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COMPLEX COMPOUNDS OF PALLADIUM (II) WITH γ – GLUTAMIC ACID AMIDE^{1,2}H.I. Gasanov, ¹A.N. Azizova, ²N.M. Kuliyeva, ¹Sh.G. Gasimov¹Azerbaijan Medical University, Scientific Research Center²Western Caspian University

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Abstract: This study examined the formation of palladium (II) complex compounds with γ -glutamic acid amide in aqueous solutions and calculated the complex stability constants, also known as formation constants. After the complexes were separated from one another, each compound's structure and characteristics were studied individually. Based on data from NMR, IR, and UV spectroscopy it was established, that two ligand molecules coordinate in a monodentate manner along the donor nitrogen atoms of the amino group and in a bidentate manner along the nitrogen atoms of the amino group and oxygen. A planar square internal coordination sphere is formed in the trans- structure, respectively, in the complexes $[Pd_2N_{amine}2Cl]$ ($[PdL_2Cl_2]$), $[Pd_2N_{amine}2O_{carb}]$ ($[Pd(HL)_2]$).

Keywords: palladium (II), glutamine, ligand, dentation, coordination

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Introduction

A systematic study of the composition-structure relationship and biological activity of palladium compounds revealed some abilities of its complexes to stabilize the cell membrane, which served as one of the prerequisites for searching among palladium complexes with radioprotective properties [1]. At the same time, the literature also contains information about the high antitumor activity of palladium complexes with organic ligands [1]. Low toxicity is one of the requirements for biologically active compounds. Palladium compounds are characterized by significantly lower toxicity compared to platinum complexes.

Despite the huge number of known and thoroughly characterized coordination compounds of noble metals, the interest of researchers in their synthesis and study does not

decrease. Recently, complexes of which ligands are bioactive natural substances containing amino acids and, in particular, glutamine, have become attractive. Information regarding glutamine's anticancer activity can be found in Ref. [2]. It is of scientific and practical interest that a coordination compound containing the metal complexing agent palladium (II) ion and the polydentate ligand glutamine has been formed. This combination has not been reported in any literature and shows promise as an anticancer medication.

The effort involved studying the interaction between palladium (II) and the γ -amide of L-glutamic acid, as well as establishing the structures of the produced coordination compounds.

Experimental part

Palladium dichloride (PdCl_2), potassium tetrachloropalladate ($\text{K}_2[\text{PdCl}_4]$) of chemically pure grade and γ - L-glutamic acid amide (L-glutamine, Qln) of reagent grade were used as starting compounds.

IR spectra of the complexes and the ligand were recorded on Thermoscientific, Nikoletis 10 and Bruker IFS-113V spectrometers in vaseline or the suspension of fluorinated oils, as well as in the form of tablets with KBr; and electronic absorption spectra were taken on a Shimadzu UV-Vis-240 Evolution-60S device. NMR spectra were recorded on a Bruker NMR 400 MHz NMR spectrometer. Elemental analysis of non-metals was performed on a CHNS-O EMA 502 analyzer. Palladium analysis was carried

out using our own method.

The thermal behavior of the complexes was studied on a STA 449 F3 Jupiter NETZSCH derivatograph at a heating rate of 10 degree/min up to 800° C.

Complex compounds were synthesized at room temperature in an aqueous solution at a ratio of $\text{Pd}^{2+} : \text{L}^- = 1 : 2$. After two days, plate-like light yellow crystals precipitated from the solution, which were then washed with water, ethanol, ether and dried at 40–50° C. Since the routes for carrying out syntheses are not so different, it is more appropriate to describe them briefly. The results of elemental analysis are listed in Table 1.

Results and discussion

In amino acid amides, the molecule composition contains three potential donor atoms - the nitrogen of the amino and amido groups and the oxygen of the carboxyl group. The donor properties of nitrogen (electronic state sp^3) of the amino group are appeared in a greater degree than of the amido groups (electronic state sp^2), since the free electron pair

of the nitrogen atom in the first case is more mobile than in the second, where the same pair of electrons is located in the p-orbital. This causes it to be moved in the direction of the carbon atom, making the nitrogen atom of the amide group less able to make a bond through the donor-acceptor mechanism [2].

