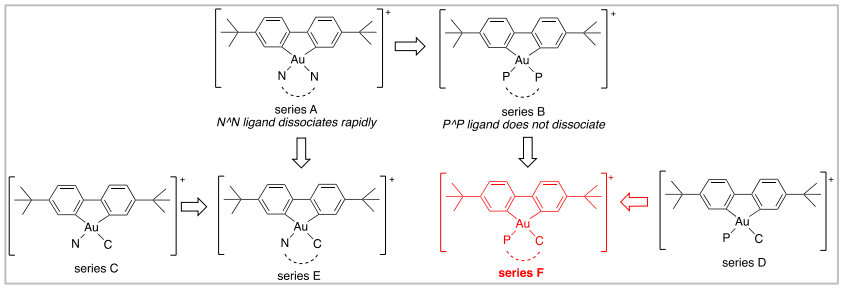
18-month post-doctoral position available in the Chembio team of the Institut Parisien de Chimie Moléculaire (IPCM) at Sorbonne Université, Paris, France

Project title: Synthesis of a novel series of organogold(III) complexes with anticancer properties; reactivity and structure-activity relationship studies

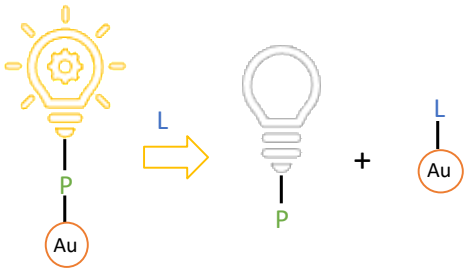
Context: Many molecular gold(III) compounds display anticancer activity on cell cultures and some of them are even active in vivo. But, in contrast to the isoelectronic and isostructural platinum(II) compounds such as cisplatin and oxaliplatin, these complexes do not appreciably target DNA but rather act via different modes of action that are still not fully uncovered.

Project: We recently introduced several series of cationic biphenyl gold(III) complexes comprising a variety of P, N or C mono- or bidentate ligands (series A-E) that show remarkable stability under reducing conditions, conversely to other gold(III) complexes that

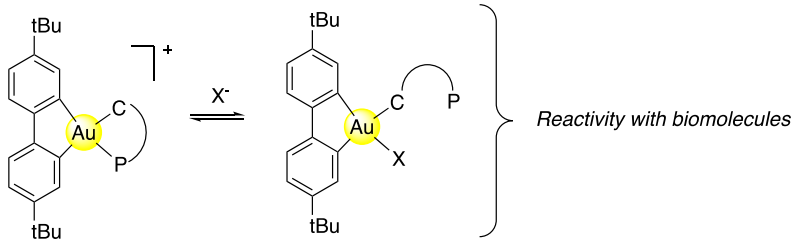


are readily reduced in the presence of glutathione. All these complexes display antiproliferative activity on lung as well as on triple negative breast cancer cells with IC_{50} in the nanomolar to the low micromolar range. Synchrotron radiation X-ray fluorescence (SR-XRF) microscopy of cells exposed to a complex from series B showed preferential accumulation of gold in the mitochondria whereas X-ray absorption spectroscopy (XAS) demonstrated that the compound remained unchanged after 4 h incubation. This indicated that the biological activity is linked to the complex structure. In contrast, compounds of series C preferentially accumulate in the mitochondria or the lysosomes according to the ability of the phosphine ligand to dissociate and liberate a vacant coordination site. XAS analysis of cells treated by the same complexes clearly evidenced a change of the coordination sphere with probable coordination of a sulfur ligand instead of the phosphine. In this case, the biological activity is (partially) linked to the complex reactivity.

In the frame of the Goldspec project that aims at elucidating biotransformations occurring to complexes in cellular context, the first task will be devoted to the synthesis of a fluorescent on/off probe to monitor the dissociation of the phosphine ligand in cells using fluorescence microscopy or flow cytometry. To achieve this goal, a luminophore-containing phosphine and the corresponding complex (series D) will be synthesized. The phosphine is expected to be poorly fluorescent owing to quenching via PET while the corresponding complex is expected to be highly fluorescent.



The second task will involve the synthesis of phosphine-containing bidentate ligands and the biphenyl gold(III) complexes (series F). The ligand is expected to be hemilabile with a propensity of the phosphine part to dissociate depending on the substituents on the phosphorus and the length of the alkyl bridge. This flexible hemilability should in turn induce a modulation of the cytotoxicity according to the ratio between the close and open forms, enabling to establish a relationship between structure and activity.



Profile: Applicants should hold a PhD in chemistry and less than 2-year postdoctoral experience. They should demonstrate strong expertise in organic / organometallic chemistry. Interest in biology will be an asset. Salary 3000 € / month excluding taxes. Candidates should send a detailed (2-page) CV, a letter of motivation and two letters of recommendation by email to benoit.bertrand@sorbonne-universite.fr. Deadline for applications 15 June, 2024; interviews between 16 June and 30 June; Provisional contract start 1 September 2024.