] (**4**)	135.1(2)	132.04(10)	0.05	0.0359(4)	[28]
$[Cd(L^4)Cl_2]$[c] (**5**)	133.90(6)	129.49(6)	0.07	0.7691(2)	[28]
$[Cd(L^5)I_2]$[d] (**6**)	138.93(7)	132.20(10)	0.11	0.7638(3)	[29]
$[Cd(L^6)Br_2]$[e] (**7**)	134.55(8)	127.09(6)	0.12	0.8459(3)	[30]

[a] L^2 = 5-methyl-1-(pyridin-2-yl)-*N*′-[pyridine-2-ylmethylidene]pyrazole-3-carbohydrazide

[b] L^3 = *N*,*N*,*O*-di-2-pyridyl ketone thiophene-2-carboxylic acid hydrazone

[c] L^4 = di-2-pyridyl ketone benzoylhydrazone

[d] L^5 = 1′-methyl-2′-(2′′-pyridylmethylene)-hydrazino-1-methyl carbonic hydrazide

[e] L^6 = methyl-2-pyridyl ketone picolinoyl hydrazone

Table 4. Intermolecular π···π interaction parameters for **1**.

Cg(I)[a]	Cg(J)[a]	Cg(I) –Cg(J)[b] (Å)	α[c] (°)	β[d] (°)	γ[e] (°)	Slippage[f] (Å)	Sym. code on (J)
Cg(1)	Cg(1)	3.870(3)	0	28.3	28.3	1.833	2–x, 1–y, 2–z
Cg(1)	Cg(2)	5.239(4)	0.99(14)	49.2	50.0		2–x, 1–y, 2–z
Cg(2)	Cg(2)	3.508(3)	0	17.1	17.1	1.029	2–x, –y, 2–z
Cg(1)	Cg(2)	3.674(3)	0.99(14)	23.7	24.4		2–x, –y, 2–z

[a] Labels of aromatic rings: (1) = N(1),C(1)–C(4),C(9); (2) = C(4)–C(9).

[b] Cg(I)–Cg(J) = Distance between ring centroids (Ang.).

[c] α = Dihedral angle between planes (I) and (J) (Deg).

[d] β = Angle between Cg(I)–Cg(J) vector and normal to plane (I) (Deg).

[e] γ = Angle between Cg(I)–Cg(J) vector and normal to plane (J) (Deg).

[f] Slippage = Distance between Cg(I) and perpendicular projection of Cg(J) on ring I (Ang).

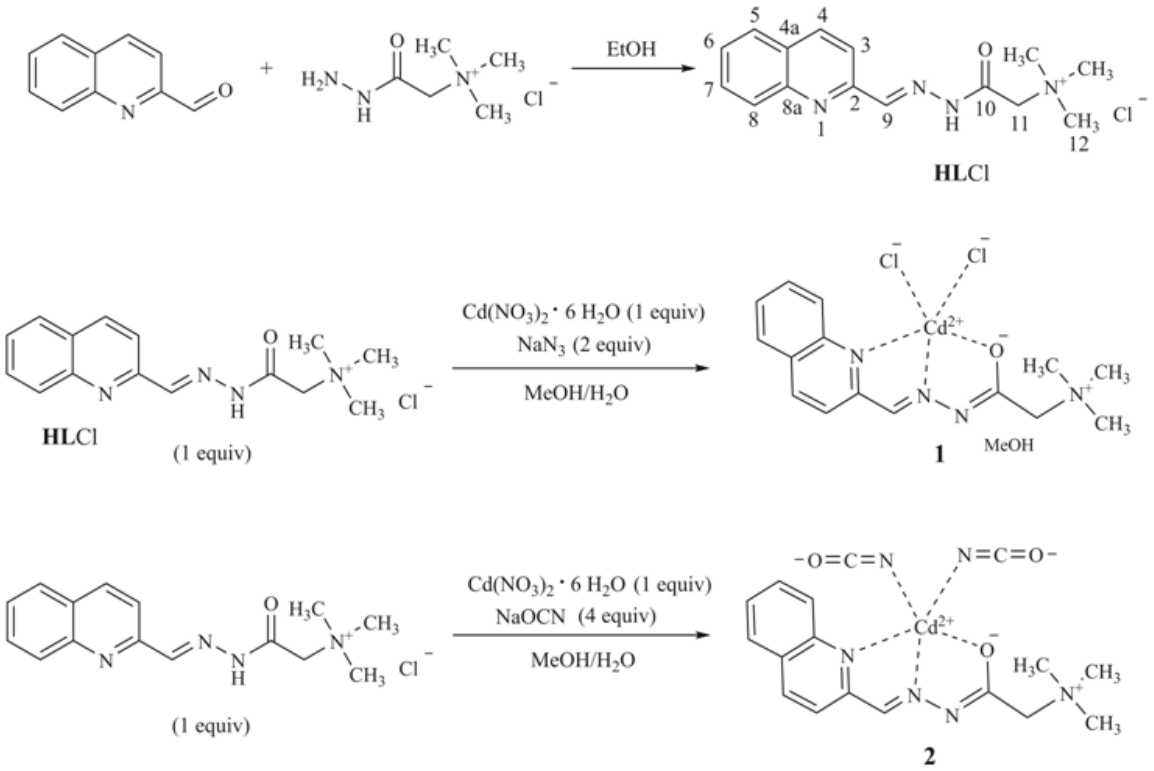
Table 5. Selected average bond lengths and angles obtained by DFT for Cd-1, Cd-2 and Cd-3.

