Tuesday Afternoon

HEESCHER Carolin

Studies concerning a Stereoselective Synthesis of Elaeocarpine

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Synthetic approach toward nhatrangins A and B

PIERRE Cathleen

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Dr. DAUBAN Philippe

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Challenge in Crop Protection Research
A case study: Natural product as lead structure for discovery

STUDIES CONCERNING A STEREOSELECTIVE SYNTHESIS OF ELAEOCARPINE

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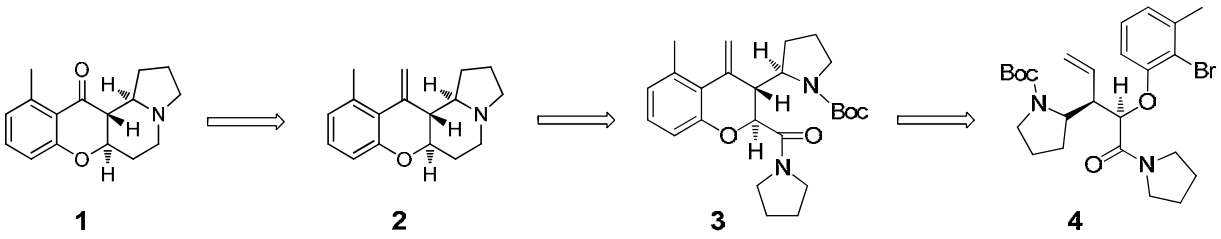
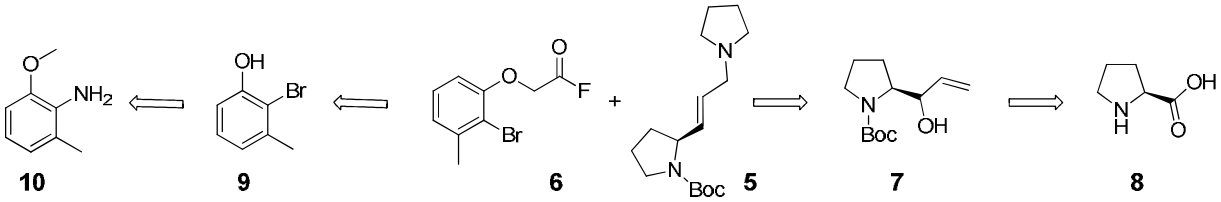
Elaeocarpine **1** is an Indolizidine alkaloid found in the plant *Elaeocarpus polydactylus*, which grows in the rain forest of New Guinea.[1] Carolle et al. proved that Indolizidine alkaloids like Elaeocarpine **1** show a very high affinity to the human δ-opioid receptor, so they offer a strong antinociception without unintentional side effects like respiratory depression.[2]

The stereoselective total synthesis of Elaeocarpine **1** using a zwitterionic Aza-Claisen rearrangement as a key step to introduce the stereogenic centres was the aim of the present project.[3] Elaeocarpine **1** should be generated by ozonolysis of **2** as the last step of the pathway. The Indolizidine core in **2** should be completed starting from amide **3** by BOC-cleavage, dibromomethane addition, intramolecular Grignard reaction and ketone reduction. The benzopyrane moiety in amide **3** should be assembled by intramolecular Heck reaction using the rearrangement amide **4** as a key intermediate within the total synthesis.



The Aza-Claisen rearrangement enables to react the chiral allyl amine **5** and the acid fluoride **6** to form the desired amide **4** with high simple diastereoselectivity and a high 1,2-asymmetric induction. In this connection, the stereogenic centre in **5** induces the passing of a single chair-like transition state within the rearrangement. In combination with a defined Z-enolate geometry a single diastereomer is obtained in very high yields during the key step of the synthesis. Allyl amine **5** is built-up from (*S*)-proline **8** via allyl alcohol **7** using standard procedures. Activation of the alcohol in **7** and S_N2' reaction with pyrrolidine finally affords allyl amine **5**. Phenole **9** is synthesized from aniline **10** by diazotation, subsequent Sandmeyer reaction and cleavage of the methyl ether. Finally the reaction with chloro acetic acid provides the phenoxy acetic acid derivative that is converted into the acid fluoride **6** upon reaction with cyanuric fluoride.



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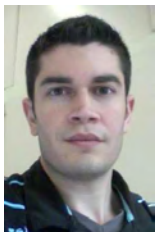

SYNTHETIC APPROACH TOWARD NHATRANGINS A AND B

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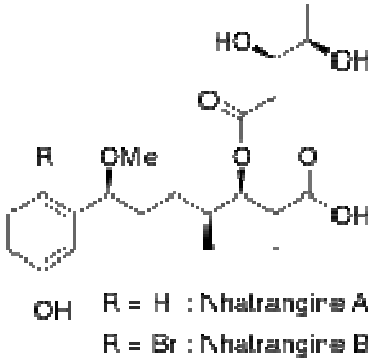
Cyanobacteria are well known from the scientific community for the numerous bioactive molecules they secrete.[1] In particular, *Lyngbya majuscula* has shown to be the source of several secondary metabolites. Among them, Nhatrangins A and B, which were isolated in 2010 by Orjala's group, turned out to be related to the aplysiatoxins.[2] Interestingly, compounds from this family have often shown either teratogenic or therapeutic properties.[3] The lack of information about these two new products bioactivity makes them appealing synthetic targets.



During our work, several synthetic pathways involving olefin metathesis as key step have been investigated, leading to disappointing results. The choice of a more linear sequence, using notably a diastereoselective alkylation and aldolisation turned out to be much more efficient and allowed the formation of an advanced intermediate to both molecules.

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SYNTHESIS OF POLYCYCLIC MOLECULES BY PALLADIUM CATALYSED C(sp^3)-H ACTIVATION

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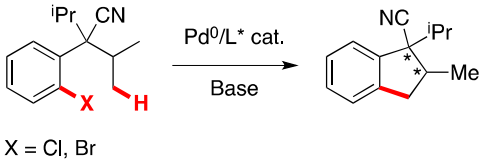
In recent years, transition-metal-catalyzed C-H functionalization has emerged as a powerful tool to transform otherwise unreactive C-H bonds. In this context, our group[1] and others[2] recently described a series of new reactions involving intramolecular Pd(0)-catalyzed C(sp^3)-H activation from bromoarenes. In particular, these reactions led to various types of useful fused carbocycles and heterocycles.