Table 1. The result of the elemental analysis for the synthesized complex compounds

Coordination compounds	Pd		N		Cl		C		H	
	Found	Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found	Calc.
$[\text{PdL}_2\text{Cl}_2]$	22.47	22.66	11.74	11.93	15.32	15.10	25.41	25.56	4.47	4.26
$[\text{Pd}(\text{HL})_2]$	26.71	26.56	14.16	13.98			30.15	29.98	5.66	5.49

To establish the purity and individuality of the resulting complexes, their X-ray photographs were taken. The uniqueness and purity of the ligand are confirmed by the stark differences in its X-ray diffraction patterns from those of the produced complexes (Fig. 1).

Depending on the synthesis conditions, coordination compounds with mono- (nitrogen atom of the amino group) or bidentately coordinated (nitrogen and oxygen atoms of the amino and carboxyl groups) glutamine molecules (HQln) might be expected to occur in the palladium (II) γ -glutamine-water system.

Consequently, the internal coordination sphere can be supplemented with both water molecules and chlorine ions.

Individual amino acids and metal complexes with their participation are prone to the so-called glass transition [3], which we observed during the synthesis process and made it very difficult to isolate them in crystalline form for X-ray diffraction analysis. Therefore, the conclusion about the structure of the complexes we synthesized was made on the basis of NMR data, vibrations physical spectroscopy and electronic absorption spectra.

NMR spectra for the starting amino acid (pH 5.65) and the synthesized complexes - $[\text{PdL}_2\text{Cl}_2]$, $[\text{Pd}(\text{HL})_2]$ (pH 6.04 and 6.71, respectively) were recorded in deuterated water (D_2O). In the spectrum of the amino acid, two multiplets are visible, corresponding to the CH and CH_2 groups; the NH_2 group is quickly deuterated, and therefore it is not detected by a separate signal. The data we obtained is as

follows: for the α -carbon atom, the signal is presented as a doublet of a doublet with δ equal to, ppm: 4.109; 4.082; 4.079 and 4.066, and for the γ -atom – as a multiplet with δ equal to, ppm: 3.065; 3.056; 3.008; 2.091; 2.951; 2.937; 2.929 and 2.909. The presence of a multiplet in the signal corresponding to the CH_2 group can be explained by the influence of the neighboring amide group.

