Institut
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I E C B

Looking to the Future

10th workshop of candidates for group leader positions at IECB

Thursday October 5th, 2017

IECB Auditorium, free & open to all

2017 pre-selected candidates for group-leader positions at IECB

Dr. Mathieu Pucheault

Institute of Moleculars Sciences - ORGA group - University of Bordeaux, France

Amine Boranes : unified reagents for borylation of aromatics.

Owing to their specific properties, aminoborane and amine borane complexes can be used as borylating reagents. We developed during the last decade a unified method for the borylation of aromatic triflates, chlorides, bromides, iodides and diazonium salts. Depending on substrates the reaction proceeds smoothly with diisopropylaminoborane in the presence of some catalysts, centered on palladium[1] or iron,[2] sometimes in its absence. One major advantage of this technology is related to the facile access to all boron derivatives using this unique borylating agent including, boronic acids, boronates, trifluoroborates, diaminoboranes, MIDA esters… we can even use the intermediate directly in cross-coupling reaction, typically Suzuki-Miyaura cross coupling.

Recent development of this technology will be presented and encompasses the discovery of water and air stable reagents, amine borane complexes[3] which undergo a dehydrogenation/coupling sequence enabling direct access to boronic acids[4] and borinics[5] in high yields.

[1] H D.S. Guerrand, L D. Marciasini, Mélissa Jousseaume, M Vaultier, M Pucheault, Chem. Eur. J.,* ***2014****, 5573–5579*

[2] a.) L D. Marciasini, M Vaultier, M Pucheault, Tetrahedron Lett.,* ***2014****, 1702–1705 b). L D. Marciasini, N Richy, M Vaultier, and M Pucheault,* Adv. Synth. Catal.,* ***2013****, 355, 1083–1088*

[3] H D.S. Guerrand, L D. Marciasini, T Gendrineau, O Pascu, S Marre, S Pinet, M Vaultier, C Aymonier, and M Pucheault Tetrahedron,* ***2014****, 6156-6161 b. H. D. S. Guerrand, M. Vaultier, S. Pinet and M. Pucheault*, Adv. Synth. Catal.,* ***2015****, 6, 1167-1174*

[4] a. M. Pucheault, M. Vaultier, B. Cacciuttolo, L. Marciasini, 16/06/2015, ***FR15/555515***

[5] L. Marciasini, B. Cacciuttolo, M. Vaultier, M. Pucheault , Org Lett.,* ***2015****, 3532-3535*

Prof. Xiao-Feng Wu

Leibniz-Institute for Katalysis, University of Rostock (LIKAT) Rostock, Germany

A trip on Carbonylative Functionalization of C-H Bonds

Due to the importance of heterocycles, our research group has been focused on the developing of new procedures for the synthesis of heterocyclic compounds during the past years. Based on the concept of carbonyl group generation, numerous heterocycles have been prepared effectively with our newly developed methods. And the carbonyl groups are mainly generated via carbonylative transformations or with oxidation procedures.

Dr. Vladimir Torbeev

Proteins chemical laboratory, supramolecular engineering and science Institute University of Strasbourg, France

Conformational dynamics in protein function studied by chemical protein synthesis.

Conformational dynamics is essential for protein function. Dissecting the contribution from different conformational isomers of a protein on a molecular level is however very challenging. In this lecture I will illustrate how chemical protein synthesis can provide with unique insights into functional role of different protein conformers. Examples will include understanding the role of protein dynamics in enzyme catalysis (*Proc. Natl. Acad. Sci. USA* **2011**, *108*, 20982), protein misfolding and aggregation (*J. Am. Chem. Soc.* **2015**, *137*, 2524) and function of intrinsically disordered proteins (*Chem. Commun.* **2017**, *53*, 7369).

Dr. Sebastian Falk

Department of Structural Cell Biology, Max Planck Institute of Biochemistry, Martinsried, Germany

Structural and functional insights into the nuclear RNA Exosome

RNA degradation serves a multitude of functions in all domains of life. The main cellular machinery responsible for degrading RNAs in the 3'-to-5' direction is the RNA exosome complex. The exosome is a multisubunit macromolecular machine that associates with a distinct set of cofactors in the cytoplasm and the nucleus. In the nucleus the exosome mediates the processing and decay of a large variety of transcripts, including defective pre-mRNAs and non-coding RNAs such as rRNAs, sn(o)RNAs and tRNAs. I will give an overview about my recent progress on the the structural and functional characterization of the nuclear exosome cofactors Mpp6 and the two Mtr4 helicase containing complexes TRAMP and NEXT.