We extended this work to the first efficient and general palladium-catalyzed intramolecular C(sp^3)-H arylation from aryl and heteroaryl chlorides.[3] The use of aryl chlorides as coupling partners greatly improved the C-H arylation scope by facilitating the access to reaction substrates such as heterocycles. We report herein that intramolecular C(sp^3)-H arylations can be combined with inter- or intramolecular C(sp^2)-H arylations in the presence of the same palladium catalyst.[4] These new types of double C-H arylations allow the rapid construction of molecular complexity and provide an efficient access to original polycyclic molecules.

More recently, our work on asymmetric intramolecular C(sp^3)–H arylation led to the first diastereo- and enantioselective synthesis of indanes by using a chiral Pd/Binepine catalyst.[5]



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APPLICATION OF C,N-DIGLYCOSYLATED HETEROCYCLES FOR THE SYNTHESIS OF MODIFIED ESL-1 GLYCOPEPTIDES

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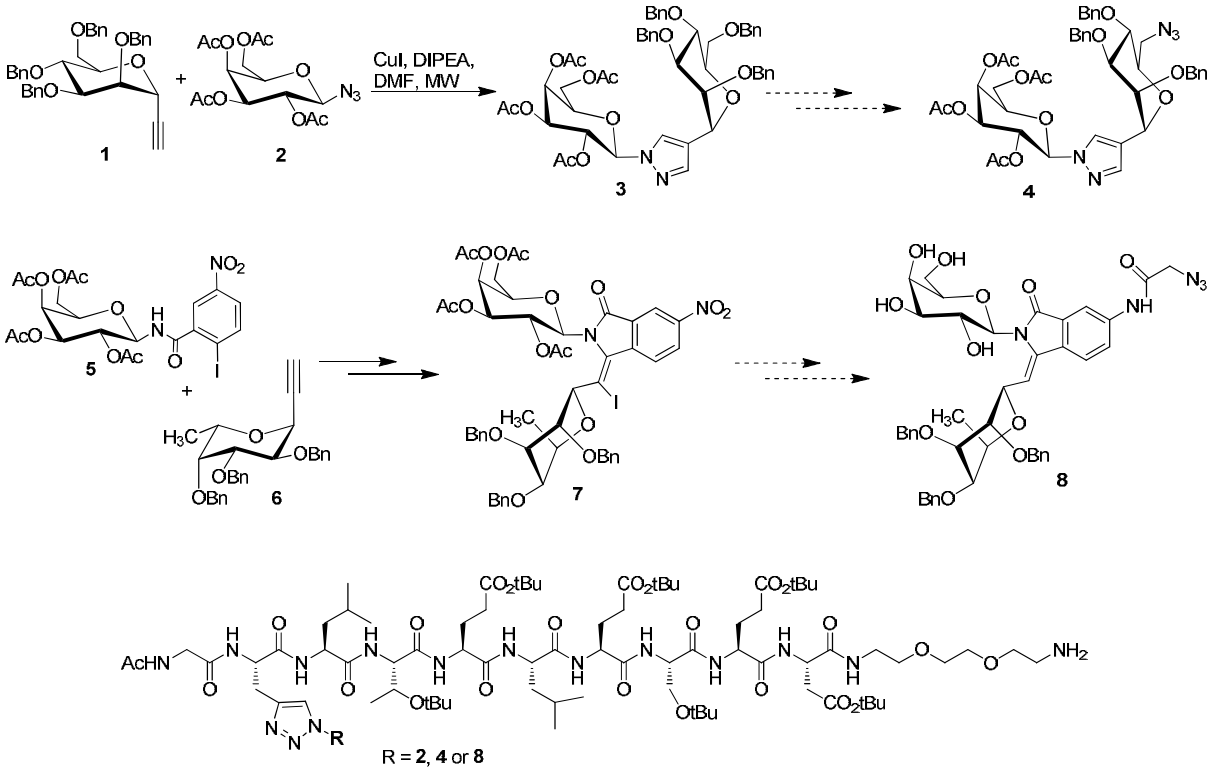
The selectin-mediated cell adhesion[1] forms the initial step of the inflammatory cascade, a physiological reaction on potentially harmful stimuli. At its beginning, P- and E-selectin are expressed on the endothelial surface and interact with the glycopeptides PSGL-1 and ESL-1 presented by leukocytes. The latter can then migrate into the inflamed tissue. Undesired cell-cell interactions do not only lead to chronically inflammatory diseases[2] but also play an important role in tumor metastasis.[3] Therefore, we aim to synthesize soluble Sialyl-Lewis^X-mimetics as competitive inhibitors of the aforementioned cell adhesion with improved stability towards enzymatic degradation. To achieve this, the natural *O*-glycosidic bonds are replaced by *C*- and *N*-glycosidic ones.[4] Also, as previously reported,[5] a central part of the natural oligosaccharide can be substituted by carbo- or heterocyclic systems. The presented triazoles and isoindolin-1-ones shall then be connected to the modified repeat unit of ESL-1 to construct glycopeptides.



