

# INFORMATION

## News

### Third Solvias Science Day

Hans-Ulrich Blaser  
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The Solvias mission statement reads: "Our business is scientific and technical services and products. Our philosophy is to foster innovation and tread new paths." As a technology-oriented service company with a strong research culture, Solvias has to ensure that its high scientific reputation remains undisputed both inside the company and for its customers. This is one of our motivations to organize a 'Solvias Science Day' for our colleagues in research, development, and production in the life science and fine chemicals industry. The third Science Day took place on November 20, 2003 under the motto 'New Strategies, Technologies, and Concepts in Research and Development' and focused on new developments in the areas of synthesis, catalysis as well as analytical methodologies. About 140 persons from eight countries attended the four sessions with ten invited presentations. This occasion was also a suitable setting for honoring one of the winners of the 'Solvias Ligand Contest 2003'. Looking back, the event was clearly a success: All comments from customers and colleagues showed us that also the third Solvias Science Day achieved its goals concerning science, information and – yes – also marketing the Solvias services.

#### Solvias Ligand Contest Award Lecture

The Solvias Ligand Contest invites researchers to submit accounts describing new or improved applications for Solvias ligands. For the year 2003, the jury has awarded the first prize *ex aequo* to two winners in recognition of their significant contributions in the area of chiral catalysis utilizing Solvias' Josiphos ligands:

To *Erick M. Carreira* (co-author C. Czekelius) for his contribution 'Catalytic Enantioselective Conjugate Reduction of  $\beta,\beta$ -Disubstituted Nitroalkenes' recognizing "the great synthetic potential of this catalytic reaction and the significant extension of the scope of Josiphos-type ligands". Erick M. Carreira is Professor of Chemistry at ETH Zurich. Prof. Carreira received his award during the Solvias Science Day USA, which took place on 3. December 2003 in Boston.

To *Bruce H. Lipshutz*, Professor in the Department of Chemistry at the University of California, Santa Barbara (co-author J.M. Servesko) in recognition of "his significant contributions to the development of the Cu catalyzed enantioselective reduction of  $\alpha,\beta$ -unsaturated ketones, the synthetic potential of this catalytic reaction, and the significant extension of the scope of Josiphos-type ligands".

Dr. Hans-Ulrich Blaser, Chief Technology Officer at Solvias presented the Award to Prof. Lipshutz and congratulated him for this achievement. In his award lecture 'Asymmetric Reductions Catalyzed by Nonracemically Ligated CuH: Quick, Clean, Very Selective, and Almost for Free', Prof. Lipshutz gave a short overview on his research in the field of copper-catalyzed reactions followed by a very lively description of the award-winning results. Copper, ligated by selected bidentate phosphines such as Josiphos induces very high levels of asymmetric induction in the reduction

of imines, cyclic as well as acyclic  $\beta$ -substituted conjugated ketones, and  $\beta$ -substituted  $\alpha,\beta$ -unsaturated esters.



Foto: Bruce H. Lipshutz in discussion

The other presentations can be grouped into two categories: 'Catalysis and synthesis' and 'Analytical methods'.

#### Catalytic Methods and Organic Synthesis

Prof. *Alois Fürstner* (Max-Planck-Institut für Kohlenforschung, Mülheim/Ruhr, Germany) gave a lecture entitled 'Metathesis: a Superb Strategic Tool for Target Oriented Synthesis' where he first described how the progress made in the understanding of fundamental aspects of metal alkylidene- and alkylidyne complexes has triggered an 'avalanche of interest' in the application of the metathesis reaction in organic synthesis. He went on to summarize his recent applications of ring closing alkene and alkyne metathesis to the total synthesis of bioactive natural products such as the strongly cytotoxic agents epothilone and salicylhalamide, the complex glycolipid woodrosin and congeners, and various members of the prostaglandin series.

Prof. *Olivier Riant* (Université catholique de Louvain, Belgium) lectured on 'New Concepts in Asymmetric Catalysis with Titanium and Copper Complexes'. In a first part of the talk he described the development of one of the first examples of stereochemical control of radical anion chemistry, namely the enantioselective pinacol coupling of aromatic aldehydes mediated by a new family of low-valent chiral Ti-hemialen complexes with enantioselectivities up to 91%. In a second part, a new and efficient method for the asymmetric hydrosilylation of ketones with a new family of copper (I) catalysts, with yields reaching >90% and good catalyst activities. Surprisingly, it was found that the reaction is strongly accelerated by oxygen.