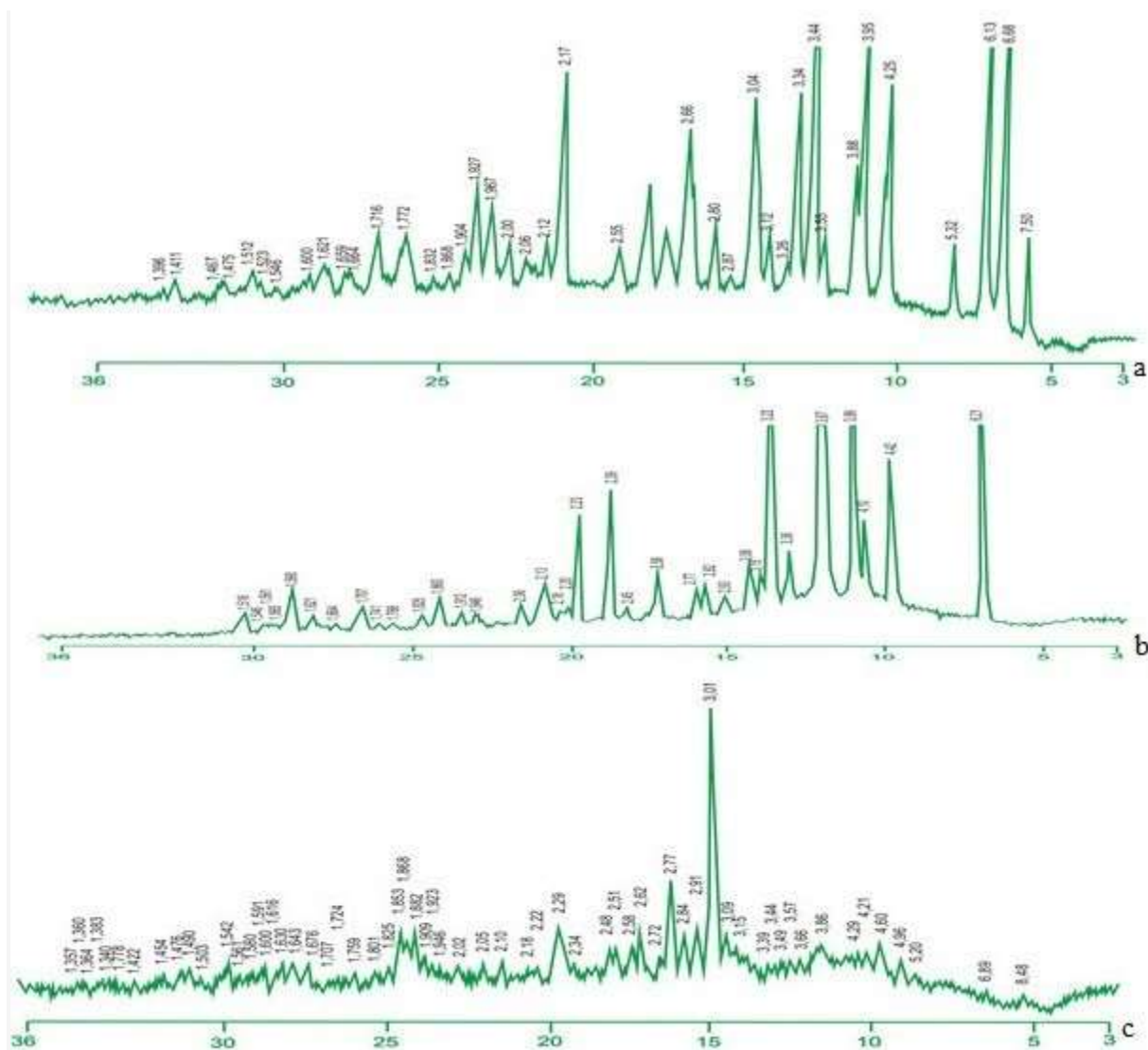


Fig.1. X-ray diffraction patterns of the ligand-HQIn (a) and complexes $[\text{PdL}_2\text{Cl}_2]$ (b), $[\text{Pd}(\text{HL})_2]$ (c)

The NMR spectrum of both synthesized palladium(II) complexes with glutamine shows two broadened signals: 5.126–4.969 ppm and 3.936–3.838 ppm, corresponding to CH and CH_2 groups. The absence of multiplets and the shift of signals towards a weaker field compared to the signals of CH and CH_2 groups in the ligand is due to the formation of a palladium (II)

complex with glutamine.

In order to determine the coordination of the ligand in the molecule of the synthesized complexes of palladium (II) with glutamine, electronic absorption spectra of aqueous solutions with a concentration of complexes $[\text{PdL}_2\text{Cl}_2]$, $[\text{Pd}(\text{HL})_2]$ $-5 \cdot 10^{-3} \text{ mol l}^{-1}$ ($\text{Pd}^{2+} : \text{L}^- = 1 : 2$) without adding a ligand and at a

glutamine concentration of 1×10^{-2} mol l⁻¹ in an excess of ligand Pd²⁺ : L⁻ = 1 : 4 in weakly acidic solutions (pH 6.71 and 5.84, respectively) were recorded. Prepared solutions of complexes with a concentration of 10⁻³ M for determining electrical conductivity are not subject to hydrolysis.

