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Synthesis, crystal structures, and antimicrobial activity of square-planar chloride and isocyanate Ni(II) complexes with the condensation product of 2-(diphenylphosphino) benzaldehyde and Girard's T reagent

MILICA MILENKOVIĆ†, ANDREJ PEVEC‡, IZTOK TUREL‡, MARINA MILENKOVIĆ§, BOŽIDAR ČOBELJIĆ†, DUŠAN SLADIĆ†, NATALIJA KRSTIĆ¶ and KATARINA ANĐELKOVIĆ*†

†Faculty of Chemistry, University of Belgrade, Belgrade, Serbia
‡Faculty of Chemistry and Chemical Technology, University of Ljubljana, Ljubljana, Slovenia
§Faculty of Pharmacy, Department of Microbiology and Immunology, University of Belgrade, Belgrade, Serbia
¶Institute of Chemistry, Technology and Metallurgy, University of Belgrade, Belgrade, Serbia

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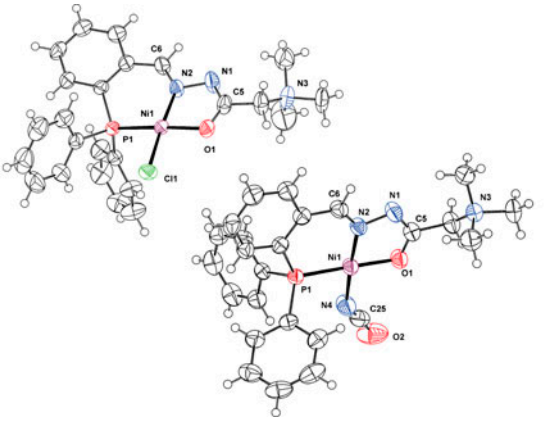


Square-planar isocyanate and chloride Ni(II) complexes with tridentate PNO condensation product of 2-(diphenylphosphino)benzaldehyde and Girard's T reagent have been synthesized and their crystal structures were determined. These Ni(II) complexes with different monodentate ligands, chloride, cyanate, and thiocyanate were tested for their antimicrobial activities against pathogenic microorganisms. The ligand and Ni(II) complexes were active not only against laboratory control strains of bacteria and yeast, but also on clinical isolates of *Escherichia coli* and *Pseudomonas aeruginosa* strains resistant to most of the clinically used antibiotics.

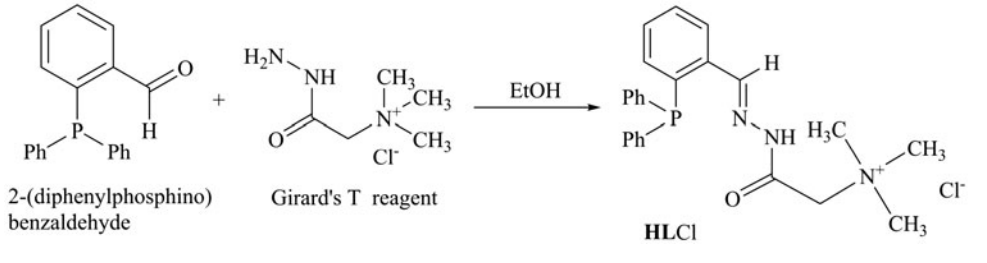
Keywords: Ni(II) complexes; 2-(diphenylphosphino)benzaldehyde; Girard's T reagent; X-ray structure; antimicrobial activity

*Corresponding author. Email: kka@chem.bg.ac.rs

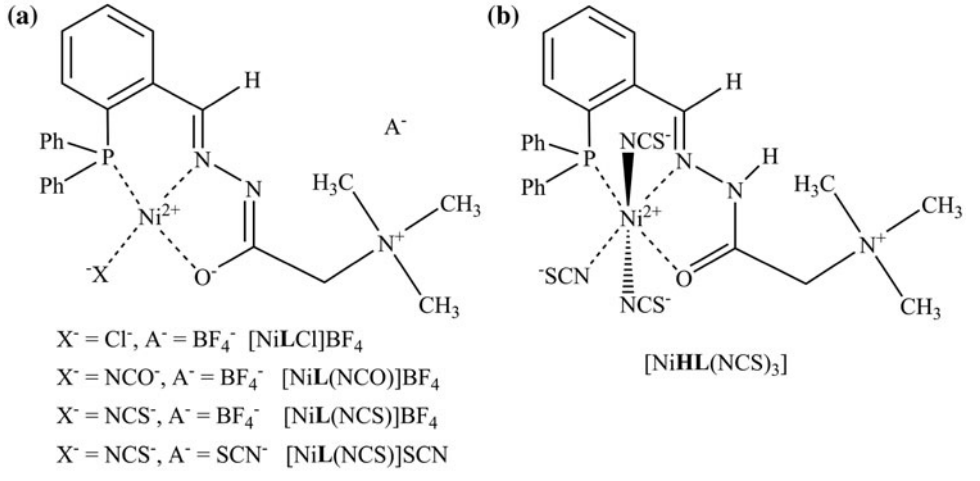
1. Introduction

The resistance of pathogenic microorganisms to standard antimicrobial agents results in a growing demand for development of new drugs. Due to their structural diversity, metal complexes can be a significant source of new chemotherapeutics. Schiff bases are an important class of compounds due to their role as ligands in metal coordination chemistry [1–3]. The coordination properties depend on conformational flexibility of the ligand, the nature of the central metal as well as on the presence of other species capable to compete for coordination sites. Significant biological activity of Schiff base ligands attracted our attention as this frequently increases after complexation with metal ions [1–14]. Schiff bases of 2-(diphenylphosphino)benzaldehyde continue to be a primary research area of our group. Acylhydrazones of 2-(diphenylphosphino)benzaldehyde and their complexes show significant antimicrobial activity; in most cases, biological activity was enhanced upon complexation. A connection between the biological activity and structure of the compounds was established. Antimicrobial activity is influenced by geometry, hydrophobicity, and charge of complexes, so that the highest antibacterial activity was observed for octahedral, electrolytic complexes, while square-planar, neutral complexes showed better antifungal activity. Also, it was determined that in square-planar complexes, a positive charge of the ligand led to decrease in antifungal activity and to increase in antibacterial activity. On the other hand, in the case of octahedral complexes, the opposite situation occurs and uncharged ligand led to better antibacterial activity, while positively charged ligand led to higher antifungal activity [15–19].

