

**PROGRAMME INTITUTS ET INITIATIVES**

**Appel à projet – campagne 2021**

**Proposition de projet de recherche doctoral (PRD)**

**ISim - Initiative Sces et ingénierie moléculaires**

**Intitulé du projet de recherche doctoral (PRD): Low Valent Metals : Organometallic Reactivity (LoVaMOR)**

**Directeur.rice de thèse porteur.euse du projet (titulaire d'une HDR) :**

NOM : **CHEMLA** Prénom : **Fabrice**  
Titre : Professeur des Universités ou  
e-mail : [fabrice.chemla@sorbonne-universite.fr](mailto:fabrice.chemla@sorbonne-universite.fr)  
Adresse professionnelle : IPCM - Campus Pierre et Marie Curie - T32-42 bureau 410 - case courrier  
(site, adresse, bât., bureau) 229

**Unité de Recherche :**

Intitulé : Institut Parisien de Chimie Moléculaire  
Code (ex. UMR xxxx) : UMR 8232

**École Doctorale de rattachement de l'équipe (future école doctorale du.de la doctorant.e) :** ED406-Chimie Moléculaire Paris Centre

**Doctorant.e.s actuellement encadré.e.s par la.e directeur.rice de thèse (préciser le nombre de doctorant.e.s, leur année de 1<sup>e</sup> inscription et la quotité d'encadrement) : 1, 2021, 50%**

-----  
**Co-encadrant.e :**

NOM : **HALBERT** Prénom : **Stéphanie**  
Titre : Maître de Conférences des Universités ou HDR   
e-mail : [stephanie.halbert@sorbonne-universite.fr](mailto:stephanie.halbert@sorbonne-universite.fr)

**Unité de Recherche :**

Intitulé : Laboratoire de Chimie Théorique  
Code (ex. UMR xxxx) : UMR 7616

**École Doctorale de rattachement :** ED388-ChimiePhysiqueChimieAnalytique ParisCentre  
Ou si ED non Alliance SU :

**Doctorant.e.s actuellement encadré.e.s par la.e co-directeur.rice de thèse (préciser le nombre de doctorant.e.s, leur année de 1<sup>e</sup> inscription et la quotité d'encadrement) : 1, 2017, 30%**

## Grandes lignes de la demande

*Titre du projet/ Title of the project : **Low Valent Metals : Organometallic Reactivity***

*Acronyme : **LoVaMOR***

*Porteurs de projet :*

***Fabrice CHEMLA (Professeur) : Equipe “Réactivité Organométallique et Catalyse pour la Synthèse” (IPCM – UMR 8232, Sorbonne Université)***

***Stéphanie Halbert (Maîtresse de Conférences) : Equipe “Inorganic, Organometallic and Organic Chemistry” (LCT – UMR 7616, Sorbonne Université)***

*Summary of the project*

**The proposed combined experimental and theoretical research project is focused on the examination of the reactivity of low-valent Zn(I)- and Mg(I)-based bimetallic compounds, with a particular interest in the potential for the functionalization of C–C multiple bonds and the controlled reduction of carbonyl or imine functions to access unpoled  $\alpha$ -hydroxy- or  $\alpha$ -amino anion equivalents.**

# Fabrice CHEMLA

Equipe ROCS – Tour 32-42 Bureau 412 – IPCM, CNRS UMR 8232 – Sorbonne Université – Faculté des Sciences et Ingénierie – CC 229 | 4 Place Jussieu | 75252 Paris Cedex 05 – + 33 (0)1 44 27 64 36 – fabrice.chemla@sorbonne-universite.fr

## Cursus

depuis 2002		<b>Professeur – UPMC</b> , puis <b>Sorbonne Université</b> (Institut Parisien de Chimie Moléculaire). <i>Thèmes de recherche : Chimie Organométallique des Groupes Principaux</i>
2000		<b>Habilitation à Diriger des Recherches – UPMC</b>
1994–2002		<b>Maître de Conférences – UPMC</b> (Equipe Pr. J. Normant).
1992-1994		<b>ATER – UPMC</b> (Pr. J. Normant)
1992		<b>Postdoctorat – Université de Marburg</b> (Pr. R. W. Hoffmann)
1989–1992		<b>Doctorat – Ecole Normale Supérieure</b> (Pr. M. Julia)
1989		<b>Ingénieur de l'E.S.P.C.I</b>

