Conference Report

DOI: 10.1002/anie.201406309

Chemistry in Stereo: The 49th Bürgenstock Conference

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In memory of André S. Dreiding,
Father of the Bürgenstock Conference

There are likely only a few annual international chemistry conferences that can look back at almost 50 years of brilliant history. The Bürgenstock Conference on Stereochemistry held in Brunnen at beautiful Lake Lucerne in the middle of the Swiss Alps has mastered this task by obeying a set of well-known rules that have become a good tradition. Despite sticking to these rules, the meeting is far from being an outmoded conference dinosaur. On the contrary, we have never seen a more carefully selected, scientifically diverse, and timely lecture program of core fields in organic chemistry, combined with emerging interdisciplinary chemistry-driven research. This, together with the in-depth and vibrant discussions of all presentations are truly unique features of the Bürgenstock Conference. Having had the opportunity to be a part of it was an inspiring experience to us that we wish to share with you in this brief report.

The meeting started on Sunday May 4th with the conference dinner, where this year's President Antonio Echavarren (ICIQ, Tarragona) welcomed all participants, in particular this year's guest of honor Javier De Mendoza (ICIQ, Tarragona). Peter Schreiner (University of Gießen) subsequently kicked off the scientific program. In his vivid talk, he showed us that Switzerland is the ideal place for a chemistry conference as the Swiss landscape looks very much like energy profiles of chemical reactions. Throughout the evening, he convinced the audience that tunneling can play a significant role in controlling chemical reactions and is sometimes able to override kinetic and thermodynamic factors. This was exemplified by the pyrolysis of pyruvic acid and trapping of the formed hydroxycarbene, which then undergoes a 1,2-hydrogen shift to the corresponding aldehyde by tunneling a barrier of 28 kcal mol^{-1}![1]

On Monday morning, Christophe Copéret (ETH Zurich) demonstrated the potential of well-defined, silica-supported single-site catalysts, for example, in alkene metathesis or the polymerization of ethylene.[2a] He furthermore highlighted direct NMR investigations on structural characteristics of such silica-based materials, which are strongly hampered by limited sensitivity, by using dynamic nuclear polarization surface enhanced NMR spectroscopy (DNP SENS), an impressive method that might even become applicable to molecular imaging of biomolecules.[2b] Anne Mapp (University of Michigan) subsequently introduced her work on synthetic transcriptional modulators. Using the GACKIX domain of the coactivator CBP/p300 as an example, she demonstrated how a ligand discovery strategy of tethering can be used to identify small molecules that efficiently stabilize conformationally dynamic proteins, thus enabling their crystallographic analysis.[3a] Mapp furthermore stressed the huge potential of the structural space found in natural-product libraries, exemplified by the identification of the most effective, while still highly selective, small molecules targeting the dynamic binding interfaces of the GACKIX domain—sekikaic and lobaric acid.[3b] After a lunch and afternoon break, the first poster session of the conference was kicked off by five short poster talks selected by the Organizing Committee.

The Monday evening lecture began with a tribute to André S. Dreiding (Figure 1), the initiator of the "Bürgenstock Conference", who unfortunately passed away on Christmas Eve 2013. Dreiding was not only famous for establishing the Dreiding model, but also well-known for his broad interest in chemistry.[4] His research spanned from investigations on biosynthetic pathways, structure elucidation, and total synthesis of natural products, over stereochemistry, methodology, exploration of reaction mechanisms, to even going deep into theoretical and physical chemistry. In 1965, he put his idea into practice to create a platform for intense discussions on stereochemistry by establishing the Bürgenstock Conference and chairing the first meeting. Dreiding was convinced that such a meeting will not only be of interest to a small group of chemists, but will attract scientists from all fields of chemistry. We are sure that everybody who ever participated in any Bürgenstock Conference will agree that he was completely correct.

For the rest of the "scientific" evening, Kenichiro Itami (Nagoya University) took the stage and gave us an impressive overview on the power of C–H activation. He presented the latest results of his laboratory in establishing and using C–H activation as a tool to play "molecular LEGO", thus opening

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Figure 1. Prof. Dr. André S. Dreiding.

the field, for example, for late-stage modifications of lead structures in order to tackle biological problems. He furthermore demonstrated the impact of C–H activation on materials science by presenting a template-driven ring-to-tube synthesis that supplied well-defined nanocarbons as well as new members of the nanocarbon family such as the grossly warped nanographene shown in Figure 2.[5]

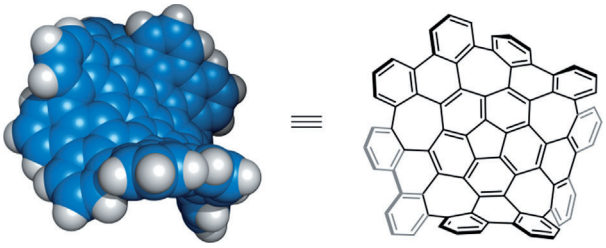
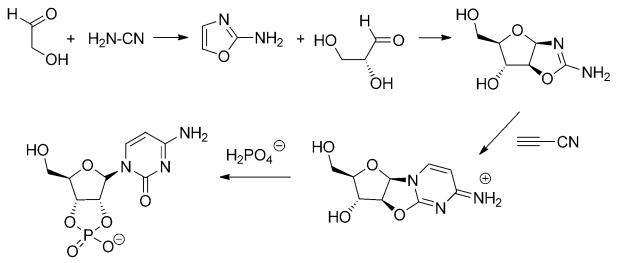