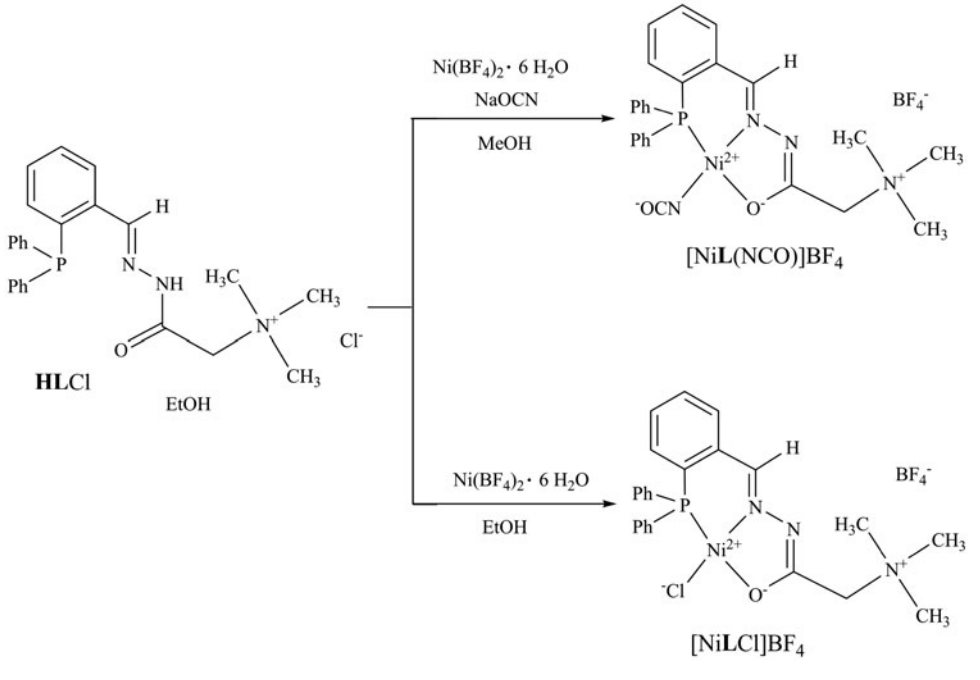
In this article, synthesis and structural characterization of isocyanate ([Ni**L**(NCO)]BF_4) and chloride ([Ni**L**Cl]BF_4) Ni(II) complexes with condensation product of 2-(diphenylphosphino)benzaldehyde and Girard's T reagent (**HL**Cl) are described (scheme 1). Antimicrobial potential of the newly synthesized Ni(II) complexes ([Ni**L**Cl]BF_4 and [Ni**L**(NCO)]BF_4) as well as three previously synthesized related complexes ([Ni**L**(NCS)]BF_4, [Ni**L**(NCS)]SCN, and [Ni**HL**$(NCS)_3$]) with condensation product of 2-(diphenylphosphino)benzaldehyde and Girard's T reagent and three different monodentate ligands, i.e., chloride, cyanate, and thiocyanate have been investigated (scheme 2).



Scheme 1. Synthesis of **HL**Cl.



Scheme 2. Square-planar (a) and octahedral (b) Ni(II) complexes with condensation product of 2-(diphenylphosphino)benzaldehyde and Girard's T reagent and different monodentate ligands.



Scheme 3. Synthesis of [Ni**L**Cl]BF_4 and [Ni**L**(NCO)]BF_4.

2. Experimental

2.1. *Material and methods*

2-(Diphenylphosphino)benzaldehyde (97%) and Girard's T reagent (99%) were obtained from Aldrich. **HL**Cl was obtained by condensation of 2-(diphenylphosphino)benzaldehyde and Girard's T reagent using a previously reported method [19]. IR spectra were recorded on a Perkin–Elmer FT-IR 1725X spectrometer using the ATR technique from 4000 to 400 cm^{-1}. Elemental analyses (C, H, and N) were performed by standard micromethods 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. *Escherichia coli* and *Pseudomonas aeruginosa* strains (clinical isolates) were kindly supplied by dr Mirjana Kovačević, Poliklinika Beo-Lab (Belgrade, Serbia).

2.2. *Synthesis of [NiLCl]BF_4*

HLCl, 0.11 g (0.23 mmol), was dissolved, by heating, in ethanol (20 mL) and solid Ni$(BF_4)_2{\cdot}6H_2O$, 0.08 g, (0.23 mmol), was added. The reaction mixture was heated at 72 °C for 2 h. The color of the solution changed from green to red. The reaction solution was left to stand at room temperature, while orange-reddish crystals arose from the solution. Yield: 0.07 g (52%) IR (vs-very strong, s-strong, m-medium, w-weak): 3060 (w), 2969 (w), 1610 (w), 1572 (s), 1481 (m), 1435 (m), 1334 (m), 1058 (vs), 999 (m), 926 (w), 752 (m), 694 (m), 540 (w), 504 (w). Elemental analysis calcd for $C_{24}H_{26}BClF_4N_3NiOP$: N 7.19%, C 49.32%, H 4.48%, found: N 7.21%, C 49.27%, H 4.51%. Λ_M (1 mM, DMSO): 28 Ω^{-1} cm^2 mol^{-1}. λ_{max} (nm) (DMSO): 292, 328, 342 and 364.