Dr. *Marc Thommen* (Solvias AG) discussed 'What Makes a Chiral Ligand Industrially Successful?'. He stressed that for an

industrial application not only the catalyst performance (selectivity, activity, and productivity) is important but also aspects such as the availability of the ligands for screening, the supply chain for large scale use but also how IP rights are handled. He used the concept of Solvias as an illustration how these problems can be approached and solved. Important characteristics are modular ligand families with common key intermediate allowing effective hydrogenation of a wide range of substrate types, the availability of a comprehensive Ligand Kit and the inclusion of the IP rights in the price of the ligand without additional royalties.

Three contributions described two successful collaborations between teams of Solvias, and Novartis and Syngenta, respectively. In both cases, the Solvias team specialized in enantioselective hydrogenation was able to provide a solution for the enantioselective key step in the synthesis designed by the partner team.

Dr. *Gerhard Penn* (Novartis Pharma AG) started off with 'Process Development for a Chiral 3-Amino-2-hydroxy-phosphinic Acid: A Case Study in Asymmetric Synthesis', where he described various approaches to the synthesis of 3-amino-(2*S*)-hydroxy-propyl-methyl-phosphinic acid, a GABA-B receptor agonist in preclinical development. Of special concern were the supply situation and special handling conditions of phosphorus-containing starting materials. Key step of the final synthesis was the asymmetric hydrogenation of a  $\beta$ -keto-phosphinate.

Dr. *Clemens Lamberth* (Syngenta Crop Protection AG) described 'Stereoselective Multi-Component Reactions in Fungicide Research' where he presented substituted mandelamides as a novel class of agrochemical fungicides. Since there is indication that the two enantiomers do not contribute equally to the biological efficacy, enantioselective syntheses are required. Dr. Lamberth showed that one way of obtaining mandelamides with high ees is the three-component Passerini reaction of an aldehyde, an isocyanide using 1,2,3,4-tetra-O-acetyl- $\alpha$ -D-galacturonic acid as chiral inducer. A second approach carried out in collaboration with Solvias started from the corresponding  $\alpha$ -keto amides and esters.

Dr. *Felix Spindler* (Solvias AG) talked about 'Enantioselective Hydrogenation for the Synthesis of Bioactive Molecules' which he characterized to be a mature technology for the preparation of enantiomerically pure bioactive molecules in gram to multi ton scales. He described the results obtained in catalyst screening and optimization programs carried out in collaboration with the teams of Novartis and Syngenta. Upon optimization of catalyst structure and reaction conditions, both compounds were prepared with ees >90% on a kilogram scale.

### Analytical Methods for Organic Synthesis and Quality Control

There is little doubt that progress in the analytical sciences is a prerequisite for more effective control of organic synthesis as well as improved quality control in the pharmaceutical industry and in environmental protection. In this context some important issues were discussed in the three lectures summarized below.

Prof. *Michael Oehme* (University of Basel) gave a lecture entitled 'Modern Separation Methods in Organic Analysis – a Rich Field for Systematic Errors and Surprises'. He stressed that even though chromatographic separation techniques are indispensable for any laboratory dealing with synthesis and structure elucidation, the introduction of newly developed techniques is often hampered by their limited suitability for routine operations or by unexpected difficulties. In his presentation Prof. Oehme discussed selected examples in the areas of enantiomer separations using chiral GC on modified cyclodextrins as well as liquid chromatography combined with mass spectrometry. He explained how systematic errors can be detected and avoided using simple tests.

Prof. *José C. Menezes* (Technical University of Lisbon) discussed the application of on-line analytics 'Using Process Analyt-

ical Technologies in an Industrial Catalytic Hydrogenation of an Active Pharmaceutical Ingredient'. Process analytical technologies (PAT) are systems for analysis and control of manufacturing processes to assure acceptable end-product quality (quality by design). In his talk he illustrated this philosophy with the integrated use of FT-NIR as on-line process monitoring technique for an industrial catalytic hydrogenation of an API. After establishing a suitable technique to monitor multiple parameters of relevance, a kinetic model was established and validated for the process under very diverse conditions. Based on these results, the best operating conditions were established, leading to the highest reactant conversion as well as the desired product selectivity.

*Marco Zeller* (Solvias AG) lectured on 'Reference Substances – Problems and Solutions' where he described the consequences of new regulations concerning the use of reference substances. Using the re-certification of the nucleotide uridine-5'-monophosphate disodium salt as an example, he illustrated some of the problems and described the approach chosen to solve these problems. He stressed the importance of the formal quality criteria and requirements regarding identity, purity and quantitative testing as well as of documentation under the strict requirements of the cGMP quality system.

