

Obtaining and research of palladium complexes with 4-aminopyridine

Gultakin Ajalova, Khudayar Gasanov, Seljan Nurullayeva, Ziya Babayev
Scientific-Research Center of Azerbaijan Medical University,
Baku
Azerbaijan

Abstract— The obtaining and investigation of various complex compounds of the biologically active aromatic heterocyclic ligands with platinum and palladium are of interest due to their potential medical applications. To that end, 4-amino pyridine containing cyclic and exocyclic nitrogen atoms has been used. The main aim of this work is to clarify which nitrogen atom of the ligand composes stronger and more stable bond.

For that purpose, the synthesis of palladium salts with ligand has been accomplished within a wide interval of pH (3-12) and temperature (50-800C). The cation-anion and neutral complex compounds have been obtained depending on stoichiometric ratio of the reacting components, temperature and pH and was further studied.

As a result of IR-spectroscopic investigation of synthesized complexes, the acquired information demonstrated that the pyridine nitrogen atom of the ligand is protonated and composes outer sphere as monocharged cation. However, tetraacidoanion is formed in the inner sphere.

In the alkaline medium the ligand is monodentately coordinated with palladium through nitrogen atom of pyridine. The exocyclic nitrogen atom of the ligand does not participate in the coordination regardless of pH of the medium and stoichiometric ratio of the taken compounds. As a result of investigation of the thermal stability of the complexes it was determined that the neutral complexes are decomposed without melting at higher temperature than cation-anion complexes. It has been found that one of the factors that affects thermal stability is the steric structure of the complexes.

The initial biological probes were accomplished and the correlation between their biological activities, composition and structures of complexes were determined. Despite the fact of taking the same medium and ligand, the

cation-anion complexes indicate completely different biological activities than neutral ones..

Keywords—Palladium, bidentate ligand, 4-aminopyridine, nitrogen atom of pyridine, biological activity.

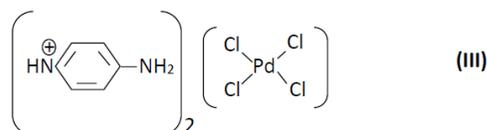
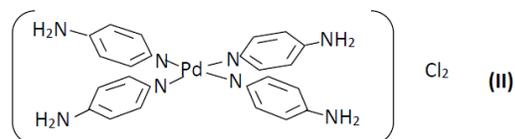
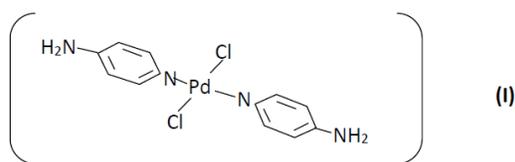
I. INTRODUCTION

In recent years, coordination complexes of platinum group metals with bio ligands have been studied thoroughly. The ligands including N-, O-, S-donor atoms as a parts of the different functional groups are of the special interest for research due to the fact that above-mentioned donor atoms play an important role in the Biosystems as an organogenic element [1, 2]. In order to study transmission of many genetic diseases, obtaining and research of the simple models of the nitrogenous bases which are the parts of DNA and RNA, or commonly of coordination complexes of nitrogen-containing aromatic ligands with palladium (II) inspire interest [3,4].

Considering the synergetic properties of biogenic metals, the study of changes in biological systems as a result of penetration of the N  ligand 4-aminopyridine as coordination compound into an organisms was selected as a research object and inspired a great interest. On the other hand, the ligand has two nitrogen donor atoms with differential characteristics. Therefore, determining which of them bonds more strongly with palladium will have a place in future researches.

EXPERIMENTAL PART

The results of physicochemical investigations indicate that the synthesized complexes have following structural formulas.



II. SYNTHESIS OF COMPOUND I.

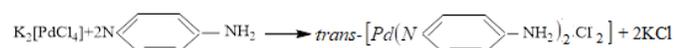
0.29 g (0.9mmol) of K_2PdCl_4 was dissolved in 10 ml of water and filtered. 0.19g (2.1 mmol) the ligand 4-aminopyridine was dissolved in 7 mL of water and added at the stirring to K_2PdCl_4 solution. It should be paid attention that the ligand should be taken at 15% excess. The reaction mixture was stirred using a magnetic stirrer at 70°C for 2 hours and the pH was set to 10, after that, yellow crystalline product became precipitating. The reaction mixture was kept in a water bath at 40°C for 3 hours, then, placed in a refrigerator. After complete finishing the precipitation process the mixture was filtered with a glass filter and washed with a mixture of ethanol and water (2: 1) and ether. The obtained precipitate was dried in vacuum upon $CaCl_2$ down to constant weight. Yield: 0.27 g (82%).

