At the Frontiers of Knowledge in Chemistry: The 47th Bürgenstock Conference**

Olga García-Mancheño and Manuel Alcarazo**

Can You Tell Me Who Is Presenting?

This was one of the first questions that everybody was asking as soon as the participants arrived in Brunnen. But this complete secret regarding the names of the plenary lecturers and moderators is only one of the traditions that make "the Bürgenstock" a different meeting. Other rules strictly limit attendance or dictate that scientists are only allowed to speak there only once during their entire career. However, all these peculiarities wouldn't create the same atmosphere without the magnificent view of the Alps and the shores of Lake Lucerne just ten meters from the conference venue (Figure 1).

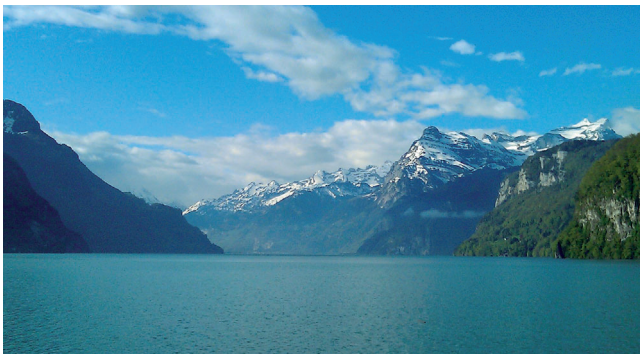


Figure 1. View of the Alps from the conference venue.

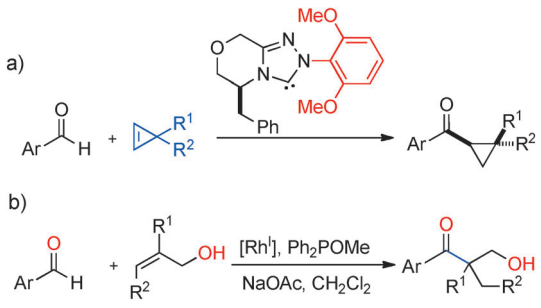
The meeting started on the 29th of April with a dinner, during which this year's president, Andreas Pfaltz (University of Basel), gave his opening speech from the dining hall's balcony and warmly welcomed everybody, and in particular the "Guest of Honor", Albert Eschenmoser (ETH Zurich). He subsequently pointed out several particular aspects of this year's meeting, such as the participation of 15 junior scientists, and he ended his speech by acknowledging the support of this year's Organizing Committee. The spectacular program, consisting of 14 lectures and 2 poster sessions, was about to start … just after the dinner!

A few main topics such as organic synthesis and catalysis, chemical biology, theoretical chemistry, and bionanotechnology were recurrent and appeared in no particular order during the whole symposium. It is impossible to relate in this short report all the interesting chemistry that was described and the vibrant discussions generated after the lectures. This summary intends however to provide a flavor of what we experienced.

The scientific program started with the impressive inaugural evening lecture by Roger Y. Tsien (University of California, San Diego), who presented his studies on engineered fluorescent proteins. These were designed to provide intraoperative guidance to help surgeons identify tumor borders and residual malignancy by in vivo imaging of protease activity. The combination of the captivating personality of the speaker and the obvious interest of the topic made this first lecture remarkable. The experience was so captivating that the audience failed to realize that microphones were not working during the talk!

Catalysis Everywhere

Catalysis is a traditional core area at the Bürgenstock Conference and this year's meeting was no exception. During the first morning lecture, Frank Glorius (University of Münster) demonstrated the applicability of Rh-catalyzed C–H activation processes for the preparation of important classes of molecules such as indoles.[1] He also presented his recent impressive results on N-heterocyclic carbene (NHC) chemistry ranging from the NHC–Ru-catalyzed asymmetric hydrogenation reactions of (hetero)aromatic compounds to the organocatalyzed enantioselective hydroacylation of electron-neutral olefins (Scheme 1 a).[2] Immediately afterwards, Vy Dong (University of Toronto) continued the session with a related topic. She spoke about developing new strategies to prepare macrocyclic polyketides, including methods to stereoselectively hydroacylate olefins and ketones (Scheme 1 b).[3]