## Production scientifique :

**86 publications dans des revues internationales de rang A**

**9 chapitres d'ouvrage**

**48 conférences sur invitation**

## Publications représentatives :

- Radical Germylzincation of  $\alpha$ -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.
- Catalytic chemo and stereoselective semi-hydrogenation of alkynes to *E*-alkenes using the combination of Pd catalyst and ZnI<sub>2</sub>, Maazaoui, R.; Abderrahim, R.; Chemla, F.; Ferreira, F.; Perez-Luna, A.; Jackowski, O. *Org. Lett.* **2018**, *20*, 7544-7549.
- Stereodivergent silylzincation of  $\alpha$ -heterosubstituted alkynes, Fopp, C.; Romain, E.; Isaac, K.; Chemla, F.; Ferreira, F.; Jackowski, O.; Oestreich, O.; Perez-Luna, A. *Org. Lett.* **2016**, *18*, 2054-2057.
- Domino Methylenation/hydrogenation of Aldehydes by Combining Matsubara's Reagent and Wilkinson's catalyst, Maazaoui, R.; Gervais, K.; Pin Nó, M.; Abderrahim, R.; Chemla, F.; Ferreira, F.; Jackowski, O.; Perez-Luna, A. *Eur. J. Org. Chem.* **2016**, 5732-5737.
- Zinc Radical Transfer-Based Modular Approach to Enantiopure Alkylidene- $\beta$ -prolines from *N*-(*tert*-butanesulfinyl)  $\alpha$ -aminomethyl acrylates, Beniazza, R.; Romain, E.; Chemla, F.; Ferreira, F.; Jackowski, O.; Pérez-Luna, A. *Eur. J. Org. Chem.* **2015**, 7661-7665.
- Ring-Opening of *N-tert*-Butanesulfinyl Ethynylaziridines with Lithium Tris(dimethylphenylsilyl)zincate: Stereoselective Access to 4-Amino-1-Allenylsilanes, Bochatay, V. N.; Sanogo, Y.; Chemla, F.; Ferreira, F.; Jackowski, O.; Pérez-Luna, A. *Adv. Synth. Cat.* **2015**, *357*, 2809-20814.

## Domaine de Compétences :

**Chimie Organique et Organométallique, Catalyse, Synthèse de Molécules Bioactives**  
**Pilotage et Management de l'Enseignement Supérieur.**

## Responsabilités :

2004 – 2008		Responsable de la <b>Spécialité « Chimie Organique et Bioorganique »</b> du Master de Chimie
2007 – 2010		Membre élu du Bureau de la Division de Chimie Organique de la Société Chimique de France
2008 – 2016		Membre élu du <b>Conseil des Etudes et de la Vie Universitaire</b> de l'UPMC
2009 – 2012		Responsable du <b>Directoire des Formations</b> de l'UPMC
2012 – 2016		<b>Vice-Président Formation Initiale et Continue</b> de l'UPMC
2016 – 2017		<b>Vice-Président Ressources et Moyens</b> de l'UPMC
2018 – 2019		<b>Vice-Président Alliance et Partenariats Territoriaux de Sorbonne Université</b>

# Stéphanie Halbert

**Maitresse de conférences** (Associate Professor) since 2015 at Sorbonne Université (SU)

Laboratoire de Chimie Théorique (LCT) UMR CNRS 7616,

12-13, 4ème étage CC137 - 4, place Jussieu 75252 Paris.

stephanie.halbert@sorbonne-universite.fr

<https://www.lct.jussieu.fr/pagesperso/halbert/>

## Previous experiences:

- 2014-2015: **Attachée Temporaire d'Enseignement et de Recherche** (ATER), Université Pierre et Marie Curie (UPMC), LCT  
Research project: Copper-free allylic alkylation with Grignard reagents.
- 2013-2014: **Post-doctoral** research associate, UPMC, LCT.  
Research project: Mechanism and selectivity of the conjugate addition of the dialkylzinc reagents to dienones catalyzed by copper complexes (ANR grant).  
Principal investigator: Pr. H. Gérard.
- **PhD** in Chemistry (*Theoretical chemistry*), Institut Charles Gerhardt de Montpellier, Université Montpellier 2, July 4th 2013 under the supervision of Pr. O. Eisenstein and Dr. C. Raynaud.  
Title: Study of the dynamical behavior of the alkylidene Schrock catalysts grafted on the silica nanoparticle.
- **Master** in Chemistry (*Fine Chemistry, Materials and Nanosciences*), Université d'Angers, 2010.  
Internship in Laboratoire de Mécanismes Réactionnels (UMR 7651 CNRS), Ecole Polytechnique, Palaiseau, France.

Scientific production: **15** publications in international journals, **10** communications (5 conferences and 5 seminars) and **8** poster presentations.