2.3. *Synthesis of [NiL(NCO)]BF_4*

A mixture of 0.08 g (0.23 mmol) $Ni(BF_4)_2{\cdot}6H_2O$ and 0.11 g (0.23 mmol) of **HL**Cl was dissolved in methanol (20 mL), and then, 0.05 g (0.77 mmol) NaOCN was added. The mixture was heated at 72 °C for 2 h. The reaction solution was left to stand at room temperature and orange crystals arose from the solution. Yield 0.08 g (59%). IR: 3057 (w), 2190 (vs), 1612 (w), 1570 (s), 1483 (m), 1436 (m), 1336 (m), 1085 (s), 1048 (s), 1003 (m), 927 (w), 751 (m), 693 (m), 541 (w), 488 (w). Elemental analysis calcd for $C_{25}H_{26}BF_4N_4NiO_2P$: N 9.48%, C 50.81%, H 4.43%, found: N 9.54%, C 50.79%, H 4.46%. Λ_M (1 mM, DMSO): 29.3 Ω^{-1} cm^2 mol^{-1}. λ_{max} (nm) (DMSO): 284 and 332.

2.4. *Synthesis of [NiL(NCS)]BF_4, [NiL(NCS)]SCN, and [NiHL$(NCS)_3$]*

All isothiocyanate complexes of Ni(II) with condensation product of 2-(diphenylphosphino) benzaldehyde and Girard's T reagent were synthesized using the previously described method [20].

2.5. *X-ray structure determination*

Crystal data and refinement parameters of [Ni**L**Cl]BF_4 and [Ni**L**(NCO)]BF_4 are listed in table 1. The X-ray intensity data were collected at room temperature with an Agilent

Table 1. Crystal data and structure refinement details for [Ni**L**Cl]BF_4 and [Ni**L**(NCO)]BF_4.

	[Ni**L**Cl]BF_4	[Ni**L**(NCO)]BF_4
Formula	$C_{24}H_{26}BClF_4N_3NiOP$	$C_{25}H_{26}BF_4N_4NiO_2P$
Fw (g mol^{-1})	584.42	590.99
Crystal size (mm)	0.50 × 0.30 × 0.20	0.40 × 0.30 × 0.10
Crystal color	Red	Red
Crystal system	Monoclinic	Orthorhombic
Space group	*C*2/*c*	*Pbca*
a (Å)	26.6563(18)	12.5489(2)
b (Å)	10.4868(3)	15.1189(2)
c (Å)	25.6357(17)	27.5476(4)
β (°)	123.101(9)	90.00
V (Å^3)	6003.2(6)	5226.48(13)
Z	8	8
Calcd density (g cm^{-3})	1.293	1.502
F(0 0 0)	2400	2432
No. of collected reflections	15,346	46,640
No. of independent reflections	6878	5987
R_{int}	0.0232	0.0319
No. of reflectionns observed	5470	4747
No. parameters	331	349
$R[I > 2\sigma(I)]$[a]	0.0598	0.0379
wR_2 (all data)[b]	0.2088	0.1050
Goof, *S*[c]	1.052	1.031
Maximum/minimum residual electron density (*e* Å^{-3})	+1.02/−0.60	+0.54/−0.35

[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.

SuperNova dual source using an Atlas detector and equipped with mirror-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å). The data were processed using CRYSALIS PRO [21]. The structures were solved using SIR-92 [22] ([Ni**L**Cl]BF_4) and Superflip [23] ([Ni**L**(NCO)]BF_4). All the structures were refined by a full-matrix least-squares procedure based on F^2 using SHELXL-97 [24]. All non-hydrogen atoms were refined anisotropically. The C6 bonded hydrogen in both complexes were located in a difference map and refined with the distance restraints (DFIX) with C–H = 0.98 and with $U_{iso}(H) = 1.2\ U_{eq}(C)$. In our final model, a very large solvent accessible void (1228 Å^3) was found in the structure of [Ni**L**Cl]BF_4. This void is probably an indication of solvent molecules (missed in the structure model) present in the unit cell and with no chemical meaning.

CCDC 1051742–1051743 contains the supplementary crystallographic data for [Ni**L**Cl]BF_4 and [Ni**L**(NCO)]BF_4, respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

2.6. *Antimicrobial activity*

Antimicrobial activity was investigated against seven different laboratory control strains of bacteria, i.e., Gram-positive: *Staphylococcus aureus* (ATCC 25923), *Staphylococcus epidermidis* (ATCC 12228), *Bacillus subtilis* (ATCC 6633); Gram-negative: *E. coli* (ATCC 10536), *Klebsiella pneumoniae* (ATCC 13883), *P. aeruginosa* (ATCC 27853), and *Salmonella enterica* subsp. *abony* (NCTC 6017) and one strain of yeast *Candida albicans* (ATCC 10231). Antibacterial activities of compounds were tested on clinical isolates, i.e., five *E. coli* and nine *P. aeruginosa* strains.

