Organometallics group

Group leader: Arnaud Gautier

News

Permanent group members (Arnaud Gautier, Jean-Louis Canet et Federico Cisnetti) as well as the students present during June 2016.

Staff

PERMANENT MEMBERS

M. Jean-Louis CANET

M. Arnaud GAUTIER
NON PERMANENT MEMBERS

- Kévin Fauché, PhD
- Julien Buzenet (M2)
- Mickaël Desroches (M1)

FORMER MEMBERS (BY YEAR OF DEPARTURE):

- 2017 Leslie Bitard, Deborah Cardoso (Sigma)
- 2016 Aurore Bonnemoy (technician), Amélie Maure (undergraduate), Anca G. Coman (Erasmus visiting PhD student), Delphine Rouzeyrol (undergraduate), Ebrahim Ettarabti (undergraduate), Moussa N'Diaye (undergraduate)
- 2015 Zohra Kouidri (engineering school student), Quentin Roche (Master), Théo Rongère (Master), Mélanie Krywalsky (undergraduate)
- 2014 Clémentine Gibard (PhD), Pierre Adumeau (PhD), Houssein Ibrahim (Post-doc), Frederick Lacemon (Master), Victoria Garcia (undergraduate), Manon Chevrier (undergraduate).
- 2013 Michela di Giannantonio (Erasmus), Olivier Piebourg (Master), Aurore Bonnemoy (undergraduate), Diane Delbège (Master)
- 2012 Carolina Valerio Barra, Fillipe Vieira Rocha (brazilian PhD students), Nicolas Candelon (post-doc), Bernard Bidon (undergraduate)
- 2011 Marine Gagnevin (undergraduate), Christelle Gaulier (Master), Claire Gaillard (post-doc)
- 2010 Pauline Labeaume (undergraduate), Loic Donato (Master), Audrey Hospital (Master), Vijetha Mogilireddy (Master, India), Aurélien Chevry (PhD), Xianmin Guo (post-doc), Denise Dugat (CNRS researcher)
- 2009 Zein Chamas (Master), Marie-Lauré Teyssot (lecturer)
- 2008 Antony Peixoto (undergraduate), Patricja Serafin (Master, Erasmus), Aurélie Maisonial (Master)

OLD GROUP PHOTOS:
Research subjects

Area of expertise: organic and organometallic chemistry, chemistry-biology interface

RESEARCH SUBJECTS

- Metallocarbenes: synthetic methodologies.
- Click chemistry (new catalysts, metallocarbene and biomolecule functionalisation).
- Anti-cancer platinum chelates, and coinage metal (Cu, Ag, Au) metallocarbenes.
- Click lanthanide chelates: luminescence studies, lanthanide complexes-protein interaction.
  Inclusion in nanoparticles for medical imaging.
- Biological activity of metallocarbenes: anticancer and antibacterial
Our research projects rely on efficient chemistry. **Organometallic and coordination complexes** are synthesized in straightforward and modular fashions in order to study them in the biological context. On the one hand, the **biological activity** of these compounds is determined. On the other hands, they are considered as **catalysts** - including for biomolecule functionalisation - or as luminescent probes for imaging applications.

All of the above-mentioned project rely on the so-called "**click chemistry**" approach. We develop highly efficient systems to perform copper-catalysed azide-alkyne cycloadditions (CuAAC) at low catalyst loading. The triazole heterocycle such obtained is at the heart of the molecular system of biological interest. For instance, triazoles may participate to platinum chelation to yield cisplatin analogues, may play the role of antennae in sensitized luminescence of lanthanide complexes and expand their possibilities of intermolecular interaction with proteins or may introduce a functionalisation site distant to the carbenic core in metal N-heterocyclic carbenes (NHC) for solubility modulation and biomolecule conjugation.

**RESEARCH HIGHLIGHTS**

**Chemical Communications, 2014** : \(((\text{Cu}(\text{IPr})_{2}(-\text{OH}))\text{(BF4)}) : synthesis and halide-free CuAAC catalysis.\)

The preparation under protic conditions of the first -hydroxo dicopper(I)–NHC complex is reported. Its application as a CuAAC catalyst was investigated, evidencing a remarkable enhancement of catalytic efficiency in the presence of 4,7-dichloro-1,10-phenanthroline and highlighting the beneficial effect of the absence of coordinating halides.