A predominantly square planar structure of the coordination site is typical for palladium(II) complexes [4]. In the electronic absorption spectra of palladium(II) complexes with a square planar structure, three spin-allowed d-d transitions are possible, the energies of which are close, which determines the presence of one broadband in the absorption spectra, the location of the latter depends on the donor atoms of the ligand environment of the central atom [5–8]. In the case of the synthesized complexes, specifically such absorption broadband was recorded in the

region 31120–3140 cm⁻¹ confirming the square planar structure of the coordination site.

The conclusion about the composition of the ligand environment of the central atom was made by comparing the values of the experimentally determined frequency of the maximum absorption band with those theoretically calculated for various chromophores using the formula $\nu_{\max} = n_i \cdot \nu_i$, where n_i is the number of donor atoms of each type; ν_i is the increment value for donor atoms of each type (Table 2). Taking into account the synthesis conditions for the theoretically most possible chromophores, the coordination site of palladium (II) of various compositions, including with mono- and bidentately coordinated glutamine, was calculated using known increment values ν_{\max} : Cl- 5165; O_{H₂O}- 6570; O_{carbox}- 6780; N_{amin}- 8450 [9].

Table 2. The composition of the chromophore and the value of the maximum absorption band of a number of palladium (II) complexes*

Composition of the complex particles	Chromophore	$\nu_{\max \text{ calc.}, \text{ cm}^{-1}}$
[PdL(H ₂ O) ₂]	PdN _{NH₂} O _{carbox} O _{H₂O}	28380
[PdL ₂ (H ₂ O) ₂]	Pd2N _{NH₂} 2O _{H₂O}	30070
[Pd(HL) ₂]	Pd2N _{NH₂} 2O _{carbox}	30450
[PdL ₄]	Pd4N _{NH₂}	33830
[PdL ₂ Cl ₂]	Pd2N _{NH₂} 2Cl	27250
[PdL ₂ ClH ₂ O]	Pd2N _{NH₂} ClO _{H₂O}	28660
[PdLCl ₂]	PdN _{NH₂} 2O _{carbox} 2Cl	25570

*The charges of complex particles are not given.

As can be seen from Table 2's data, the most satisfactory experimental value for the complex [Pd(HL)₂], of which ν_{\max} is equal to 31112 cm⁻¹, corresponds to the calculated value of 30452 cm⁻¹, and for the [PdL₂Cl₂] complex, of which ν_{\max} is equal to 27165 cm⁻¹, corresponds to the calculated value 27250 for the chromophores Pd2N_{NH₂}2O_{carbox} and Pd2N_{NH₂}2Cl, respectively. These data may indicate the synthesis of a planar-square structure of the coordination compound of palladium (II), in which two glutamine molecules, in the first case, are bidentately coordinated with the nitrogen atom of the amino group and the oxygen atom of the carboxyl group, and in the second case – monodentate via the nitrogen atom of the amino group.

IR spectra were recorded in a wide range of wave numbers from 4000 to 200 cm⁻¹. The shape of the obtained spectra satisfactorily coincides with the characteristic vibrational frequencies of the spectra of amino acids given in the literature [10–12]. There are no IR spectroscopic data for the palladium (II) complex with glutamine in the literature. In the IR spectra, maxima are visible that are responsible for the structure of the ligand. In the high-frequency region of the amino acid spectrum, two stretching vibrations (symmetric ν_s and asymmetric ν_{as}) of free NH bonds of the amide group, which correspond to absorption bands of 3456 and 3410 cm⁻¹, and of the amine group, 3112 and 2932 cm⁻¹, are observed. Deformation (δ) vibrations of the NH bond of

the amide group appear in the spectrum in the region of 1638 cm^{-1} and 1420 cm^{-1} . Stretching vibrations of the carbonyl group (C=O) of the amide were detected in the region of 1680 cm^{-1} . The absorption maximum of 1584 cm^{-1} observed in the spectrum of glutamine corresponds to bending vibrations (NH^{+3}) for amino acids, which confirms the zwitterionic form of glutamine [12–14].