Supervisions: 3 Licence, 4 Master, 1 PhD (30%, 2017-2020), 2 post-docs (LabEx MiChem),

## Main collective responsibilities:

- Member of **Comité de Sélections** for the recruitment of Assistant Professors (2019).
- Member of **Parcoursup** committee at Sorbonne Université (2020).
- President of French Young Chemists' section Ile-de-France (**RJ-SCF-IdF**) Network (2016-2019), member of Administration Council of SCF (since 2019), Secretary of RJ-SCF (since 2020)
- Member of organizing committee of **IUPAC 2019** (young scientists program) and **SCF'21**.

## Other activities:

- Science **outreach** (Fête de la Science SU 2016, 2017, 2018, 2019; Journeys from Alchemy to Chemistry UNESCO 2019).
- Organization of **professional integration events** (Academic careers 2017, Professional integration event for Master Students 2016).

## Selection of 5 significant publications:

1. "Catalytically active species in Copper/DiPPAM-Catalyzed 1,6-Asymmetric Conjugate Addition of Dialkylzinc to Dienones: a computational overview" S. Halbert, J. Lauberteaux, C. Blons, R. Marcia de Figueiredo, C. Crévisy, O. Baslé, J.-M. Campagne, M. Mauduit and H. Gérard, *ChemCatChem*, **2019**, *11*, 4108.
2. "Computational Study of the Cu-Free Allylic Alkylation Mechanism with Grignard Reagents: Role of the NHC Ligand" A. I. Poblador-Bahamonde and S. Halbert, *Eur. J. Org. Chem.*, **2017**, *39*, 5935-5941.
3. "Copper-Catalyzed Asymmetric Conjugate Addition of Dimethylzinc to Acyl-N-methylimidazole Michael Acceptors: Scope, Limitations and Iterative reactions" S. Drissi-Amraoui, T. E. Schmid, J. Lauberteaux, C. Crévisy, O. Baslé, R. Marcia de Figueiredo, S. Halbert, H. Gérard, M. Mauduit and J.-M. Campagne, *Adv. Synth. Catal.*, **2016**, *358*, 2519.
4. "Elucidating the Link between NMR Chemical Shifts and Electronic Structure in d0 Olefin Metathesis Catalysts" S. Halbert, C. Copéret, C. Raynaud, O. Eisenstein, *J. Am. Chem. Soc.* **2016**, *138*, 2261.
5. "Hydrofluoroarylation of Alkynes with Ni Catalysts. C-H Activation via Ligand-to-Ligand Hydrogen Transfer, an Alternative to Oxidative Addition" J. Guihaume, S. Halbert, O. Eisenstein, R. N. Perutz, *Organometallics* **2012**, *31*, 1300.

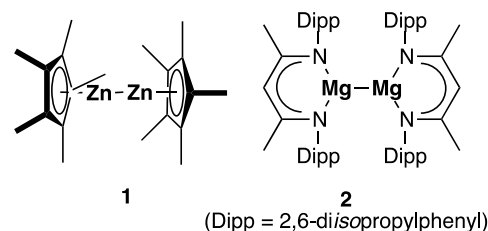
## Scientific description

### Objectives and description of the project

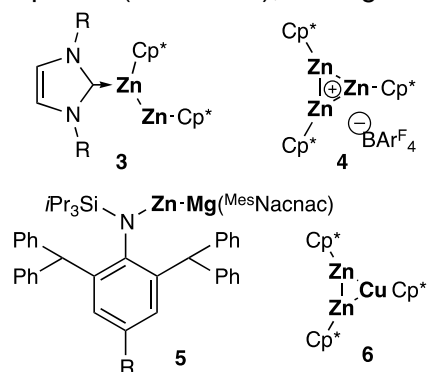
Main-group organometallic compounds having a **metal–metal bond** are well known when the metal is a group 13 element. Particularly dibora compounds, considered for a long time as structural curiosities, have found during the past decade widespread applications in organic and organometallic chemistry.<sup>[1]</sup> Analogous dialuminum reagents have also been known for a long time<sup>[2]</sup> and have raised a considerable theoretical interest,<sup>[3]</sup> but have found so far less applications in organic synthesis.<sup>[4]</sup>

On the other hand, homologous main group dimetallic compounds **having Zn–Zn or Mg–Mg bonds have been discovered more recently**. In 2004, Carmona reported<sup>[5]</sup> the first preparation and characterization of compound **1**, a molecular organometallic complex bearing a Zn(I) functionality and a Zn–Zn bond. In 2007, Jones reported the first analogue Mg(I) complex **2** (Scheme 1).<sup>[6]</sup> The bonding was described by theoretical chemistry, in particular the M–M bond length, its dissociation energy (BDE) and its electronic properties (population, orbital contributions).<sup>[7]</sup> For instance, complexes **1** and **2** exhibit a strongly covalent bonding involving the metal's orbitals (BDE ~ 60 kcal.mol<sup>-1</sup> and d(Zn–Zn) = 2.331 Å in **1**).<sup>[5,8]</sup>