**ChemMedChem, 2014** : High-Throughput Screening of Metal-N-Heterocyclic Carbene Complexes against Biofilm Formation by Pathogenic Bacteria.

A set of molecules including a majority of metal-N-heterocyclic carbene (NHC) complexes (metal=Ag, Cu, and Au) and azolium salts were evaluated by high-throughput screening of their
activity against biofilm formation associated with pathogenic bacteria. This research was performed in collaboration with the universities of Strasbourg and Paris VI as well as the Biofilm Control company.

Organometallics, 2013 : Simplified Preparation of Copper(I) NHCs Using Aqueous Ammonia.

The use of aqueous ammonia as a coordinating and basic reagent for the metalation of imidazol(in)ium salts derived from (S)IPr and (S)IMes with simple inorganic copper precursors is reported. The synthesis of copper carbene complexes was performed using aqueous/alcoholic media in mild conditions (room temperature to 60 °C) with short reaction times.

Organometallics, 2012 : CuAAC functionalization of azide-tagged copper(I)-NHCs acting as catalyst and substrate.

We have developed copper(I) NHC complexes bearing azide functions. These species are able to act both as catalyst and substrate and provide an original entry to functionalised metallocarbenes. This article is included in the Organometallics special issue « Copper Organometallic Chemistry»

Chemical Communications, 2012 : A Water Soluble CuI–NHC for CuAAC ligation of unprotected peptides under open air conditions.

Using water-soluble copper(I)-NHC, CuAAC functionalisation of oligopeptides was efficiently performed in buffered aqueous media, in the presence of air without any sacrificial reducing agent. This study was performed in collaboration with Agnès Delmas and Vincent Aucagne from Molecular Biophysics Centre of Orléans.

The unprecedented mechanism of action of silver(I)-NHCs against cancer cells was recently elucidated. Induction of apoptosis proved to follow an original pathway. These study was performed in collaboration with Sylvain Roland (Parisian Institute of Molecular Chemistry), Thierry Cresteil (Institute of Chemistry of Natural Substances, Gif-sur-Yvette) the GReD laboratory as was as the Charles Friedel Laboratory of the National Superior School of Chemistry of Paris.


Novel trisdipicolinate-lanthanide complexes with triazole groups obtained by CuAAC are reported. Their use as phasing agents for accurate X-ray crystallographic structural determination of proteins is described. The CuAAC modification allows efficient protein co-crystallization with significantly lower concentration of lanthanide complexes in comparison to unmodified analogues.

Network, collaborations, projects

COLLABORATION NETWORK

Local academic:

- GReD, UMR 6247 CNRS/ UMR 931 INSERM (Biology).
- RGM Laboratory
- ICCF, Inorganic Materials Team.
- IMTV (U990) (Biology)
French and international academic:

- Laboratory of Crystallography and Biological NMR, UMR8015, Paris Descartes University.
- Parisian Institute of Molecular Chemistry, UMR7201, Pierre and Marie Curie University.
- Laboratory of Coordination Chemistry, Institute of Chemistry of Strasbourg, University of Strasbourg.
- Molecular Biophysics Centre of Orléans (UPR CNRS 4301)
- Institute of Structural Biology (CNRS/CEA/UJF), Grenoble.
- Canceropôle Lyon Auvergne Rhône-Alpes.
- Imperial College, London, Great Britain
- University of York, Great Britain
- Freie Universität Berlin, Germany
- UNESP, Araraquara, Brazil

Industrial:

- Biofilm Control, a high-technology company specialised in bacterial biofilm detection and treatment.
- Orgapharm
- Givaudan
- Afyren

CURRENTLY FUNDED PROJECTS

- ANR EasyMiniProt, coord. V. Aucagne (CBM-Orléans), partner: A. Gautier. 2015-

FORMER FUNDED PROJECTS

- Antibacterial Metallocarbenes, funding by Auvergne region, F. Cisnetti, 2012-2014.