



Synthesis and Structure of Platinum (II) Complexes with the Decomposition product of Cystamine Dihydrochloride

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ABSTRACT

The interaction of dithiodiethylamine (cystamine) (L^1) with platinum compounds in aqueous medium has been studied and it has been shown that in aqueous solutions in an acidic medium, the disulfide bond L^1 is cleaved, followed by coordination of platinum to form β -mercaptoethylamine (mercamine, LH). Depending on the reaction conditions, binuclear complexes of composition $\mu(S)[Pt_2(LH)_2C1_4]$ (I), $\mu(Cl)[Pt_2(LH)_2C1_4]$ (II) with bridging chlorine or sulfur atoms are formed. At 70°C, a compound with a bridged position of sulfur atoms (complex I), and at lower temperatures (30-50°C) with a bridged position of chlorine atoms (complex II) are formed. X-ray structural analysis of the complex $[Pt_2(LH)_2C1_4]$ (I) was carried out. Crystals I are rhombic, with $20^\circ Ca = 17.282(1)$, $b = 9.986(1)$, $c = 8.0188(9)$ Å; $R = 0.029$. Molecule I is a binuclear complex in which platinum atoms are linked by a pair of bridging thiolate ligands ($-SCH_2-CH_2-MH_3^+$). The Pt_2S_2 metallocycle is bent along the sulfur-sulfur line, so that the dihedral angle between the coordination planes of platinum atoms is equal to 138° . The S-S distance, equal to $2.909(1)$ Å, is noticeably shorter than the doubled van der Waals radius of the sulfur atom (3.60 Å). The structure of the complexes was also confirmed by IR spectroscopy data.

Keywords: platinum, bidentate ligand, cystamine, disulfide bonds, mercamine, cis-, trans-structures, gauche conformation

Received 15.10.2023

Revised 27.11.2023

Accepted 24.12.2023

INTRODUCTION

It is known that cystamine has the ability to prevent or facilitate the course of the general radiation reaction of the body, which occurs under the action of large doses of x-rays and gamma rays. In this case, the disulfide bond is cleaved with the formation of β -mercaptoethylamine (mercamine) at the first stage [1,2]. The study of the interaction of cystamine $NH_2CH_2CH_2S-SCH_2CH_2NH_2$ (L^1) with palladium, mercury, silver, and copper compounds showed that this also leads to the cleavage of the disulfide bond with the metal coordinating the formed deprotonated molecules of β -mercaptoethylamine $HSCH_2CH_2NH_2$ [3]. Information about complex compounds of platinum with cystamine was not found in the literature prior to our study. However, it is of particular interest to consider the data available in the literature on the complexes of palladium with β -mercaptoethylamine. (LH).

It follows from the literature data that LH forms two types of compounds with palladium(II): the mononuclear complex PdL_2 and the trinuclear complex $[Pd_3L_4]Cl_2$. The PdL_2 compound was first synthesized by reacting stoichiometric amounts of $K_2[PdCl_4]$ with an alkaline solution $LH \cdot HC1$ [4]. The authors [5] studied the structure of this complex by IR spectroscopy using metal isotope substitution ($^{104}Pd/^{110}Pd$) and amino groups (NH_2/ND_2) and proved that in the PdL_2 complex the PdN_2S_2 skeleton has a cis-configuration, as evidenced by the presence of two bands of stretching vibrations $\nu(PdN)$ ($421, 309$ cm^{-1}), such $\nu(PdS)$ (368 and 337 cm^{-1}).

Changing the ratio of the initial reagents leads to the formation of trinuclear palladium complexes: both homometallic $[Pd_3L_4]Cl_2$ [4] and heterometallic: $[PdNi_2L_4]Cl_2$ or $[Pd_2NiL_4]Cl_2$. During the interaction of the $[Pd_2NiL_4]Cl_2$ complex with the tetrachloromercurate anion in an aqueous solution, Ni is replaced by Hg to form the complex $[Pd_2HgL_4][HgC1_4]$ [6].

Our earlier studies [7] of the interaction of platinum salts with Our earlier studies of the interaction of platinum salts with $L1 \cdot 2HC1$ in alkaline medium (pH 10) showed that a compound is formed with the ratio $Pt : L1 : C1 = 3 : 4 : 2$, similar in composition to the compound obtained by interaction with β -mercaptoethylamine - $[Pt_3L_4]Cl_2$ [6]. However, as a result of X-ray diffraction studies, it was found that not a trinuclear, but a hexanuclear complex of the noncluster type is formed $[Pt_6L_8C1_4]$ [7,8].

