



**SORBONNE
UNIVERSITÉ**

CHINA SCHOLARSHIP COUNCIL

Appel à projets

Campagne 2022

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Title of the research project :

Organic Pi-acid Molecules for the Implementation of Anion-pi Catalysis

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Research Unit

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Doctorate School

Thesis supervisor's doctorate school (candidate's futur
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PhD student currently supervised by the thesis supervisor (number, year of the first inscription) :

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(2; 2018, 2021)

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École doctorale

Joint supervisor's doctorate school :

Or, if non SU :

PhD student currently supervised by the joint supervisor (number, year of the first inscription) :

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 pericyclic reactions and metal-insertion into electron-rich haloarenes are amongst the transformations that should benefit from this new catalytic paradigm.

2- State of the art

If supramolecular chemistry is seen as collective behavior on the molecular scale, non-covalent interactions are the intermolecular relationships governing molecular assemblies. Specific, selective and reversible in nature, these interactions 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 with the π -cation electrostatic bond.¹ However, π -anion interactions were overlooked and came to light not even a decade ago.² Indeed, while the interaction of a cation with the electronic cloud on either sides of the plane of an aromatic ring is easily conceived, the interaction of an anion, electrostatic in nature, is much less intuitive. It was demonstrated that CTCs of electron-deficient arenes with halides or with electron-rich molecules had spectral, thermodynamic and structural properties closely related.³

CTC have been extensively studied in materials science owing to their inherent properties, mainly in the field of charge transport, light emission, nonlinear optics and external stimuli responsiveness.⁴ Their π -acid component are UV absorbers and their color changes upon contact with either π or Lewis bases which provides evidence for CTC formation.⁵ Interestingly, CTCs have also been exploited for liquid chromatography separation of electron-rich polyaromatic hydrocarbons. The association constant of the complex formed being correlated to the retention time, it was further possible to sort the different electron-poor arenes into three categories: weak, medium and strong π -acceptors.⁶

Their propensity to absorb light has been advantageously used to excite molecules and trigger reactivity. This photocatalytic activity has been reviewed recently.⁷ Yet, the use of the π -acidity to stabilize anions in the context of catalysis has hardly been studied. Indeed, the feasibility has only been demonstrated by the seminal reports by Matile and coworkers⁸ using π -acid molecules based on naphthalene diimide and fullerene. 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.⁹ As such, the potential of this interesting prospect has yet to be established.

3- Specific aims

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

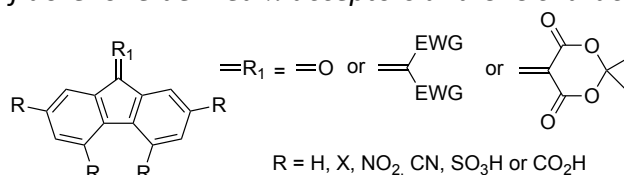


Figure 1: Fluorenone-derived π -acceptors

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).¹⁰ 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.

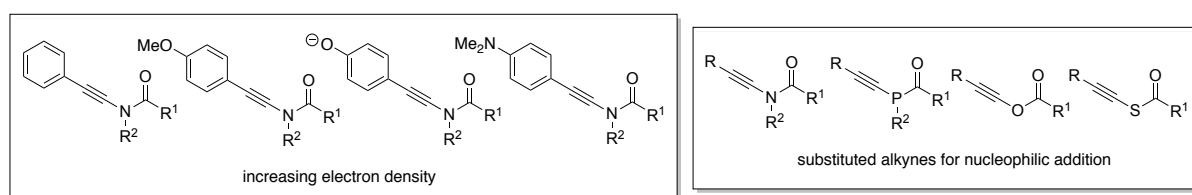


Figure 2: Electron-donors for CTC characterization

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.¹¹ 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.



Scheme 1: Additions of electron-rich species across the triple bond of ynamides

4- References

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; Mascial *et al.* *J. Am. Chem. Soc.* **2002**, *124*, 6274; 3) Kochi *et al.* *Angew. Chem. Int. Ed.* **2004**, *43*, 4650; 4) Zhang, J., Zhang *et al.* *Chem. Eur. J.* **2020**, *27*, 464; Osakada *et al.* *Chem. Eur. J.* **2014**, *20*, 4762 ; 5) Sulzberg and Cotter US patent 3637798 25 (1972); 6) Felix *et al.* *Chromatographia* **1992**, *34*, 177; 7) Melchiorre *et al.* *J. Am. Chem. Soc.* **2020**, *142*, 5461; 8) Matile *et al.* *Nat. Commun.* **2014**, *5*, 3911; Matile *et al.* *Chem. Sci.* **2015**, *6*, 6219; 9) Matile *et al.* *Angew. Chem. Int. Ed.* **2017**, *56*, 13066; 10) 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; 11) 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.

5- Scientific Know-how of each supervisor

The ROCS team at IPCM (Réactivité Organométallique et Catalyse pour la Synthèse) is well established in the development of synthetic methodology using either main group or transition metals for the development of new synthetically useful transformations leading to more sustainable synthetic methods.

Dr Myriam Roy has developed a strong expertise in the areas of π -acid molecules, CTCs and material sciences. On her arrival in 2018 to the ROCS team, she considered the implementation of this know-how in the context of chemical synthesis.

Dr Alejandro Perez Luna, head of the ROCS team has a long-standing experience of addition of main group metals onto alkynes and alkenes, including catalysis.

6- Relevant Publications of the supervisors

- *Radical Germylzincation of α -Heteroatom-Substituted Alkynes.* de la Vega-Hernández, K.; Romain, E.; Coffinet, A.; Bijouard, K.; Gontard, G.; Chemla, F.; Ferreira, F.; Jackowski, O.; Perez-Luna,* A. *J. Am. Chem. Soc.* **2018**, *140*, 17632–17642.
- *Stereodivergent Silylzincation of α -Heteroatom-Substituted Alkynes.* Fopp, C.; Romain, E.; Isaac, K.; Chemla, F.; Ferreira, F.; Jackowski, O.; Oestreich,* M.; Perez-Luna,* A. *Org. Lett.* **2016**, *18*, 2054–2057.
- *Trans-Selective Radical Silylzincation of Ynamides,* Romain, E.; Fopp, C.; Chemla, F.; Ferreira, F.; Jackowski, O.; Oestreich,* M.; Perez-Luna,* A. *Angew. Chem. Int. Ed.*, **2014**, *53*, 11333-11337.

7- 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.