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SYNTHESIS OF TYLOPHORINE AND SUBSTITUTED DERIVATIVES

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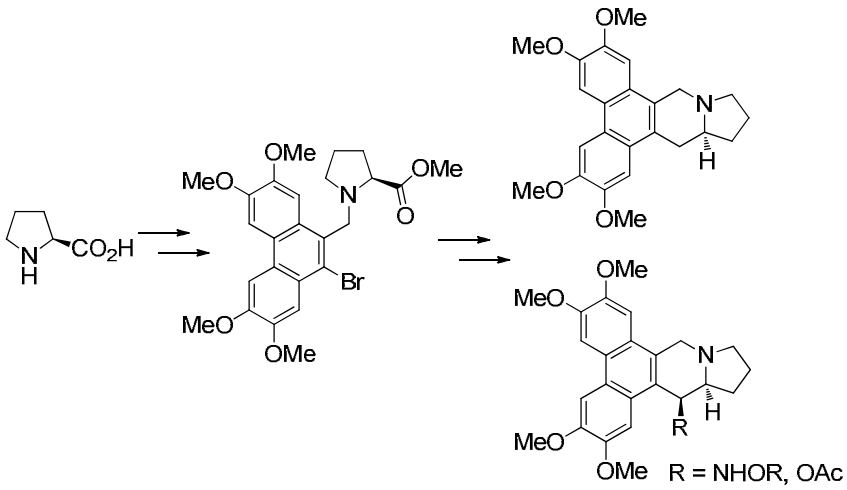
Phenanthroindolizidine and phenanthroquinolizidine alkaloids represent a large group of pentacyclic natural products isolated mainly from *Tylophora, Cynanchum*, and *Pergularia* species[1] and are of significant interest for medical research.[2] Due to their influence on protein and nucleic acid biosynthesis, some of these compounds exhibit cytostatic and antiinflammatory effects, as well as strong antiviral activity.[3] The naturally occurring tylophorine is the (*R*)-(–)-enantiomer and was found to be more active as an antiviral agent than the unnatural (*S*)-(+)-tylophorine. In contrast, the dextrorotatory alkaloid turned out to be the more potent inhibitor of cancer cell growth.
To date, no specific cellular target protein or nucleic acid has been identified.
(*S*)-(+)-tylophorine was synthesized from L-proline in nine linear steps including an oxidative ring closure and a free-radical cyclization of an *N*-aziridinylimine as radical acceptor according to the method of Kim[4] as the key steps.[5]



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THE SYNTHETIC CHEMISTRY OF NITRENES: TO SELECTIVE CATALYTIC C-H AMINATION AND BEYOND

Philippe DAUBAN

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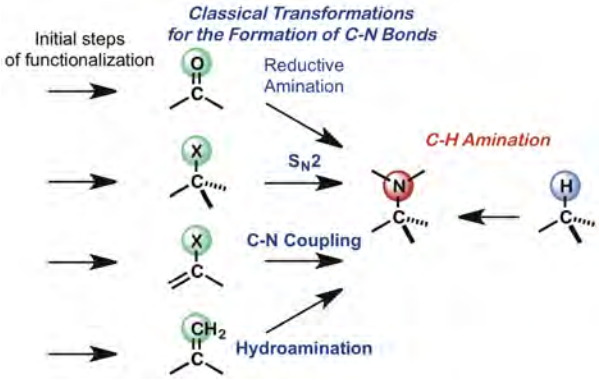
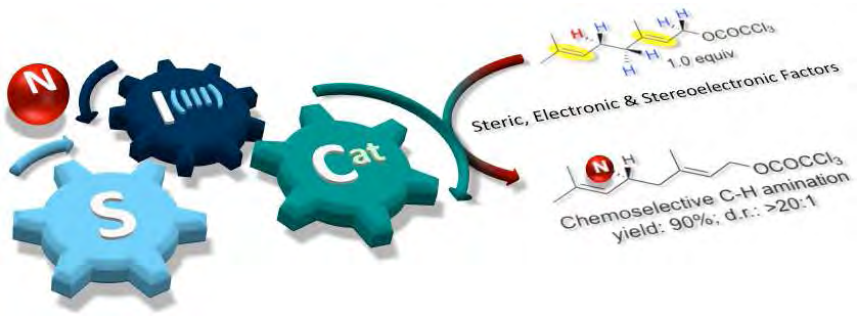
The fundamental importance of nitrogen in chemistry and biology has inspired organic chemists since Wöhler's urea synthesis. Great attention is still paid to the search for mild conditions allowing selective formation of C-N bonds.[1] Key reactions include Buchwald-Hartwig couplings, reductive amination of carbonyl compounds, or alkene hydroamination. In this context, the development of mild conditions for the selective direct amination of C-H bonds with nitrenes offers unique opportunities in synthesis.



The application of catalytic C-H functionalization reactions in total synthesis depends on their level of predictability. Whereas good control can be achieved in intramolecular reaction, the intermolecular version remains much less predictable, and even more challenging as the number of C-H bonds increases. The conception of such a reaction requires a clear understanding of the steric, electronic, and stereoelectronic factors influencing the reactivity of C-H bonds. To this end, the application of metal-catalyzed nitrene transfers has allowed gaining useful insights into the inherent reactivity of various substrates. In this lecture, the results of our investigations aimed to better predict the site of C-H amination of complex molecules will be presented. The reaction relies on the combination of an iodine(III) oxidant with a transition metal catalyst and a sulfur-based aminating agent. Application of the reaction conditions has also revealed that the synthetic chemistry of nitrenes might have a wider scope than anticipated.



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CHALLENGE IN CROP PROTECTION RESEARCH A CASE STUDY: NATURAL PRODUCT AS LEAD STRUCTURE FOR DISCOVERY

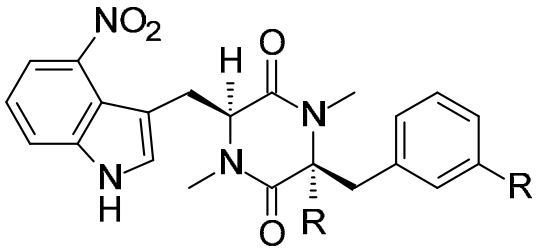
Frederick Calo, William Moberg, Eike Huppe and Liliana Parra.

BASF SE, Crop Protection Chemistry Research, 67056 Ludwigshafen

The presentation will focus on the importance of modern Crop Protection Research today and will highlight:

- Why do we need Crop Protection Research?
- What are the challenges that Crop Protection Research face?
- How can we find new chemical classes as starting point?

