Aryl-BIAN Copper Complexes as Highly Efficient Catalysts

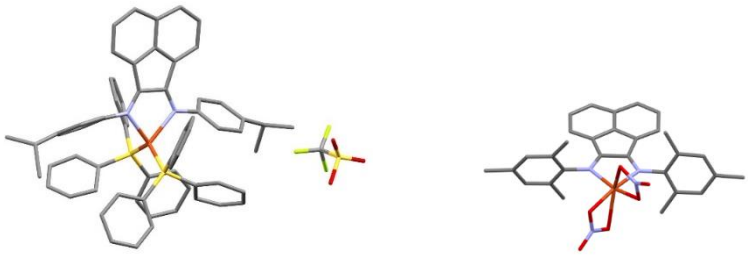
Clara S. B. Gomes,* Maria S. Viana, Beatriz P. Machado and Vitor Rosa

LAQV-REQUIMTE, Departamento de Química, Faculdade de Ciências e Tecnologia, Universidade NOVA de Lisboa, Caparica Portugal

* e-mail: clara.gomes@fct.unl.pt

Copper complexes are important synthons that find applications in different fields, ranging from drugs to photochemistry, homogenous and heterogeneous catalysis. One of such homogeneous catalytic processes is the CuAAC – copper catalyzed azide-alkyne cycloaddition. This is the well-known "click chemistry" approach that selectively gives rise to 1,4-disubstituted-1,2,3-triazoles, firstly reported by Sharpless in 2001 [1]. Since then, several Cu-based catalysts were developed, and part of its mechanistic details disclosed [2]. Nevertheless, there are still drawbacks to overcome, such as the need to use halides or additives, high catalyst loadings or temperature. Moreover, in the last two decades, several synthetic methodologies have been developed towards more sustainable and economical processes. One of these is mechanochemistry, which has the advantages of being an effective and cheap technique, for the synthesis of both organic and inorganic/coordination compounds [3] and for various other applications in Chemistry.

Herein, some of our recent developments on solution-based and mechanochemical synthesis and structural characterization of copper (I) and copper (II) complexes containing steric- and electronically versatile bis-aryl-diiminoacenaphthene (BIAN) ligands will be presented (Figure 1). Catalytic studies for the CuAAC reaction including comparative studies to determine the influence of the counterion or the polarity of solvents on their activity, were performed.



(a) (b)

Figure 1. Examples of derivatives synthesized in this work: (a) [Cu(*p*-iPrBIAN)$(PPh_3)_2$]OTf and (b) [Cu(Mes-BIAN)$(NO_3)_2$].

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Peptide-ionic liquid conjugates towards the treatment of skin infections

A. Gomes,[a] L. J. Bessa,[a,b] I. Fernandes,[a] L. Aguiar,[a,c] R. Ferraz,[a,d] C. Monteiro,[e,f] M. C. L. Martins,[e,f,g] N. Mateus,[a] P. Gameiro,[a] C. Teixeira,[a] P. Gomes[a]

[a]LAQV-REQUIMTE, Departamento de Química e Bioquímica, Faculdade de Ciências, Universidade do Porto, Portugal

[b] *current affiliation*: CIIEM, Egas Moniz - Cooperativa de Ensino Superior, Almada, Portugal

[c] *current affiliation*: Gyros Protein Technologies, Tucson, AZ 85714, United States of America