These two dimetallic complexes opened a totally new and very interesting research area, devoted to the design, preparation, characterization and theoretical understanding of various molecular complexes bearing a M–M bond where M is a main group metal.<sup>[7]</sup> For example, species of the Zn family with different substitution patterns on each Zn atom have been reported (Scheme 2), among them the dizinc(I) mono-



Scheme 1 : Seminal Zn–Zn and Mg–Mg complexes

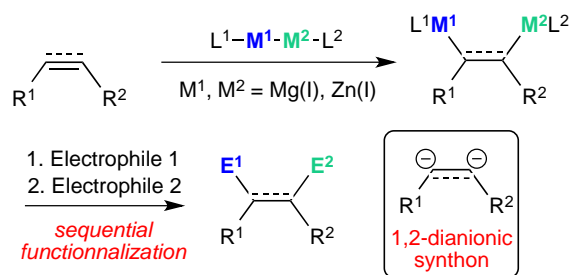


carbene complex **3**<sup>[9]</sup>, the trizinc cation **4** (where each Zn-atom presents a formal oxidation state of 1,33)<sup>[7]</sup>. The dissymmetry caused by the ligands in **3** affects the nature of the LM–ML' bonding as it changes the electronic distribution between the two metal centers and in consequence the properties and the reactivity of the species. Rationalizing by theory the effect of ligands on the nature of this bond seems mandatory to understand and control the reactivity of these complexes on route to applications. Conversely, mixed low valent complexes were also described, bearing a Zn(I)–Mg(I) functionality as **5**<sup>[10]</sup> or a Zn(I)–Cu(I) one as **6**<sup>[7]</sup>. In the case of these mixed M–M' bond as well as in the case of trimetallic species (i.e.

**4**), traditional electronic descriptors such as oxidation degrees are no more unequivocally determined. In such species, an accurate description of the M–M bond is yet to be established<sup>[11]</sup> and thus these dimetallic complexes remains to be investigated from a theoretical view point.

The above-selected recent examples showcase the remarkable recent diversity, thermal stability and strong M–M bonding of di- or trimetallic complexes with Zn(I) and/or Mg(I) metal centers. Surprisingly however, by contrast with the dibora species, **very little is known about the reactivity of such low valent molecular main-group organometallic species**, despite their relative ease of access.

The proposed research project is focused on the examination of the reactivity of such low-valent bimetallic compounds, **with a particular interest for the functionalization of C–C multiple bonds**. Our aim is to develop a straightforward approach to 1,2-bimetallic alkenes (or alkynes) through the addition of M–M species onto alkynes (resp. alkenes, Scheme 3).



Scheme 3 : Dimetallation of alkenes or alkynes and sequential functionalizations

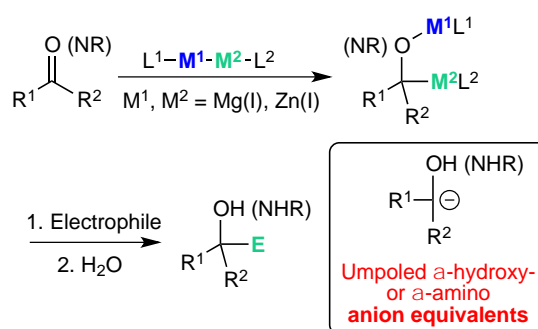
This approach will be tackled through an **intertwined synthetic and theoretical approach** in order to fully characterize the chemical potential of these uncommon dimetallic low valent reagents. To our knowledge, for the time being, only two examples of addition across multiple C–C bond were reported, involving the reaction of dimagnesium compound **2** with 1,1-diphenylethylene.<sup>[12]</sup> The addition was found to

be *reversible* and thus non-synthetically useful. However, the reaction was recently promoted by the presence of an external carbene ligand.<sup>[13]</sup> We anticipate that tuning the M–M versus M–Ligand bonding will represent a valuable general approach to control the addition process. A similar process was demonstrated recently for the CO reduction by dimagnesium reagents<sup>[14]</sup> and for the stabilization of dialuminum reagents.<sup>[15]</sup> The introduction of ligands to tune the selectivity could also pave the way for the development of asymmetric variants that have not been considered so far. Notably, chiral analogues of **3** prepared from readily accessible chiral NHC ligands could be particularly well suited and would represent a real breakthrough in this chemistry.

