Program

Thursday, 16 May 2019

08.45 Opening of the symposium's reception desk & Welcome Coffee

09.30 Opening of the 14. Freiburger Symposium
Address of welcome by
Dr. Roger Marti, HTA-FR
Dr. Bernhard Urwyler – Board Director of DIAC
Dr. Remo Gamboni – Introduction to the program

09.45 *Optimization of Catalysts with virtual High Throughput Screenings, Genetic Algorithms, and Machine Learning*
Dr. Marek P. Checinski, Founder and CEO of CreativeQuantum GmbH, Berlin, Germany

10.30 *Tackling Challenges in Industrially Relevant Homogeneous Catalysis: The Catalysis Research Laboratory (CaRLa), an Industrial−Academic Partnership*
Dr. Thomas Schaub, BASF SE, Ludwigshafen, Germany

11.15 *Olfactory Pleasures: How to Access Kg-Quantities of a Thiadiazole without Lawesson Reagent?*
Dr. Gabriel Schäfer, Idorsia Pharmaceuticals Ltd., Allschwil, Switzerland

12.00 Lunch break and Poster Session

14.00 *Use of Catalysis in Fine Chemical Industry – From Research to Manufacturing – Case Study*
Dr. Bastien Monnerat, Syngenta Crop Protection, Monthey, Switzerland

14.45 *Biocatalysis in the Flavor & Fragrance Industry*
Dr. Fredi Brühlmann, Firmenich SA, Geneva, Switzerland

15.30 Coffee break

16.00 *(Swiss) Innovations in Selective Heterogeneous Hydrogenations – from the 1950s to the Present Day*
Dr. Jonathan Medlock, DSM Nutritional Products, Kaiseraugst, Switzerland

16.45 Keynote Lecture: *Catalysis - an important tool in Siegfried's offering*
Dr. Jürgen Roos, CSO, Member Executive Committee Siegfried AG, Zofingen, Switzerland

19.00 Aperitif and Symposium Dinner

Friday, 17 May 2019

08.30 Opening of the symposium's reception desk & coffee

09.00 Sandmeyer Award Lecture 2019
Arsenic and other Geogenic Contaminants in Groundwater – a Global Challenge
Dr. Andreas Voegelin and **Dr. Stephan Hug**, Eawag, Dübendorf, Switzerland

10.00 Sandmeyer Award Lecture 2018
Design, Synthesis and Biological Evaluation of Strigolactone and Strigolactam Derivatives for Potential Crop Enhancement Applications in Modern Agriculture
Dr. Alain De Mesmaeker and **Dr. Raymonde Fonné-Pfister**, Syngenta Crop Protection Research, Stein, Switzerland

10.45 Coffee break

11.00 *Enzyme Catalysis in the Synthesis of Ipatasertib, AKT Inhibitor*
Dr. Hans Iding, F. Hoffmann-La Roche Ltd., Basel, Switzerland

11.45 *Application of Transition-metal Catalysis and Biocatalysis as State-of-the-art Technologies in the Manufacture of a Key Intermediate of Entresto*
Dr. Florian Kleinbeck, Novartis Pharma AG, Basel, Switzerland

12.30 Lunch break

14.00 *Catalysis at Johnson Matthey: On the Cost Effective Use of Catalysis for Complex Synthesis*
Dr. Antonio Zanotti-Gerosa, Johnson Matthey, Cambridge, UK

14.45 *Engineering of 3D Printed Catalytic Reactors*
Prof. Simon Kuhn, KU Leuven, Belgium

15.30 *Catalysis Engineering for Sustainable Technologies*
Prof. Dr. Javier Pérez-Ramirez, ETH Zürich, Switzerland

16.15 Closure of the Symposium

Optimization of Catalysts with virtual High Throughput Screenings, Genetic Algorithms, and Machine Learning