The spectrum of palladium (II) complexes with glutamine $[\text{Pd}(\text{HL})_2]$, $[\text{PdL}_2\text{Cl}_2]$ shows absorption bands with maxima at 3456, 3430 and 3460, 3420 cm^{-1} , respectively, which correspond to symmetric and asymmetric stretching vibrations (NH) of the amide group. The frequencies 3310.3072 and 3305.3050 cm^{-1} correspond to the stretching vibrations (ν_s and ν_{as}) of the amine NH group. Bending vibrations

of the amide NH group are visible at 1638.1640 and 1426.1430 . In the IR spectrum of the $[\text{Pd}(\text{HL})_2]$ complex, stretching vibrations of the carbonyl group (C=O) are observed at 1686 cm^{-1} , and the maximum at 1650 cm^{-1} that appears in the spectrum of the palladium (II) complex with glutamine confirms the fact that the ligand is in zwitterionic form.

We did not identify the assignment of all absorption bands in the obtained spectra; the characteristic bands for the starting amino acid and the synthesized complex were only considered (Table 2).

It is known [11, 15] that Pd-N and Pd-O bonds correspond to band maxima in the low-frequency region of the spectrum, which are often difficult to recognize due to mixing with other skeletal vibrations.

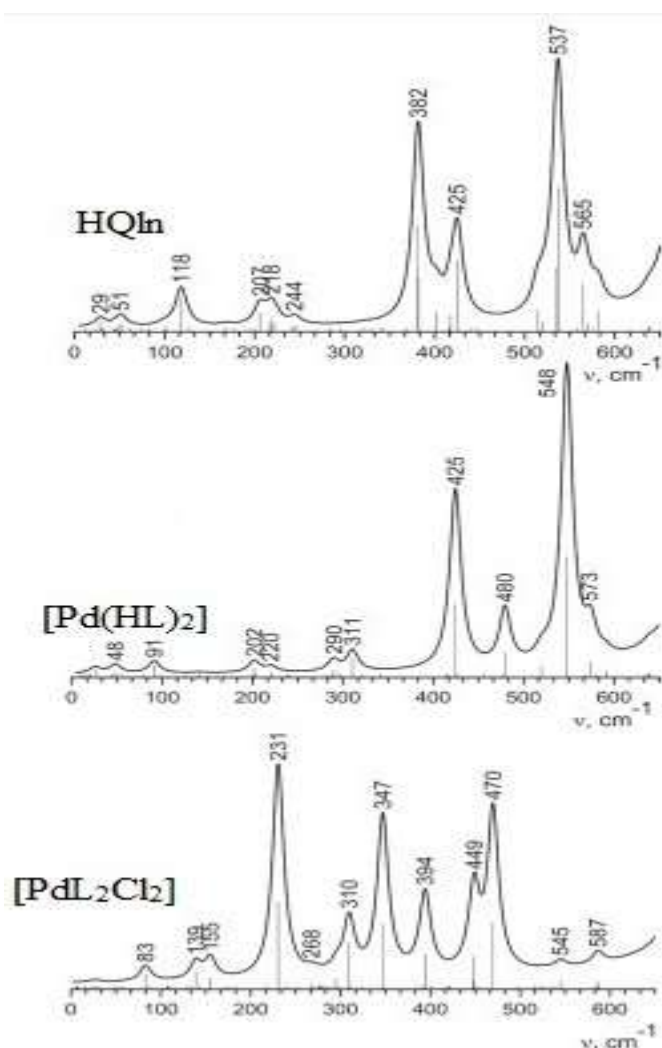


Fig.2. IR spectra of HQln and complexes $[\text{Pd}(\text{HL})_2]$ and $[\text{PdL}_2\text{Cl}_2]$

However, after comparing the absorption bands of the amino acid and the palladium

complex in the spectra, maxima are visible at 470 and 449 cm^{-1} , which are absent in the

spectrum of the starting amino acid, which we referred to the stretching vibrations of Pd-N and Pd-O bonds, respectively, which satisfactorily coincides with the data for the palladium (II) complex with amino acids [15]. One clear absorption band at 347 cm^{-1} observed in the IR spectrum of the complex $[\text{PdL}_2\text{Cl}_2]$ was

attributed to Pd-Cl valence bonds. The presence of one band for each Pd-N, Pd-O and Pd-Cl bonds in the spectrum indirectly indicates the *trans*-isomeric form of the synthesized complexes [15]. The qualitative thiocarbamide reaction of N.S. Kurnakov was used to prove this judgment.

