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Conference Report

SCS-Syngenta Symposium 2015: Chirality, Upsides for Chemical Innovation

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In mid-October 2015, the third Swiss Chemical Society (SCS) – Syngenta symposium 'Chirality: Upside for Chemical Innovation' was hosted at Syngenta R&D Center in Stein, Switzerland. Building on the success of the first two joint symposia on *Catalysis* in 2011 and *Fluorine* in 2013, this third event added to the reputation for excellent quality of science and knowledge sharing between different industries and academia.

In his opening remarks, Dr. ***Gerardo Ramos***, Head of Syngenta Crop Protection Research & Development (CP R&D), reminded everybody that "chemistry has significantly improved people's quality of life, and that Syngenta is proud to continue the tradition of making significant advances in chemistry to ensure sustainable agriculture and help meet the global food challenge we are now facing". He also reminded the audience that the synthesis of chiral agrochemicals on an industrial scale had long been considered a pipe dream. In the 1990s, the synthesis of herbicide (S)-Metolachlor by iridium-mediated hydrogenation was developed by Ciba-Geigy in Switzerland (a Syngenta legacy company) in collaboration with Solvias and remains the biggest asymmetric process in the world by tonnage. This symposium took the opportunity to review the latest advances in chirality across different fields.

Knowledge Sharing

The symposium was designed as an interactive knowledge-sharing platform between Syngenta, the different Swiss industries, postgraduate students and leading academics in the field of chirality. This one-day event brought together more than 180 participants from Switzerland, France and Germany for a series of ten cutting-edge lectures and a poster session, where latest results and breakthroughs were discussed. At the end of this intense day, Dr. ***Camilla Corsi***, Head of Chemical Research, concluded that "we have all enjoyed an wonderful day of exiting science". Three poster prizes were awarded to ***Lukas Delvos*** (TU Berlin, Germany), ***Michael Lüscher*** (ETH Zürich, Switzerland) and ***Julia Pedroni*** (EPF Lausanne, Switzerland) for their outstanding results and presentation skills.

Prof. ***Peter Kündig***, Professor at the University of Geneva, Switzerland, and president of the Swiss Chemical Society (SCS) was equally enthusiastic about the outcome of the joint symposium: "This was an excellent day of science, with outstanding scientists and excellent speakers presenting to a full house; the symposium was perfectly organized and was exciting from start to finish". The SCS-Syngenta symposium 2017 is now being developed and more information will be available by early 2017 on the SCS-Syngenta website.

Dr. Alain de Mesmaeker and Prof. Peter Kündig

Morning Session – Chairman: Prof. Peter Kündig (University of Geneva, President of the Swiss Chemical Society)

Prof. ***Ben Feringa*** (University of Groningen, NL) opened the day with a lecture on asymmetric catalysis and in particular monodentate phosphoramidite ligands for the addition of organozinc-, organomagnesium- and organolithium reagents to electrophiles. Complete regio- and enantioselectivity were achieved in Michael-addition to α,β-unsaturated carbonyl compounds and also in SN2/SN2' reactions. He went on to present a new catalytic method for the direct cross-coupling of organolithium reagents with aryl halides using classical palladium catalysis under well-defined solvent and temperature conditions. The lecture concluded with a detour in supramolecular chemistry and the amplification of chirality using light-induced molecular switches.

Prof. ***Oliver Trapp*** (University of Heidelberg, D) gave a thought-provoking talk on foil-induced Coulomb explosion imaging and how this has been used in his laboratory to visualize directly the sense of chirality of enantiopure (*R*,*R*)-2,3-dideuterooxirane and confirm unambiguously the absolute configuration of (+)-glyceraldehyde.[1]

Dr. ***Alexander Mayweg*** from Roche then presented an overview on the importance of chirality in biological systems. Small-molecule drugs are designed to target proteins and consequently, enantioselective recognition of the binding partners is often observed. Chirality is now seen to be crucial to escape the flat aromatic chemical space associated with non-specific binding of drug candidates and he presented an example where this was successfully applied to BACE1 inhibitors to target Alzheimer's disease.