Depending on the nature of the starting organometallic complex and of the attached non-innocent ligands, sequential functionalizations will be envisioned, leading to **polyfunctionalized alkenes or alkanes**.

It should be noted that whereas the known dimetallic complexes are difficult to isolate, they are surprisingly easy to prepare. We will thus focus on **one-pot approaches, without any isolation of the mixed dimetallic structures**. In this context, the synergetic approach between computational study of reaction mechanisms and experimental development of synthetic procedure will allow “in silico” characterization of the intermediate and sampling of the possible competitive reactions.

In another field of application, the reducing ability<sup>[16]</sup> of these complexes will also be examined, in order to define new and selective strategies involving the **controlled** reduction of carbonyl or imine functions. Only the reduction of carbon monoxide<sup>[14]</sup>, esters<sup>[17]</sup> and nitriles<sup>[18]</sup> are reported to date, as well as the reaction of isocyanates with the dizinc compound **2**,<sup>[19]</sup> and the cyanosilylation of ketones catalyzed by the dimagnesium compound **3**.<sup>[20]</sup> A particularly interesting prospect related to the controlled reduction of aldehydes, ketones or imines is the possibility to access **umpoled  $\alpha$ -hydroxy- or  $\alpha$ -amino anion equivalents** (Scheme 4). The expertise of the theoretical group on the regiocontrolled conjugate addition of dienone catalyzed by Cu–Zn bimetallic complex will be highly beneficial for this part.<sup>[21]</sup> Indeed, it was demonstrated that the observed selectivity relied on the distinct roles played by the two metals (Zn and Cu) of the bimetallic species. Here again, the use of chiral NHC-complexes would open a route to chiral *disubstituted*<sup>[22]</sup>  $\alpha$ -hydroxy- or  $\alpha$ -amino anions and thus to enantioenriched tertiary alcohols or amines.



Scheme 4 : Reduction of carbonyls or imines

### ***Feasibility. Risk assessment and management***

Dizinc and dimagnesium compounds are generally simple to prepare and to handle : although being sensitive to water and oxygen, they show a remarkable thermal stability and solubility. They have been demonstrated to be reactive towards CO,<sup>[14,23]</sup> esters,<sup>[17]</sup> alkylidene-cyclopropanes,<sup>[24]</sup> azides<sup>[25]</sup> and nitriles.<sup>[18,26]</sup> In our project, the acceptor substrates for the addition reactions show complementary polarities (C–C and C–O(N) multiple bonds) and different activation modes; this is offering a broad reactivity scope and this would help in the project success. The synergistic approach between computational study of reaction mechanisms and experimental development of synthetic procedure in real time that we want to implement, will allow deciphering the details of these two action modes and is thus a key to allow a real progress of this study. The feasibility of the addition towards C=C bonds has been demonstrated by very recent work from the Jones laboratory,<sup>[14,15]</sup> which also pointed out one of the main difficulties of this project: the non-innocent ligands involved in the stabilization of dizinc or dimagnesium compounds have been shown to react in some extent, depending on the structure of the complex involved and particularly on the M–M bond length and strength. These can be predicted on the bases of DFT calculations, yielding understanding of uncontrolled reactivity and helping design more efficient systems. Although keeping in mind the possibility of modulating the non-innocent ligands and of designing new bimetallic complexes, we will rather focus on the reactivity tuning of reported complexes with additional ligands in order to play with the M–M bond polarizability.

### ***Position of the project within national and international context***

By contrast to dibora compounds, which have found during the past decade widespread applications in the area of the multiple carbon-carbon bonds functionalization,<sup>[1,27]</sup> homologous main group dimetallic compounds presenting a Zn–Zn or a Mg–Mg bond **have found to date very few synthetic applications**. Some organometallic research groups over the world (C. Jones (Melbourne), M. R. Crimmin (London), X.-J. Yang (Xi'an), ...) are engaged in this field, and their efforts are mainly focused on the organometallic structure determination and inorganic reactivity of dimagnesium compounds. After some time during which the field has remained quite specialized, it is now clearly emerging into a “hot topic” (as evidenced by the number of publications which has been multiplied by 3 within the last two years) that holds potential for rich and promising further developments.

