A Kaleidoscope of Contemporary Organic Chemistry: The 46th Bürgenstock Conference**

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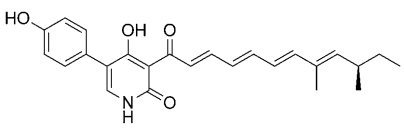
An event with tradition(s)

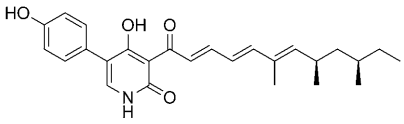
That is the way that the organizational framework of the Bürgenstock Conference could be described. This annual meeting held in the heart of Switzerland is surely one of the most esteemed conferences in chemistry. Its unique atmosphere is not only created by the constantly outstanding scientific quality of the lectures and the idyllic surrounding of Lake Lucerne, but also by a set of rules that have remained unchanged over the years. The number of participants is limited to about 120, and their names (and particularly those of the speakers) are a well-kept secret prior to the beginning of the conference. Scientists are only allowed to speak there once in their lifetime, and all participants are expected to stay for the whole duration of the meeting. The one-hour lectures are followed by half-hour discussions, thus offering the chance for thorough insights into the topics. As in former years, chemists from academia and industry attended, and young scientists had the opportunity to meet esteemed colleagues. This year's conference president, Jeremy K. M. Sanders (University of Cambridge), promised a "liberal interpretation" of the term "stereochemistry" during the opening dinner. He was supported by the organizing committee, which consisted of Donald Hilvert, Jérôme Lacour, Reto Naef, Philippe Renaud, Jay S. Siegel, and Helma Wennemers, in achieving this goal. Together they had compiled a program consisting of 14 lectures and two poster sessions. Sadly, Sanders had to remind the participants at the opening that this year's meeting's "Guest of Honor" Dudley Williams (University of Cambridge) had passed away a few months prior to the conference. Out of respect for the late colleague and as recognition of his achievements, no other "Guest of Honor" was selected, and the position was still granted to Williams posthumously.

Chemical Biology as a Recurring Theme

The lecture program of the 2011 conference offered world-class science from the heart of organic chemistry (total synthesis and catalysis) as well as from related interdisciplinary fields. Chemical biology played a key role in this setting. Already with the first evening lecture after the opening of the meeting, Shankar Balasubramanian (University of Cambridge) impressively demonstrated the opportunities resulting from chemistry addressing biological challenges. Besides his work on transcription factors and G-quadruplexes,[1] he focused on the "Solexa" method for DNA sequencing, which was co-invented by him.[2] The subsequent discussion led to a lively conversation about ethical consequences resulting from sequencing of whole human genomes becoming a part of everyday life. In the following first morning lecture, Karl Gademann (University of Basel) showed that less can sometimes be more in natural products chemistry. With three examples (the inhibition of biofilm formation on surfaces,[3] control of nucleocytoplasmic protein transport,[4] and neuritogenesis), he demonstrated that the "molecular editing"[5] of natural products can lead to truncated structures that are already suitable for the modulation of biological processes. The natural products of the farinosone and militarinone type investigated by the Gademann group could thus provide small molecule stimulators of neuritogenesis and therefore therapeutic agents against neurodegenerative deseases (Scheme 1).[6]



farinosone A



militarinone D

Scheme 1. Pyridone natural products as agents for the stimulation of neuritogenesis.

With organic synthesis being a key technology in the Gademann work, it was fitting that the next lecture was dedicated to a firework of demanding total syntheses presented by Mohammad Movassaghi (Massachusetts Institute of Technology). The biomimetic approach played a particular role in his work. Movassaghi thus accomplished the preparation of epipolythiodiketopiperazine alkaloids with oligosulfide motifs[7] as well as a novel highly efficient strategy for the synthesis of agelastatine alkaloids.[8]

After the first poster session, which was introduced by five short oral presentations, the evening lecture led back into chemical biology, with Alanna Schepartz (Yale University) presenting her eminent work on β-peptides.[9] Towards the end of her talk, a question arose that was not finally answered and that also stimulated the subsequent discussion to a major extent: Why has nature selected α- and not β-amino acids as

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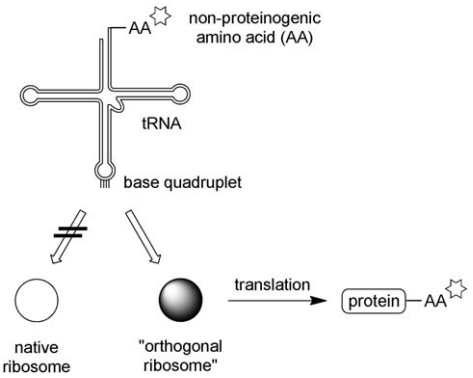
building blocks for proteins? The next morning lecture continued the biological focus, with Jason Chin (Medical Research Council, Cambridge) presenting new ways for reprogramming the genetic code. It was particularly impressive how Chin achieved the translation of modified proteins in vivo using an "orthogonal ribosome". This artificially evolved additional ribosome is capable of recognizing base quadruplets on modified tRNAs that encode non-proteinogenic amino acids (Scheme 2).[10] Chin used this and other innovative techniques to reprogram the genetic code for numerous applications,[11] for instance the direct ribosomal translation of proteins that are normally posttranslationally modified.[12]



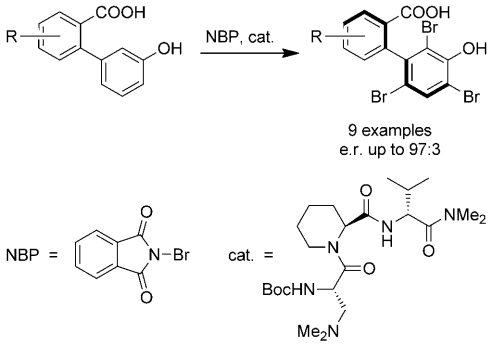
Scheme 2. "Orthogonal ribosome" for reprogramming the genetic code using base quadruplets.