Finally a case study will be presented using a thaxtomin natural product as a lead structure for herbicide discovery. (Fig. 1)



Thaxtomin A R = OH
Thaxtomin D R = H

Figure 1. Structure of thaxtomins

Wednesday Morning

PRADHAN Anirban

Strongly twisted arenes by scholl cyclizations with unexpected regioselectivity

EL HELLANI Ahmad

Evaluation of the electronic properties of carbon(0)-based compounds through gold catalysis and X-ray structure analysis

KONIEV Oleksandr

Screening for selective chemical ligation reactions

BURA Thomas

Water-soluble phosphonate-substitutes bodipy derivates with tunable emission channels

IBRAHIM Farah

Synthesis of new chiral calix-salen complexes and application in asymmetric heterogeneous catalysis

YANG Jing

Facile synthesis of new rare earth catalysts and their application for varied Michael-type reactions

FRATH Denis

Boranil: a new easily accessible, versatile and highly fluorescent dye

RAYA Paco

Design and synthesis of modified aminoglycosides: towards new antibacterial and antiviral agents

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Dr. DE MESMAEKER Alain

From Natural Products to commercial compounds for Crop Protection

STRONGLY TWISTED ARENES BY SCHOLL CYCLIZATIONS WITH UNEXPECTED REGIOSELECTIVITY

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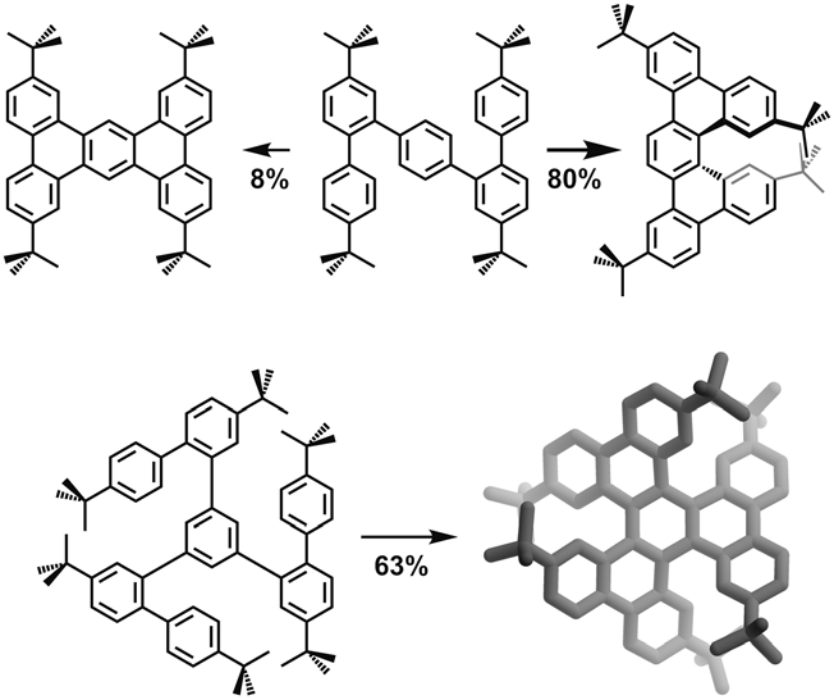
In order to better apprehend the well-known but still only partially understood intramolecular Scholl reaction (i.e. arene-arene dehydrocyclization in the presence of a Lewis acid), its regioselectivity has been investigated with the study of test molecules bearing bulky *tert*-butyl substituents and offering competing cyclization pathways to non-congested transoid products and highly congested cisoid alternatives. It has been shown that, against all expectation, even a strong steric hindrance has no marked effect on regioselectivity and highly twisted cisoid polycyclic aromatic hydrocarbons are preferentially formed, whereas their flat and more symmetrical transoid isomers are only obtained in minority. These results, especially the successful and efficient Scholl synthesis of highly twisted, triply helical hexa-*tert*-butyl-hexabenzotriphenylene, also suggest that the Scholl reaction is powerful enough to be considered for the development of organic synthesis of helicenes and other highly strained polycyclic aromatic hydrocarbons, which have recently become the targets of considerable synthetic efforts.



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EVALUATION OF THE ELECTRONIC PROPERTIES OF CARBON(0)-BASED COMPOUNDS THROUGH GOLD CATALYSIS AND X-RAY STRUCTURE ANALYSIS

EL HELLANI Ahmad, BOUR Christophe, GANDON Vincent

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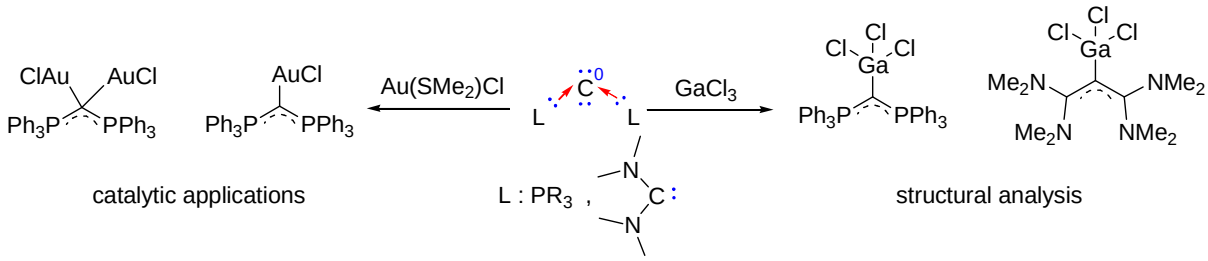
Most organic compounds which are stable in the condensed phase contain tetravalent carbon atoms, where all four valence electrons are being engaged in chemical bonds. On the other hand, the chemistry of divalent carbon(II) was only recognized after the isolation of a stable persistent carbene by Bertrand and co-workers in 1985.[1] Such products display one б-type lone pair orbital and are thus good ligands. Earlier on, concern was also paid to a new family of compounds, first reported in 1961 by Ramirez and co-workers.[2] They can be considered as divalent carbon(0) derivatives with two lone pairs at the central carbon, with a possibility of double coordination of two Lewis acids to this carbon. This feature was proposed by Kaska in 1973,[3] and verified later by the isolation of di-metalated adducts.[4] From 2006, these compounds were the centre of extensive theoretical investigations by Frenking,[5] which led to the isolation of new members of this family by Fürstner[6] and Bertrand.[7] This family is now referred to as “carbones”, of general formula CL_2 (L =PR_3 or carbene).

“Carbones” are still virtually unused in catalysis. Thus, we have decided to study these derivatives, especially in the field of gold catalysis, and to compare them with well-known ligands such as NHCs, phosphines and phosphites.[8] More recently, we were able to synthesize their corresponding $GaCl_3$ complexes and to rationalize their electronic properties through Gutman’s rule for Lewis acid/Lewis base adducts.[9, 10]



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SCREENING FOR SELECTIVE CHEMICAL LIGATION REACTIONS

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Discovery of selective coupling reactions is an important and difficult challenge in organic chemistry.
In order to study systematically selectivity towards different chemical functions present in biological media, we use two-steps model study. During the preliminary stages of screening we use the model reaction between a reactive function and different models of chemical functions presented in complex biological media. Screening is done via HPLC, which allows us to check quickly and efficiently the selectivity and the activity of defined functional group.
Functional groups, which exhibited selectivity on the first stage of the screening, are used in the second step of model study. This second step consists of reactivity tests versus tag-modified functional group in the model complex media (for instance, trypsin digest of lysosyme). During this step functional group of interest can be tested in real biological conditions and compared with other chemical groups described in literature as selective reagents for ligation reactions.
By these means we are intending to discover reliable selective ligation reactions that can be further tested on real biological objects.