This work is devoted to the study of the interaction of platinum (II) with cystaminedihydrohalide in aqueous medium in the pH range 1 -7.

MATERIAL AND METHODS

We used cystaminedihydrochloride (Fluka) without additional purification. $H_2[PtCl_4]$, obtained by the method [9].

Synthesis of the $[Pt_2(LH)_2C_{14}]$ complex (bridging sulfur atoms, I). To a filtered solution of 1.17 g (0.65 mmol) of $H_2[PtCl_4]$ in a mixture of 5 mL of water with 5 mL of concentrated HCl was added with stirring 0.78 g (0.65 mmol) of $L_1 \cdot 2HCl$ dissolved in 10 mL of water, while the color of the solution became pale red. When this solution was evaporated in a water bath at a temperature of 70-75°C, a precipitate formed to a small volume, containing yellowish-red crystals, which were taken under a microscope and analyzed. The substance is slightly soluble in water and insoluble in alcohol, acetone, chloroform, carbon tetrachloride, benzene, ether.

Synthesis of the complex $[Pt_2(LH)_2C_{14}]$ (bridging chlorine atoms, II). To a filtered solution of 0.67 g (0.38 mmol) $H_2[PtCl_4]$ in a mixture of 5 ml H_2O with 5 ml concentrated HCl was added a solution of 0.46 g (0.38 mmol) $L_1 \cdot 2HCl$ in 10 ml water with stirring. The color of the solution changed from light red to yellow. After 5 min. at a temperature of 35-40°C, a dark yellow precipitate precipitated from the solution. The precipitate was filtered off and dried first in air and then in vacuum to constant weight. Yield 0.93 g (48%). The substance is slightly soluble in water and insoluble in alcohol, acetone, chloroform, carbon tetrachloride, benzene, ether. Analytical data for complexes I and II are given in Table 1.

Table 1. Results of elemental analysis of the complexes I,II

Complex	Brutto-formula	Content (calculated/found), %			
		Pt	C1	S	N
I	$C_4H_{14}N_2S_2Pt_2C_{14}$	56.86/56.41	20.66/20.87	9.34/9.60	4.08/4.20
II	$C_4H_{14}N_2S_2Pt_2C_{14}$	56.86/56.63	20.66/20.57	9.34/9.51	4.08/4.31

The IR spectra of the starting substances and complexes were measured on ThermoScientific, Nicoletis 10 and Bruker IFS-113V spectrometers in vaseline or suspension of fluorinated oils, as well as in the form of tablets with KBr in the range of 100-4000 cm^{-1} , in the solid state (suspension in vaseline or fluorinated oils, tablets with KBr and CsI).

X-ray photoelectron spectra (XES) (obtained on a Varian VIEE-15 spectrometer. The Cls - 285.0 eV line was used as a standard. The reproducibility of the electron detachment energies was ± 0.1 eV.

X-ray diffraction data - unit cell parameters and intensities of 1619 reflections with $I > 2\sigma$ - were obtained on a Bruker X8 APEX automatic four-circle diffractometer equipped with a two-coordinate SDS detector at 273(2)K using molybdenum radiation and a graphite monochromator according to the standard method ($\lambda MoK\alpha$, graphite monochromator, $\theta/2\theta$ -scanning, 2θ max = 56°). The structure was solved by the heavy atom method and refined by the least squares method (LSM), first in the isotropic and then in the anisotropic approximation. In the difference synthesis, all hydrogen atoms calculated geometrically were revealed. The final refinement of the least squares in the full-matrix anisotropic approximation for non-hydrogen atoms and in the isotropic approximation for hydrogen atoms is brought to $R = 0.029$; $RW = 0.044$ over 1551 reflections with $F_2 > 3\sigma$. The atomic coordinates are given in Table 1. 2, bond lengths and bond angles are given in Table. 3

RESULTS AND DISCUSSIONS

The study of the interaction of cystaminedihydrochloride with platinum showed that the nature of the products formed depends on the reaction conditions.