Table 3. Some absorption bands of the IR spectra of glutamine and diglutamine complex of palladium (II)

HL	$[\text{PdL}_2\text{Cl}_2]$	$[\text{Pd}(\text{HL})_2]$	Absorption band assignment
3456 and 3410	3460 and 3420	3456 and 3430	ν_s and ν_{as} NH in the amide group
3112 and 2932	3305 and 3050	3310 and 3072	ν_s and ν_{as} NH in the amine group
1680	1686	1688	ν (C=O)
	346		ν (Pd-Cl)
1638	1640	1638	δ (NH)
1584	1686	1650	$\delta(\text{NH}^{+3})$ for aminoacids containing NH_2 group
1420	1430	1420	δ (NH)
-	-	476	ν (Pd-N)
-	-	439	ν (Pd-O)

On the heating curve of the $[\text{PdL}_2\text{Cl}_2]$ compound, endothermic effects are observed at temperatures of 122, 197 and $342\text{ }^\circ\text{C}$, as well as many exothermic effects. The first endothermic effect corresponds to the removal of two ligand

molecules and a chlorine atom. The DTA curve of the compound $[\text{Pd}(\text{HL})_2]$ shows only two endothermic effects at 190 and $208\text{ }^\circ\text{C}$, as well as many exothermic effects.