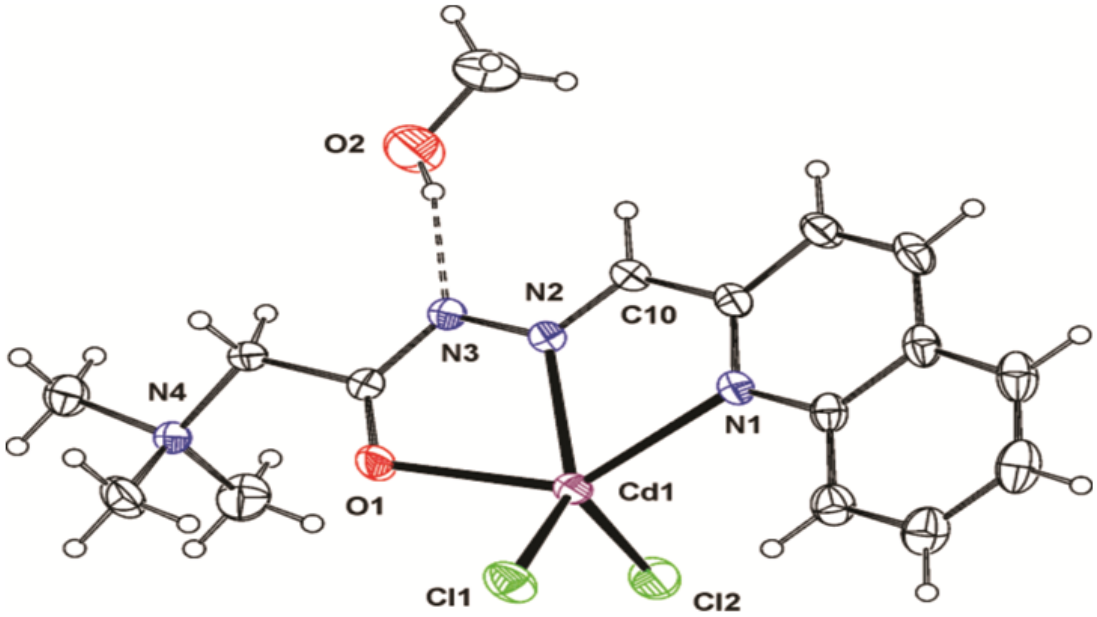
Compound	Cd-1	Cd-2	Cd-3
Distance, Å			
Cd-NCO	2.150		2.197
Cd-OCN		2.170	2.150
Angle, °			
Cd–N–C	155.5		
Cd-O-C		118.3	121.0
N-C-O	178.2	178.7	179.0
OCN-Cd-NCO	124.5		
OCN-Cd-OCN			118.6
NCO-Cd-OCN		114.2	

