

AAP China Scholarship Council – CSC 2023 PROJET DE RECHERCHE DOCTORALE (PRD)

Titre du PRD : Organic Pi-acid Molecules for the Implementation of Anion-Pi Catalysis

DIRECTION de THESE

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Ecole Doctorale de rattachement : ED406 – Chimie moléculaire de Paris Centre

Nombre de doctorants actuellement encadrés : Aucun

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CO-TUTELLE INTERNATIONALE envisage : OUI X NON

Organic π -acid Molecules for the Implementation of Anion- π Catalysis

1- Objectives and description of the project

This project is aimed at developing a new type of catalysis based on π -anion interactions, a type of supramolecular interactions recently identified. Such noncovalent interactions should allow the achievement of new catalytic transformations with the potential to solve long-standing problems in synthetic methodology. Our specific aims are:

- 1) To prepare fluorenone derivatives with strong and tuneable π -acidity.
- 2) To characterize their charge transfer complexes (CTCs) with electron-rich compounds.
- 3) To demonstrate their potential for innovative catalysis. Important reactions such as element-metal additions across electron-rich alkynes are amongst the transformations that should benefit from this new catalytic paradigm.

2- State of the art

In supramolecular chemistry, non-covalent interactions are the intermolecular relationships governing molecular assemblies. Specific, selective and reversible in nature, they can be easily tuned by external stimuli, thus allowing the engineering of dynamic processes and the adaptive response of a given system. While hydrogen bonds are well substantiated, the weaker π -interactions were harnessed only in the late 80s using cations.¹ However, π -anion interactions were overlooked and came to light not even a decade ago.²

CTC have been extensively studied in materials science owing to their inherent properties, mainly in the fields of charge transport, light emission, nonlinear optics and external stimuli responsiveness.³ Their π -acid component are UV absorbers and their color changes upon contact with either π or Lewis bases provides evidence for CTC formation.⁴ Interestingly, CTCs have also been exploited for liquid chromatography separation of electron-rich polyaromatic hydrocarbons.⁵ In addition, it is worthy to note that CTCs of electron-deficient arenes with halides or with electron-rich molecules have spectral, thermodynamic and structural properties closely related.⁶

The propensity of CTCs to absorb light has been advantageously and massively used in photocatalysis.⁷ Yet, the use of the π -acidity to stabilize anions or electron-rich species in the context of catalysis has hardly been studied.⁸ Indeed, the feasibility has only been demonstrated by the seminal reports by Matile and coworkers.⁹ However, his main interests lay in reproducing biologically relevant processes like anion transport through membranes and polyketide/terpenoid biosynthesis (i.e. malonate/enolate chemistry). Additionally, a single report on the catalysis of Diels-Alder reactions was disclosed.¹⁰ Currently, we have implemented a nitrogen activation methodology using CTC. However, the full potential of this interesting prospect has yet to be established.

¹ Dougherty *et al.* *J. Am. Chem. Soc.* **1988**, *110*, 1983; Dougherty *et al.* *Angew. Chem. Int. Ed.* **1990**, *29*, 915.

² Frontera *et al.* *Angew. Chem. Int. Ed.* **2011**, *50*, 9564; Mascal *et al.* *J. Am. Chem. Soc.* **2002**, *124*, 6274.

³ Zhang, J., Zhang *et al.* *Chem. Eur. J.* **2020**, *27*, 464; Osakada *et al.* *Chem. Eur. J.* **2014**, *20*, 4762.

⁴ Sulzberg and Cotter US patent 3637798 25 (1972).

⁵ Felix *et al.* *Chromatographia* **1992**, *34*, 177.

⁶ Kochi *et al.* *Angew. Chem. Int. Ed.* **2004**, *43*, 4650.

⁷ Melchiorre *et al.* *J. Am. Chem. Soc.* **2020**, *142*, 5461.

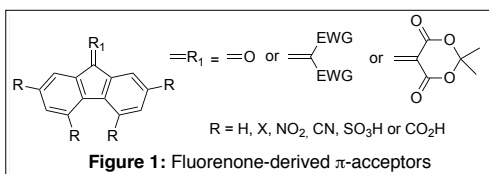
⁸ García Mancheño *et al.* *Synthesis* **2022**, *54*, 3907.