Based on the many comments of our colleagues both during and after the Science Day we can conclude that it was an unqualified success. We have every intention to continue the series in the fall of 2004.

### Novartis ehrt Wissenschaftler für herausragende Beiträge

Basel, 9. Dezember 2003. – Novartis ehrte zehn Wissenschaftler der Novartis Institutes for BioMedical Research (NIBR) und Pharma-Entwicklung für ihre herausragenden Beiträge im Bereich Forschung und Entwicklung. Die Novartis Scientist Awards – sie wurden 2003 zum sechsten Mal vergeben – haben zum Ziel, die Kreativität und Innovationskraft in der Forschung und Entwicklung zu fördern.

#### Der Distinguished Scientist Award

Die höchste interne Auszeichnung im wissenschaftlichen Bereich auf Unternehmensebene ist der Distinguished Scientist Award. Er ist mit CHF 40'000 dotiert und gibt dem Gewinner das Recht, den Titel 'Novartis Distinguished Scientist' zu tragen. Die begehrte Auszeichnung wurde Dr. *Jürg Zimmermann*, Leiter Kombinatorische Chemie, 'Discovery Technologies', Novartis Institute for BioMedical Research in Basel, verliehen. Seine herausragenden medizinischen Beiträge auf dem Gebiet der onkologischen Forschung waren für zahlreiche Projekte von entscheidender Bedeutung. So synthetisierte er insbesondere einen vielversprechenden Wirkstoff, aus dem schliesslich Glicec<sup>®</sup> wurde, die lebensrettende Behandlung bei chronisch-myeloischer Leukämie, aber auch der erste Proteinkinasehemmer, der auf den Markt kam.

#### Der Leading Scientist Award

Die höchste Auszeichnung im wissenschaftlichen Bereich auf Divisionsebene ist der Leading Scientist Award. Er ist mit CHF 25'000 dotiert und gibt den Gewinnern das Recht, den Titel 'Novartis Leading Scientist' zu tragen. Die Auszeichnung wurde an folgende Wissenschaftler der NIBR und Pharma-Entwicklung verliehen: Dr. *Jonathan Hall*, Dr. *René Lattmann*, Dr. *Jürgen Maibaum*, Dr. *Paolo Paganetti*, Dr. *Markus Rudin* und Dr. *Mira Susa Spring* (NIBR) sowie Dr. *Murat Acemoglu*, Dr. *Paul Gallo* und Dr. *Hans-Joachim Walny* (Pharma-Entwicklung).

Daneben wurde der Leading Scientist Award auch fünf Wissenschaftlern von Animal Health und Sandoz verliehen: Dr. *Ute Isele* (Animal Health) sowie Dr. *Gerhard Fleissner*, Dr. *Stefan Horkovics-Kovats*, Dr. *Heinrich Matous* und Dr. *Herbert Schleich* (Sandoz).

## Honors/Ehrungen

Der Ruzicka-Preis 2003 ging an Dr. *Matthias Ernst* (39) vom Laboratorium für Physikalische Chemie der ETH Zürich für seine Arbeit auf dem Gebiet der Kernresonanzspektroskopie. Der mit CHF 10'000 dotierte Preis, der nach dem Nobelpreisträger Leopold Ruzicka benannt ist, wird seit 1957 an junge Forscher vergeben, die eine herausragende Arbeit auf dem Gebiet der Chemie veröffentlicht haben.

Prof. em. *Dieter Seebach*, Laboratorium für Organische Chemie der ETH Zürich, wurde von der American Peptide Society der 2004 Vincent du Vigneaud Award verliehen.

Dr. *Pavel Pospisil*, Institut für Pharmazeutische Wissenschaften der ETH Zürich, wurde anlässlich des Computational Chemistry Workshops in Wuppertal der Bayer Award for Excellence in Computational Chemistry zugesprochen.

Prof. *Hanns Möhler*, Institut für Pharmazeutische Wissenschaften der ETH Zürich, wurde vom Max-Planck-Institut für Psychiatrie mit der Goldenen Kraepelin-Medaille geehrt.