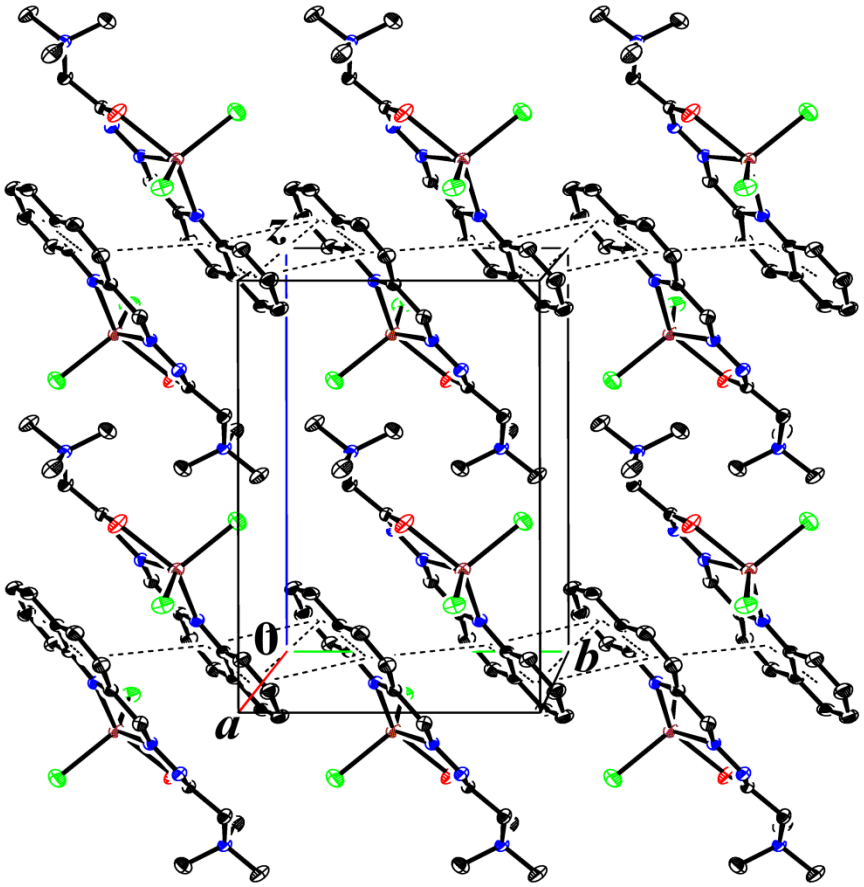
Table 6. Antimicrobial activity of HLCl, **1**, **2**, NaOCN and $Cd(NO_3)_2 \cdot 4H_2O$ (MIC values are given in mM).

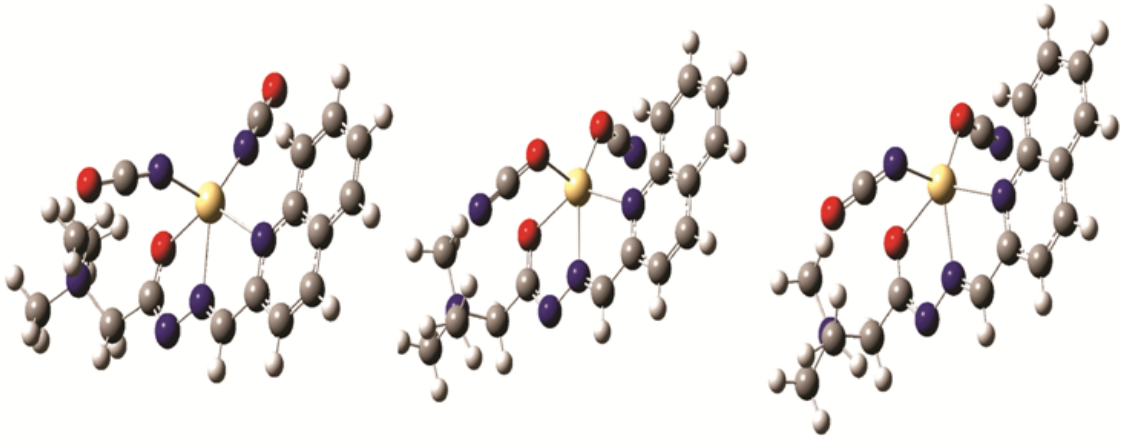
Microorganisms	HLCl	**1**	**2**	NaOCN	$Cd(NO_3)_2 \cdot 4H_2O$	Meropenem *	Amphotericin *
S. aureus ATCC 6538	1.630	2.204	0.535	> 15.385	3.241	0.004	n.t.
S. epidermidis ATCC 12228	1.630	0.551	0.535	> 15.385	3.241	0.003	n.t.
B. subtilis ATCC 6633	3.260	1.102	0.535	> 15.385	0.202	0.005	n.t.
E. coli ATCC 10536	> 3.260	1.102	0.268	> 15.385	0.404	0.006	n.t.
K. pneumoniae ATCC13883	1.630	2.204	0.535	> 15.385	0.808	0.008	n.t.
P.aeruginosa ATCC 9027	> 3.260	> 2.204	1.071	> 15.385	3.241	0.010	n.t.
S.enterica ATCC 6017	> 3.260	2.204	0.535	> 15.385	3.241	0.006	n.t.
C. albicans ATCC 10231	> 3.260	0.551	0.535	> 15.385	0.202	n.t.	0.0005

n.t. not tested
* reference antimicrobial drugs









a) b) c)