Marek P. Checinski

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Recent success of advanced atomistic computational chemistry in predicting chemical reactivity, or materials properties, rendered them a valuable and accepted means to tackle problems in academia and nowadays in industry. The development of new simulation methods and new computer architectures enables an enormous improvement of the productivity of research and development of new chemical synthesis.
Approaches like virtual high throughput screenings are highly scalable and allow a deep and very fast insight into the impact of new promising system modifications. These improvements can be accessed with much less time, material, and staff. Thus, the time to application and risk of new synthesis development can be decreased significantly.
The field of computational chemistry is diverse and offers a number of inherently different approaches suitable for different problems, targeting isolated molecules in the gas phase to extended solids, polymers and liquids. Simulating not only energy and derivative properties, but adding a time domain to the problem, accesses the dynamics of the system of interest. New methods are enabling the access to molecular level morphology and dynamics of a materials and catalysts, which can have a crucial impact on activity and stability.
We present the application of modern quantum mechanics in chemical reaction analysis/optimization. We show how hundreds, or thousands of new reactions or material derivatives can be investigated in few days at high accuracy with virtual high throughput screenings and modern optimization algorithms. We present how material morphology and dynamics looks like on atomic level, and what we can learn from that new insight. As well we show how machine learning research is reaching the research and development in chemistry.
Finally, we present how two recent R&D projects in conventional catalysis and electro catalysis leads to two new patents, starting from the simulation approach and keep the focus only on the promising experiments within a few months.

Tackling Challenges in Industrially Relevant Homogeneous Catalysis: The Catalysis Research Laboratory (CaRLa), an Industrial−Academic Partnership

Thomas Schaub

BASF SE, Ludwigshafen, Germany

Industrial-academic collaborations are broadly used for the development of new industrial processes. To achieve a strong and deep collaboration in the field of homogenous catalysis, BASF and the University of Heidelberg have been running the Catalysis Research Laboratory (CaRLa) together in Heidelberg since 2006. This lecture highlights the concept of this laboratory and our experiences over the last few years in this joint laboratory. How this collaboration works is explained in more detail using three selected projects: sodium acrylate based on CO_2, the selective decomposition of cyclohexylhydroperoxide to cyclohexanone and the asymmetric amination of ketones with NH_3/H_2

Olfactory Pleasures: How to Access Kg-Quantities of a Thiadiazole without Lawesson Reagent?

Gabriel Schäfer

Idorsia Pharmaceuticals Ltd., Allschwil, Switzerland
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To avoid the handling of Lawesson reagent or other thiation agents on scale, a new robust route to a thiadiazole building block needed to be developed. The key to success was the use of a commercially available amino-thiadiazole, which was converted into the desired building block via a sequence of Sandmeyer bromination and Suzuki coupling. The different parameters of the Pd-catalyzed coupling have been studied in detail, and the learnings from these studies allowed the reaction to be performed under mild conditions at room temperature.

Use of Catalysis in Fine Chemical Industry – From Research to Manufacturing – Case Study

Bastien Monnerat

Syngenta Crop Protection Monthey SA

Catalysis plays an important role and is widely used in the manufacturing of both chemical intermediates and active ingredients at Syngenta. Catalytic processes involving single phase, two phases as well as three phases liquid-solid-gas are implemented at large scale in several sites of production around the world and particularly at Monthey.
The presentation will cover the main important steps during the research, the development and the industrialisation of a three-phase heterogeneous chemical reaction taking place in the synthesis of a key intermediate of one of Syngenta's fungicide. Catalysts screening, process development as well as chemical reaction engineering aspects, process safety, optimisation and operational challenges at industrial scale will also be covered during this presentation.

Biocatalysis in the Flavor & Fragrance Industry

Fredi Brühlmann

Firmenich SA, Geneva, Switzerland

The flavor and fragrance industry exploits various approaches for accessing a large and diverse palette of ingredients that serve the creative work of flavorists and perfumers. Botanical, animal or microbial raw materials traditionally were important sources for ingredients, although they are no longer the primary source. Additionally, many companies utilize petro-based synthetic chemistry for ingredients within given cost and regulatory constraints. More recently, biotechnology has enabled opportunities for development of new ingredients and novel routes to known ingredients & intermediates. The use of biosynthetic tools both in vivo as well as in vitro enables a growing array of chemistries under benign conditions often in combination with synthetic chemistry. Powerful engineering tools allow tackling stability, productivity, or selectivity issues of biocatalytic systems by tuning biocatalysts for performance under process conditions. Consequently, biotechnology continues to fuel the development of innovative processes and products that transform the F&F industry.

(Swiss) Innovations in selective heterogeneous hydrogenations – from the 1950s to the present day.

Jonathan Medlock

DSM Nutritional Products, Kaiseraugst, Switzerland
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Vitamins are essential for human and animal life and can have other applications e.g. as antioxidants. Since production quantities can exceed 10,000 t/a, even small improvements in production efficiency can yield high benefits. Selective hydrogenation reactions are crucial for the cost-effective production of vitamins.
In this presentation we will describe the development of selective hydrogenation reactions, in particular the reduction of alkynes to alkenes, for the synthesis of vitamins, carotenoids and aroma compounds. Starting from the well-known “Lindlar catalyst” we will highlight recent developments/improvements including our success in developing a lead-free, continuous semi-hydrogenation process using 3D-printed reactor technology.