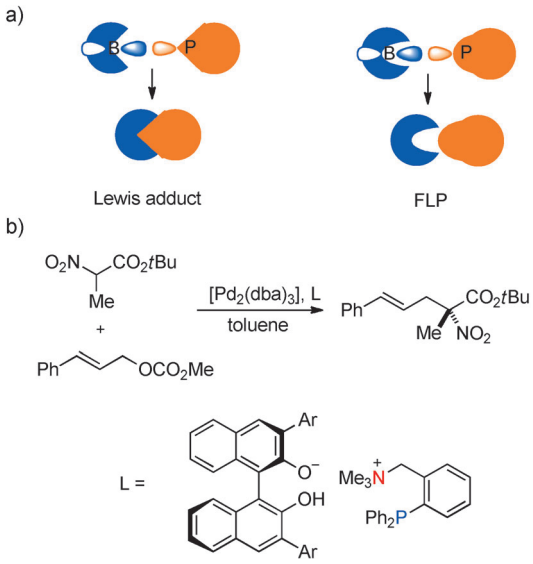


Scheme 1. a) Organocatalytic hydroacylation of cyclopropenes. b) Rh-catalyzed hydroacylation of allylic alcohols.

[*] Dr. O. García-Mancheño
Institut für Organische Chemie
Westfälische Wilhelms-Universität Münster
Corrensstrasse 40, 48149 Münster (Germany)
E-mail: olga.garcia@uni-muenster.de
Dr. M. Alcarazo
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, 45470 Mülheim an der Ruhr (Germany)
E-mail: alcarazo@mpi-muelheim.mpg.de

[**] We wish to thank the Junior Scientist Participation (JSP) Program of the Bürgenstock conference for generous financial support.

Two days later, on Thursday morning, Douglas W. Stephan (University of Toronto) returned to catalysis. He first revitalized the audience after the get-together from the previous night by introducing the concept of frustrated Lewis pairs (FLPs). In addition, he demonstrated that this a priori very simple concept can be employed for the metal-free activation of a huge variety of small molecules such as H_2, CO_2, and in particular cases, even C–H bonds (Scheme 2a). The ability of FLPs to carry out direct reductions of imines and olefins by using H_2 as reductant was also described.[4]



Scheme 2. a) Basic concept governing FLP chemistry; b) typical reaction and an example of an ion-paired chiral ligand L.

The evening lecture on the same day by Ei-ichi Negishi (Purdue University) focused on the development of the Zr-catalyzed enantioselective carboalumination of alkenes (ZACA reaction) and its applications in natural product synthesis.[5] Finally, during the morning session on the last day, Takashi Ooi (Nagoya University) also delivered a very insightful presentation that strongly focused on catalysis. He spoke about the molecular design of chiral quaternary onium salts with the aim of understanding the relationship between the structure of chiral organic ion pairs and their reactivity and selectivity as catalysts. Specifically, he focused on the design of chiral triazolium ions and other chiral ion-paired ligands comprising an achiral molecule carrying a quaternary ammonium and a phosphino ligand and a chiral binaphtholate (Scheme 2b).[6]

Poster Sessions

The first poster session was dedicated to emerging scientists. Six posters were selected for short oral presentations that gave some promising European young chemists the opportunity to introduce their recent developments in eight-minute slots that were strictly controlled by Helma Wennemers (ETH Zurich). The selected speakers this year were Stuart Conway (University of Oxford), Syuzanna Harutyunyan (University of Groningen), Rubén Martín (ICIQ), Nuno Maulide (MPI for Coal Research), Jerôme Waser (EPFL), and Manuel Alcarazo (MPI for Coal Research). During the second poster session, established scientists also shared their achievements. We had the pleasure of listening to short communications by Tekahiko Akiyama (University of Gakushuin), Martin Albrecht (University of Dublin), Christian Hackenberger (Free University of Berlin), Yujiro Hayashi (Tokyo University of Science), Corey Stephenson (Boston University), and Hayato Tsuji (University of Tokyo).

