Chemical reactivity, photochemistry and DNA interaction of a ruthenium nitrosyl complex with cyclam appended with anthracenyl fluorophore

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Nitrosyl ruthenium complexes with tetraazamacrocyclic ligands, such as cyclam (1,4,8,11-tetraazacyclotetradecane) and related species, have demonstrated potential for controlled nitric oxide (NO) release.[1,2] The chemical versatility of cyclam allows its functionalization by appending selected groups to N or C atoms of the macrocycle and provides an interesting strategy to tailor the properties of complexes as well as their potential interactions in biological milieu.

The *trans*-[Ru(NO)(H_2O)(cyclam-ant)](ClO_4)$_3$ complex (**I**) (ant=anthracenylmethyl, Figure 1), which was previously synthesized and characterized, has now its chemical reactivity, photochemistry and interaction with DNA investigated in this work.

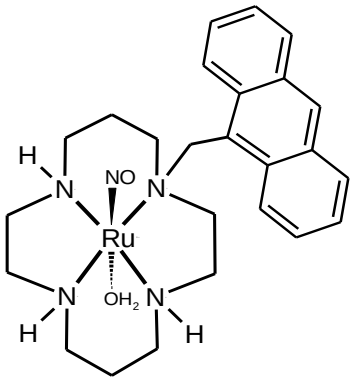

Figure 1: Structural representation of complex **I**.

Electrochemical studies (DPV, pH 1, μ = 0.1 mol L^{-1}) showed two cathodic peaks at negative potentials centered at the $\{RuNO\}^6$ moiety, E_{cp1} = -0.4 V (*vs* Ag/AgCl), $\{RuNO\}^{7/8}$, E_{cp2} = -0.1 V (*vs* Ag/AgCl), $\{RuNO\}^{6/7}$ along with one at +1.1 V, which is assigned to a reduction process centered at anthracenyl group. Under irradiation with light (two LED sources, λ_{irr} = 365 nm, 73 Wm^{-2}) of an aqueous solution of **I** (25 μmol L^{-1}, pH 7.4), it was observed a systematic decrease in the absorption of the quartet characteristic of anthracenyl group in the region 360-400 nm of the electronic spectra. This feature suggests its photobleaching. The presence of known NO scavengers, such as oxymyoglobin, did not indicate NO release. On the other hand, chemical reduction of **I** in aqueous solution (pH 1) with Eu(II) promotes NO release with the production of the corresponding *trans*-bis aqua complex, as inferred by DPV and FTIR. Reduction of **I** with Eu(II) is accompanied by a six fold increase in metal complex fluorescence emission (λ_{ex} = 370 nm, λ_{em} = 395 nm, slit 5) thus NO release can be monitored by this technique in real time. Interaction of **I** with DNA (fish sperm) was studied by absorption titration in solution (Tris-buffer pH 7.4). Hypochromism of 54% (at 378 nm), a bathochromic shift ($\Delta\lambda_{max}$= 6 nm), and two isosbestic points (at 310 and 422 nm) were observed. These results are consistent with interaction by intercalation of anthracenyl group with DNA, with an estimated binding constant of $1.89x10^3$ M^{-1}. This interaction mode is consistent with hyperchromism and hypsochromic shift observed during the titration with NaCl of a solution of **I** saturated with DNA. Together, since **I** interacts with DNA and releases NO upon reduction, it could be used to delivery nitric oxide specifically to mitochondria and/or nucleus.

References

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