Conference Report

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Merging Art and Science—The 53rd Bürgenstock Conference**

Job Boekhoven and Dorian Didier**

At the end of April 2018, the 53rd Bürgenstock Conference took place in Brunnen, Switzerland. This world-class conference on stereochemistry gathered some of the most gifted researchers in the field to exchange on current chemistry topics in an interdisciplinary setting. During the final dinner, Conference President Ilan Marek honored his longtime colleague Yitzhak Apeloig, the Guest of Honor, and the former President, E. W. Meijer (Figure 1). Marek acknowledged the hard work of the 53rd Organizing Committee: Alain de Mesmaeker, Cristina Nevado, Christian Bochet, and Fabrice Gallou, and concluded his speech by wishing good luck to Véronique Gouverneur, the current Vice President and next year's President.



Figure 1. Photograph of the President, his predecessor, and the Organizing Committee of the 53rd Bürgenstock conference.

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[**] 53rd EUCHEM Conference on Stereochemistry in Brunnen (Switzerland), April 29th—May 3rd, 2018. The authors are grateful to the Organizing Committee and the sponsors of the Junior Scientists Participation (JSP) program.

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The opening lecture on Sunday was held by Helmut Schwarz Technische Universität Berlin), who challenged the concept of methane activation. Through a combination of gas-phase mass spectrometry experiments and computational approaches (density functional theory), he set the tone for the high quality of the conference by presenting his results and mechanistic interpretation on the use of transition-metal oxides for tackling this "methane challenge."[1a] A detailed theoretical analysis of "doping effects" was given to support the dramatic selectivity improvements of homonuclear metal clusters for the activation of CH_4 and other hydrocarbons.[1b] The last part of his talk was focused on the activation of C–H bond by metal carbides for the formation of C–C bonds in the gas phase.[1c]

James P. Morken (Boston College, USA) opened Monday's lecture series with his astonishing work on enantioselective diborylations of unactivated alkenes using simple, yet highly efficient catalytic systems.[2a,b] The high point of his lecture focused on his original palladium- and nickel-catalyzed "stereoselective conjunctive coupling" reaction, showcasing remarkable assembly of borylated stereocenters in acyclic systems.[2c–g]

Nuno Maulide (University of Vienna) took us on a journey through aspects of his research during the following lecture. First, he presented an unusual route to α-functionalization of carbonyl derivatives by thoroughly designed umpolung strategies.[3a] In situ access to novel "electrophilic enolates" (Figure 2a) enabled efficient and stereoselective nucleophilic

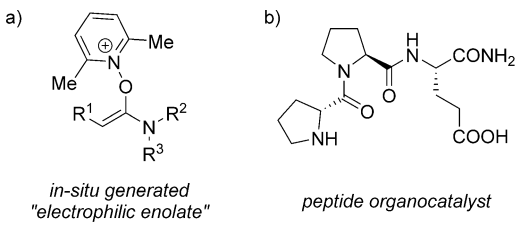

Figure 2. a) Nuno Maulide's "electrophilic enolates."[3a] b) Helma Wennemers' chiral peptide organocatalyst.[6a]

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additions towards molecular sophistication, including fluorination reactions and C–C bond formation. Acyclic stereocontrol was also achieved through stereoselective sulfoxide rearrangements, providing full stereodivergence in the construction of adjacent stereocenters.[3b–d] His presentation was concluded by a well-envisioned application of 4π-electrocyclic ring opening as an alternative to unselective macrolactonization.[3e–f]

On Monday afternoon, the focus shifted towards the use of synthetic chemistry for biomolecular applications. Shigehiro Yamaguchi from the Institute of Transformative Bio-Molecules at Nagoya University gave an inspiring lecture towards that goal. His mission is to develop photostable fluorescent dyes with near-infrared emission for live cell 4D imaging. The strategy of his group has been to introduce main-group elements into the aromatic skeleton of conventional fluorophores, such as fluorescein or rhodamine. The resulting compounds display drastic red shifts compared to the unmodified dyes, which makes them more suitable for near-infrared imaging compared to their nonmodified counterparts. More importantly, the new dyes are highly photostable.[4a] Shigehiro demonstrated the practicality of the latter by beautiful time-lapse imaging of living cells (Figure 3).[4b–c]