Minimum inhibitory concentration (MIC) was determined by broth microdilution method according to Clinical and Laboratory Standards Institute guidelines [25]. The tested compounds were dissolved in 1% DMSO and then diluted to the highest concentration. Twofold serial concentrations of the compounds were prepared in a 96-well microtiter plate (ranging from 31.2 to 500 μg/mL) with addition of 0.05% 2,3,5-triphenyl-2*H*-tetrazolium chloride (Sigma–Aldrich) as a growth indicator. All tests were performed in Müller–Hinton broth for the bacterial strains and in Sabouraud dextrose broth for *C. albicans*. All of the MIC determinations were performed in duplicate, and two positive growth controls were included. 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*

Our previous attempts to synthesize Ni(II) complexes with condensation product of 2-(diphenylphosphino)benzaldehyde and ethyl carbazate or 4-phenylsemicarbazide with chloride in the fourth coordination place in the reaction of the appropriate acylhydrazone and $NiCl_2{\cdot}6H_2O$ in methanolic or ethanolic solutions were unsuccessful since these complexes were unstable in reaction solutions and decomposed to starting compounds. The reaction of **HL**Cl with $Ni(BF_4)_2{\cdot}6H_2O$ results in formation of square-planar ([Ni**L**Cl]BF_4) (scheme 3). In this reaction, the source of chloride was the ligand itself. In the reaction of

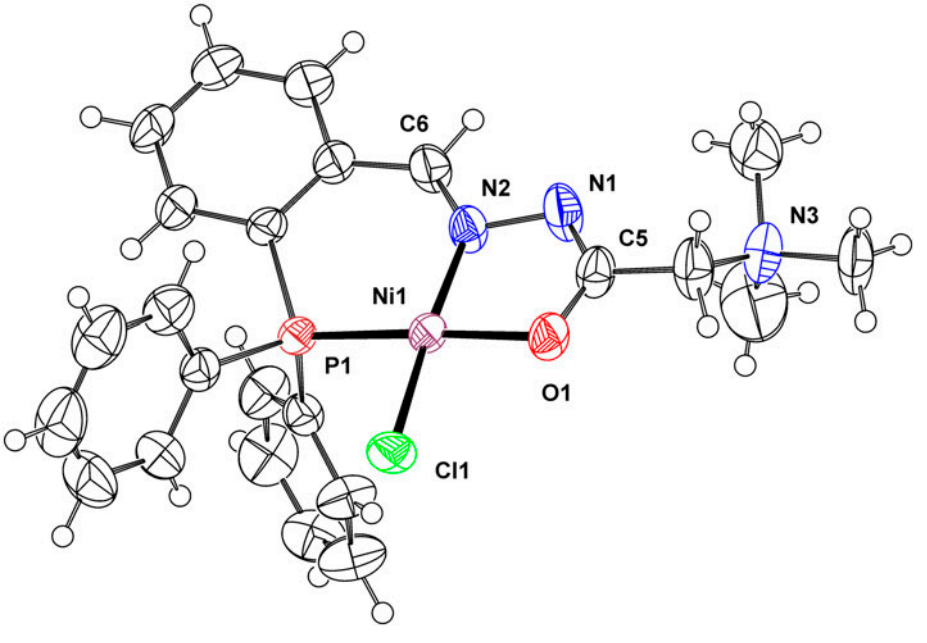


Figure 1. ORTEP plot of [Ni**L**Cl]BF_4 with thermal ellipsoids at 50% probability for non-H atoms and circles for hydrogens. The BF_4^- was omitted for clarity.

$Ni(BF_4)_2{\cdot}6H_2O$ and NaOCN with **HL**Cl in methanol, [Ni**L**(NCO)]BF_4 was obtained (scheme 3). In ([Ni**L**Cl]BF_4 and [Ni**L**(NCO)]BF_4), coordination spheres contain deprotonated zwitter-ionic form of acylhydrazone ligand coordinated in tridentate PNO fashion and monodentate chloride or cyanate in the fourth coordination position.

The reactions of acylhydrazones of 2-(diphenylphosphino)benzaldehyde with Ni^{2+} and OCN^- resulted in four-coordinate metal ion formation [17, 18, 26]. Geometries of these cyanate Ni(II) complexes depend on the nature of the acylhydrazone, i.e., tetrahedral complex was obtained with condensation product of 2-(diphenylphosphino)benzaldehyde and semioxamazide [26], while square-planar complexes were formed with condensation product of 2-(diphenylphosphino)benzaldehyde and ethyl carbazate [17] or 4-phenylsemicarbazide (scheme 4) [18]. Ambidentate OCN^- could be coordinated via N or O and both types of coordination were observed. Theoretical calculations at OPBE/TZ2P level have shown that Ni–N coordination is favored by 17.0 kcal mol^{-1} for NCO^- versus OCN^- [18].

Syntheses of [Ni**L**(NCS)]BF_4, [Ni**L**(NCS)]SCN, and [Ni**HL**$(NCS)_3$] were previously described [20]. Reaction conditions, i.e., the source of Ni^{2+} and SCN^- influenced stoichiometry and geometry of complexes. Coordination of ligand in deprotonated zwitter-ionic form results in formation of square-planar complexes, while coordination of monocationic form of undeprotonated ligand leads to octahedral geometry [20].

