

Platinum (IV) complexes Reduction: a electronic and thermodynamical study

Bruna Lemes Silva^{1*}, Juliana Fedoce Lopes²

^{1,2LaQC} UNIFEI, Itajubá, Minas Gerais, Brasil

*e-mail: brunalemessilva@gmail.com

However, Cisplatin¹ *cis*-[Pt(NH₃)Cl₂], a well known anticancer drug has limitations such as: low water solubility, side effects and resistance. Therefore, the development of a new generation of similar drugs is has been pursued². An approach to try overcome the cisplatin disadvantages is use Pt(IV), as pro-drugs. These are more stable to be administered orally, diminishing side effects can also modulate their pharmacological properties⁴. Several platinum (IV) compound with bioactive axial ligands were studied, like: Iproplatin, Ormaplatin and Satraplatin. Many studies indicate that to be active, the Pt(IV) compound is reduced given the square-planar Pt(II) complexes by axial ligand leaving^{5,4}. Experimental studies indicate, however, that there is formation of products formed by loss of equatorial ligands^{6,7}. In this work, the reduction mechanism was studied by electronic and thermodynamic analyses for Iproplatin. The LUMO of these complexes are directly connected to the reduction. Our results shows that

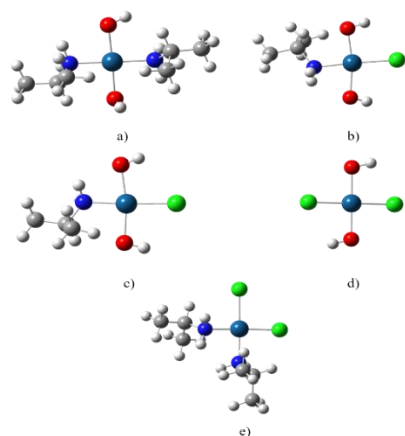


Figure 1. Iproplatin Reduction
Pt(II) Products

LUMO has dx^2-y^2 symmetry, which could happens specially for OH⁻ be a good electron donor. Calculations were done using the Gaussian 09 software in gas phase and solvent effect, using MP2, the basis function 6-31G (d,p) for light atoms and LanL2dz for platinum. Considering the LUMO symmetry, the equatorial ligands (products A, B, C and D) were removed and, assuming that it would follow the classical mechanism the product E, was also studied. Figure 1 shows all these possible products. Observing Table 1, the Gibbs free energy of the products in gas phase indicate a spontaneous and exothermic mechanism. In aqueous phase, the enthalpic contribution due to increased interaction with the solvent and all mechanisms present as spontaneous. The product E (by loss of OH⁻ axial ligands) is favored in both phases. * The calculations for the product A with the *cis*-geometry is being performed.

**Table 1: Reduction reaction
Gibbs free energy in kcal.mol⁻¹**

	Gas phase	Solvent (water)
	ΔG	ΔG
A*	-42,73	-193,80
B	-54,79	-187,08
C	-47,87	-180,91
D	27,83	-167,24
E	-55,73	-311,22

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