Dr. Rémi Sonneville

MRC Protein Phosphorylation and Ubiquitylation Unit, The Sir James Black Centre, University of Dundee, Scotland, UK

The end of DNA replication

Chromosomes must be precisely duplicated to preserve genome stability during cell division. The assembly of the CMG helicase (CDC-45-MCM-GINS), which unwinds DNA at the replication fork, is the key regulated step during initiation of DNA replication in eukaryotes. Replisome disassembly is the final step of DNA replication; it involves the ubiquitylation and CDC-48/P97/VCP-dependent dissolution of the CMG helicase. Using *Caenorhabditis elegans* early embryos and Xenopus egg extracts, we show that the CUL-2^{LRR-1} ubiquitin ligase associates with and drives CMG disassembly together with CDC-48 and its co-factors UFD-1 and NPL-4. Interestingly, depletion of the ubiquitin ligase revealed a novel backup mechanism that drives CMG disassembly during mitosis and required the CDC-48 cofactor UBXN-3, orthologous to the human tumour suppressor FAF1. Partial inactivation of *lrr-1* and *ubxn-3* leads to synthetic lethality, suggesting potential approaches to selectively kill *faf1* deficient cancer cells.

Dr. Mikayel Aznauryan

Department of Chemistry and Interdisciplinary Nanoscience Center (iNANO), Aarhus University, Denmark

Single-molecule microscopy of protein and nucleic acid conformational dynamics in crowded solutions and living cells

The cellular interior represents an extremely complex and crowded environment with little resemblance to the isolated experimental conditions *in vitro*. Therefore, major efforts are currently undertaken to develop tools to directly study biomolecules in their native cellular environment. Among those is the single-molecule Forster Resonance Energy Transfer (FRET) microscopy that has developed into an important method for probing the structure and dynamics of individual biomolecules [1].

Here I will discuss our recent results where single-molecule FRET was utilized to investigate the conformational dynamics of telomeric nucleic acids in cell-mimicking crowded solutions. In addition, I will present our recent method developments that enabled performing single-molecule FRET measurements directly in living cells and allowed for probing the conformational dynamics, thermal stability and kinetics of intrinsically disordered and folded proteins in their native cellular environment [2].

(1) Plitzko, J. M.; Schuler, B.; Selenko, P. Structural Biology outside the box—inside the cell. Curr Opin Struc Biol 2017, 46, 110.

(2) Konig, I.; Zarrine-Afsar, A.; Aznauryan, M.; Soranno, A.; Wunderlich, B.; Dingfelder, F.; Stuber, J. C.; Pluckthun, A.; Nettels, D.; Schuler, B. Single-molecule spectroscopy of protein conformational dynamics in live eukaryotic cells. Nature methods 2015, 12, 773.

Looking to the Future Workshop Program

Thursday October 5th, 2017

11.30 - 12.00 Amine Boranes : unified reagents for borylation of aromatics

Dr. Mathieu Pucheault
Institute of Moleculars Sciences - ORGA group - University of Bordeaux, France

12.00 – 14.00 Cocktail lunch

14.00 - 14.30 A trip on Carbonylative Functionalization of C-H Bonds

Prof. Xiao-Feng Wu
Leibniz-Institute for Katalysis, University of Rostock (LIKAT) Rostock, Germany

14.30 - 15.00 Conformational dynamics in protein function studied by chemical protein synthesis

Dr. Vladimir Torbeev
Proteins chemical laboratory, supramolecular engineering and science Institute
University of Strasbourg, France

15.00 - 15.30 Structural and functional insights into the nuclear RNA Exosome

Dr. Sebastian Falk
Department of Structural Cell Biology, Max Planck Institute of Biochemistry, Martinsried, Germany

15.30– 16.15 Coffee break

16.15 - 16.45 The end of DNA replication

Dr. Rémi Sonneville
MRC Protein Phosphorylation and Ubiquitylation Unit, The Sir James Black Centre, University of Dundee, Scotland, UK

16.45 - 17.15 Single-molecule microscopy of protein and nucleic acid conformational dynamics in crowded solutions and living cells

Dr. Mikayel Aznauryan
Department of Chemistry and Interdisciplinary Nanoscience Center (iNANO), Aarhus University, Denmark