Arsenic and other Geogenic Contaminants in Groundwater – a Global Challenge

Andreas Voegelin and Stephan Hug

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Groundwater is the main drinking and irrigation water resource in many regions around the world. Natural contamination of groundwater with geogenic contaminants (e.g., arsenic, manganese, fluoride, uranium, thallium) poses a major health threat to hundreds of millions of people worldwide. Especially problematic is arsenic due to its abundance and toxicity. To find solutions to this global challenge, it is essential to not only understand the biogeochemical mechanisms that control the release of geogenic contaminants and their fate in soils and aquifers, but also to predict areas at risk of contamination and to design strategies for water treatment and for minimizing contaminant transfer into the food chain. Our team addresses these challenges by combining fundamental and applied research as well as experimental and modeling approaches, thereby contributing to the mitigation and prevention of public health hazards related to geogenic contaminants.

Design, synthesis and biological evaluation of Strigolactone and Strigolactam derivatives for potential Crop Enhancement applications in modern agriculture

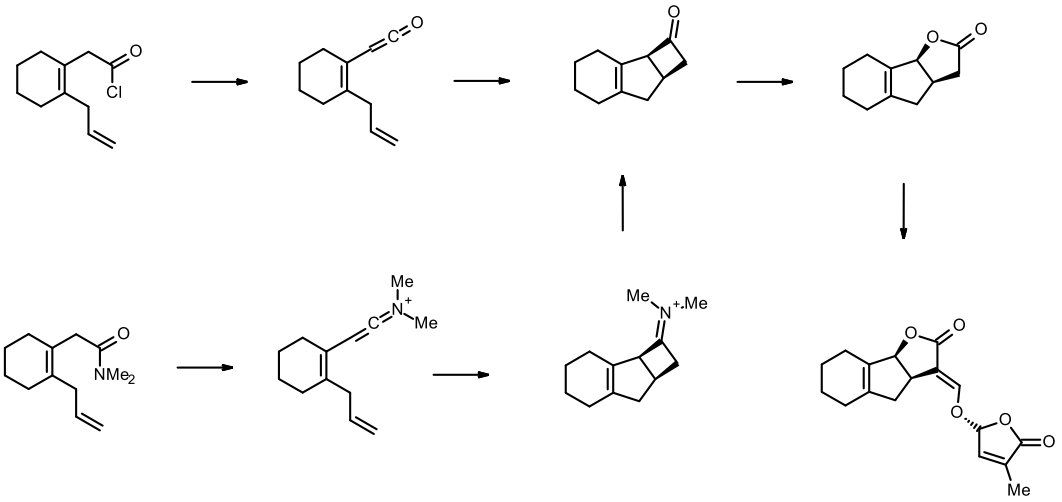
Raymonde Fonné-Pfister,[a] Claudio Screpanti,[a] Harro Bouwmeester,[b] Alain De Mesmaeker [a]

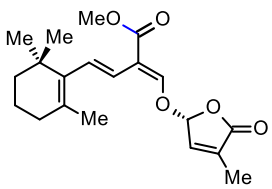
[a] Syngenta Crop Protection, Research Chemistry, CH-4332 Stein, Switzerland
[b] University of Amsterdam, Faculty of Sciences, Science Park 904 Amsterdam, Netherlands

Strigolactones are the last discovered phytohormones. Among the numerous roles that strigolactones play in plant growth and development, they have been shown to control the root and shoot architecture, having significant consequences on plant adaptation to environmental conditions and abiotic stress. In addition, strigolactones signaling might influence the harvest yield of field crops.

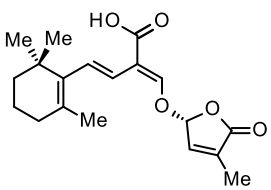
We describe the stereoselective synthesis of natural strigolactones as well as of their derivatives displaying improved biological performance using ketene-iminium salts as key intermediates. We disclose also the synthesis of non-canonical strigolactones as methyl carlactonoate and carlactonic acid. In addition, we illustrate the use of ketene-iminiums intermediates in other Crop Protection projects leading to small rings derivatives as well as to aromatic compounds.