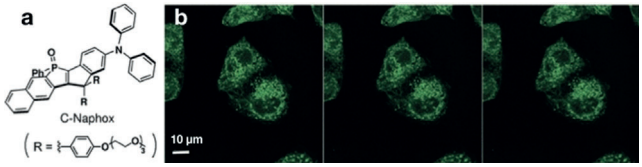

Figure 3. a) Structure of the photostable dye Naphox-C. b) Fluorescence micrographs over time of the dye show bright fluorescence, but no photobleaching.[4a]

The first poster session started with selected short oral presentations given by Job Boekhoven, Charles E. Diesendruck, Sunkyu Han, Monica Perez-Temprano, and Marcos G. Suero.

In the evening lecture, Andreas Marx from the University of Konstanz demonstrated his approach to further understanding the information layer beyond the genome sequence. The main message of his talk was that the complexity of organisms can only in part be attributed to the size of the genome, and part of complexity should be found elsewhere, such as post-synthesis modification of proteins and nucleic acids. His team aims to understand how these modifications affect their biological function.[5a,b] To that end, they used smart nucleic acid modifications as well as protein modification to gain a better understanding of the role of ubiquitination and methylation of nucleotides in biology. As an example, the group has developed new tools to study the mechanisms in DNA repair by synthesis of nonnatural NAD+ derivatives.[5b,c]

Tuesday was kicked off by a lively morning lecture by Helma Wennemers (ETH Zurich). She uses polyketide-inspired peptides that can asymmetrically catalyze the conversion of malonic acid half-thiols.[6a] She also used the Pro–Pro–Xaa tripeptide scaffold to catalyze aldehyde olefin additions with high reactivity and stereoselectivity (Figure 2b). She talked us through her thorough understanding of the reaction mechanism[6b,c] and the conformation of the tripeptide catalyst during the catalytic action. These studies have enabled her group to modify the peptide to increase stereoselectivity[6d] and also to catalyze aldehyde maleimide addition.[6e]

Ashraf Brik (Technion, Israel) gave an overview of his approach to using organic chemistry to create synthetic proteins in order to investigate the mode of action of their native counterparts.[7a] Specifically, his group aims at a better understanding of the process of ubiquitination and de-ubiquitination of proteins.[7b] Site-specific ubiquitination of proteins is crucial for regulating their controlled cellular degradation. However, recapitulating the ubiquitination process ex vivo is extremely challenging, in part due to the hundreds of enzymes involved. His group thus developed smart synthetic organic approaches, including a modified native chemical ligation, which can modify specific lysine or cysteine with various ubiquitin derivatives, negating the use of enzymes.[7c,d] Those combined approaches have enabled systematic studies that help understand protein degradation by proteases.[7e]

On Tuesday evening, we were entertained by a concert performed by three excellent musicians. We started with classical works, but brought to us with a scientific pitch by Nuno Maulide. In his performance, Nuno talked us through the science behind cymatics and he showed us his take on how science and classical music often go hand in hand. Amnon Stanger (Technion) took over the piano with his jazz interpretation of Pink Floyd's *Atom Heart Mother*. Renana G. Poranne (ETH Zurich) joined him on the stage for a breathtaking performance of Leonard Cohen's *Hallelujah*.

Wednesday morning's session started with a talk from Rubén Martín (ICIQ, Tarragona) who showed us his vision of site-specific carboxylation from a remote position.[8a] The use of simple nickel complexes allowed him to activate C–X bonds in alkyl chains to trigger a "metal walk" through reversible H-shifts (Figure 4).[8b,c] This unique strategy was further applied to diene dicarboxylation,[8d] hydrocarboxylation of unsaturated hydrocarbons in water[8e] and umpolung arylation of ambiphilic α-bromo boronic esters,[8f] among other beautiful transformations.