3.2. *Crystal structures of [NiLCl]BF_4 and [NiL(NCO)]BF_4*

[Ni**L**Cl]BF_4 and [Ni**L**(NCO)]BF_4 crystallized in monoclinic and orthorhombic crystal systems with space groups *C*2/*c* and *Pbca*, respectively. ORTEP of the structures are given in figures 1 and 2, while bond lengths and angles are listed in table 2. The complex cations in [Ni**L**Cl]BF_4 and [Ni**L**(NCO)]BF_4 consist of one tridentate deprotonated PNO ligand coordinated to Ni(II) and coordinated chloride or isocyanate forming a square-planar geometry. BF_4^- ion acts as counterion in the crystal structure of both complexes. Bond distances and angles in [Ni**L**Cl]BF_4 and [Ni**L**(NCO)]BF_4 are in accord with reported values for the similar square-planar complex where thiocyanate is coordinated through nitrogen to Ni [20]. The sum of the nickel-containing angles in [Ni**L**Cl]BF_4 and [Ni**L**(NCO)]BF_4 is 360°. The position of Ni(II) is 0.0520(13) ([Ni**L**Cl]BF_4) and 0.0039(10) ([Ni**L**(NCO)]BF_4) out of the best plane that contained the coordination sphere. In the structures of both complexes, there is no evidence for significant non-covalent interactions.

3.3. *Spectroscopy*

In IR spectra of complexes instead of the carbonyl band of the uncoordinated ligand at 1686 cm^{-1}, a new band appeared at 1572 cm^{-1} in the spectrum of [Ni**L**Cl]BF_4 and at 1570 cm^{-1} in the spectrum of [Ni**L**(NCO)]BF_4. The observed bands indicate coordination of the ligand in deprotonated form via carbonyl oxygen and electron delocalization [N=C–O^- ↔ $^-$N–C=O] of the deprotonated hydrazide in the bound ligand. Coordination of imine nitrogen was confirmed from the batochromic shifts of ν(C = N) from 1657 cm^{-1} in the spectrum of the free ligand to 1610 and 1612 cm^{-1} in spectra of [Ni**L**Cl]BF_4 and [Ni**L**(NCO)]BF_4, respectively. Similarly, as in the case with previously reported Ni(II) complexes of 2-(diphenylphosphino)benzaldehyde acylhydrazone ligands, there are no significant changes in position of ν(C–P) vibration (1433 cm^{-1} in the spectrum of ligand, 1435 cm^{-1} in the spectrum of [Ni**L**Cl]BF_4, and 1436 cm^{-1} in the spectrum of [Ni**L**(NCO)]BF_4)

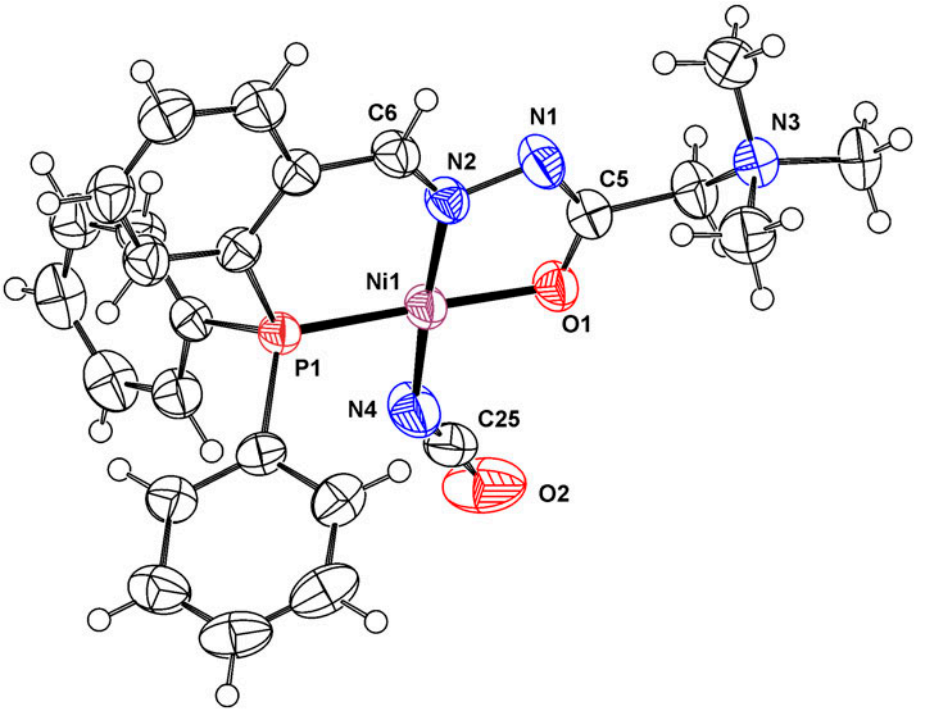
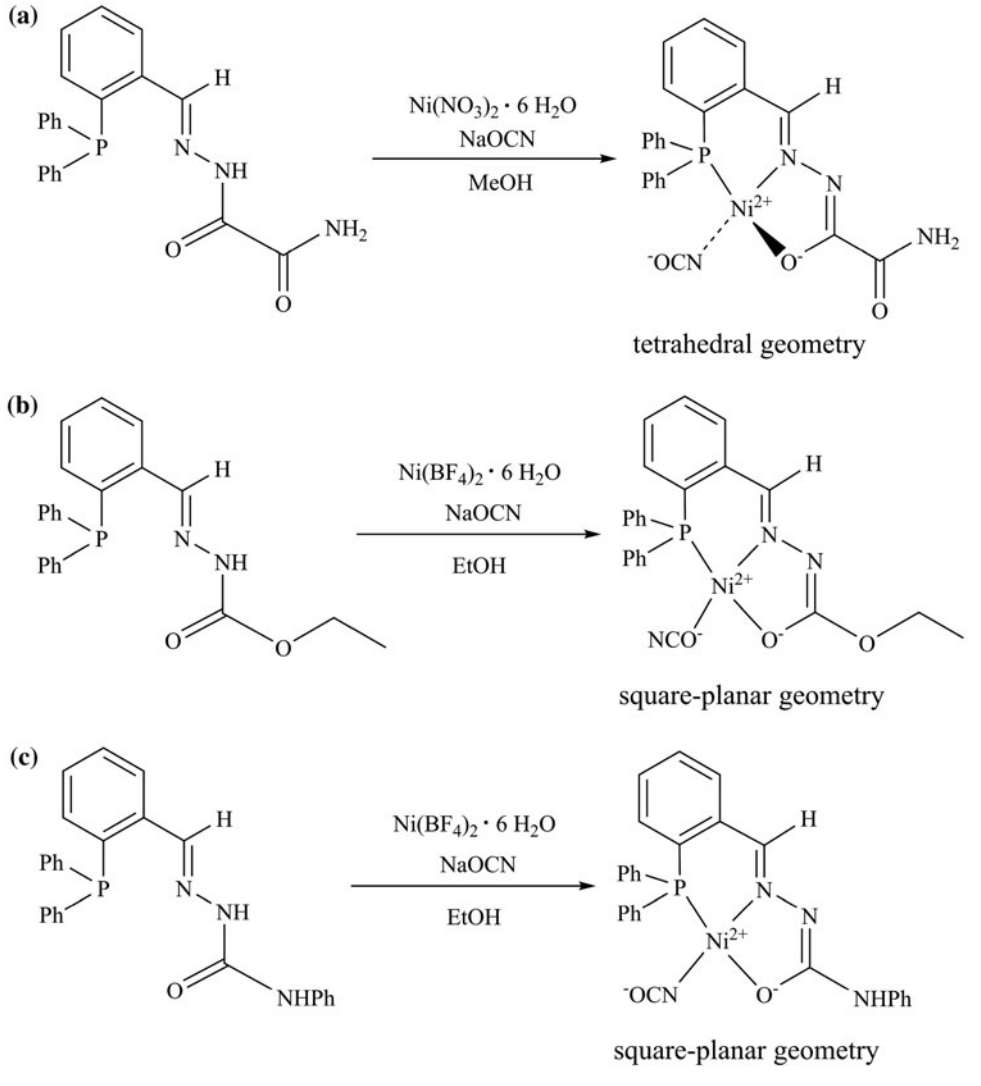