The development of new methodologies allowing for the double functionalization of C-C multiple bonds by using elements such as Zn or Mg, as environmentally benign as B, but showing a different and sometimes orthogonal reactivity remains highly desirable within the context of eco-compatible and step-economy chemistry. The expertise of the experimental team in the functionalization of multiple C-C bonds has been already demonstrated.<sup>[28]</sup> Concerning the theoretical part, this project is in line with the expertise of the team in mechanisms and selectivity in organometallic and organic chemistry.<sup>[21]</sup>

### ***Position of the project in regard to the iSiM objectives***

The goal of LovaMor is to develop cutting-edge synthetic methodologies through the implementation of an interdisciplinary investigation covering the preparation, reactivity studies and theoretical understanding of a family of molecular complexes that has remained almost unexplored so far. This fundamental research is expected in the medium term to impact the fields of synthesis and catalysis with a focus on main-group metals such as Zn, Mg or Al that offer the potential to progress towards more sustainable chemistry. Clearly, LovaMor aims to develop high-level molecular science to meet the objectives of iSiM.

It will involve two partners: Institut Parisien de Chimie Moléculaire (ROCS team, Partner 1) and Laboratoire de Chimie Théorique (Inorganic, Organometallic and Organic Chemistry, Partner 2). These two partners belong to two different laboratories, two different federations and two different doctoral schools, what gives a consortium that allows to blur the lines between physical and organic chemistry.

### **Partners complementarity :**

The team “Réactivité Organométallique et Catalyse pour la Synthèse” from IPCM (UMR 8232, Sorbonne Université) comprises 8 perm. researchers working in the area of metal-mediated synthesis. The team has a general expertise in the preparation and handling of main-group functionalized organometallics, including Zn, Cu, Si or Ge derivatives, as well as bimetallic reagents. F. CHEMLA (PR) and A. PEREZ-LUNA (DR CNRS) will be involved in the project. The team “Inorganic and Organometallic Chemistry” at LCT (UMR 7616, Sorbonne Université) has a general expertise in combining reaction pathway determinations with a large variety of interpretative methods to analyse, understand and control reactivity in transition-metal-, main-group-, and purely-organic chemistry. S. HALBERT (MCF) and H. GERARD (PR) will be involved in the quantum chemical approaches.

Hence, LoVaMOR brings together two partners that share a common interest in studying original reactive intermediates to develop innovative applications, and relies on the combination of their complementary expertise. A synergistic approach between computational study of reaction mechanisms and experimental development of synthetic protocols will be applied. The structure, analysis of the bonding and mechanisms of the surmised dimetallic species will be studied through computational study and compared to experimental results. The interplay between experiment and theory (answers/requests/questions) in real time is key to allow a real progress of this study. The quantitative analyses offered by computational study are thus a powerful tool to understand the factors that govern the selectivity issues. Such a collaborative work between the partners has already been implemented on other topics.<sup>[29]</sup>

### **Research program**

The research program proposed hereafter aims to implement a synergistic approach between computational study of reaction mechanisms and experimental development of synthetic methods. The project being experimentally-driven yet fueled through a constant interplay between experiments and theory, the Ph.D. student involved in the project will conduct experimental work and theoretical modelling at the same time. The project team will take care to recruit a **candidate having good experimental skills in organic and/or organometallic chemistry, and a consistent curiosity in theoretical chemistry and its tools**. A specific training concerning some theoretical aspects will be provided, thanks to the courses of the Label of Chimie Théorique or summer/winter school in theoretical chemistry and to the expertise of the LCT team.

Experimentally, the reactivity of various dizinc compounds with alkynes will be first examined, using preliminary results obtained during the first semester 2021 in the ROCS team.<sup>[30]</sup> In particular, we expect  $\alpha$ -heteroatom-substituted alkynes to be suitable substrates for dimetallation. These results, associated to those from literature, will be used to determine and validate a model (functional, modelling of the environment, ...) to represent the structures and energetics of dizinc and dimagnesium compounds.

Having these results in hand, a first task will be dedicated to probe diverse non-innocent ligands (cyclopentadienyl, aminyl, bis-aminyl...) as it has been shown that their size or nature has a direct influence on the M–M length and thus presumably on the reactivity of the bimetallic complex towards multiple C–C bonds.<sup>[13,14]</sup> This experimental work will be conducted jointly with computations focused on the description of the influence of the additional ligands on the properties and reactivity of these di- or bimetallic compounds relative. BDE and electronic properties of the M–M bond (using Electron Localization Function (ELF), Atoms In Molecule (AIM) or through Natural Bond Orbital (NBO)) will be examined in symmetric M–M or mixed M–M' complexes with different coordination sphere to build a database of reactivity indexes. Their correlation with reaction quantities (energies or activation barrier) will be examined in order to design potential reactional compounds, to be implemented experimentally. The reactivity of analogous dimagnesium(I) compounds with alkynes will then be examined, as well as the reactivity with alkenes. The feedback from these experimental tests will help improving the computational approach, as expected from our synergistic approach developing both aspects within the framework of the same doctoral project.