## Lectures

### Basler Chemische Gesellschaft

Donnerstag, 17.30 Uhr  
Institut für Organische Chemie, St. Johannis-Ring 19, Kleiner Hörsaal

25. März 2004 Prof. *C. Mioskowski*  
University de Strasbourg, Dept. Chemie  
Title to be disclosed

### Berner Chemische Gesellschaft

Mittwoch, 16.30 Uhr  
Hörsaal EG 16, Departement für Chemie und Biochemie, Freiestr. 3  
(Kaffee um 16.10 Uhr vor dem Hörsaal)

31. März 2004 Prof. *Patrick Aebischer*  
Président de l'Ecole Polytechnique Fédérale de Lausanne  
'Investing in Science and Education for the Future of Switzerland'

### Département de Chimie Organique, Université de Genève

Sciences II, Auditoire A-100, 16 h 30  
30, quai Ernest Ansermet, Genève

Jeudi  
4 mars 2004 Prof. *Frank Wuerthner*  
Department of Organic Chemistry, University of Wuerzburg, Wuerzburg, Germany  
'Complex Dye Architectures by Hierarchical Self-Organization'

Jeudi  
11 mars 2004 Prof. *Yannick Landais*  
Université de Bordeaux I, Bordeaux, France  
Title to be announced

Jeudi  
18 mars 2004 Prof. *Ivo Stary*  
Institute of Organic Chemistry and Biochemistry, Academy of Sciences, Prague, Czech Republic  
'The Organometallic Approach to the Synthesis of Helicenes and Their Derivatives'

### Institut de Chimie, Université de Neuchâtel

Mercredi  
10 mars 2004 Colloque du 3e cycle  
Prof. *Dirk Guldi*  
10 h 30 University of Notre Dame, Indiana, Etats Unis  
Petit Auditoire Le titre sera annoncé plus tard

Vendredi  
12 mars 2004 Colloque du 3e cycle  
Prof. *Dirk Guldi*  
Heure à fixer University of Notre Dame, Indiana, Etats Unis  
Auditoire à fixer Le titre sera annoncé plus tard

Jeudi  
25 mars 2004 Gastronomie Moléculaire  
17 h 00 Dr. *Imre Blank*  
Aroma & Taste Impact, Nestlé Research Center, Lausanne  
Petit Auditoire 'Flavour Generation During Cooking'

### Zürcher Hochschule Winterthur

Abteilung Chemie und Biologische Chemie  
Freitag,  
12. März 2004 Dr. *Karl Höhener*  
20.00 h Temas AG (in Zusammenarbeit mit NGW)  
Laborgebäude, L201  
'Das Geheimnis des Milliardstelometers'

Donnerstag,  
25. März 2004 Prof. Dr. *Heiner Bührer*  
17.00 h Industrielle Chemie, ZHW Winterthur  
Chemiegebäude, C402  
'Abschiedsvorlesung'

### Novartis Chemistry Lectureship 2003/2004

Location: Novartis Pharma AG  
Auditorium Horburg, WKL-430.3.20  
Müllheimerstrasse 195, CH-4057 Basel

Time: 10.30 am ('Get Together': 10.00 am)

March 10, 2004 Prof. *Daniel H. Rich*  
University of Wisconsin, Madison  
'Design and Synthesis of Peptidase Inhibitors. What Challenges Remain?'

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**Congresses – Conferences – Workshops**

**PGS**

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 POLYMER GROUP OF SWITZERLAND

**ONE-DAY SYMPOSIUM**  
**Polymers in Life Sciences**

Jointly organized by: University of Basel, Physical Chemistry Dept. and PGS

31. March. 2004

Basel, Pharmazentrum Hörsal 1, Klingelbergstrasse 50/70

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MARCUS TEXTOR, ETHZ	Polymer-based surface modification for applications in the biomaterials and biosensor field
HARRY HEINZELMANN CSEM NE	Polymeric self-assembly on surfaces
STEVEN ARMES, SUSSEX UNIVERSITY GB	Biocompatible phosphorylcholine-based homopolymers and block copolymers: synthesis and applications
HOLGER PETERSEN NOVARTIS	Degradable polymers for microparticle preparation
FALKO SCHLOTTIG SYNTHES – STRATEC	Resorbable polymers for trauma repair and reconstructive procedures
MICHAEL MÖLLER UNIVERSITY of GENEVA	Poly(ortho esters) for injectable, biocompatible and degradable drug delivery systems
AART MOLENBERG STRAUMAN	Use of PEG hydrogels for tissue regeneration
JEFFREY HUBBELL EPFL	Cell-responsive polymer systems in regenerative medicine and drug delivery

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