Figure 2. ORTEP plot of [Ni**L**(NCO)]BF_4 with thermal ellipsoids at 50% probability for non-H atoms and circles for hydrogens. The BF_4^- was omitted for clarity.

Table 2. Selected bond lengths (Å) and angles (°) for [Ni**L**Cl]BF_4 and [Ni**L**(NCO)]BF_4.

	[Ni**L**Cl]BF_4	[Ni**L**(NCO)]BF_4
Ni1–Cl1	2.1550(10)	
Ni1–N2	1.863(3)	1.8542(18)
Ni1–N4		1.851(2)
Ni1–O1	1.891(2)	1.8896(15)
Ni1–P1	2.1358(9)	2.1477(6)
N1–N2	1.422(4)	1.413(3)
N1–C5	1.293(5)	1.299(3)
N2–C6	1.294(5)	1.288(3)
O1–C5	1.281(5)	1.274(3)
P1–Ni1–Cl1	90.32(4)	
P1–Ni1–N2	94.70(9)	95.97(6)
P1–Ni1–N4		89.05(7)
P1–Ni1–O1	173.13(9)	178.26(6)
N2–Ni1–Cl1	174.95(10)	
N2–Ni1–N4		174.81(9)
N2–Ni1–O1	83.85(12)	84.14(7)
N1–N2–C6	112.5(3)	112.51(18)
N1–C5–O1	124.7(3)	125.4(2)
N2–N1–C5	109.3(3)	108.75(18)
N4–C25–O2		176.0(3)



Scheme 4. (a) Synthesis of cyanate Ni(II) complex with condensation product of 2-(diphenylphosphino)benzaldehyde and semioxamazide. (b) Synthesis of cyanate Ni(II) complex with condensation product of 2-(diphenylphosphino)benzaldehyde and ethyl carbazate. (c) Synthesis of isocyanate Ni(II) complex with condensation product of 2-(diphenylphosphino)benzaldehyde and 4-phenylsemicarbazide.

[17, 18, 20, 26]. A band at 2190 cm^{-1} observed in the IR spectrum of [Ni**L**(NCO)]BF_4 corresponds to cyanate coordination. The appearance of strong bands at 1058 cm^{-1} in the spectrum of [Ni**L**Cl]BF_4 and at 1048 cm^{-1} in the spectrum of [Ni**L**(NCO)]BF_4 indicates the presence of tetrafluoroborate in the outer sphere of both complexes.

3.4. *Antimicrobial activity*

All the complexes showed moderate activity against all the tested microorganisms. The ligand and the complexes showed similar activities. [Ni**L**(NCS)]BF_4 showed the best

Table 3. Antimicrobial activity of tested compounds (MIC values are given in mM).