From Organic Synthesis to Disease Treatments

Synthetic organic chemistry has always been present at the Bürgenstock Conference. Introduced by Mohammad Movassaghi, Paul Wender (Stanford University) delivered a vibrant lecture presenting several examples of his research group's total syntheses of complex natural products such as bryostatin I or prostratin, as well as structurally simplified analogues. He also introduced studies designed to determine the mode of action, binding assays, and the biological function of these molecules (Figure 2).[7]

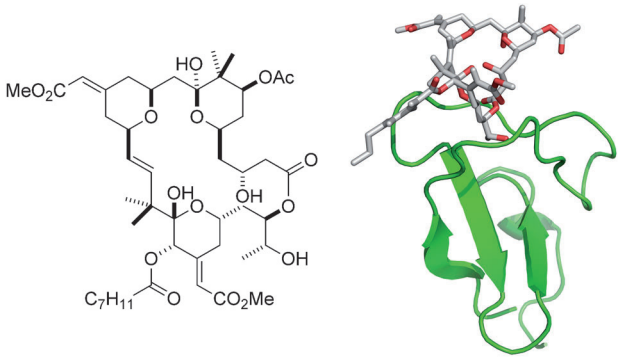
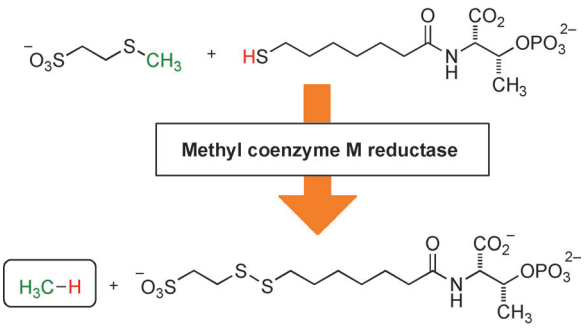


Figure 2. Molecular structure (left) and mode of action (right) of bryostatin I.

Bioorganic Chemistry and Chemical Biology

A prominent focus of this year's conference was on topics from the area of chemical biology. On Tuesday, Sarah E. O'Connor (John Innes Centre and University of East Anglia) opened the morning session with a lecture entitled "Elucidation, evolution and mechanistic analysis of natural products pathways". O'Connor described her work towards the elucidation and manipulation of plant metabolism in order to understand the fundamental biochemical processes that underlie the biosynthesis of specific natural products.[8] Subsequently, Virginia Cornish (Columbia University) offered a journey on how to bring together modern methods in chemical synthesis and DNA technology by manipulation of biological systems.[9]

The next morning, Bernhard Jaun (ETH Zurich) delivered his talk about the mechanism of action of methyl coenzyme M reductase, which is the key enzyme for methane formation and functionalization by archaea (Scheme 3).[10] Thomas R.



Scheme 3. Synthesis of methane by archaea that employ methyl coenzyme M reductase.

Ward (University of Basel) also lectured on metalloenzymes, in his case, artificial ones. By incorporating catalytically active organometallic moieties within a protein host, he has created artificial metalloenzymes with properties reminiscent of both homogeneous and enzymatic catalysis. These hybrid systems could be exploited in hydrogenation, alkylation, and sulfoxidation reactions with excellent enantioselectivities.[11]

Theoretical Chemistry

Stefan Grimme (University of Bonn) delivered the only seminar of the symposium that was dedicated completely to theoretical chemistry. He explained clearly to a mainly non-expert audience the importance of dispersion effects and the large errors derived from not introducing dispersion corrections in routine DFT calculations. He even showed several illustrative examples of organic molecules such as hexaphenylethane and some derivatives in which these effects play a significant role in their stability and allowing their synthesis and isolation (Figure 3).[12]

Bionanotechnology

Last but not least, bionanotechnology was also very present during the conference, with talks by Luisa De Cola (University of Münster) and Milan Mrksich (Northwestern University). De Cola, the current conference Vice-President, lectured about the amazing applications of functionalized zeolite L as new biofunctional materials and for in vitro and in vivo imaging. She presented her results on new classes of trifunctional hybrid nanoparticles that are able to simultaneously target, label, and photoinactivate pathogenic, antibiotic-resistant bacteria.[13]

