UFR CHIMIE & BIOLOGIE Université Grenoble Alpes

Master in Chemistry

Sujet de stage de Master 2

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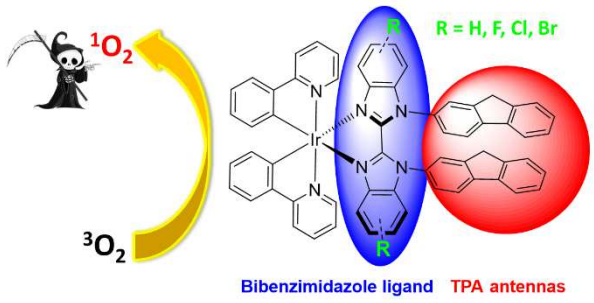
Parcours de Master 2 (*Rayer la/les mention(s) inutile(s)*) :
Chemistry for Life Sciences (CLS)
~~Polymers for Advanced Technologies (PTA)~~
Organic Synthesis (SOIPA)

Titre du sujet : *Iridium(III) complexes for imaging and photodynamic therapy against cancer*

Objectifs visés du stage : Synthesis and study of a family of iridium(III) complexes as therapeutic and contrast agent.

Intérêts pédagogiques et compétences visées : The multidisciplinary subject require a motivated candidate who will have the opportunity to discover different fields of chemistry, from organic synthesis and metal complexes to physical-chemistry characterization such as emission spectroscopy.

Résumé : Photodynamic therapy (PDT) uses photosensitizers (PS) which become cytotoxic upon light-irradiation. Transition-metal complexes, in particular Ir(III) based ones, are promising PS due to their long excited-state lifetimes, and high photo-stability.[1] However, these PSs usually absorb light in the UV/Vis region, whereas the optimal tissue transparency is in the NIR. Two-photon absorption (TPA) can overcome this issue, with simultaneous absorption of two low-energy NIR-photons leading to the same excited state as one higher-energy photon absorption. We envisage to synthesize a series of iridium(III) complexes for PDT, bearing two TPA antennas grafted on original dibenzimidazole ancillary ligand. A number of approved drugs have on their skeleton halogen atom(s).[2,3] The presence of these elements has a dramatic impact on the drug activity through two major effects, being lipophilicity enhancement which will facilitate the membrane penetration, and through the generation of non-specific hydrophobic interaction in proteins.[3] Thus, we will incorporate these elements on the ancillary ligand framework. The complexes will be characterized by NMR, mass, UV-visible, luminescence (steady state and time resolved spectroscopies) and the Φ_Δ will be measured in our facilities. We will also pay attention to the solubility of the complexes in aqueous media for the PDT application. TPA measurement will be carried out by our collaborators at ENS Lyon who have a dedicated set-up for TPA cross section characterization. The complex(es) displaying the best "figure of merit" (σ_{TPA} x Φ_Δ, where σ_{TPA} is the effective TPA cross section at a given wavelength)[4] will be submitted to in vitro PDT studies.



Approches & matériels utilisés : Usual organic synthesis techniques (inert atmosphere, Schlenk techniques), structural characterization by single crystal X-ray diffraction, characterization in solution (NMR, mass spectrometry) and emission spectroscopy.

Domaines de compétences souhaitées du candidat : The candidate should have a strong background in organic synthesis and the associated characterization techniques (NMR, Mass spectrometry…). In addition, she/he will have an interest physical-chemistry such as luminescence spectroscopy.

Dates du stage : January -June 2024 (the date can be changed without exceeding a 6 months period)

Références:

[1] L. K. McKenzie, H. E. Bryant, J. A. Weinstein, *Coord. Chem. Rev.* **2019**, *379*, 2–29.
[2] S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320–330.
[3] Z. Xu, Z. Yang, Y. Liu, Y. Lu, K. Chen, W. Zhu, *J. Chem. Inf. Model.* **2014**, *54*, 69–78.
[4] L. Beverina, M. Crippa, M. Landenna, R. Ruffo, P. Salice, F. Silvestri, S. Versari, A. Villa, L. Ciaffoni, E. Collini, et al., *J. Am. Chem. Soc.* **2008**, *130*, 1894–1902.