Microorganism	**HL**Cl	[Ni**HL**$(NCS)_3$]	[Ni**L**(NCS)]BF_4	[Ni**L**(NCS)]SCN	[Ni**L**(NCO)]BF_4	[Ni**L**Cl]BF_4	$Ni(BF_4)_2 \cdot 6H_2O$	NaOCN	KSCN	Cefotaxime	Amphotericin B
S. aureus ATCC 25923	0.129	0.191	0.206	0.210	0.106	0.107	1.469	7.691	5.145	0.027	n.t.
S. epidermidis ATCC 1228	0.257	0.191	0.206	0.105	0.212	0.214	1.469	>7.691	>5.145	0.007	n.t.
B. subtilis ATCC 6633	0.064	0.191	0.103	0.105	0.106	0.107	1.469	>7.691	>5.145	0.027	n.t.
K. pneumoniae ATCC 13883	0.257	0.191	0.206	0.210	0.212	0.214	1.469	>7.691	>5.145	0.055	n.t.
E. coli ATCC 25922	0.257	0.191	0.206	0.210	0.212	0.214	>1.469	>7.691	>5.145	0.014	n.t.
S. enterica NCTC 6017	0.257	0.191	0.206	0.210	0.212	0.214	1.469	>7.691	>5.145	0.007	n.t.
P. aeruginosa ATCC 27853	0.257	0.191	0.103	0.210	0.106	0.214	>1.469	>7.691	>5.145	0.027	n.t.
C. albicans ATCC 10231	0.257	0.191	0.206	0.210	0.212	0.214	1.469	7.691	>5.145	n.t.	0.007

Table 4. Antibacterial activity of tested compounds against different *P. aeruginosa* isolates (MIC values are given in mM).

	1[a] (uroculture)	2[b] (wound)	3[c] (uroculture)	4[d] (wound)	5[d] (wound)	6[e] (ear)	7[e] (ear)	8[f] (uroculture)	9[g] (uroculture)
HLCl	0.257	0.257	0.514	0.257	0.257	0.257	0.257	0.257	0.257
[Ni**HL**$(NCS)_3$]	0.191	0.191	0.191	0.191	0.191	0.191	0.191	0.191	0.191
[Ni**L**(NCS)]SCN	0.210	0.210	0.210	0.210	0.210	0.210	0.210	0.210	0.210
[Ni**L**(NCO)]BF_4	0.212	0.212	0.212	0.212	0.212	0.212	0.212	0.212	0.212
[Ni**L**Cl]BF_4	0.214	0.214	0.214	0.214	0.214	0.214	0.214	0.214	0.214

Resistant to:
[a]Amoxiclav, cefixime, cephalexin, fosfomycin, nitrofurantoin, sulfamethoxazole/trimethoprim.
[b]Amoxiclav, ampicillin, cefixime, cephalexin, sulfamethoxazole/trimethoprim.
[c]Amoxiclav, ampicillin, cefixime, ciprofloxacin, cephalexin, ceftriaxone, cefepime, gentamicin, sulfamethoxazole/trimethoprim.
[d]Amoxiclav, cefixime, cephalexin, sulfamethoxazole/trimethoprim.
[e]Amoxiclav, ampicillin, cefixime, cephalexin, chloramphenicol, tetracycline, sulfamethoxazole/trimethoprim.
[f]Amoxiclav, cefixime, ciprofloxacin, cephalexin, gentamicin, fosfomycin, pipemidic acid, sulfamethoxazole/trimethoprim.
[g]Amoxiclav, ampicillin, cefixime, ciprofloxacin, cephalexin, ceftriaxone, cefepime, gentamicin, sulfamethoxazole/trimethoprim.

Table 5. Antibacterial activity of tested compounds against *E. coli* strains isolated from uroculture (MIC values are given in mM).

	HLCl	[Ni**HL**$(NCS)_3$]	[Ni**L**(NCS)]BF_4	[Ni**L**(NCS)]SCN	[Ni**L**(NCO)]BF_4	[Ni**L**Cl]BF_4
1[a]	0.514	0.381	0.206	0.210	0.423	0.214
2[b]	0.514	0.381	0.206	0.210	0.423	0.214
3[c]	0.514	0.381	0.206	0.210	0.423	0.214
4[d]	0.514	0.381	0.412	0.210	0.423	0.214
5[e]	0.514	0.381	0.206	0.210	0.423	0.214

Resistant to:
[a]Amoxiclav, piperacillin, cephalexin, cefepime, cefixime, ceftazidime, ceftriaxone, ciprofloxacin, gentamicin, pipemidic acid.
[b]Ciprofloxacin, gentamicin, sulfamethoxazole/trimethoprim, pipemidic acid.
[c]Amoxiclav, cephalexin.
[d]Nalidixic acid.
[e]Ampicillin, sulfamethoxazole/trimethoprim.

activity against *B. subtilis* and *P. aeruginosa*, [Ni**L**(NCS)]SCN against *S. epidermidis* and *B. subtilis*, [Ni**L**(NCO)]BF_4 against *S. aureus*, *B. subtilis,* and *P. aeruginosa*, [Ni**L**Cl]BF_4 against *S. aureus* and *B. subtilis*, while in the case of [Ni**HL**$(NCS)_3$], the same activity was observed against all the tested microbial strains. All the tested compounds, except [Ni**HL**$(NCS)_3$], exhibited best activity against *B. subtilis* although with this strain the highest activity was observed for ligand itself (table 3). The activities of all complexes to *K. pneumoniae*, all complexes except [Ni**HL**$(NCS)_3$] to *B. subtilis*, the newly synthesized complexes to *S. aureus* and isocyanate and isothiocyanate complexes with BF_4^- as the counterion to *P. aeruginosa* are similar to cefotaxime. Of particular significance is the fact that the ligand and Ni(II) complexes showed moderate activity against *P. aeruginosa* (table 4) and *E. coli* (table 5) strains (clinical isolates from different origin) resistant to most of the clinically used antibiotics.