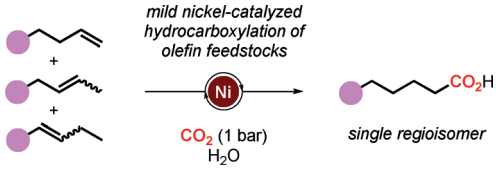

Figure 4. Rubén Martín's regioconvergent "nickel walk."[8e]

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Ang Li (Shanghai Institute of Organic Chemistry) subsequently took the stage to describe some of his recent achievements in total synthesis. He shared his view of architecture design for the construction of complex terpenoid structures, such as daphnilongeranin B and E,[9a] among others. An impressive sequence of 6π-electrocyclization/aromatization was also assembled as a key step in the synthesis of daphenylline (Figure 5).[9b]

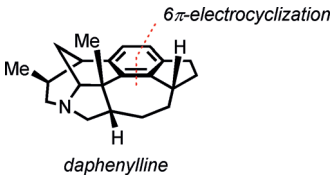

Figure 5. Ang Li's 6π-electrocyclization strategy in total synthesis.[9b]

The afternoon session started with a vision on reaction-mechanistic interpretation through computational chemistry from Odile Eisenstein (Université de Montpellier and University of Oslo). Based on the simple idea that NMR spectroscopic data of structural intermediates could be directly correlated to the computational analysis of shielding/deshielding arising from their paramagnetic term, Eisenstein presented a detailed study of the well-known metathesis reaction by comparing measured and estimated ^{13}C NMR chemical shifts.[10a–f] Her way of analyzing chemical shifts in terms of electronic structure certainly provides the community with an alternative vision on reactivity.

Appetizers for the second poster session were then served by Roey J. Amir, Gabriel Lemcoff, Amandine Collet, Thomas N. Snaddon, and Christof Sparr as flash presentations. Both poster sessions were a hive of activity and detailed discussions took place between all participants.

The evening lecture was given by Philippe Renaud (École Polytechnique Fédérale de Lausanne) who introduced us to his vision on how to tackle challenges in radical chemistry. He presented several exciting strategies based on radical generation, such as chlorosulfonylation of dienes for the formation of five-membered rings,[11a] fluorination with organoboranes, smooth radical-promoted reduction with catecholboranes, deuterative deiodination reaction with D_2O,[11b] or concepts for repairing the thiol–ene coupling reaction. The epilogue of his presentation disclosed the hydroalkoxylation of substituted alkenes by means of a radical chain process.

The final day of the meeting was dedicated to the supramolecular chemistry of cages and molecular frameworks. Jonathan R. Nitschke (University of Cambridge) started the day with his take on supramolecular cages that spontaneously form driven by imine-based dynamic covalent chemistry.[12a] These beautiful structures can selectivity host small molecules ranging from potent greenhouse gases such as SF_6 to the highly reactive P_4.[12b] Besides the binding of small molecules, these cages can even be used to carry out chemical reactions, analogous to molecular flasks. In very recent work, he showed that the cages can be used to selectively capture and isolate salts from a two-phase solution.[12c]

In the final lecture, Omar M. Yaghi (University of California, Berkeley) talked about the atom, the molecule, and the covalent framework. This gave an overview of his work on "reticular chemistry",[13a] which is the chemistry of linking molecules and building blocks by strong bonds to make extended crystalline structures. He focused on the challenges involved in the synthesis of covalent organic frameworks, especially the difficulty in simultaneously synthesizing and crystallizing these materials. When his team understood the importance of microscopic reversibility, that is, molecules should be given sufficient time to crystallize into their most favorable configuration, the field took off.[13b] He has shown the use of these materials in a plethora of examples, which include a catalytic CO_2 reduction in water.[13c,d]

The 53rd Bürgenstock Conference was closed by Ilan Marek with the announcement of Janine Cossy as the Vice-President of the 54th Bürgenstock Conference.

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Meeting Reviews

Conference Report

J. Boekhoven,*
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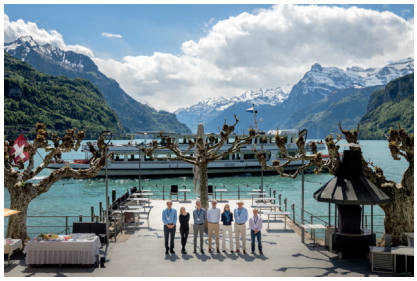

For the 53rd time, the Bürgenstock Conference gathered some of the most gifted scientists and rising stars in organic, physical, and bioorganic chemistry. Orchestrated by Ilan Marek (President) and his successor, Véronique Gouverneur, the synergy between art and science took place in Brunnen, Switzerland, with an beatiful view over Lake Lucerne.

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