[d]CQBM, Escola Superior de Saúde, Politécnico do Porto, Portugal

[e]i3S - Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Portugal

[f]INEB - Instituto de Engenharia Biomédica, Porto, Portugal

[g]ICBAS - Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, Portugal

The treatment of complicated skin infections, like diabetic foot ulcers and other chronic wounds, are often associated with persistent polymicrobial biofilms that delay and difficult the healing process.[1] The most severe cases culminate in inpatient hospital admission, where infections can be exacerbated by hospital-acquired pathogens, in particular, if caused by the so-called ESKAPE pathogens, for which few efficient antibiotics are available.[2] The current biomedical approaches to chronic wounds aim at providing both protection against multidrug-resistant (MDR) bacteria and a matrix scaffold, often collagen-based, to boost the reestablishment of healthy skin.[3] Therefore, new options and new antibiotics are urgently needed and having that in mind our strategy is to use: i) antimicrobial peptides (AMP) to prevent or treat infection in the open wound; ii) collagen-inducing peptides (CBP)[4] to induce fast healing; iii) and ionic liquids (IL)[5] with intrinsic antimicrobial activity and a chemical permeation enhancement properties for an improved skin permeation. Through different combinations of these three types of building blocks, we aim to find a new class of active pharmaceutical ingredients suitable for topical application in the treatment of complicated skin infections. All the different conjugates designed and tested *in vitro* thus far will be presented.[6-8] The most promising ones, result from conjugation of CBP with IL, delivering a new type of conjugate with potent antibacterial, antifungal, and collagen-inducing effects on human dermal fibroblasts.[9] Hence, these peptide-ionic liquid conjugates are promising leads towards the development of a topical formulation for the treatment of complicated skin infections.

References:

1. doi:10.2147/IDR.S172366; 2. doi:10.3389/fmicb.2019.00539; 3. doi:10.2147/dmso.s36024; 4.doi:10.3390/molecules22101743; 5. doi:10.3390/ijms222111991; 6. doi:https://doi.org/10.3390/ijms21176174; 7. doi:10.3389/fmicb.2019.01915; 8. doi:10.3390/pharmaceutics13111962; 9. doi:10.1128/spectrum.02291-21;

Influence of the molecular structure on the luminescence pathway

Samuel Guieu

LAQV-REQUI*M*TE and Department of Chemistry, University of Aveiro, Aveiro, Portugal.

Email: sguieu@ua.pt

Organic fluorophores are very versatile, with applications ranging from lightning devices to sensors and molecular probes for biological imaging. It is well established that their photophysical properties are strongly influenced by their structure and their environment, and it is possible to fine-tune their emission color by modifying their conjugation or substituents. But upon excitation, an organic fluorophore has various ways to return to the ground state: non-emissive relaxation through vibrations, fluorescence, phosphorescence, and it can even re-organize its structure in the excited state before the emission process. Understanding the relation between the structure of the dye and the different luminescence pathways is of fundamental importance, in order to reveal the full potential of organic dyes and develop practical applications.

Here, we will present some of our recent results, focusing on two approaches:

- Aggregation-Induced Emission Enhancement, or Restriction of Intramolecular Motions, which favor the emission pathway over the non-emissive relaxation, thus increasing the luminescence intensity, and how it can be used in molecular probes (Figure 1);
- Excited State Intramolecular Proton Transfer, and more generally proton transfer, and its influence on the emission color of organic dyes (Figure 2).

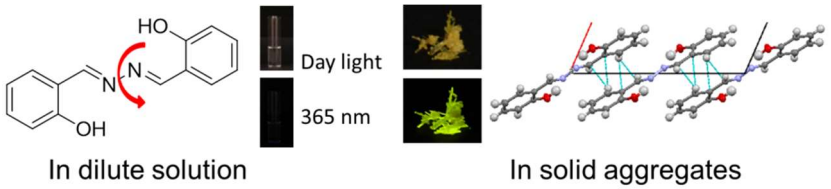

Figure 1: Example of organic dye presenting an enhanced emission in the solid state.

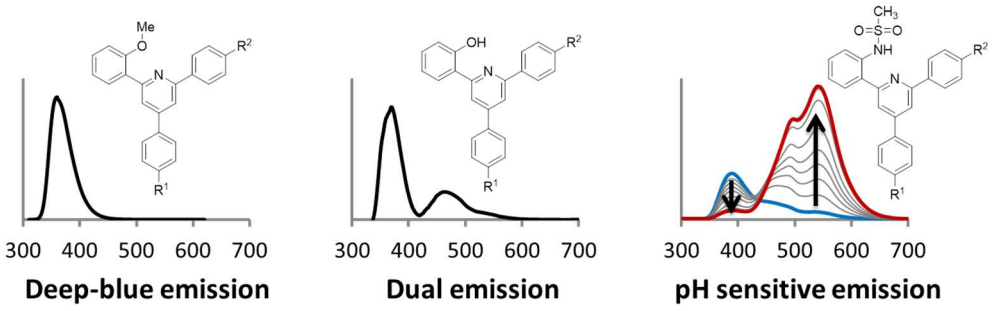

Figure 2: Representative emission spectra of different families of triarylpyridines.