⁹ Matile *et al.* *Nat. Commun.* **2014**, *5*, 3911; Matile *et al.* *Chem. Sci.* **2015**, *6*, 6219.

¹⁰ Matile *et al.* *Angew. Chem. Int. Ed.* **2017**, *56*, 13066.

3- Specific aims

Task 1: Development of fluorenone-derived π -acceptors and CTC characterization

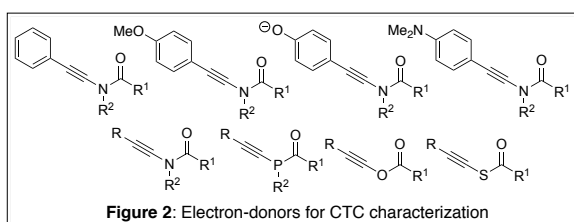


To meet success, the project requires a flexible access to an array of π -acceptors in order to fine tune the π -accepting strength and to control the inertness of the acceptor under the required catalytic reaction conditions. The fluorenone motif provides the desired

assets and several synthetic methodologies for its derivatization have been described (Figure 1).⁶ For further development, introduction of chirality can be easily achieved on these skeletons by the introduction of an amino acid via peptide coupling or imine formation.

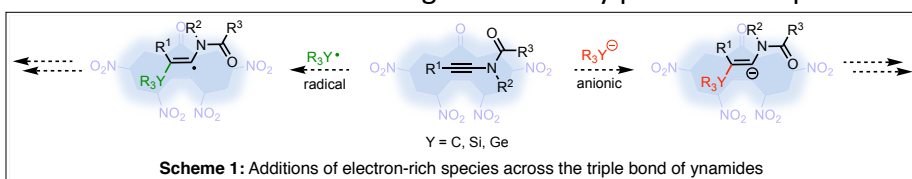
With the different π -acceptors in hand, CTC formation with several donors of increasing electron density will be assessed (Figure 2).¹¹ The enthalpies of complexation will be thus determined by spectrophotometric titrations at variable temperature and a systematic

structure-reactivity investigation will provide quantitative information on the amount of charge transferred from the electron-donor to the electron deficient species. Additionally, X-ray analysis of crystallized CTC should provide valuable information on the physical-chemical properties of these supramolecular entities.



Task 2: Innovative catalytic processes exploiting supramolecular π -anion interactions

The objective of task 2 is to substantiate the generality of anion- π catalysis, which would ensure a high impact of our work among the community. Illustratively, such activation mode should be ideally suited to trigger additions to electron-rich alkynes. For instance, the reactivity of electron rich ynamides toward mild nucleophiles will be assessed and element-metal addition reactions with organometallic reagents (either through radical or anionic processes) will be studied (Scheme 1). This is one of the recognized fields of expertise of the ROCS group.¹² Note that the more electron-rich the alkyne, the greater the charge transfer would be and thus, the greater the activation, which is counter-intuitive to usual nucleophilic additions and should lead to original reactivity patterns complementary to existing ones.



4- Student profile

We are looking for a motivated student with a

strong background in catalytic methodologies. Experience in transition metal chemistry and/or supramolecular chemistry would be advantageous but not necessary. We expect him/her to possess excellent interpersonal skills, a high level of professionalism, and to develop a high degree of intellectual independence and creative thinking during the course of the PhD.

¹¹ Drago *Physical Methods in Chemistry*, Saunders, Philadelphia, 1977; Mulliken *et al. Molecular Complexes*, Wiley, New York, **1969**; Ballester *et al. J. Am. Chem. Soc.* **2014**, *136*, 3208.

¹² A. Perez-Luna *et al. J. Am. Chem. Soc.* **2018**, *140*, 17632 ; A. Perez-Luna *et al. Org. Lett.* **2016**, *18*, 2054; Perez-Luna *et al. Angew. Chem. Int. Ed.*, **2014**, *53*, 11333.

AVIS de l'Ecole Doctorale :