Scheme





methyl-carlactonoate



carlactonoic acid

Enzyme Catalysis in the Synthesis of Ipatasertib, AKT Inhibitor

Hans Iding

F. Hoffmann-La Roche Ltd., Basel, Switzerland

Biotransformations have the potential to deliver enantiopure active pharmaceutical ingredients (API) in an economic fashion. The highly efficient asymmetric synthesis of Akt kinase inhibitor ipatasertib generates all three stereogenic centers using bio- or metal catalysis: (i) a kinetic resolution of the starting material using a nitrilase gives access to the (R)-nitrile; (ii) a diastereoselective biocatalytic reduction of a sterically demanding bicyclic ketone creates the (R,R)-alcohol; (iii) the side chain of the synthesis is based on a Ru-catalyzed asymmetric hydrogenation of a vinylogous carbamic acid to produce (S)-α-aryl-β-amino acid. All three catalytic steps proceed with high stereoselectivity.
The presentation focuses on the process development of the two biocatalysis steps highlighting the opportunity to tune the enzymes by protein engineering. The key features of the enzymes – enantioselectivity, stability and activity – have been improved.

Application of Transition-metal Catalysis and Biocatalysis as State-of-the-art Technologies in the Manufacture of a Key Intermediate of Entresto

Florian Kleinbeck

Novartis Pharma AG, 4002 Basel, Switzerland

Entresto® is a novel oral treatment for patients suffering from chronic heart failure that combines two active pharmaceutical ingredients – sacubitril as neprilysin inhibitor and valsartan as angiotensin II receptor blocker – in a single chemical entity. In contrast to valsartan, which has been an established API for already many years, a manufacturing process suitable for large-scale commercial production had to be developed for sacubitril. The use of both transition-metal catalysis and biocatalysis as state-of-the-art technologies was crucial to efficiently build up the molecular structure of sacubitril and achieve the defined performance targets required for the commercial manufacturing process.

Catalysis at Johnson Matthey: On the Cost Effective Use of Catalysis for Complex Synthesis

Antonio Zanotti-Gerosa

Johnson Matthey, Cambridge, UK

Catalysis offers a great opportunity for cost-effective, sustainable routes to the complex synthetic targets of the fine chemicals, pharmaceutical, agro and F&F spaces. However, a number of hurdles must be overcome to achieve the most efficient processes, including optimization of catalyst loadings, catalyst commercial availability, catalyst recycling (when possible), understanding of the impact of reaction conditions and substrate purity on the reaction. The talk will focus on hydrogenation and transfer hydrogenation using homogeneous and heterogeneous catalysts. New research directions and opportunities associated with the use of achiral, highly active homogeneous catalysts will be discussed (e.g. ester hydrogenation).

Engineering of 3D printed catalytic reactors

Simon Kuhn

KU Leuven, Belgium

The impact of digital fabrication on the field of catalytic technology and chemical engineering is steadily increasing. Additive manufacturing, also referred to as 3D printing, closes the gap between theory and experiment, by enabling accurate fabrication of geometries optimized through modelling and the experimental evaluation of their properties. This rapid and seamless transition between digital data and physical objects will be of increasing value in streamlining both research and manufacture of reactors and structured catalysts, enabling creative contributions from researchers with a core expertise in fields such as catalytic technology and chemical engineering. The introduction of flow chemistry at the lab scale would enable the exploration and scale-up of a broader range of synthesis conditions (e.g. not deemed safe in batch reactors) and therefore enable protocols and products currently not accessible at the production scale.
Nevertheless, improvements are still needed, for instance in decreasing printing costs, controlling the surface roughness of reactor internals, standards and standardized test protocols, etc. A broader impact of 3D printing in reaction engineering would be facilitated as well by increasing the thermal and chemical compatibility of the build materials.
The goal of this contribution is to highlight the interaction at the crossroads of chemistry, materials science, and reactor engineering to implement digital fabrication in the field of catalytic technology and chemical engineering.

Catalysis Engineering for Sustainable Technologies

Javier Pérez-Ramírez

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Heterogeneous catalysis is quite possibly the most relevant discipline in the chemical industry, spearheading improvements in process sustainability by improving the exploitation of raw materials, enabling the transition from fossil to renewable feedstocks, reducing energy consumption, and minimizing the environmental footprint. To confront these challenges head on, this vibrant discipline is becoming increasingly design-driven, a shift which is facilitated by the availability of increasingly powerful tools that enable the continued development of fundamental knowledge over different time and length scales. The design of a heterogeneous catalyst, a dream not long ago, is becoming a reality. In this talk, I will discuss recent examples from my laboratory to illustrate how this intellectual growth in the understanding of catalyzed processes can kindle revolutionary technological advancements.