Table 2. Coordinates of non-hydrogen atoms ($\times 10^5$) in complex I

Atoms	x	y	z
Pt(1)	16492(2)	17828(3)	15691(4)
C1(1)	0.12306	0.00451	0.01324
C1(2)	0.04669	0.24053	0.05361
S(1)	21332(5)	38109(10)	23615(14)
N(1)	5649(30)	53159(60)	26109(70)
C(1)	17819(30)	51079(50)	9429(70)
C(2)	12209(3)	60409(50)	18149(90)

Table 3. Bond lengths and bond angles in complex I

Bonds	d, Å	Angle	ω , grad
Pt(1)-C1(1)	2.353(1)	S(1)Pt(1)Cl(2))C1(2)	96.50(4)
Pt(1)-C1(2)	2.369(1)	S(1)Pt(1)S(1A)	79.31(4)
Pt(1)-S(1)	2.280(1)	S(1A)Pt(1)Cl(1) A)Pc1(1)C1(1)	93.45(4)
Pt(1)-S(1 A)	2.275(1)	C1(1)Pt(1)C1(2)	91.55(4)
S(1)-C(1)	1.826(5)	Pt(1)S(1)Pt(1A)	91.72(3)
C(1)-C(2)	1.515(8)	Pt(1)S(1)C(1)	109.4(2)
C(2)-N(1)	1.491(8)	Pt(1A)S(1)C(1)	108.4(2)
		S(1)C(1)C(2)	111.1(4) 11.2(4)
		C(1)C(2)N(1)	112.6(4)

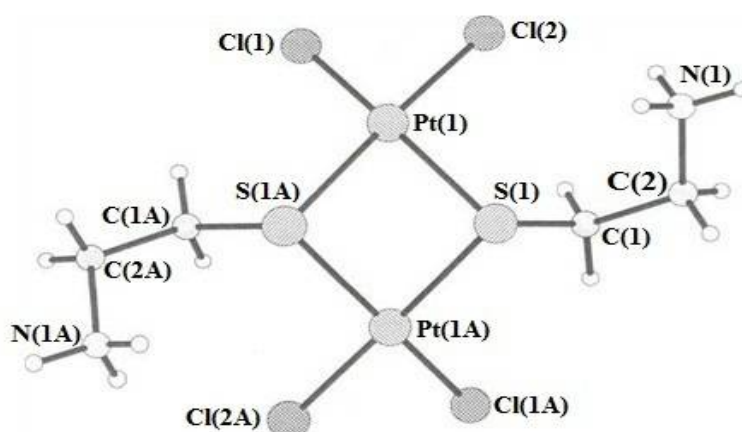


Fig 1: Molecular structure and numbering of atoms of the complex1.

The structure of complex I was established by X-ray diffraction analysis (XRD). Crystals of I are rhombic, at 200 C $a = 17.282(1)$ Å, $b = 9.986(1)$, $c = 8.0188(9)$ Å; $V = 1383.0(3)$ Å³, $Z = 4$ sp. gr. Rsp. The molecule is located in a particular position on axis 2.

Molecule 1 (figure) is a binuclear complex in which platinum atoms, each having two terminal chlorine atoms, are linked by a pair of bridging thiolate ligands $-\text{SCH}_2\text{CH}_2\text{NH}_3^+$. Axis 2 passes through the middle of the metal cycle, perpendicular to its root-mean-square plane. Platinum atoms have square-planar coordination. The Pt_2S_2 metalocycle is bent along the sulfur-sulfur line, so that the dihedral angle between the coordination planes of platinum atoms is 138° . The angle $\text{Pt}(1)\text{S}(1)\text{Pt}(1\text{A})$ is 91.720 and the angle $\text{S}(1)\text{Pt}(1)\text{S}(1\text{A})$ is 79.310 . The Pt-Pt distance in the cycle ($3.270(1)$ Å) actually coincides with the sum of the van der Waals radii (3.26 Å), while the S-S distance ($2.909(1)$ Å) is noticeably shorter than twice the van der Waals radius of the atom sulfur (3.60 Å) [10]. However, this last distance is significantly longer than in the cystamine molecule. (2.06 Å) [11].

Thus, X-ray diffraction studies have established that under the conditions of a chemical reaction, the sulfur-sulfur bond of the initial cystamine molecule is broken, followed by coordination of the resulting β -mercaptoethylamine protonated at the amino group and deprotonated at the sulfhydryl group.