WATER-SOLUBLE PHOSPHONATE-SUBSTITUTED BODIPY DERIVATIVES WITH TUNABLE EMISSION CHANNELS

Thomas BURA , Raymond ZIESSEL

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Over the past decade there has been a renewed interest in the design of highly luminescent dyes for use as probes in biological systems[1]. However, among the myriad of available synthetic fluorescent molecules (e.g., fluorescein, rhodamine, acridine, anthracene, phenanthrene, pyrene, quinoline, benzofuran, dansyl, naphthalimide, squaraines, cyanines and indacene) exhibiting high extinction coefficients, high quantum yields, narrow emission bands, and photostability[2]. However, many such dyes have limited utility due to poor solubility. For most biological applications both good water solubility and resistance to the formation of nonfluorescent dimer and higher aggregates (especially after conjugation to biological material) are essential. We focused our attention on the synthesis of water-soluble Bodipy dyes[3] (a cyanine derivative) on which different phosphonate fragments were introduced. Several probes highly water soluble were designed with emission wavelength spanning from 500 to 700 nm.[4]

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SYNTHESIS OF NEW CHIRAL CALIX-SALEN COMPLEXES AND APPLICATION IN ASYMETRIC HETEROGENEOUS CATALYSIS

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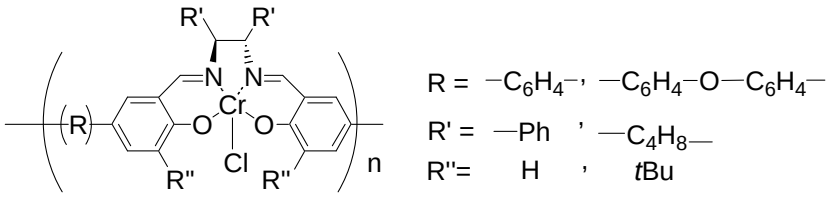
Hadath, Beyrouth, Liban.

Chiral salen complexes have been intensively studied because they constitute one of the main catalyst families that can be used to prepare valuable, highly enantioenriched synthons. In line with the idea of green chemistry, one major goal is now to establish efficient procedures for the recovery and reuse of such catalysts. Several heterogenization procedures have been described that involve the modification of the salen structures through covalent grafting or non-covalent interactions with various supports[1,2]. Another approach consists in the preparation of polymers from appropriately modified salen or corresponding complexes. In this context, the most common procedure involves polycondensation reactions between properly modified diamines and disalicylaldehyde derivatives[3].

We have thus developed a polymer synthetic methodology by polycondensation of various modified disalicylaldehyde derivatives with different chiral diamines[4]. Maldi-Tof analyses showed that the targeted polymers possessed a macrocyclic structure, named calixsalen, in a mixture of 2-, 3-, 4- and 5-mers.



General structure of calixsalen synthesized by polycondensation

These new chiral calixsalen derivatives have been complexed with chromium salts and tested as heterogeneous catalysts in asymmetric reactions (Henry Reaction). After reduction of the imine functions, the corresponding reduced catalysts will be complexed with copper salts and tested to promote the same transformation for a comparison of the efficiency of both catalysts type. Their recyclability will be examined.

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FACILE SYNTHESIS OF NEW RARE EARTH CATALYSTS AND THEIR APPLICATION FOR VARIED MICHAEL-TYPE REACTIONS

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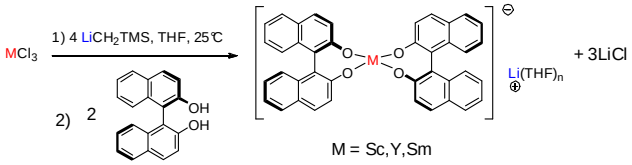
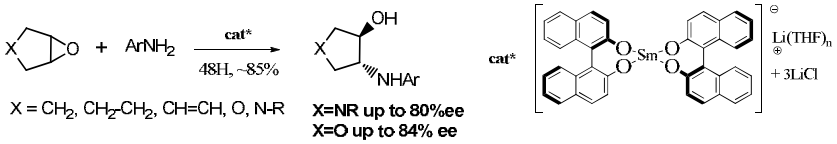
ICMMO, LCM, UMR 8182, Université Paris Sud 11, 91405 Orsay Cedex, France.

A new family of chiral lanthanide complexes derived from (S)-binaphthol has been firstly synthesised by a one pot procedure.

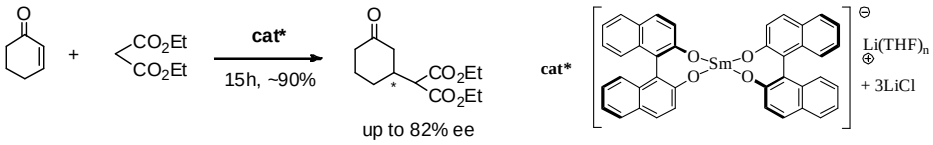


Three main advantages of this preparation are practiced. Using only commercially available substrates was firstly considered. Secondly, modification of these catalysts is highly accessible. At last, the potential of these catalysts to be a heterobimetallic/bifonctionnal catalyst which is a new concept for designing more efficient asymmetric catalyst.

Most lanthanide complexes were considering being a good Lewis acid. Hence, these complexes were primarily evaluated for the aminolysis of meso-epoxides and proved to be efficient enantioselective catalysts.



Asymmetric catalysts based on the concept of bifonctionnal catalysis have emerged as a particularly effective class, enabling simultaneous activation of multiple reaction components. In order to practicing this concept, Michael type reaction is chosen to demonstrate the heterobimetallic ability of this new family catalysis.



Excellent yields and moderate to good excess were obtained. Meantime, these results give the first evidence that our catalysts have a role both of Lewis acid and bronsted base. Inspired by these results, we are deciding to expand the broad of substrate. Including linear Michael acceptor and varies hetero-nucleophiles were evaluated.