The general formula $C_{10}H_{12}N_4PdCl_2$

Found: Pd– 29.23, Cl– 19.56, N – 15.41, C – 33.01, H – 3.39

Calculated: Pd– 29.11, Cl– 19.40, N – 15.32, C – 32.86, H – 3.28

The equation of the reaction is described by the following scheme:



The stoichiometric ratio of the reactants during the reaction is taken 1:2. The ligand forms chemical bond by donor-acceptor mechanism replacing two chlorine atoms from coordination sphere of palladium.

III. SYNTHESIS OF COMPOUND II.

0.33 g (1.4mmol) complex $[Pd(NH_3)_4]Cl_2$ was dissolved in 15 mL of water and then 0.51 g (5.4 mmol) of 4-aminopyridine was dissolved in 10 ml water added to it, the last was stirred and filtered. The reaction mixture was stirred using the magnetic stirrer at 80°C for 4 hours and the pH was gradually set to 8. After that, the yellow crystalline compound precipitated from transparent solution. The precipitation

process continued under the temperature = (60°C) for 3 days. The precipitate was filtered using the glass filter and then washed with cold water, alcohol, ether and dried upon $CaCl_2$ up to constant weight. Yield: 0.57g (76%).

The general formula $C_{20}H_{24}N_8PdCl_2$

Found: Pd–19.09, Cl– 12.69, N – 20.09, C – 43.56, H – 4.47

Calculated: Pd– 19.22, Cl– 12.80, N – 20.23, C – 43.39, H – 4.33.

The reaction takes place in accordance with the following scheme:



The stoichiometric ratio between metal and ligand must be taken like 1:4 for coordination of four ligands with palladium. Thereby, four molecules of the ligand form chemical bonds by donor-acceptor mechanism replacing completely four molecules of ammonia from coordination sphere of palladium.

IV. SYNTHESIS OF COMPOUND III.

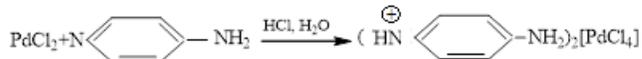
0.39 g (2.2mmol) of $PdCl_2$ powder was mixed with 0.41g (4.4mmol) of 4-aminopyridine powder, then 20 ml of water was added. Continuously stirring with a magnetic stirrer at 80°C for two hours we set the pH of solution to 5.5. After that, the obtained warm homogeneous solution was filtered using a paper filter and transferred into a porcelain basin, then evaporated to a small volume at 60°C in a water bath. The brown needle-like crystals were precipitated cooling of this concentrated solution. The precipitate was filtered using a glass filter, washed with cold ethanol, then with ether. The obtained complex was dried in vacuum upon $CaCl_2$ up to constant weight. The yield was 0.85 g (89%).

The general formula $C_{10}H_{14}N_4PdCl$.

Found: Pd– 24.39; Cl– 32.51, N – 12.98, C – 27.58, H – 3.34

Calculated: Pd– 24.27, Cl– 32.35, N – 12.77, C – 27.40, H – 3.19.

The reaction takes place in accordance with the following scheme:



The nitrogen atom of pyridine of ligand is protonated in acidic medium differently from other reaction modes and generates the outer sphere of coordination complex. Composed tetrachloro anion $[PdCl_4]^{2-}$ constitutes the inner sphere.

4-aminopyridine has been purchased from “Reanal” company and used without additional purification.

$K_2[PdCl_4]$ and $[Pd(NH_3)_4]Cl_2$ salts were synthesized by known technique [14]. Analytical grade $PdCl_2$ was purchased and used.

The purity of the synthesized complexes was controlled by “Commander Sample ID (Coupled Two Theta/Theta)” WL=1.54060 marked X-ray analyzer. The elemental analysis was carried out using “CHNSOE Carlo ERBA” device. The records for IR and DTA analysis were got by “Thermo

Scientific Nicolet IS 10” and “STA 449 F3 Yupiter” devices of “NETZSCH” company, respectively.

V. CONCLUSION

The regulated conditions and specified ratio of reactants during the experiment are optimal and it is possible to obtain pure substances with a high yield only under these conditions. To avoid some problems throughout the IR analysis, the bromide analogues of some coordination complexes have been synthesized and investigated. On the other hand, first of all, IR spectra of the reacting ligand and metal salts were recorded and compared with the IR spectra of the complex and proper results are deduced.

