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Synthesis and Platinum (II) Complexes of Different Polyazacyclophane Receptors

Begoña Verdejo[1,*], Estefanía-Delgado-Pinar[1], Javier Pitarch-Jarque[1], Lorena Magraner-Pardo[2], J. Vicente de Julián-Ortiz[2], Enrique García-España[1]

[1] Institut de Ciència Molecular, Universitat de València, Paterna, Valencia, Spain
[2] Innotecno Development SL, Parc Científic, Paterna, Valencia, Spain.
* Author to whom correspondence should be addressed; E-Mail: begona.verdejo@uv.es
Tel.: +34-963544401

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Abstract:

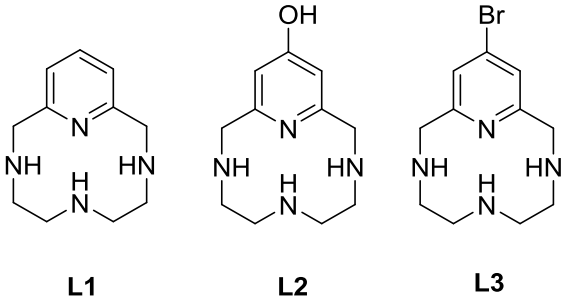
The interaction of $PtCl_4^{2-}$ with different polyazacyclophanes containing a pyridine unit as aromatic spacer has been studied by ^{1}H and ^{195}Pt NMR spectroscopy, Analysis of the recorded spectra of D_2O solutions containing L and $PtCl_4^{2-}$ in a 1:1 molar ratio at acidic pH shows the evolution with time of the ^{1}H and ^{195}Pt signals. Different crystal structures have been solved by X-ray diffraction analysis. At acidic pHs, the metal ion is coordinated by the central amino group of the macrocyclic cavity and three chloride or bromide atoms, in a square planar geometry. Formation of $[Pt(H_2\mathbf{L1})Br_3]Br$ (**1**) and $[Pt(H_2\mathbf{L2})Br_3]Br$ (**2**) reveals the rapid substitution of chloride ligands in $PtCl_4^{2-}$ by bromide ligands. However, as reveals the crystal structure obtained for $[Pt^{IV}\mathbf{L3}Br_2](PtBr_4)(H_2O)$ (**4**), at slightly higher pH values, the metal ion is coordinated through all nitrogen atoms of the macrocyclic cavity and an oxidation to Pt(IV) occurs.

Keywords: platinum complexes, polyazacyclophanes, coordination chemistry

1. Introduction

During the last years, research on coordination chemistry of platinum has aroused great interest due to their potential biological applications in drug design. [1-7]

Here, we communicate some initial results on coordination chemistry of Pt(II) with different azapyridinacyclophanes (see Chart 1), These triaza macrocycles, have been shown to display interesting properties in their coordination to metal ions.[8, 9]



L1 **L2** **L3**

Chart 1

2. Results and Discussion

Crystals suitable for x-ray diffraction were obtained from K_2PtCl_4 and L·3HBr in I:1 molar ratio. In accordance with a behaviour previously reported by García-España *et al.*,[10] the crystal structures obtained for [Pt(H_2**L1**)Br_3]Br (**1**) [Pt(H_2**L2**)Br_3]Br (**2**) and [Pt^{IV}**L3**Br_2]($PtBr_4$)(H_2O) (**4**) reveal the rapid substitution of chloride ligands in $PtCl_4^{2-}$ by bromide ligands.

For [Pt(H_2**L1**)Br_3]Br (**1**), each unit includes one [Pt(H_2**L1**)Br_3]$^+$ cation and a bromide counterion. Due to the presence of two protonated amino groups (N2 and N4), the metal ion cannot be accommodated in the macrocyclic cavity. Thus, Pt(II) presents the characteristic square planar geometry, coordinated by three bromide lignds and the central amino group of the macrocycle. (see Figure 1). The different [Pt(H_2**L1**)Br_3]$^+$ cations are interconnected, through an intermolecular hydrogen-bond array in which the bromide counterion links through hydrogen bonding the protonated amino groups of two contiguous units (Br4-H···N4=2.280Å and Br4-H···N2=2.238Å). At the same time, another hydrogen bond can be observed between the protonated amino group N2 and one of the bromide ligands coordinated to the metal ion (Br2-H···N2=2.737Å). It is noteworthy that [Pt(H_2**L2**)Br_3]Br (**2**) and [Pt(H_2**L1**)Cl_3]Cl (**3**) present an analogous structure to the described for [Pt(H_2**L1**)Br_3]Br (**1**).