Schematically, the structure of complex I can be represented as follows:

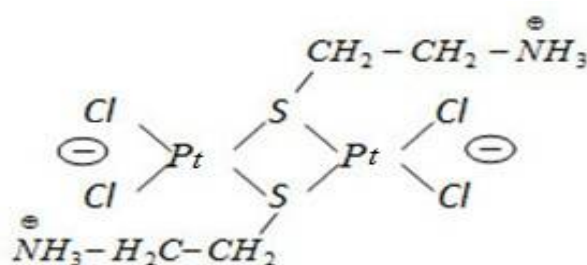


Fig 2: structure of complex I

Positive charges are localized on nitrogen atoms and negative charges on chlorine atoms. Both Pt-S bonds (2.280 and 2.275 Å) are aligned but noticeably shorter than in other platinum complexes, in which the metal atoms are linked by a pair of bridging thiolate ligands (2.282 – 2.454 Å, the average value is 2.359 Å

[11–13]). Such a shortening of the Pt-S distances in complex I is apparently due to its zwitterionic nature. The length of the Pt-C1 bond in various platinum complexes can vary within fairly wide limits, in particular, depending on the nature of the *trans* ligand. For those complexes in which a ligand with a weak π -acceptor ability is located in the *trans* position to the Pt-C1 bond, the length of the Pt-Cl bond is 2.30–2.34 Å [14,15]. If the ligand is capable of exhibiting a significant *trans* effect (σ -bonded carbon atom, carbene ligand), then the Pt-Cl bond lengthens to 2.35–2.45 Å [16, 17]. In complex I, the Pt-C1(1) and Pt-C1(2) bond lengths (2.353 and 2.369 Å) are close to the lower limit of values characteristic of the second group of complexes with the Pt-C1 bond. At the same time, in the binuclear $[\text{Pt}_2\text{Cl}_6]^{2-}$ dianion, the bond lengths of platinum with terminal chlorine atoms are 2.25–2.27 Å [18,19], i.e. shorter than in the complex I studied by us and than in the platinum complexes discussed above and belonging to the first group. A small but significant (16 σ) difference in the Pt-Cl(1) and Pt-Cl(2) bond lengths in complex I should be noted. that, apparently, the proposed above color-ion scheme of the structure of the complex does not fully reflect the nature of the delocalization of the negative charge in it and the degree of participation of two chlorine atoms in this delocalization.

Comparison of the interatomic distances in coordinated mercamine and mercamine hydrochloride [20] shows that, upon platinum coordination, the lengths of the C-C and C-N bonds in the ligand practically do not change; however, the C-S bond shortens from 1.86 Å in free mercamine hydrochloride to 1.826 Å in complex 1, while the SC(1)C(2) angle also decreases from 112.6° in the free ligand to 111.1° in complex I. As in the free ligand, β -mercaptoethylamine in complex I has a *gauche* conformation with an angle rotation of 55° (the angle between the SCC and CCN planes) around the C-C bond.

And, finally, in the crystal, I molecules form a three-dimensional network of intermolecular hydrogen bonds Cl(1)···H(Nⁱ1)-Nⁱ1, C1(2)···H(Nⁱ1)-Nⁱ1 (distances C1···H 2.41, 2.46 Å; C1···N 3.196, 3.238 Å, respectively, transformation i [(-x)(-0.5 + y)(0.5 - z)]; transformation j [(x)(0.5 - y)(-0.5 - z)]). The third hydrogen atom does not participate in the system of hydrogen bonds. There are no grounds for the conclusion about the existence of an intramolecular interaction $\text{MH}_3^+ \cdots \text{S}$ in complex I.

The IR spectral data (Table 4) are in good agreement with the XRD results, according to which the central Pt_2S_2 metallocycle in complex I is non-planar (bent along the sulfur-sulfur line) and has local C_2v symmetry. The most characteristic in the spectra of Pt chloride complexes are the frequencies of stretching vibrations $\nu(\text{PtCl})$, which give intense bands in the region of 300–380 cm^{-1} . For vibrations of Pt-C1 bonds (types A1 + B1 + B2).