Whoever thought that everything about antimicrobial peptides was understood was proven wrong by the lecture of John Robinson (University of Zurich). Robinson works on mimetics of peptidic β-hairpin structures.[13] These investigations also led to cationic antimicrobial peptides, which normally act by a membranolytic mechanism. In contrast, Robinson found peptides with nanomolar antibacterial activity that display a novel unprecedented mode of action.[14]

New Results from Organo- and Palladium Catalysis

Peptidic structures also were the topic of the next evening lecture given by Scott Miller (Yale University), though in a completely different context. Miller uses peptide-based organocatalysts for highly efficient synthetic processes and demonstrated this principle being exemplified by the Rauhut–Currier reaction,[15] epoxidations,[16] and the atropisomer-selective bromination of biaryls (Scheme 3).[17]

A bridge leading back into synthetic chemistry was built this way, and consequently, organocatalysis was followed by palladium catalysis in the next section. Melanie Sanford (University of Michigan) showed how versatile the chemistry of palladium(IV) catalysis has become and which promising methods for organic synthesis result from it.[18] Jin-Quan Yu (Scripps Research Institute) offered a journey into the world of palladium-mediated C–H activations and showed how to employ the directing principle of weak palladium coordination for such transformations.[19] Overall, two impressive talks



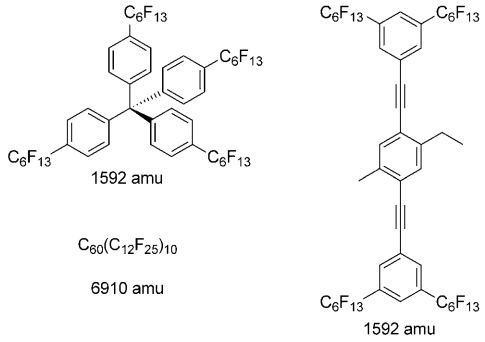
Scheme 3. Organocatalytic atropisomer-selective bromination of biaryls. Boc = *tert*-butoxycarbonyl.

have reminded the attendees that the research on palladium in organic synthesis has not come to an end with the 2010 Nobel Prize, but continues to play a central role in chemistry.

DNA Nanotechnology and the Interface with Physics

Following the traditional concert, for which the president of the conference had selected works for string quartet by Mozart, Bloch, and Borodin, the next scientific session was dedicated to DNA chemistry. The use of the intrinsic properties of DNA (selective molecular recognition, formation of defined three-dimensional structures) for nanotechnological applications is a very vital field of research. In the lecture of Yamuna Krishnan (National Centre for Biological Sciences, Bangalore), it was demonstrated how to perform DNA nanotechnology in living systems. Krishnan has developed a DNA nanoobject which can be switched between two states in a pH-triggered fashion. It is thus applicable as an intracellular pH sensor, a principle even working in *C. elegans*.[20] Furthermore, polyhedric DNA constructs as potential drug delivery systems were presented.[21] Hanadi Sleiman (McGill University) showed that DNA nanostructures can be made even more versatile by the incorporation of "foreign molecules", such as *m*-terphenyls. Besides her work on oscillating triggered DNA cage structures,[22] she also presented results on polymer–DNA conjugates[23] and on the site-specific metallation of DNA.[24]

With the nanotechnological aspect of these two talks, it was a logical step to aim for the interface between chemistry and physics as another interdisciplinary topic of the meeting besides chemical biology. Following the second poster session, which had been initiated by five oral presentations again, Marcel Mayor (University of Basel) thus showed how to address physical questions by means of organic chemistry. Besides his work on nanotechnological projects,[25] he also impressed the audience with results on molecular interferometry. Using wave–particle duality in form of the de Broglie relation, Mayor diffracts whole organic molecules at nanomechanical gratings and has already accomplished the quantum interference of molecular units with masses greater than 6000 amu (Scheme 4).[26]



Scheme 4. Examples of organic molecules used for quantum interference in molecular interferometry.

In the final session of the conference, Wilhelm Huck (Radboud University Nijmegen) took advantage of another Bürgenstock tradition. As there are no abstracts for lectures and a strict restriction of photography, new ideas can also be presented without the danger of eventually losing them to competitors. Huck is currently working on a new scientific orientation of his group and presented his concept to use picoliter droplets[27] to mimic the "crowded" intracellular environment—an interesting approach that we will surely hear a lot about in the future. Ivan Huc (University of Bordeaux, CNRS) finished the conference's lecture program by presenting his work on foldamers. He demonstrated how to employ artificial molecular units to construct defined and predictable three-dimensional structures. His group thus accomplished the preparation of a helix zipper[28] as well as of oligohelices.[29] Foldamer-based objects can also be used for directed molecular motion.[30]

The liberal interpretation of the term stereochemistry promised by the conference's president Jeremy K. M. Sanders was hence brought to convincing completion. The defined spacial orientation of molecular units was indeed a *cantus firmus* of the meeting. However, as the take on stereochemistry was not too restricted, the opportunity was created to present modern organic chemistry in all aspects, particularly at the border to neighboring disciplines, such as biology and physics. This year's vice president Andreas Pfaltz (University of Basel) will be president of the 47th Bürgenstock conference in 2012. He will also no doubt manage to use the unique atmosphere and tradition of this meeting to offer a world-class scientific program. The participants of the next conference may look forward to six thrilling days at Lake Lucerne!

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