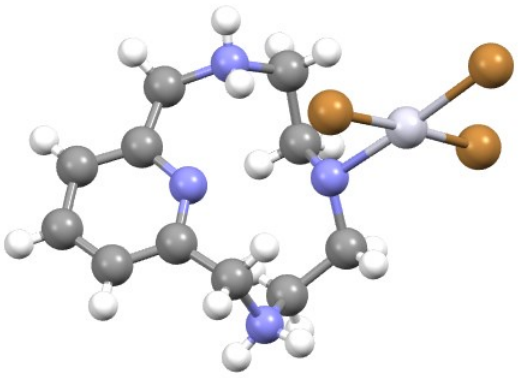


Figure 1. X-Ray crystal structure of the cation [Pt(H_2L1)Br_3]$^+$

However, as reveals the crystal structure obtained for [Pt^{IV}**L3**Br_2]($PtBr_4$)(H_2O) (**4**), at slightly higher pH values, the metal ion is coordinated through all nitrogen atoms of the macrocyclic cavity and two bromide ligands complete the octahedral geometry, indicating that an oxidation to Pt(IV) occurs. As can be seen in Table 1, the Pt-N bond distances in the [Pt^{IV}**L3**Br_2]$^{2+}$ cation are shorter than the obtained for the bromide ligands. Furthermore, the [Pt^{IV}**L3**Br_2]$^{2+}$ cations are interconnected through intermolecular hydrogen-bonds with the $[PtBr_4]^{2-}$ anions. This counterion links through hydrogen bonding one of the benzylic amino groups of a unit (Br6-H···N2=2.323Å) with the same amino group of the following unit creating chains that are isolated and do not show any kind of interconnection

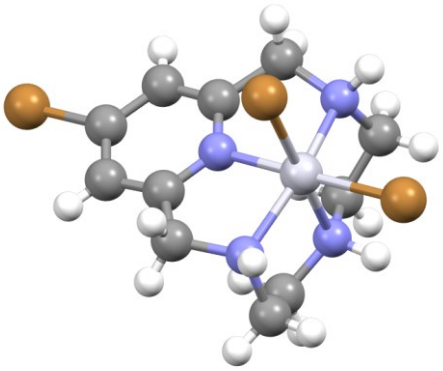


Figure 2. X-Ray crystal structure of the cation [Pt^{IV}**L3**Br_2]$^{2+}$

Figure 3 shows the evolution with time of ^{1}H and ^{195}Pt NMR spectra of D_2O solutions containing K_2PtCl_4 and **L1**·3HCl in 1:1 molar ratio recorded at acidic pH. Initially, the ^{195}Pt spectrum consists of a signal at - 1660 ppm which can be attributed to $[PtCl_4]^{2-}$.[11] After 2 days, a new signal at -2030 ppm appears and can be attributed to a platinum(II) ion coordinated to three chlorides and to a nitrogen atom of the macrocycle,, in accordance with the crystal structure obtained for this receptor, [Pt(H_2**L1**)Cl_3]Cl (**3**).

These ^{195}Pt NMR spectral changes are accompanied by significative variations in the ^{1}H NMR spectra. The initial ^{1}H NMR spectrum, which corresponds to the fully protonated free receptor presents, in the aliphatic region, a singlet signal at 4.55 which can be assigned to the benzylic protons, and two triplet signals at 3.20 and 2.95 ppm assigned to the protons of the ethylenic chains. In the aromatic region, a triplet and a doblet signals appear at 8.00 ppm and 7.48 ppm respectively. As the reaction proceeds, although the symmetry is essentially preserved,

new signals with more complex spin systems appear.

Table 1. Selected distances and angles

[Pt(H$_2$**L1**)Br$_3$]Br (**1**)				[Pt^{IV}**L3**Br$_2$](PtBr$_4$)(H$_2$O) (**4**)			
Distances (Å)		**Angles(°)**		**Distances (Å)**		**Angles(°)**	
Pt1-N1	2.077(5)	Br1-Pt1-Br2	92.22 (2)	Pt1-N1	1.974(5)	N1-Pt1-N2	82.21 (2)
Pt1-Br1	2.374 (3)	Br2-Pt1-Br3	91.30(2)	Pt1-N3	2.055(5)	N2-Pt1-N3	84.35 (2)
Pt1-Br2	2.406(5)	Br1-Pt1-N3	85.40(3)	Pt1-N2	2.080(3)	Br2-Pt1-Br3	91.64(2)
Pt1-Br3	2.410(6)	Br3-Pt1-N3	91.08(2)	Pt1-Br2	2.446(5)	Br2-Pt1-N2	85.57(3)
				Pt1-Br3	2.414(6)	Br2-Pt1-N1	87.86(2)
						Br3-Pt1-N2	97.83(2)
						Br3-Pt1-N3	88.76(2)

3. Materials and Methods

The synthesis of **L1-L3** has been carried out by slightly modifications on the general procedures described in literature.[8,9,12] All reagents and chemicals were obtained from commercial sources and used as received. Solvents used for the chemical synthesis were of analytical grade and used without further purification.

Synthesis of [Pt(H$_2$L1)Br$_3$]Br (1). To an aqueous solution (5 mL) of **L1**·3HBr, K$_2$[PtCl$_4$)] in water (5 mL) in a 1.1 molar ratio was added dropwise with stirring. After the mixture was stirred for 2 h at room temperature, it was filtered. Orange crystals suitable for X-Ray analysis were obtained by slow evaporation of the solvent.