Table 4. Main vibrational frequencies (cm^{-1}) in the IR spectra of the complexes I,II

Assignment	I	II
	Cl	Cl
$\nu(\text{NH}_3^+)$ $\nu(\text{NH}_2)$	3200-2000	3200-2000
$\delta(\text{NH}_3^+)$	1582	1570
$\delta(\text{NH}_2)$	1559	1561
$\nu(\text{PtX}_k)$	376	359
	364	
	330	
$\nu(\text{PtX}_M)$		308
		287
$\nu(\text{PtS}_k)$		380
$\nu(\text{PtS}_M)$	285	
	271	

Indeed, in the IR spectrum of complex 1, three $\nu(\text{PtCl})$ bands with frequencies of 376, 364, and 330 cm^{-1} are observed, which is consistent with the nonplanar structure of the metallocycle in this complex. Stretching vibrations $\nu(\text{PtS})$ correspond to bands at 285 and 271 cm^{-1} . The protonated amino group is characterized by broad absorption in the region of 2000–3200 cm^{-1} and bands of bending vibrations $\nu(\text{NH}_3^+)$ near 1582 and 1559 cm^{-1} .

XPS data are also consistent with the presence in complex I of a protonated NH_3^+ group ($E_b(\text{N}_{1s}) = 401.4$ eV), the same as in the initial cystamine hydrochloride ($E_b(\text{N}_{1s}) = 401.4$ eV), and a sulfur atom, platinum coordinated ($E_b(\text{S}_{2p}) = 163.4$ eV).

The IR spectrum of complex II differs significantly from the spectrum of complex I. It also contains three bands $\nu(\text{PtCl})$ at 359, 308 and 287 cm^{-1} . The reduced values of the last two frequencies in the spectra of II suggest that they refer to stretching vibrations $\nu(\text{PtClM})$ with the participation of bridging rather than

terminal halogen atoms. The frequency 359 cm^{-1} lies in the region characteristic of vibrations of the terminal bonds $\nu(\text{PtClK})$. The presence of two bands $\nu(\text{PtXM})$ and one band $\nu(\text{PtClK})$ is characteristic of binuclear complexes of the $[\text{Pt}_2\text{L}_2\text{Cl}_4]$ type with halide bridges and trans position L [20,21]. This suggests the following structure of complex II:

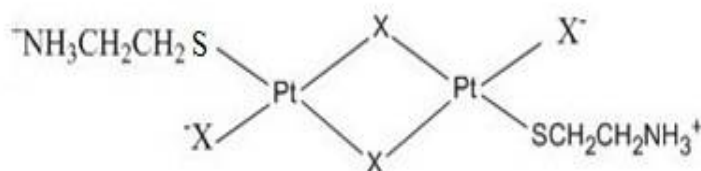


Fig 3: structure of complex II

The stretching vibrations of the Pt-S bonds in the IR spectra of complex II have a frequency of 390 cm^{-1} . The presence of one $\nu(\text{PtS})$ band is consistent with the trans structure of these complexes. The $\nu(\text{PtS})$ vibrations in the case of complex II have higher frequencies compared to $\nu(\text{PtS})$ in the spectrum of I, which is determined by the terminal rather than bridging nature of these bonds. The protonated amino group in complex II has the same frequencies as in complex I.

Thus, the study of the interaction of cystamine dihydrochloride with platinum in aqueous solutions in an acidic medium showed that in all cases the formation of complexes with the product of cystamine cleavage at the disulfide bond - (β -mercaptoethylamine (mercamine) (LH) occurs.

In acidic medium, $[\text{Pt}_2(\text{LH})_2\text{Cl}_4]$ complexes are formed with a protonated amino group and the ligand is coordinated by a platinum atom through a sulfur atom. In this case, depending on the reaction temperature, it is possible to synthesize complexes of the same composition but different structures: at 70°C , a compound with a bridging position of sulfur atoms is formed (complex I), and at lower 500°C with bridging position of chlorine atoms (complex II).

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CITATION OF THIS ARTICLE

Kh.I. Hasanov, N.M. Quliyeva, A.N. Azizova, Sh.Q. Qasimov. Synthesis and Structure of Platinum (II) Complexes with the Decomposition product of Cystamine Dihydrochloride. *Bull. Env. Pharmacol. Life Sci*, Vol 13 [1] December 2023: 316-321