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Conference Report

Solvias Science Day 2008

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The major goal of the Solvias Science Day is the presentation and discussion of new strategies, concepts, and solutions in the field of synthetic and analytical chemistry by leading experts from universities, the life science industry, and by Solvias' scientists. The Science Day 2008 took place on November 18, 2008. About 120 colleagues from research, development and production in the life science and fine chemicals industry attended the four sessions with eight presentations. This occasion was also a suitable setting to honor the winner of the Solvias Ligand Contest 2008. Looking back, the event was clearly a success: All comments from customers and colleagues showed us that the seventh Solvias Science Day achieved its goals concerning science, information and – yes – also marketing the Solvias services.

The presentations can be grouped into the three categories: 'Synthetic and Catalytic Methodologies', 'Analysis of Biologicals', and the Award Lecture.

Synthetic and Catalytic Methodologies


Antonio Togni

Prof. ***Antonio Togni*** (ETH Zürich) started off with a lecture entitled 'Pursuing New Catalytic Functionalization Reactions'. In his lecture he illustrated the approach he has followed in the past few years to develop and study new catalytic reactions for the enantioselective formation of carbon heteroatom bonds. In a first part, he explained how the first transition-metal-catalyzed enantioselective fluorination reaction was discovered and developed to a preparative level. Furthermore, he described mechanistic studies which led to a concept permitting the extension of this methodology to the formation of C–Cl, C–S and C–O bonds with good to high levels of enantioselectivity. In a second part, Prof. Togni described the search for a suitable reagent for the catalytic electrophilic trifluoromethylation based on the concept described above. Indeed a hypervalent trifluoromethyl iodine compound was found well suited to allow not only the α-trifluoromethylation of carbonyl compounds but also of arenes, thiols and even phosphines. The lecture ended with a short discussion of the mode of action of a nickel–Pigiphos catalyst, one of the rare examples of a chiral triphosphine, which is effective in the activation of cyanoolefins towards secondary amines and phosphines as nucleophiles.

Prof. ***Karl Gademann*** (ETH Lausanne) talked about the synthesis and immobilization of natural products under the title 'Natural Product Hybrids: Synthetic … and on the Rocks'. In a short introduction he explained his motivation to utilize natural products for the understanding of biological processes on a molecular level and to apply hybridization of natural products as a powerful strategy to combine different bioactivities or mechanisms in one compound. In a first part of his lecture, Prof. Gademann described the preparation of antimicrobial surfaces *via* natural product derived hybrids. In this work, surface binding was ensured by the catechol derived from the siderophore anachelin, a PEG spacer bestowed the surface with protein and cell-resistant properties, and the glycopeptide vancomycin was responsible for the antibiotic activity. Immobilization of these hybrids on TiO_2 ("on the rocks") allows for the generation of antimicrobial surfaces, which present an appealing strategy for the prevention of hospital-acquired infections. In the second part of the lecture, the total synthesis and biological evaluation of anguinomycin C was described, using modern metal mediated transformations such as a Cr(III) catalyzed hetero Diels Alder reaction, hydrozirconation/Negishi cross coupling and a B-alkyl Suzuki Miyaura coupling. This synthetic work permitted biological studies demonstrating that anguinomycin C is an inhibitor of CRM1 mediated nuclear export.


Karl Gademann


Manfred Reetz

Prof. ***Manfred Reetz*** (MPI Mühlheim, Germany) talked about 'Directed Evolution of Enantioselective Enzymes as Catalysts in Organic Chemistry'. First he briefly summarized work he started in the 1990s where a fundamentally new approach to asymmetric catalysis was developed, namely the directed evolution of enzymes. This approach is based on the combination of gene mutagenesis, expression and screening. Several such cycles are transversed, thereby building up evolutionary pressure – a sort of Darwinism in the test-tube. Prof. Reetz then discussed in more detail how this methodology was developed further in order to render this type of protein engineering more effective by reducing the number of experiments. In particular, he focused on iterative saturation mutagenesis where selected amino acids around the complete binding pocket of an enzyme are randomly replaced in a combinatorial manner. Such focused enzyme libraries are then systematically screened for properties such as enantioselectivity, substrate scope or thermal stability. Prof. Reetz demonstrated the power of these new strategies on the examples of an epoxide hydrolase and a Bayer-Villigerase where very high levels of enantioselectivities where reached with relatively few experiments.