The observed 501 and 362 cm^{-1} absorption bands of compound I in the IR spectra were assigned to the coordination bonds stretching $\nu_{\text{Pd-N}}$ and $\nu_{\text{Pd-Cl}}$, respectively. The metal-to-nitrogen and metal-to-chlorine bonds were observed with one absorption band in infrared spectra of the coordination complex according to the C_{2v} choice rule, which shows that they locate in trans- position relatively to each other (Fig.1). This fact is also confirmed in the literature [5–7]. If the ratio of metal:ligand is taken like 1:4, then four metal-to-(palladium)-nitrogen bonds of the ligand are formed in the coordination sphere of palladium.

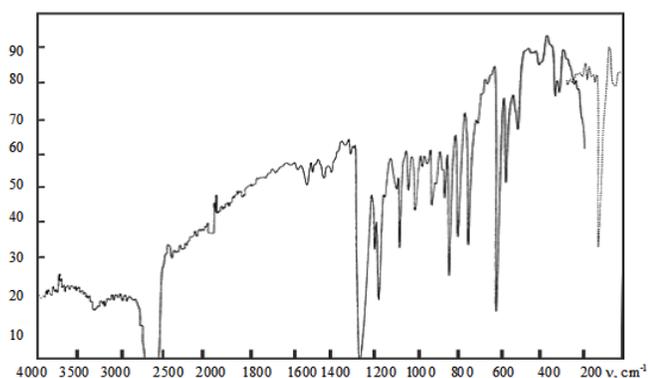


Figure 1. IR spectra of compound II

The existence of one strong absorption band of 470 cm^{-1} in IR spectra of the obtained coordination compound II confirms the results of the chemical experiments. It means that in the flat square plane of palladium, when the central atom forms coordination complexes with ligands of equal strength

like $\begin{matrix} \text{N} & & \text{N} \\ & \diagdown & / \\ & \text{Pd} & \\ & / & \diagdown \\ \text{N} & & \text{N} \end{matrix}$ tetra mine, according to the D_{4h} Choice Rule, the $\nu_{\text{Pd-N}}$ bonding is really characterized by one adsorption band in the absence of any displacement [8,9]. In both IR spectra of the coordination compounds I and II the absorption bands at 3609 cm^{-1} , 3616 cm^{-1} and 1422 cm^{-1} weak, 1240 cm^{-1} medium, 1420 cm^{-1} weak and 1245 cm^{-1} medium were observed. They belong to the δ_{CH} plane of pyridine ring and proves participation of nitrogen atom of pyridine in the coordination (Fig.2, Tab 1.).

Tab 1. Some basic IR data of synthesized complexes

Complexes	IR spectra (ν , cm^{-1})					
	$\nu_{\text{Pd-Cl}}$	$\nu_{\text{Pd-N}}$	ν_{NH_3}	$\delta_{\text{N-H}}$	$\delta_{\text{C-H}}$	$\delta_{\text{N...H}}$
$\text{trans-[Pd(N} \begin{matrix} \text{C}_6\text{H}_4\text{-NH}_2 \end{matrix} \text{)]}_2\text{Cl}_2$	362	501			1422 1240	
$[\text{Pd(N} \begin{matrix} \text{C}_6\text{H}_4\text{-NH}_2 \end{matrix} \text{)]}_4\text{Cl}_2$		470			1420 1248	
$(\text{NH} \begin{matrix} \text{C}_6\text{H}_4\text{-NH}_2 \end{matrix} \text{)}_2[\text{PdCl}_4]$	340		3514	1630 1610		3588 3596

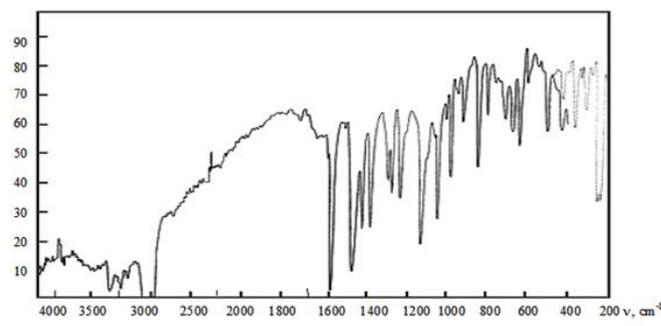


Figure 2. IR spectra of the compound II

IR spectra of cation-anion type complex was given in figure 3.

