Research Project no. MSMC21 (Area: Molecular Systems and Materials Chemistry)

Minimum duration of the research internship: 5-6 months (MSc thesis)

New Water Soluble Staining Agents for Bioimaging

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Since the first report in 1913 of N,N'-dimethyl PDI, several PDIs have found their way into industrial-scale production, especially in fiber applications and in high-grade industrial paints. Recently, the excellent optical properties of PDI's, such as near-unity fluorescence quantum yield, excitation in the visible region, strong and reversible electron-accepting character, high photochemical stability and high electron mobility, lead to a burst in the development of high performance optical molecular probes based on the PDI core for Near-InfraRed (NIR) imaging techniques. Despite the fact that NIR organic probes usually suffer from poor hydrophilicity and low quantum yields, recent progress in strategies and synthetic methods for the development of water soluble PDI have been made. For example, the applicability of water soluble PDI derivatives for selective in vivo staining of mitochondria have been already showed.

In our group, we have developed several visible and NIR PDIs with different imide and bay substituents. [*RSC Advances*, **2013**, *3*, 9171-9174; *Dyes and Pigments*, **2014**, *110*, 227-234; *J. Am. Chem. Soc.*, **2015**, *137*, 7104-7110; *ACS Appl. Mater. Inter.*, **2015**, *7*, 27720-27729] The synthesis of PDIs derivatives, starting from the commercially available perylene-3,4,9,10-tetracarboxylic acid dianhydride, allows the introduction of substituents in the imide group (affecting the aggregation, solubility or immobilization) or in the bay region (substituents affect electronic and optical properties) (Figure 1).

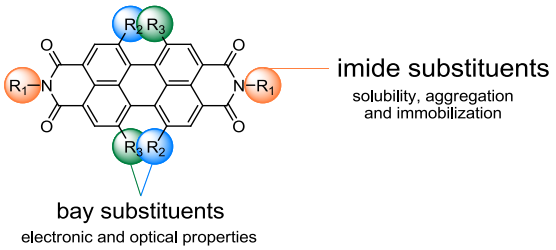

Figure 1. General structure of PDIs and influence of the different substituents position.

The GOAL of this work is the development of novel water soluble fluorescent molecular probes for advanced imaging applications. In particular, the synthesis of new perylenediimides (generically called PDI's), its photophysical characterization and cellular uptake.

Our STRATEGY is to prepare new water soluble PDIs while tunning the photophysical properties through nucleophilic displacement of the initial halogenated precursors with N- or O-nucleophiles, or by palladium coupling for the formation of C-C bonds. Substituents that can tackle water solubility as well as cell permeability of the compounds will be incorporated in the imide region.

The NOVELTY of this proposal is the preparation PDIs with near-infrared absorption and emission alongside good water solubility. Incorporation of biocompatible substituents will be made in order to optimize the fluorescent properties and enhance the cellular uptake while maintaining a reduced cytotoxicity, envisaging the selective staining of cell organelles.

The student (with appropriate knowledge of organic synthesis) will be enrolled in a dynamic and challenging research environment, and will have the opportunity to contact with several spectroscopic and microscopic characterization techniques.