4. Conclusion

The synthesized square-planar Ni(II) complexes contain a common tridentate ligand, condensation product of 2-(diphenylphosphino)benzaldehyde and Girard's T reagent, coordinated in deprotonated zwitter-ionic form via phosphorus, imine nitrogen and carbonyl

oxygen and chloride or isocyanate in the fourth coordination site. Tetrafluoroborate is in the outer sphere of both complexes. Condensation product of 2-(diphenylphosphino)benzaldehyde and Girard's T reagent and corresponding isocyanate, chloride, and isothiocyanate complexes possess antimicrobial properties. Comparison of their antimicrobial activity with the activity of previously examined Ni(II) complexes with acylhydrazones of 2-(diphenylphosphino)benzaldehyde [17, 18] suggests that the presence of quaternary ammonium group in the structure of ligand significantly improves antibacterial activity.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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References

[1] N.C. Saha, R. Pradhan, M. Das, N. Khatun, D. Mitra, A. Samanta, A.M.Z. Slawin, A.D. Jana, J. Klanke, E. Rentschler. *J. Coord. Chem.*, **67**, 286 (2014).
[2] X.-D. Jin, C. Xu, X.-C. Liu, X.-Y. Yin, Y.-C. Gang, Q. Yang, Y.-H. Jin. *J. Coord. Chem.*, **66**, 3970 (2013).
[3] M. Sönmez, M.R. Bayram, M. Çelebı. *J. Coord. Chem.*, **62**, 2728 (2009).
[4] M. Amirnasr, R.S. Erami, K. Mereiter, K.S. Joß, S. Meghdadi, S. Abbasi. *J. Coord. Chem.*, **68**, 616 (2015).
[5] H. Keypour, M. Shayesteh, R. Golbedaghi, A. Chehregani, A.G. Blackman. *J. Coord. Chem.*, **65**, 1004 (2012).
[6] S. Celen, E. Gungor, H. Kara, A.D. Azaz. *J. Coord. Chem.*, **66**, 3170 (2013).
[7] M.S. Aljahdali, A.T. Abedelkarim, A.A. El-Sherif, M.M. Ahmed. *J. Coord. Chem.*, **67**, 870 (2014).
[8] S.Y. Ebrahimipour, M. Mohamadi, J. Castro, N. Mollania, H.A. Rudbari, A. Saccá. *J. Coord. Chem.*, **68**, 632 (2015).
[9] D. Nartop, P. Gürkan, N. Sari, S. Çete. *J. Coord. Chem.*, **61**, 3516 (2008).
[10] V.B. Badwaik, R.D. Deshmukh, A.S. Aswar. *J. Coord. Chem.*, **62**, 2037 (2009).
[11] A.A. Nejo, G.A. Kolawole, M.C. Dumbele, A.R. Opoku. *J. Coord. Chem.*, **63**, 4367 (2010).
[12] Z. Wang, Y.-Q. Fan, L. Shi, Y.-G. Xu. *J. Coord. Chem.*, **66**, 2032 (2013).
[13] S.A. Patil, V.H. Naik, A.D. Kulkarni, S.N. Unki, P.S. Badami. *J. Coord. Chem.*, **64**, 2688 (2011).
[14] S.A. Patil, V.H. Naik, A.D. Kulkarni, U. Kamble, G.B. Bagihalli, P.S. Badami. *J. Coord. Chem.*, **63**, 688 (2010).
[15] M. Milenković, A. Bacchi, G. Cantoni, S. Radulović, N. Gligorijević, S. Aranđelović, D. Sladić, M. Vujčić, D. Mitić, K. Anđelković. *Inorg. Chim. Acta*, **395**, 33 (2013).
[16] M. Milenković, G. Cantoni, A. Bacchi, V. Spasojević, M. Milenković, D. Sladić, N. Krstić, K. Anđelković. *Polyhedron*, **80**, 47 (2014).
[17] M. Milenković, A. Bacchi, G. Cantoni, J. Vilipić, D. Sladić, M. Vujčić, N. Gligorijević, K. Jovanović, S. Radulović, K. Anđelković. *Eur. J. Med. Chem.*, **68**, 111 (2013).
[18] M. Milenković, A. Pevec, I. Turel, M. Vujčić, M. Milenković, K. Jovanović, N. Gligorijević, S. Radulović, M. Swart, M. Gruden-Pavlović, K. Adaila, B. Čobeljić, K. Anđelković. *Eur. J. Med. Chem.*, **87**, 284 (2014).
[19] K. Adaila, M. Milenković, A. Bacchi, G. Cantoni, M. Swart, M. Gruden-Pavlović, M. Milenković, B. Čobeljić, T. Todorović, K. Anđelković. *J. Coord. Chem.*, **67**, 3633 (2014).

[20] B. Čobeljić, A. Pevec, S. Stepanović, V. Spasojević, M. Milenković, I. Turel, M. Swart, M. Gruden-Pavlović, K. Adaila, K. Anđelković. *Polyhedron*, **89**, 271 (2015).
[21] Oxford Diffraction. *CrysAlis PRO*, Oxford Diffraction Ltd, Yarnton (2009).
[22] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi. *J. Appl. Crystallogr.*, **26**, 343 (1993).
[23] L. Palatinus, G. Chapuis. *J. Appl. Crystallogr.*, **40**, 786 (2007).
[24] G.M. Sheldrick. *Acta Crystallogr. A*, **64**, 112 (2008).
[25] Clinical and Laboratory Standards Institute (CLSI). Performance standards for antimicrobial susceptibility testing, 17th Informational Supplement. Approved standard. CLSI document M100-S17. Wayne, PA (2007).
[26] V. Radulović, A. Bacchi, G. Pelizzi, D. Sladić, I. Brčeski, K. Andjelković. *Monatsh. Chem.*, **137**, 681 (2006).