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Synthesis and DNA binding tests of a fluorescent pyrene bearing a Pt(II) pyridineimino complex

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Despite the long time gone respect to the discovery of cis-platinum anticancer activity, still a huge amount of research is devoted to the design of new Pt(II) complexes with enhanced biological activity [1-3].

The here presented work concerns the synthesis of a fluorescent pyridinimino platinum(II) complex (Figure 1), where the presence of a cis-platinum moiety linked to an extended aromatic residue could provide interesting properties as for binding to biosubstrates. In fact, covalent Pt(II) binding can occur, which would be strengthened by the anchoring offered by possible intercalation in nucleic acids of the pyrene fragment. Antiproliferative properties have been described for some pyridinimino [4] and pyridinamino [5] platinum(II) complexes. Moreover, similar bifunctional systems have already been tested with interesting performances [7,8].

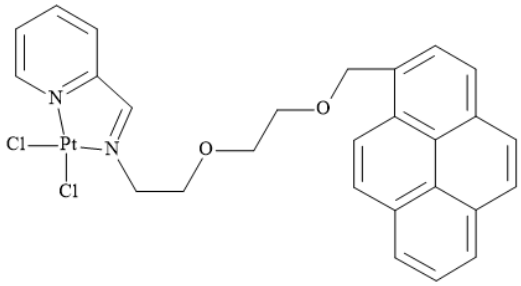

Figure 1. The metal complex synthesized and analysed in this study: [dichloro{N-[7'-(pyren-2"-yl)-3',6'-dioxahept-1-yl]-pyridyl-2-methanimine)platinum(II)]

The chelating iminopyridine ligand was prepared by a condensation reaction between pyridine-2-carboxyaldehyde and the suitably O-alkylated aminoalcohol. The platinum complex was then synthesized starting from *cis*-[$PtCl_2(DMSO)_2$], and purified by crystallization. The pure complex (elemental analysis) was spectroscopically (IR, ^{1}H-, ^{13}C and ^{195}Pt NMR) characterized. It is well soluble in DMSO and in DMSO/H_2O mixtures, where its stability was checked by ^{1}H- and ^{195}Pt NMR. The absorbance and fluorescence optical features of the dye were also checked.

Afterwards, the target Pt(II) complex was let interact with natural double stranded DNA to check its reactivity towards this biosubstrate. Spectrophotometric and spectrofluorometric titrations show that the binding does indeed occur. As for absorbance data, hypochromic and bathochromic effects suggest intercalative binding. However, the absence of a defined isosbestic point indicates

multiple equilibria. Interestingly and in agreement with this observation, the light emission behavior of the dye/DNA system is complex. Opposite fluorescence change trends are observed at different temperatures, likely related to a different contribution of DNA-templated dye aggregation. Under the (until now) explored conditions, the binding is so strong to turn to be quantitative. Further experiments are ongoing to better enlighten the binding mechanism.

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