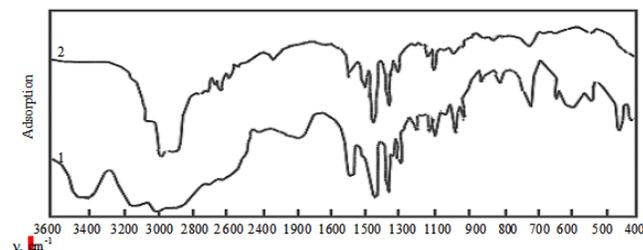


Figure 3. IR spectra of aminopyridine and its cation-anion coordination

The stability of the exocyclic nitrogen atom, i.e. of absorption bands reserved for the free NH_2 group in fourth position such in IR spectra of ligand shows that this group does not take part in the coordination. Only the nitrogen atom of pyridine behaves as monodentate ligand due to the fact that it participates in the coordination of a potential bidentate ligand 4-aminopyridine with palladium.

Cation-anion-type complex of palladium with 4 amino pyridine - compound III has been synthesized by changing the conditions of the process. The strong observed absorption band of 3514 cm^{-1} within the range of 2000-3600 cm^{-1} of the IR spectra of this complex proves that a nitrogen atom of pyridine ligand is protonated and converted into a cation. The nitrogen atom of the exocyclic amine group is not changed in an acidic medium and if we ignore the slight displacement of π electrons of $\nu_{\text{C=C}}$ bond in the pyridine ring, recorded medium 1630 cm^{-1} and strong 1610 cm^{-1} absorption bands indicate the protonation of the nitrogen atom of pyridine [10,11]. The strong adsorption band of 340 cm^{-1} in IR spectra of cation-anion type coordination complex proves the formation of tetra acido anion of palladium - $[\text{PdCl}_4]^{2-}$ [12,13]. 3588–3596 cm^{-1} broad absorption band observed in

IR spectra of the cation-anion type complex indicates the participation of protonated amino groups in hydrogen bonding [12,13].

The molar electro conductivities of compounds I, II, III have been studied in 10^{-3} mol/L aqueous-alcohol solution in a ratio of 4:1 (water: alcohol) at 25°C . It is proved that the compound III is nonelectrolyte ($42 \text{ Ohm}^{-1}\text{m}^2\text{mol}^{-1}$), compounds I and II are tri charged ionic electrolytes ($184 \text{ Ohm}^{-1}\text{m}^2\text{mol}^{-1}$). The exact value of electrical conductivity of compound III cannot be determined due to the fact that the ligand is deprotonated and transferred to the inner sphere. The molar electro conductive values of the complexes validate the proposed assumption about their structure.

The thermal stabilities of all three complexes were studied. Thermal conversion of a cation-anion type coordination complex aroused special interest. The differential thermal analysis (DTA) for the compound III shows that it is heat-resistant up to 165°C . The observed exothermic peak on the DTA curve at 182°C was followed by an endothermic peak. The remaining peaks correspond to the process of thermal decomposition of the organic part of the complex. The reasons for this are deprotonation of outer ligand as a result of the solid thermal conversion and formation nonelectrolyte type coordination complex transferring to the inner side [19–23] (Fig.4). The other two complexes are stable up to the 240 and 220°C , respectively, however, at the higher temperatures they are decomposed without melting.

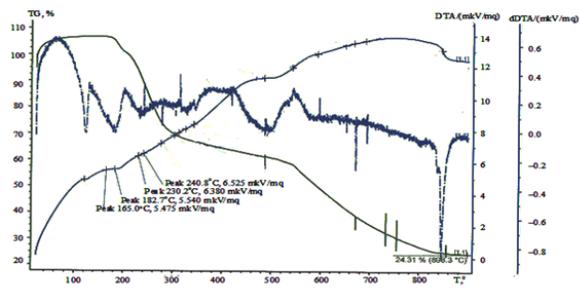
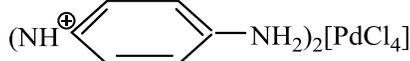


Fig.4. Thermal behavior of the complex



The biological activities of the complexes in vitro were also studied. The results of performed biological tests showed that all three coordination complexes demonstrate the different biological activities. For example, the compound I has weak antitumor effect and a strong antiviral effect.

Other complexes have antifungal-antimicrobial and radio protective properties, respectively. A short analysis of the biological activities of the coordination complexes indicates that the complexes with different compositions and structures formed by the same ligand and palladium have different biological activities. Thus, it is obvious that the structure, composition, coordination way of the ligand and kind of complex play significant role.

Thus, 4-aminopyridine that is a potential bidentate ligand is monodentally coordinated via nitrogen atom of pyridine

independently on the reaction condition and the stoichiometric ratio, whereas exocyclic amino group does not participate in coordination.

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