We will present here our recent results on the characterization of these catalysts and their application mainly on the Michael type reaction.

BORANIL: A NEW EASILY ACCESSIBLE, VERSATILE AND HIGHLY FLUORESCENT DYE

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Julien Massue, Gilles Ulrich, Raymond Ziessel

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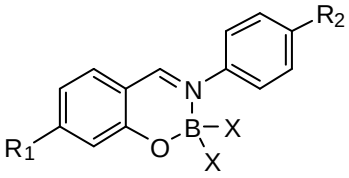
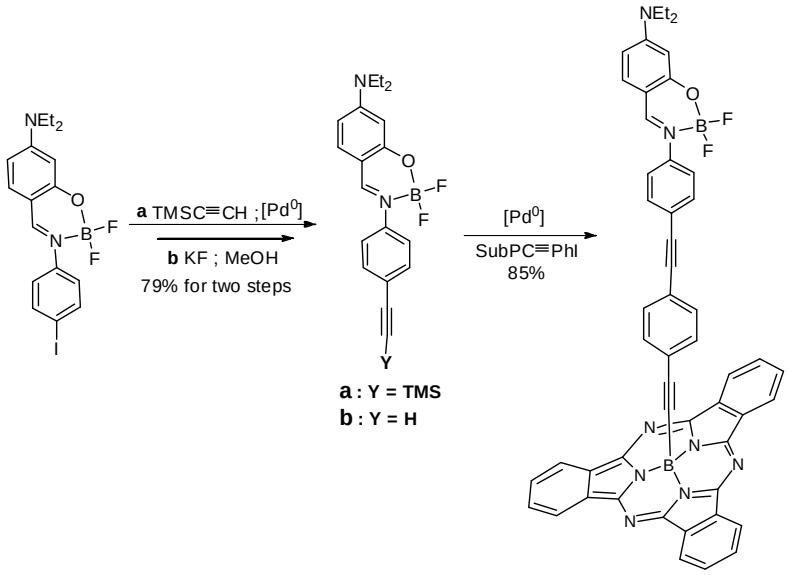
Complexation of a large variety of *Anils* (aniline-imines) with boron(III) precursors provides stable *Boranils*.[1-3] This method enables to obtain a new family of fluorophores with good yields, starting with cheap and commercially available compounds. Analysis of optical properties of these dyes reveals that the fluorescence stems from an intra-ligand charge transfer (ILCT) state with the best quantum yields reaching 90%.[3]



Interestingly *Boranils* are also chemically versatile and allows the design of a large variety of dyes with modulated properties. For instance, grafting of photoactive modules such as BODIPY, HBO borates complexes or subphthalocyanine fluorophores, opens the way to use *boranils* in multichromophoric systems.[3,4]



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DESIGN AND SYNTHESIS OF MODIFIED AMINOGLYCOSIDES: TOWARDS NEW ANTIBACTERIAL AND ANTIVIRAL AGENTS

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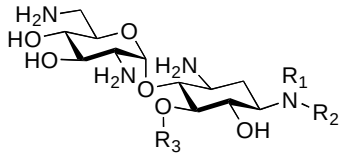
Aminoglycosides are broad-spectrum natural antibiotics well-known for their high potency against several bacterial strains. Therefore, these compounds have been used as drugs for more than fifty years. Their bactericidal properties come from their high affinity for the decoding site (A-site) of the 16S subunit of the bacterial ribosome.[1] Binding to this specific RNA loop causes a misreading of the bacterial messenger RNA, which induces the accumulation of erroneous proteins, leading to the pathogen's death.

Moreover, the field of application of these compounds is continuously expanding, as it appears they could be used for anticancer and antiviral therapy. Indeed, it was recently proved that aminoglycosides were actually able to selectively bind the Dimerization Initiation Site (DIS) of the HIV-1 RNA, which is involved in a key step of the viral replication.[2]

Unfortunately, the use of antibiotics has also led to the appearance of resistant bacteria. Propagation and multiplication of resistances among bacterial populations is now considered a major issue in hospital environment. However, the addition of a lateral chain at the N-1 position was assessed to allow aminoglycosides to bypass the defense mechanisms of resistant bacteria, as it turns out that such substituents already exist in some natural active antibiotics.



Aminoglycosides analogs

Considering the wide variety of targets aminoglycoside derivatives could interact with, we decided to develop a synthetic route to new active compounds. The design of such analogs would allow us to access a large library of substracts of clinical relevance.