Prof. ***Paul Knochel*** (LMU München, Germany) discussed the application of 'Functionalized Magnesium and Zinc-Organome-

tallics for Organic Synthesis'. Organometallic Mg and Zn reagents are widely used in organic synthesis but their application is often restricted due to a rather low tolerance of functional groups. In the last decade, Prof. Knochel has developed a number of polyfunctional organometallics which overcome many of these limitations. In a first part of his lecture, he described how the presence of LiCl allows a smooth insertion of metals like Zn, Mg or In into the C–X bond of various organic halides, providing a wide variety of stable polyfunctional organometallics. This method is very well suited for the preparation of a range of new heteroarylmagnesium species starting from cheap chlorides which can then be used for Pd-catalyzed coupling reactions. In a second part, the development of soluble tetramethylpyrrolidine magnesium bases for the preparation of polyfunctional magnesiated and zincated heterocycles was described. This strategy allows the deprotonation and functionalization of a variety of arenes and heteroarenes with high selectivity. The preparative potential of these polyfunctional organometallics was demonstrated for the synthesis of bioactive molecules *via* new cross-coupling reactions.

Paul Knochel

Analysis of Biologicals

Three lectures addressed the analysis of therapeutic biologicals for quality control, especially of glycosylated proteins, which is a problem of growing importance also for the business of Solvias.

Dr. ***Steffen Kiessig*** (Solvias AG) discussed 'N-Glycan Analysis of Therapeutic Proteins by means of Capillary Electrophoresis'. Dr. Kiessig stated that the analysis of these oligosaccharides is an important test in quality control release analysis and stability testing of therapeutic glycoproteins and described the basic strategies that allow the determination of the antennarity and the sialic acid distribution, by capillary electrophoresis. These methods are now used for batch release and stability testing as illustrated with the data of a recombinant protein production campaign.

Steffen Kiessig

In the second lecture entitled 'Glycan Analysis by CE-MS' given by Prof. ***Christian Neusüß*** (Aalen University, Germany) it was shown that the combination of capillary electrophoresis with mass spectrometry is a powerful tool to analyze not only the glycans after cleavage but also to give valuable information on the intact glycoproteins and glycopeptides. He briefly discussed the experimental set-up developed for this purpose and illustrated the impressive results obtained with this methodology.

Christian Neusüß

Finally, Dr. ***Maria Schwarz*** (Solvias AG) discussed 'Isoelectric Focusing of Therapeutic Proteins for Quality Control in the Pharmaceutical Industry: Microchip versus Capillary Electrophoresis'. IEF is an attractive technique for the identification and quantification of charged isoforms of proteins and peptides. The analytes are separated on the basis of their isoelectric point. Traditionally this is carried out in a pH gradient formed along the separation path in a capillary. In her lecture Dr. Schwarz compared results obtained with conventional capillary methods and with a novel microchip methodology for several therapeutic proteins. It could be shown that the microchip can significantly shorten the method development for quality control without notable loss in reproducibility.

Maria Schwarz

Solvias Ligand Contest Award Lecture

The Solvias Ligand Contest invites researchers to submit accounts describing new or improved applications of Solvias ligands. For the year 2008, the jury has awarded the first prize to Prof. ***Walter Baratta*** (Università di Udine, Italia) with the following laudation: "In recognition of the development of a remarkably efficient new class of catalysts based on Os – Josiphos complexes. The novel catalysts as well as the analogous Ru complexes exhibit very good enantioselectivities, very high turnover numbers and turnover frequencies for the hydrogenation of aromatic ketones. In addition there is potential for further development."

Walter Baratta receiving his award from Hans-Ulrich Blaser

Prof. Baratta entitled his award lecture 'A New Class of Highly Efficient Ru and Os Catalysts for the Reduction of Carbonyl Compounds'. He explained that the motivation for his research is the fact that selective and productive enantioselective transition metal catalysts are crucial for industrial applications, allowing the use of precious chiral complexes in low amount and leading to products with low metal content. He then went on to describe that during his studies aimed at efficient ruthenium catalysts for the transfer hydrogenation of ketones, he found that the bidentate nitrogen ligand 2-aminomethyl pyridine has a strong acceleration effect. Furthermore, he found that in combination with the Solvias Josiphos ligands high enantioselectivities can be obtained. Based on this important findings, Prof. Baratta developed several generations of Ru complexes which give excellent results both for the transfer hydrogenation well as the hydrogenation of aryl ketones. Especially terdentate pincer catalysts containing a metal-carbon bond proved to be very robust and efficient. Even more remarkable was the unprecedented discovery that the analogous osmium compounds are in some cases even more active catalysts and exhibit similar enantioselectivities. There is little doubt that these novel Ru and Os complexes have a good industrial potential for the highly enantioselective reduction of ketones with very low catalyst loadings.

From the many comments both during and after the symposium we can conclude that also the seventh Solvias Science Day was an unqualified success and we have every intention to continue the series.

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