Synthesis of [Pt(H$_2$L2)Br$_3$]Br (2). To an aqueous solution (5 mL) of **L2**·3HBr, K$_2$[PtCl$_4$)] in water (5 mL) in a 1.1 molar ratio was added dropwise with stirring. After the mixture was stirred for 2 h at room temperature, it was filtered. Orange crystals suitable for X-Ray analysis were obtained by slow evaporation of the solvent.

Synthesis of [Pt(H$_2$L1)Cl$_3$]Cl (3). To an aqueous solution (5 mL) of **L1**·3HCl, K$_2$[PtCl$_4$)] in water (5 mL) in a 1.1 molar ratio was added dropwise with stirring. After the mixture was stirred for 2 h at room temperature, it was filtered. Yellow crystals suitable for X-Ray analysis were obtained by slow evaporation of the solvent.

Synthesis of [Pt^{IV}L3Br$_2$](PtBr$_4$)(H$_2$O) (4). To an aqueous solution (5 mL) of **L3**·3HBr, K$_2$[PtCl$_4$)] in water (5 mL) in a 1.1 molar ratio was added dropwise with stirring.. After the mixture was stirred for 2 h at room temperature, it was filtered. Orange crystals suitable for X-Ray analysis were obtained by slow evaporation of the solvent.

NMR Measurements. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance AC-300 spectrometer operating at 299.95 MHz for ^{1}H. The chemical shifts are given in parts per million referenced to the solvent signal. Adjustments to the desired pH were made using drops of DCl or NaOD solutions. The pD was calculated from the measured pH values using the correlation, pH = pD − 0.4.[13]

Crystallographic analysis Analysis of single crystals was carried out with an Enraf-Nonius KAPPA CCD single-crystal diffractometer (λ =0.71073 Å). The structures were solved with using the program SHELXS-86.[14] Structure refinement was performed by means of the

program SHELXL-97.[15] Molecular plots were produced with either the program MERCURY[16] or ORTEP.[17] Crystal data, data collection parameters, and results of analysis are listed in Table 2.

Table 2. Crystal data for **1**, **2**, **3** and **4**.

Compound	**1**	**2**	**3**	**4**
Formula	$C_{11}H_{20}Br_4N_4Pt$	$C_{11}H_{20}Br_4N_4OPt$	$C_{11}H_{20}Cl_4N_4Pt$	$C_{11}H_{21}Br_7N_4O_2Pt_2$
M.W.	723.04	739.04	545.2	1190.87
T (K)	293(2)	293(2)	293(2)	293(2)
Crystal system	monoclinic	monoclinic	monoclinic	orthorhombic
Space group	$P2_1/c$	$P2_1/c$	$P2_1/c$	Pnma
a (Å)	8.0766(3)	8.1303(4)	7.8747(2)	25.8639(8)
b (Å)	19.7244(8)	20.1032(8)	19.5912(4)	11.3142(2)
c (Å)	11.4678(7)	11.0855(4)	11.3248(3)	7.5064(2)
α (°)	90	90	90	90
β (°)	106.707(5)	105.033(4)	105.741(3)	90
γ (°)	90	90	90	90
Volume ($Å^3$)	1749.77(15)	1749.86(13)	1681.61(8)	2196.59(11)
Z	4	4	4	4
ρ (g/cm^3)	2.745	2.805	2.153	3.601
λ (Å)	0.71073	0.71073	0.71073	0.71073
F(000)	1328	1360	1040	2128
μ(mm^{-1})	17.149	17.156	8.975	25.473
2Θ range	6.694 to 49.998	6.584 to 53.996	6.798 to 49.986	6.514 to 49.986
Ref. collect.	6380	7827	6380	10431
Indep. ref.	3050	3814	2955	2030
R(int)	0.0903	0.0353	0.0336	0.0365
Data/restr/param	3050/67/181	3814/37/192	2955/0/181	2030/2/136
R1 (I>4σ)	0.0984	0.0662	0.02279	0.0451
wR ^{2}	0.3075	0.1949	0.0521	0.1136
GOOF (F^2)	1.045	1.059	1.035	1.038

4. Conclusions

Interaction of $K_2[PtCl_4]$ with different pyridine azacyclophanes in aqueous solution leads to a fast replacement of the chloride ligands in $[PtCl_4]^{2-}$. by bromide ligands. The X-ray analysis of the compound shows that interaction of $[PtCl_4]^{2-}$ with L.3HBr in 1:1 molar ratio gives rise to two different complexes as function of the pH, which differ in the location of platinum in the macrocycle. At acidic pH, Pt(ll) binds to the central nitrogen of the macrocycle, while at slightly higher pH values, as the benzylic nitrogens deprotonate, the metal ion can be coordinated by all the nitrogen atoms of the macrocyclic cavity and an oxidation to Pt(IV) occurs.

We are currently trying to characterize better these complexes in solution, analyzing the effect of pH changes, as well as trying to obtain information on interaction with nucleobases and oligonucleotides.

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Conflicts of Interest

The authors declare no conflict of interest

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