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FROM NATURAL PRODUCTS TO COMMERCIAL COMPOUNDS FOR CROP PROTECTION

Alain De Mesmaeker

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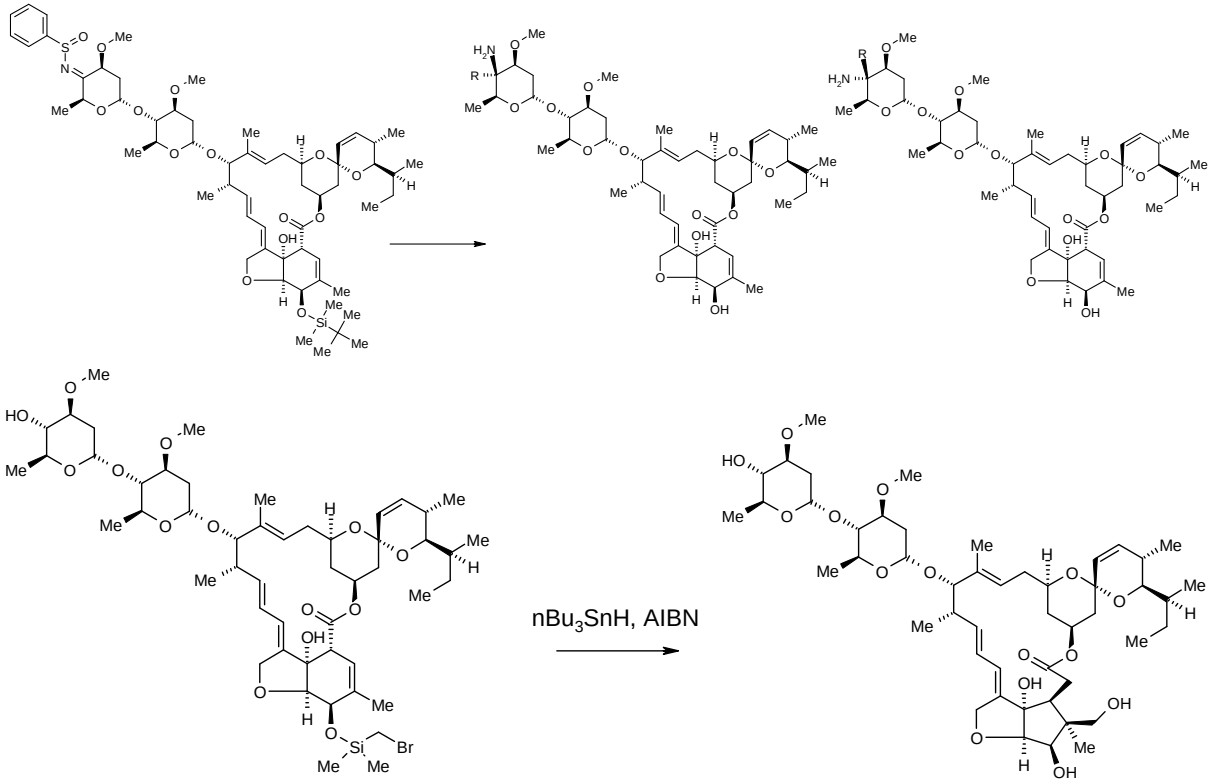
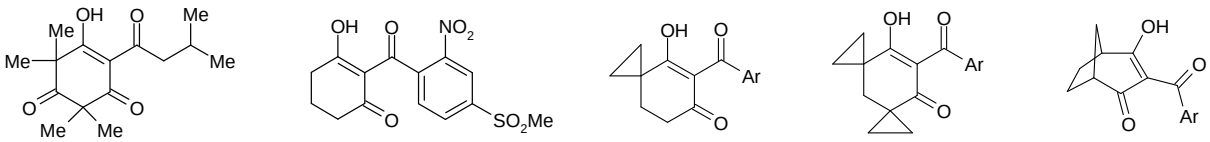
Although natural products are a very rich source of biologically active leads, generally they require further optimization through structural modifications to reach the desired performance profile.
We present two projects from Syngenta focusing on the optimization of natural products for Crop Protection. In the first example, we describe the structural modification of Mectins as potent insecticides, in particular the formation of a new C-C bond at C-4'' using addition of Grignard reagents to sulfoximines and a novel radical ring contraction reaction



In the second part of the presentation, we disclose the optimization of Leptospermone leading to novel selective broad spectrum herbicides for corn and sugar cane.



Leptospermone
Natural product

Mesotrione
Commercial herbicide

Novel analogues of Mesotrione

Thursday Morning

KOTERA Naoko

Cryptophane-based biosensor for sensitive zinc detection by ^{129}Xe MRI

MEDRAN NAVARRETE Vincent

Synthesis of a new [^{18}F]fluoropropylpyrazolo[1,5-*a*]pyrimidine acetamide for tracing the TSPO 18 kDa by positron emission tomography

MEDINA Florian

Gold (I) and (III) as catalysts for inter and intramolecular hydroamination of alkenes

MICHAUX Jérome

New *N*-hydroxynaphtalimides for aerobic oxidation

PRIEM Thomas

Design and synthesis of novel water-soluble prosthetic groups for ^{18}F labeling of peptides and proteins

CAILLOT Gilles

Furfual: a green and renewable precursor towards substituted aromatic compounds

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Dr. BERNIER David

Chemistry at Bayer CropScience: Innovation from concept to process

CRYPTOPHANE-BASED BIOSENSOR FOR SENSITIVE ZINC DETECTION BY ^{129}XE MRI

Naoko Kotera[1], **Nawal Tassali**[2], **Thierry Brotin**[3], **Patrick Berthault**[2], **Bernard Rousseau**[1]

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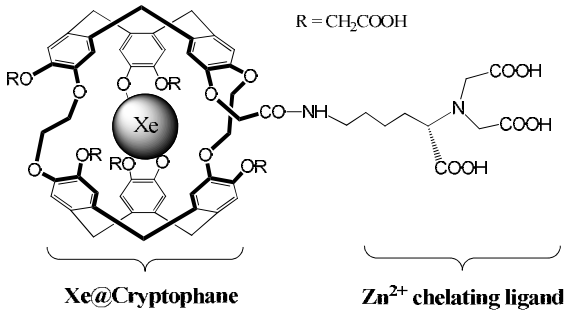
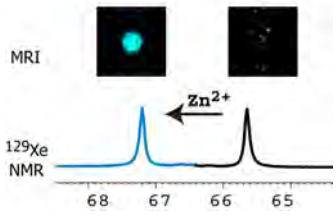
The divalent zinc cation, Zn^{2+}, is an indispensable and ubiquitous element of the body. A slight excess or lack in zinc ions can be a symptom or a cause of serious human afflictions, among which heart disease, diabetes, cancer and neurodegeneration. Detection of Zn^{2+} *in vivo* is therefore crucial for early diagnoses. Magnetic resonance imaging (MRI) is a powerful clinically-used modality for anatomic imaging. However, conventional MRI techniques rely on the observation of water protons and require the use of contrast agents as they suffer from reduced sensitivity. To the best of our knowledge, the detection threshold of free Zn^{2+} is 30 µM, a value above the total Zn^{2+} concentration of 20 µM in blood[1].

Here we propose the use of hyperpolarized ^{129}Xe nuclear magnetic resonance (NMR) for the sensitive detection of zinc ions thanks to a cryptophane-based biosensor. Hyperpolarization drastically improves the sensitivity by enhancing the nuclear spin polarization. The noble gas needs to be encapsulated in dedicated host systems bearing a ligand chelating the Zn^{2+} ions. Cryptophane cages are so far the best candidates to encapsulate xenon as they have shown the best affinities and can be easily functionalized[2].

This new biosensor was synthesized from a known hydrosoluble cryptophane and ^{129}Xe NMR results are very promising. Indeed, the chemical shift of encapsulated xenon significantly changes in presence of zinc. Thanks to this new method, we were able to detect as low as 100 nM of zinc, a sensitivity 300 times better than ever reached for *in vitro* detection.