Figure 2. The warped, "Pringles"-like nanographene.[5b]

The scientific fireworks on C–H functionalization continued on Tuesday morning, when Naoto Chatani (Osaka University) reported on his progress on C–H activation utilizing bidentate systems. The talk included recent examples of the carbonylation of unactivated C_{sp^3}–H bonds, the oxidative cycloaddition of aromatic amides to alkynes, and the direct arylation as well as alkylation of C_{sp^2}–H bonds in aromatic amides, just to name a few highlights.[6] In the subsequent talk, Marcey L. Waters (University of North Carolina at Chapel Hill) switched gears by presenting her work on deciphering noncovalent aromatic interactions—in particular cation–π interactions—in biomolecular recognition using designed miniproteins as model systems.[7a] In the second part of her talk, she expanded on the investigation of histone lysine methylation as a critical marker controlling gene expression, in particular by utilizing small synthetic receptors derived from dynamic combinatorial libraries.[7b] The evening lecture by John Porco, Jr. (Boston University) was devoted to the stereoselective synthesis and biomedical evaluation of the antitumoral natural products rocaglamides, forbaglins, and aglains.[8] Among other examples, he demonstrated the power of emulating biosynthetic processes in order to target natural products exemplified by excited-state intramolecular proton transfer (EXIPT) driven [3+2]-cycloaddition reactions.

Wednesday morning started with a talk by Christopher Chang (University of California, Berkeley) on new reaction-based imaging probes for sensing small molecules, such as H_2O_2, or metal ions, such as Cu^{2+}. Utilizing, for example, in situ generated fluorescent probes like fluorescein or luciferase facilitates the selective detection of such compounds in vivo. These investigations address fundamental questions on the influence of small molecules and metals on physiology and pathology and thus help to explore the "chemistry of humans".[9] In the following lecture by John Sutherland (University of Cambridge) on the chemical origins of life, the audience was provided with insights into chemical pathways that could lead to informational polymeric organic molecules, such as RNA, from simple small building blocks. This included the synthesis of pyrimidine ribonucleotides (Scheme 1),[10a] oligoribonucleotide ligation by chemoselective acetylation, as well as the synthesis of ribonucleotides and amino acid precursors by photoredox chemistry,[10b] all of which carried out under prebiotically plausible reaction conditions.



Scheme 1. A route to pyrimidine ribonucleotides under prebiotically feasible conditions that circumvents the chemically impossible direct fusion of the sugar unit with the nucleotide portion.[10a]

The day found additional, nonscientific highlights with the musical evening by the well-known Asasello Quartet and the postconcert get-together, where not only interesting discussions took place, but also all kinds of imaginative balloon artwork were created.

After a rather short night for many of the participants, Armido Studer (University of Münster) did a fantastic job in getting the audience excited for more science by showing the diversity of compounds accessible by electron catalysis.[11] As one of the highlights, he outlined the base-promoted homolytic aromatic substitution (BHAS) reaction in the synthesis of fluorenones or in the transition-metal-free trifluoromethylation of alkenes or aromatic isocyanides. Michelle Chang (University of California, Berkeley) subsequently presented mechanistic insights into fluorine specificity in native enzymes and how synthetic biology approaches can be used to engineer new fluorinated polyketide natural products by incorporation of fluorinated extender units.[12] She continued

describing interesting ways to efficiently produce biofuels by de novo pathway assembly and further stepwise optimization.

In the afternoon, it was time for the second round of poster presentations, which were again accompanied by intensive discussions. The evening lecture by Nazario Martín (Universidad Complutense de Madrid) took us into the world of nanocarbons. His talk included impressions of supramolecular interactions of π-extended tetrathiafulvalenes(exTTF)-modified carbon nanoforms and their application as electrically conducting materials.[13]

The final day commenced with the talk by Jesus Jiménez-Barbero (CSCI, Madrid) on molecular recognition studied by saturation transfer difference (STD) NMR spectroscopy.[14] He presented the latest on glycan receptor interactions as well as the interplay of cytotoxic small molecules, such as epothilone, with tubulins. STD NMR spectroscopy can also be used to investigate large systems, such as fibroblast growth factors, and their interactions with heparin. Last but surely not least was the contribution by Matthew S. Sigman (University of Utah) who spoke about his work on analyzing and predicting selectivity in asymmetric catalysis, a highly challenging problem because of the multidimensional relationships that have to be accounted for. He led the audience through the methodological development for this goal, starting from early work on the analysis of electronic and steric effects alone, to using STERIMOL parameters and most recently molecular vibrations.[15]

The conference was closed by a short resumé combined with copious acknowledgments to all who contributed to the success of this meeting by the Organizing Committee (Alain De Mesmaeker, Jérôme Lacour, Reto Naef, Philippe Renaud, and Helma Wennemers) and the President, before passing the reins to Antonio Togni (ETH Zurich), next year's President. We are sure he also will measure up to the expectations of the participants by putting together yet another fantastic program that will adequately celebrate the 50th anniversary of this extraordinary conference with such a unique atmosphere, top-notch science, and vivid discussions at the Seehotel Waldstätterhof in Brunnen, on the beautiful Lake Lucerne. Great things happen at great places!

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