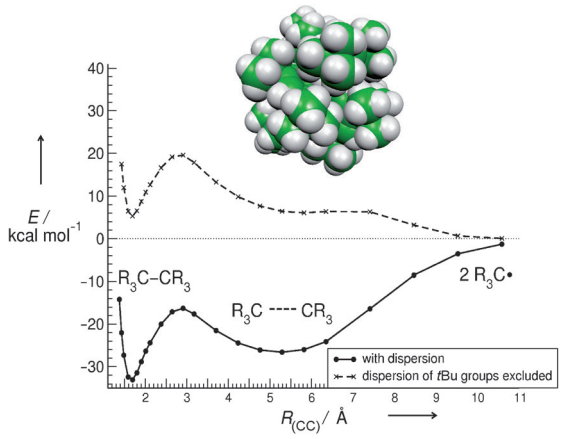


Figure 3. Effect of dispersion in the stability of dodeca(*tert*-butyl)-substituted hexaphenylethane.

Mrksich described his work on using self-assembled monolayers of alkanethiolates on gold to prepare model surfaces that are structurally defined, yet that can have complex compositions and present the ligands in spatially organized patterns.[14] He further presented the novel use of mass spectrometric analysis for the label-free screening and discovery of new reactions.

A Town Taken Over by Chemists

Two afternoons were kept free of lectures, and take-away meals were provided for those who wished to join any of the possible excursions. Climbing one of the few mountains that surround the lake, a boat trip, a walk around the city, or just having a beer in one of the "Biergärten" were the options. These two afternoons also contributed enormously to the Bürgenstock atmosphere. It was a strange situation to be in a town you have never visited before and yet know most of the "inhabitants": the guys running along the street, those enjoying an ice cream at the lake's shore, or even those making funny objects with balloons for the children.

Unfortunately, all good things have to come to an end. On Friday, May 4th, after a short speech from the President thanking the speakers and the excellent organization, the conference finished with a lunch in the main hall of the hotel. I (M.A.) had the pleasure, together with my colleague Tom Snaddon, of sharing the table with Albert Eschenmoser and his wife. We probably received the best lecture of our lives about the history of chemistry. It was really exciting to hear many histories and anecdotes about scientists such as Arigoni, Prelog, and Reppe from someone who knew them personally, and is also responsible for significant developments in chemistry.[15] Finally, we took a picture to immortalize the enjoyable conversation and said goodbye to the rest of the participants. The 47th Bürgenstock Conference was finished but we are sure that the 48th will match the exceptional standards of this one. The tradition continues …

[1] F. W. Patureau, T. Besset, F. Glorius, *Angew. Chem.* **2011**, *123*, 1096 – 1099; *Angew. Chem. Int. Ed.* **2011**, *50*, 1064 – 1067.
[2] F. Liu, X. Bugaut, M. Schedlar, R. Fröhlich, F. Glorius, *Angew. Chem.* **2011**, *123*, 12834 – 12839; *Angew. Chem. Int. Ed.* **2011**, *50*, 12626 – 12630.
[3] a) S. K. Murphy, M. M. Coulter, V. Dong, *Chem. Sci.* **2012**, *3*, 355 – 358; b) S. K. Murphy, D. A. Petrone, M. M. Coulter, V. Dong, *Org. Lett.* **2011**, *13*, 6216 – 6219.
[4] a) G. C. Welch, R. R. S. Juan, J. D. Masuda, D. W. Stephan, *Science* **2006**, *314*, 1124 – 1126; b) for a recent review on the chemistry of FLPs, see: D. W. Stephan, G. Erker, *Angew. Chem.* **2010**, *122*, 50 – 81; *Angew. Chem. Int. Ed.* **2010**, *49*, 46 – 77; c) for metal-free hydrogenation see: P. Spies, S. Schwendemann, S. Lange, G. Kehr, R. Fröhlich, G. Erker, *Angew. Chem.* **2008**, *120*,