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SYNTHESIS OF A NEW [^{18}F]FLUOROPROPYL PYRAZOLO[1,5-*a*] PYRIMIDINE ACETAMIDE FOR TRACING THE TSPO 18 kDa BY POSITRON EMISSION TOMOGRAPHY

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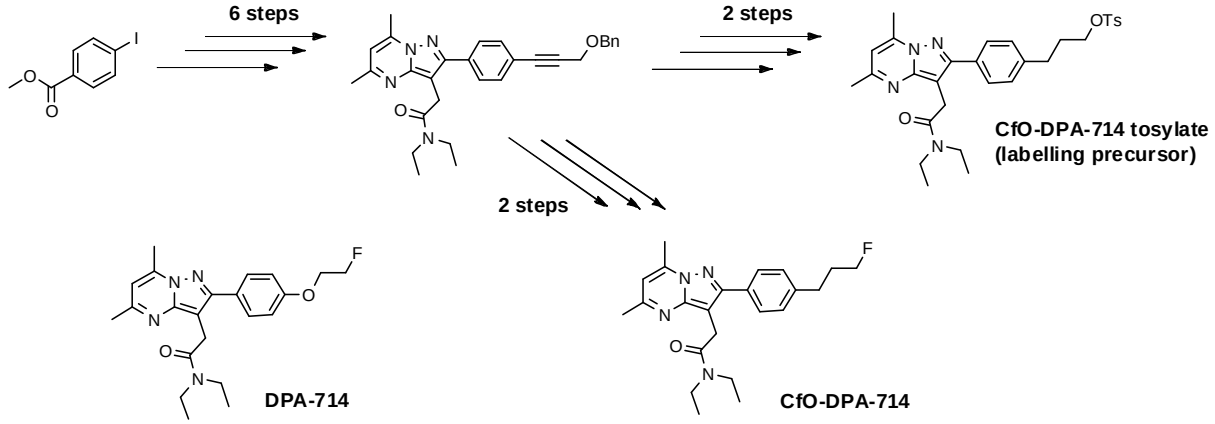
***Introduction*:** Most of the neurodegenerative pathologies such as Parkinson's or Alzheimer's disease (AD) are accompanied by inflammation involving activation of microglia cells, which overexpress the translocator protein 18 kDa (TSPO, formerly known as the peripheral benzodiazepine receptor (PBR)). Because it correlates with the extent of inflammation, this protein is a potential target for neurodegenerative disorders detection. Positron Emission Tomography (PET), an *in vivo* molecular imaging technique involving compounds labelled with a short-lived positron-emitting radioisotope, could be useful in this respect. This PhD work aims at developing radiotracers as TSPO-specific ligands which are labelled with fluorine-18 ($T_{1/2}$ = 110 min).

***Objectives and Results*:** Our work consists in designing some new TSPO radioligands belonging to the pyrazolo[1,5-*a*]pyrimidine acetamide class. In this area, a compound named [^{18}F]DPA-714 was synthesized by our group in 2008 [1]. However, beside its promising *in vitro* biological evaluation as a selective TSPO ligand, recent *in vivo* studies revealed that this molecule, which features a 2-[^{18}F]fluoroethoxyphenyl group, undergoes rapid metabolization. This partly leads to the formation of fluorine-18-labelled metabolite that results from *O*-dealkylation [2]. To circumvent the latter drawback, a new pyrazolo[1,5-*a*]pyrimidine acetamide called CfO-DPA-714 was prepared, in which the oxygen atom connecting the phenyl ring and the fluoroethyl chain is replaced by a methylene group. Its synthesis, and that of the precursor for labelling, were both achieved in 8 steps from methyl 4-iodobenzoate. It notably features a Sonogashira cross-coupling as a key step.



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GOLD (I) AND (III) AS CATALYSTS FOR INTER AND INTRAMOLECULAR HYDROAMINATION OF ALKENES.

Florian Medina, Christophe Michon, Francine Agbossou-Niedercorn

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Equipe Catalyse, Chiralité et Chimie Fine
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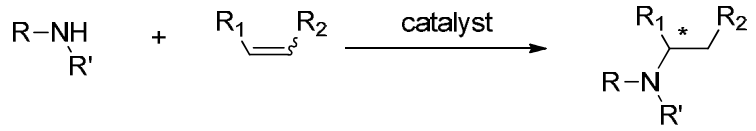
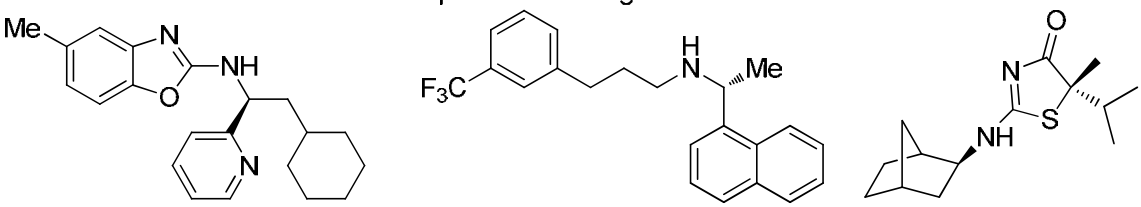
Reactions between primary or secondary amines with alkenes allow formation of secondary or tertiary amines which are useful building blocks for the synthesis of pharmaceutical compounds.[1] Catalysis can offer highly selective and atom-economic reactions but challenges remain for some reactions like the synthesis of amines.



Amines as compounds of biological interest



Ontazolast (oncology) Cinacacet (hyperthyroid) AMG 221 (anti-diabete)

Supported by ANR grant HYDROAM[2], we've been developing new methods for amine syntheses since 2009. First, we've studied Copper (I) and (II) catalysts for inter- and intramolecular hydroamination of unactivated alkenes and the role of the metal was discussed in detail.[3]
More recently, we've focused our attention on Gold (I) and (III) catalysts applied to inter- and intramolecular hydroamination of alkenes which were activated or not. Our last results will be discussed and compared with close examples from the literature. First, reactivity scope and limits of these catalysts will be explained. Second, mechanistic investigations will be highlighted focusing on the role of additives, on the synthesis of potent intermediates as well as on kinetic studies.[4] The presence of parallel reactions along these chemical transformations will be discussed.

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