Controlled reduction of carbonyl-type functionalities will then be examined in a second part of the PhD work. This step will allow both the evaluation of the versatility of the most efficient bimetallic compounds onto addition to CC multiple bonds, but also to evaluate in a different reactional context the less efficient ones. Based on the obtained experimental results, a search of reaction mechanisms in imine/carbonyls reduction with these low-valent bimetallic compounds will be engaged. In this part, we will explore the different reaction pathways, which can be envisioned due to the numerous possibilities for active species and side reactivities. The selectivities (regio-, stereo- and enantio-selectivity) thus obtained by computations will be tested and compared to the experimental results.

## Références / Bibliography

- <sup>1</sup> Neeve, E. C.; Geier, S. J.; Mkhaldid, I. A. I.; Westcott, S. A.; Marder, T. B. *Chem. Rev.*, **2016**, *116*, 9091.
- <sup>2</sup> a) Hoberg, H.; Krause, S. *Angew. Chem. Int. Edit.*, **1976**, *15*, 694 ; b) Uhl, W. *Z Naturforsch B*, **1988**, *43*, 1113.
- <sup>3</sup> Wehlschulte, R. J. The chemistry of low-valent organoaluminum species; in *The Chemistry of organoaluminum compounds*, Micouin, L.; Marek, I.; Rappoport, Z. eds, John Wiley & Sons, Ltd: Chichester, UK, 2009; Vol. 89, pp 223–252.
- <sup>4</sup> Eisenstein, O.; Gerard, H. Structure, Bonding, and Reactivity of Organoaluminum Molecular Species: A Computational Perspective; in *The Chemistry of organoaluminum compounds*, Micouin, L.; Marek, I.; Rappoport, Z. eds, John Wiley & Sons, Ltd: Chichester, UK, 2009; Vol. 89, pp 1–32.
- <sup>5</sup> Resa, I.; Carmona, E.; Gutierrez-Puebla, E.; Monge, A. *Science*, **2004**, *305*, 1136.
- <sup>6</sup> Green, S. P.; Jones, C.; Stasch, A. *Science*, **2007**, *318*, 1754.
- <sup>7</sup> Duncan Lyngdoh, R. H.; Schaefer, H. F.; King, R. B. *Chem. Rev.*, **2018**, *118*, 11626.
- <sup>8</sup> del Rio, D.; Galindo, A.; Resa, I.; Carmona, E. *Angew. Chem. Int. Edit.*, **2005**, *44*, 1244.
- <sup>9</sup> Jochmann, P.; Stephan, D. W. *Chem. Eur. J.*, **2014**, *20*, 8370.
- <sup>10</sup> Hicks, J.; Underhill, E. J.; Kefalidis, C. E.; Maron, L.; Jones, C. *Angew. Chem., Int. Ed.*, **2015**, *54*, 10000.
- <sup>11</sup> Bao, J. L.; Zhang, X.; Xu, X.; Truhlar D. G. *Phys. Chem. Chem. Phys.*, **2017**, *19*, 5839.
- <sup>12</sup> a) Boutland, A. J.; Carroll, A.; Alvarez Lamsfus, C.; Stasch, A.; Maron, L.; Jones, C. *J. Am. Chem. Soc.*, **2017**, *139*, 18190; b) Dange, D.; Gair, A. R.; Jones, D. D. L.; Juckel, M.; Aldridge, S.; Jones, C. *Chem. Sci.* **2019**, *10*, 3208.
- <sup>13</sup> Yuvaraj, K.; Douair, I.; Maron, L.; Jones, C. *Chem. Eur. J.* **2020**, *26*, 14665.
- <sup>14</sup> a) Yuvaraj, K.; Douair, I.; Paparo, A.; Maron, L.; Jones, C. *J. Am. Chem. Soc.* **2019**, *141*, 8764; b) Yuvaraj, K.; Douair, I.; Jones, D. D. L.; Maron, L.; Jones, C. *Chem. Sci.* **2020**, *11*, 3516.
- <sup>15</sup> Bonyhady, S. J.; Collis, D.; Frenking, G.; Holzmann, N.; Jones, C.; Stasch, A. *Nat. Chem.*, **2010**, *2*, 865.