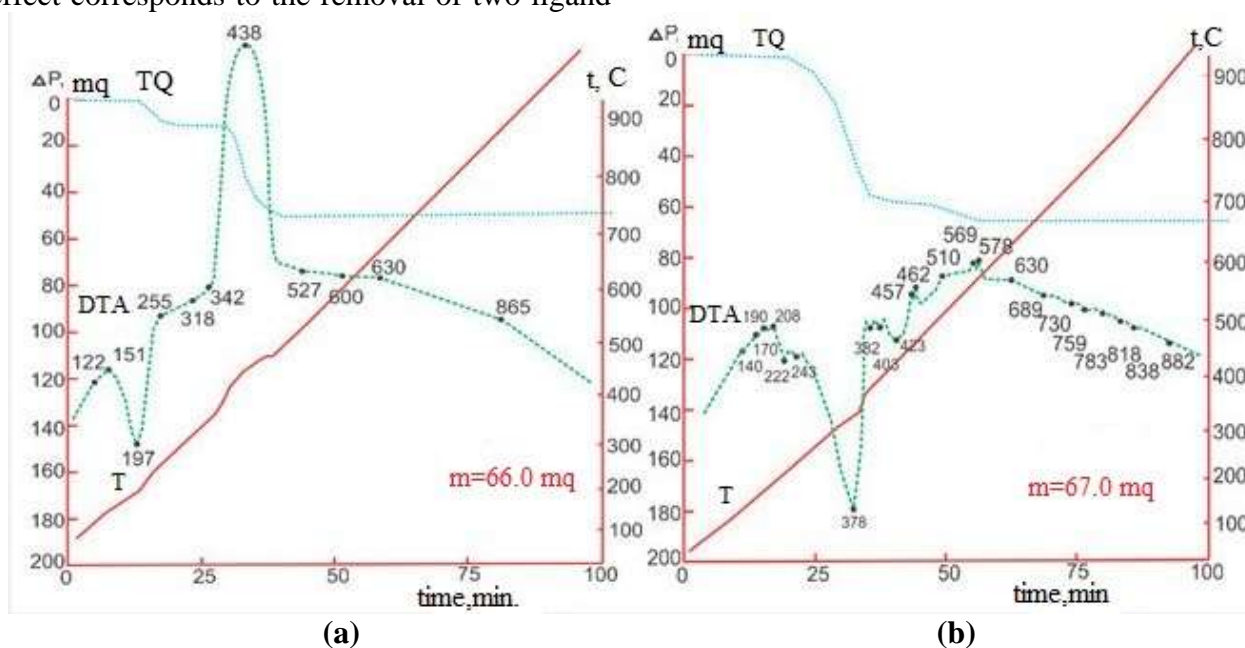


Fig. 3. Derivatograms $[\text{PdL}_2\text{Cl}_2]$ (a) and $[\text{Pd}(\text{HL})_2]$ (b)

The appearance of the first endothermic effect is consistent with the removal of two ligand molecules. Data from thermal analysis of the studied compounds showed that the complexes decompose without melting and the final product of thermolysis is metallic

palladium.

Thus, physicochemical methods confirmed the formation of a coordination compound of palladium (II) with glutamic acid in the composition $[\text{Pd}(\text{HL})_2]$ and $[\text{PdL}_2\text{Cl}_2]$.

Conclusion

1. A coordination compound of palladium (II) with glutamine with composition $[\text{Pd}(\text{HL})_2]$ is formed, in which two ligand molecules are coordinated bidentately with the donor nitrogen atoms of the amino group and the oxygen of the hydroxyl group.
2. In another obtaining complex $[\text{PdL}_2\text{Cl}_2]$, monodentate coordination of two ligand molecules is carried out at the nitrogen atom of the amino group.
3. In both complexes, the ligands are coordinated in a *trans*-position relative to each other.

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PALLADIUMUN (II) γ -AMİD QLUTAMİN TURŞUSU İLƏ KOMPLEKS BİRLƏŞMƏLƏRİ

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Xülasə: Palladiumun (II) sulu məhlullarda γ – amid qlutamin turşusu ilə kompleks birləşmələrinin alınması və əmələgəlmə sabiti öyrənilmişdir. Məhluldan komplekslər fərdi qaydada ayrılmış, quruluş və tərkibləri öyrənilmişdir.

Sintez edilmiş komplekslərdə NMR, İQ- və UB- spektroskopiya tədqiqatları ilə müəyyən edilmişdir ki, komplekslərdə iki molekul liqand azot atomları ilə monodentatlı, digər komplekslərə isə azot və oksigen atomları ilə bidentatlı koordinasiya edirlər. Müvafiq olaraq neytral tipli komplekslərdə [Pd₂Namin₂Cl] ([PdL₂Cl₂]), [Pd₂Namin₂Okarb] ([Pd(HL)₂]) daxili sferada trans-vəziyyətdə yastı kvadrat müstəvisi formalaşır.

Açar sözlər: palladium, qlutamin, liqand, dentatlılıq, koordinasiya

КОМПЛЕКСНЫЕ СОЕДИНЕНИЯ ПАЛЛАДИЯ (II) С γ -АМИДОМ ГЛУТАМИНОВОЙ КИСЛОТЫ

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Аннотация: В данной работе изучено образование комплексных соединений палладия (II) в водных растворах с γ -амидом глутаминовой кислоты и определены их константы образования. Комплексы выделены в индивидуальном виде и изучены их строение и свойства.

По данным ЯМР, ИК- и УФ- спектроскопии установлено, что происходит монодентатная координация двух молекул лиганда по донорным атомам азота аминогруппы и бидентатная - по атомам азота аминогруппы и кислорода. Формируется плоскоквадратная внутренняя координационная сфера в транс-строении, соответственно в комплексах [Pd₂Намин₂Cl] ([PdL₂Cl₂]) и [Pd₂Намин₂Окарб] ([Pd(HL)₂]).

Ключевые слова: палладий, глутамин, лиганд, дентатность, координация