7654 – 7657; *Angew. Chem. Int. Ed.* **2008**, *47*, 7543 – 7546; d) P. A. Chase, G. C. Welch, T. Jurca, D. W. Stephan, *Angew. Chem.* **2007**, *119*, 8196 – 8199; *Angew. Chem. Int. Ed.* **2007**, *46*, 8050 – 8053.
[5] a) B. Liang, E. Negishi, *Org. Lett.* **2008**, *10*, 193 – 195; b) E. Pitsinos, N. Athinaios, Z. Xu, G. Wang, E. Negishi, *Chem. Commun.* **2010**, *46*, 2200 – 2202.
[6] a) K. Ohmatsu, M. Ito, T. Kunieda, T. Ooi, *Nat. Chem.* **2012**, in press; b) K. Ohmatsu, M. Kiyokawa, T. Ooi, *J. Am. Chem. Soc.* **2011**, *133*, 1307 – 1309.
[7] a) E. A. Dubikovskaya, S. H. Thorne, T. H. Pillow, C. H. Contag, P. A. Wender, *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 12128; b) P. A. Wender, J. Kee, J. M. Warrington, *Science* **2008**, *320*, 649 – 652; c) E. A. Goun, R. Shinde, K. W. Dehnert, A. Adams-Bond, P. A. Wender, C. H. Contag, B. L. Franc, *Bioconjugate Chem.* **2006**, *17*, 787 – 796; d) P. A. Wender, J. De Brabander, P. G. Harran, J. M. Jiménez, M. F. T. Koehler, B. Lippa, C. M. Park, C. Siedenbiedel, G. R. Pettit, *Proc. Natl. Acad. Sci. USA* **1998**, *95*, 6624 – 6629.
[8] a) W. Runguphan, Q. Xudong, S. E. O'Connor, *Nature* **2010**, *468*, 461 – 464; b) D. K. Liscombe, A. R. Usera, S. E. O'Connor, *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 18793 – 18798.
[9] C. R. Jing, V. W. Cornish, *Acc. Chem. Res.* **2011**, *44*, 784 – 792.
[10] a) S. Scheller, M. Goenrich, S. Mayr, R. K. Thauer, B. Jaun, *Angew. Chem.* **2010**, *122*, 8289 – 8292; *Angew. Chem. Int. Ed.* **2010**, *49*, 8112 – 8115; b) S. Scheller, M. Goenrich, R. Boecher, R. K. Thauer, B. Jaun, *Nature* **2010**, *465*, 606 – 608; c) S. Ebner, B. Jaun, M. Goenrich, R. K. Thauer, J. Harmer, *J. Am. Chem. Soc.* **2010**, *132*, 567 – 575.
[11] T. R. Ward, *Acc. Chem. Res.* **2011**, *44*, 47.
[12] S. Grimme, P. R. Schreiner, *Angew. Chem.* **2011**, *123*, 12849 – 12853; *Angew. Chem. Int. Ed.* **2011**, *50*, 12639 – 12642.
[13] a) C. A. Strassert, M. Otter, R. Q. Albuquerque, A. Höne, Y. Vida, B. Maier, L. De Cola, *Angew. Chem.* **2009**, *121*, 8070 – 8073; *Angew. Chem. Int. Ed.* **2009**, *48*, 7928 – 7931; b) J. El-Gindi, K. Benson, L. De Cola, H.-J. Galla, N. S. Kehr, *Angew. Chem.* **2012**, *124*, 3776 – 3780; *Angew. Chem. Int. Ed.* **2012**, *51*, 3716 – 3720.
[14] a) X. Liao, R. T. Petty, M. Mrksich, *Angew. Chem.* **2011**, *123*, 732 – 734; *Angew. Chem. Int. Ed.* **2011**, *50*, 706 – 708; b) T. J. Montavon, J. Li, J. R. Cabrera-Pardo, M. Mrksich, S. A. Kozmin, *Nat. Chem.* **2012**, *4*, 45 – 61.
[15] A. Eschenmoser, *Angew. Chem.* **2011**, *123*, 12618 – 12681; *Angew. Chem. Int. Ed.* **2011**, *50*, 12412 – 12472.

DOI: 10.1002/anie.201203758