- <sup>16</sup> Jones, C. *Nat. Rev. Chem.*, **2017**, *1*, 1.
- <sup>17</sup> Boutland, A. J.; Lamsfus, C. A.; Maitland, B.; Maron, L.; Stasch, A.; Jones, C. *Chem. Eur. J.*, **2017**, *23*, 14049.
- <sup>18</sup> Wang, J.; Wang, J.; Shen, L.; Zhao, Y.; Wu, B.; Yang, X.-J. *Organometallics* **2019**, *38*, 2674.
- <sup>19</sup> Li, B.; Wölper, C.; Huse, K.; Schulz, S. *Chem. Commun.* **2020**, *56*, 8643.
- <sup>20</sup> Wang, W.; Luo, M.; Li, J.; Pullarkat, S. A.; Ma, M. *Chem. Commun.* **2018**, *54*, 3042.
- <sup>21</sup> a) Halbert, S.; Lauberteaux, J.; Blons, C.; Marcia de Figueiredo, R.; Crévisy, C.; Baslé, O.; Campagne, J.-M.; Mauduit, M.; Gerard, H. *Chem. Cat. Chem.*, **2019**, *11*, 4108; b) Drissi-Amraoui, S.; Schmid, T. E.; Lauberteaux, J.; Crévisy C.; Baslé, O.; Marcia de Figueiredo, R.; Halbert, S.; Gérard, H.; Mauduit, M.; Campagne, J.-M. *Adv. Synth. Catal.*, **2016**, *358*, 2519 c) Halbert, S.; Gerard, H. *New J. Chem.*, **2015**, *39*, 5410.
- <sup>22</sup> For related recent approaches to secondary enantioenriched alcohols, see : Yuasa, A.; Nagao, K.; Ohmiya, H. *Beilstein J. Org. Chem* **2020**, *16*, 185; Takeda, M.; Mitsui, A.; Nagao, K.; Ohmiya, H. *J. Am. Chem. Soc.* **2019**, *141*, 3664.
- <sup>23</sup> Lalrempuia, R.; Kefalidis, C. E.; Bonyhady, S. J.; Schwarze, B.; Maron, L.; Stasch, A.; Jones, C. *J. Am. Chem. Soc.*, **2015**, *137*, 8944.
- <sup>24</sup> Kong, R. Y.; Crimmin, M. R. *J. Am. Chem. Soc.* **2020**, *142*, 11967.
- <sup>25</sup> a) Gondzik, S.; Schulz, S.; Bläser, D.; Wölper, C.; Haack, R.; Jansen, G. *Chem. Commun.*, **2014**, *50*, 927; b) Stienen, C.; Gondzik, S.; Gehlhaar, A.; Haack, R.; Wölper, C.; Jansen, G.; Schulz, S. *Organometallics* **2016**, *35*, 1022; c) Bonyhady, S. J., Green, S. P., Jones, C., Nembenna, S., Stasch, A. *Angew. Chem. Int. Ed.*, **2009**, *48*, 2973.
- <sup>26</sup> Ma, M.; Stasch, A.; Jones, C. *Chem. Eur. J.*, **2012**, *18*, 10669.
- <sup>27</sup> Zhao, F.; Jia, X.; Li, P.; Zhao, J.; Zhou, Y.; Wang, J.; Liu, H. *Org. Chem. Front.*, **2017**, *4*, 2235.
- <sup>28</sup> la Vega-Hernández, de, K.; Romain, E.; Coffinet, A.; Bijouard, K.; Gontard, G.; Chemla, F.; Ferreira, F.; Jackowski, O.; Pérez-Luna, A. *J. Am. Chem. Soc.* **2018**, *140*, 17632; Fopp, C.; Isaac, K.; Romain, E.; Chemla, F.; Ferreira, F.; Jackowski, O.; Oestreich, M.; Pérez-Luna, A. *Synthesis* **2017**, *49*, 724; Fopp, C.; Romain, E.; Isaac, K.; Chemla, F.; Ferreira, F.; Jackowski, O.; Oestreich, M.; Pérez-Luna, A. *Org. Lett.* **2016**, *18*, 2054; Beniazza, R.; Romain, E.; Chemla, F.; Ferreira, F.; Jackowski, O.; Pérez-Luna, A. *Eur. J. Org. Chem.* **2015**, 7661; Romain, E.; Fopp, C.; Chemla, F.; Ferreira, F.; Jackowski, O.; Oestreich, M.; Pérez-Luna, A. *Angew. Chem. Int. Ed.* **2014**, *53*, 11333.
- <sup>29</sup> Romain, E.; de la Vega-Hernández, K.; Guegan, F.; Sanz-Garcia, J.; Fopp, C.; Chemla, F.; Ferreira, F.; Gerard, H.; Jackowski, O.; Halbert, S.; Oestreich, M.; Perez-Luna, A. *Adv. Synth. Cat.* **2021**, submitted.
- <sup>30</sup> A master-2 research training stay in the ROCS team focused on this theme has begun in February 2021.