Next Dr. ***Christoph Taeschler*** from Lonza demonstrated why chirality is generally considered to be a curse by the process chemist and how Lonza has tackled this challenge over the years exemplified by the production of L-carnitine, a food supplement. From the different routes that were initially proposed, the new LC10 process relies on a ruthenium-catalyzed asymmetric hydrogenation of a keto-ester. An intensive process development program was carried out and the optimal process in now used in production with up to 98% *ee* for the asymmetric step.

Prof. ***Manfred Reetz*** (University of Marburg, D) followed with a talk on directed evolution of enzymes and the remarkable levels of stereocontrol that can be achieved for hydrolases, monooxygenases and reductases in combination with very challenging substrates. Different strategies were presented to quickly develop optimized mutant libraries.[2] Iterative saturation mutagenesis is most efficient, in particular combined with multi-residue site mutation using a reduced amino acid alphabet. Finally, triple code saturation mutagenesis is a good compromise between structural diversity and screening effort.[3]

Afternoon Session – Chairman: Dr. Alain de Mesmaeker (Principal Fellow, Syngenta Crop Protection R&D)

Prof. ***Scott Miller*** (Yale University, USA) presented an overview of his work on small peptides as catalysts for a variety of asymmetric transformations. This was applied on complex macromolecules such as Vancomycin[4] and Teicoplanin, where a variety of peptides were used to selectively functionalize different hydroxyl groups or halogenate a single site out of several possibilities on aromatic rings. These findings were later applied to the control of atropisomers in the synthesis of quinoxazolinones.[5]

Dr. ***Eric Francotte*** (Novartis, Switzerland) then explained how the power of molecular recognition using natural chiral polysaccharides, such as cellulose triacetate, has been exploited to develop chiral chromatography over the last forty years. This led to the development of silica-coated immobilized polysaccharide derivatives, which are now routinely used for the separation, on small and large scale, of compounds in drug discovery programs.

Dr. ***Edouard Godineau*** (Syngenta, Switzerland) gave then an insight on chirality in agrochemicals where chiral molecules represent 30% of commercialized active ingredients, but only 10% are sold as non-racemic compounds. Lower application rates resulting in reduced environmental impact is a desirable feature of an agrochemical, but achieving this with low cost of goods is often a challenge. Catalytic, enantioselective methods have proven to be successful in the synthesis of (S)-Metolachlor by asymmetric hydrogenation on a multi-ton scale.

Prof. ***Jérôme Lacour*** (University of Geneva, Switzerland) described his latest results on the use of stereogenic nitrogen atoms. Tröger bases are known to racemize rapidly under a wide range of conditions, but reaction with diazocarbonyl derivatives, followed by an unreported oxidative loss of a CH_2 unit, led to the synthesis of functionalized Tröger base derivatives with excellent enantiospecificity.[6]

Prof. ***Eric Jacobsen*** (Harvard University, USA) concluded the day with a lecture on anion binding chemistry. Taking advantage of the well-established anion-binding properties of ureas and thioureas, dual activation of electrophiles and nucleophiles has been studied in the past. Examples included halide, enolate and imidate anion-binding.[7] The binding mode of the catalyst in the ground state and transition state plays a key role in defining its properties and activity. Detailed mechanistic analysis has allowed new strategies for the design of new glycosylation catalysts.

The SCS-Syngenta symposium organizing committee is Dr. Camilla Corsi (Head Chemical Research, Syngenta Crop Protection R&D), Dr. Alain de Mesmaeker (Principal Fellow, Syngenta Crop Protection R&D, Chemical Research), Dr. Jérôme Cassayre (Head Insecticide Chemistry, Syngenta Crop Protection R&D), Dr. Mathilde Lachia (Team Leader, Syngenta Crop Protection R&D, Chemical Research), Dr. Sarah Sulzer (Group Leader, Syngenta Crop Protection R&D, Chemical Research) and Prof. Peter Kündig (University of Geneva, Swiss Chemical Society President).

Symposium website: *http://www.syngenta.com/country/ch/de/Forschung/forschunginstein/symposium/Pages/Symposium.aspx*

More photos: *https://vimeo.com/142715077*

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