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ХРОНИКА

The *Balticum Organicum Syntheticum* conference returns to Riga, Latvia

A major academic event for all organic chemists in the Baltic region this year was the 9th biannual *Balticum Organicum Syntheticum* conference (BOS-2016). The first such event was held in 2000 when Victor Sniečkus, professor at the Queens University, Canada with his friends, chemists of Baltic origin from the USA, organized the first BOS in Vilnius, Lithuania.

Two very important differences of BOS-2016, compared to the previous conferences, were the financial support from EU 7th Framework Program (the InnovaBalt project) and the increased proportion of female speakers, notably, Riina Aav, Emily Balskus, Suzanne A. Blum, Inga Čikotiené, and Sarah Reisman, who offered very valuable and interesting chemistry lectures, while there had been only seven female speakers in the previous eight BOS conferences combined. Two of them were from the Baltic countries – Estonia (Riina Aav) and Lithuania (Inga Čikotiene) – they are young chemistry professors starting their own research carrier in the challenging field of organic chemistry.

Among the traditions of BOS conferences is the evaluation of research posters (there were 149 posters at BOS-2016) offered by Thieme publishers who provided prizes for the best poster presenter from the Baltic countries (Latvia, Lithuania, Estonia) and the rest of the world. The social program for the conference included an evening at the *Ziemeļblāzma* (Northern Lights) cultural center that has been an active site of cultural and educational landscape of Riga since the beginning of the 20th century. Each of the recent four BOS conferences were proceeded by pre-BOS conferences organized in Estonia (2010 and 2012) and Latvia (2014 and 2016) on some topics at the interface of medicinal chemistry and biological research. Latvian partners organized two-days long pre-BOS conference at the Latvian Institute of Organic Synthesis (LIOS) on two important directions of medicinal chemistry – anticancer agents and inflammation. The participants visited the new pharmacology and biology building during the reunion of LIOS chemists, biologists, and pharmacologists at the new multidisciplinary facility in the Teika district of Riga.

The format of the BOS-2016 conference was traditional, with 3½ days of a single conference track featuring invited speakers and a poster session at the recently built National Library of Latvia – named poetically as *Gaismas pils* (Castle of Light). There were 315 participants from 24 countries and 19 speakers both with academic and industrial backgrounds. The lectures were focused on organic chemistry, materials science, chemical biology, and the development of new drugs.

The Sunday afternoon session was started by Prof. **Frank Glorius** (University of Münster, Germany), who set high standards with his presentation about the chemistry and philosophy relevant to the discovery of new reactions and heterogenous catalysts, the design of valuable synthetic processes, and mechanism-based screening.

Dr. **Stefan Schunk** (Grünenthal GmbH, Aachen, Germany) discussed the main research directions at his company, connected to the problems of pain and inflammation. His lecture was about successful lead optimization that has resulted in the development of cebranopadol – an opioid receptor agonist, which is currently in clinical trials.

Prof. **Ryan Shenvi** (The Scripps Research Institute, La Jolla, USA) was recently awarded the *Natural Product Reports* Emerging Investigator Lectureship. This Lectureship is awarded annually to researchers who have made a significant impact in the field of natural product chemistry in their early career. The privilege of this honor is that the winner has to choose the place of the lecture. Prof. R. Shenvi had indicated Riga and particularly BOS-2016 as the place for giving this lecture. Indeed, the lecture was devoted to various stories from the recent history of natural product synthesis. At the same time, Prof. Shenvi devoted a lot of attention to active isocyanoterpenes and to the general usage of isonitriles as ligands for metalloenzymes. After the lecture, Prof. R. Shenvi was presented with a certificate given by James Anson, Deputy Editor, *Natural Product Reports* (Royal Society of Chemistry).

The second day of the conference started with a lecture by Prof. **Maris Turks** from Riga Technical University, Latvia. His lecture topic was very unusual for the mainstream organic synthetic chemists – the application of sulfur dioxide as a useful reagent and solvent in organic chemistry. Ring cleavage reactions of aziridines usually are not regioselective, but performing them in liquid SO_2 at –10°C with added LiCl allowed the reaction to go to completion with high regioselectivity. The application of SO_2 as a derivatization agent for GC analysis and the use of silyl sulfinates for sulfoxide synthesis are some of the practical outcomes of this research.

Dr. **Pavel Mykhailiuk** simultaneously represented two organizations: Taras Shevchenko National University of Kyiv, Ukraine and Enamine, a well-known Ukrainian manufacturer of rare chemicals. He continues the highly valuable expertise that Ukrainian chemists have accumulated in the field of organofluorine chemistry for several decades. His interests are centered on trifluorodiazomethane as a powerful reagent for the synthesis of trifluoromethyl heterocycles. Dr. Mykhailiuk group has synthesized >100 fluorinated proline derivatives by a photochemical cycloaddition reaction and a methodology has been developed for preparative scale synthesis of fluorinated amines, resulting in more then 500 new compounds.

Prof. **Brian Stoltz** (California Institute of Technology, USA) has pursued the synthesis of complex, recently discovered natural

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products exhibiting interesting biological properties that present difficult challenges even to the most skilled synthetic chemists. For example, his research group has developed a target-directed synthesis of aspeventin B. Another strategy used by Prof. B. Stoltz group is target-driven methodology development. They have perfected the applications of some well known reactions, for example, enantioselective Tsuji allylation. Such reactions were used in natural product synthesis and formation of quaternary Mannich adducts by Pd-catalyzed allylic alkylation.

Prof. **Peter Nielsen** (University of Copenhagen, Denmark) presented the situation at the crossroads of chemistry and biology, looking at peptide- and nucleic acid-based translation of genetic information and evolution of prebiotic systems. His research has been focused on the role of epigenetic processes in ribosomes.

Prof. **Nuno Maulide** (University of Vienna, Austria) surprised the audience at least three times. First of all, it was chemistry with efficient solutions for achieving various molecular rearrangements and atom-economical transformations for the synthesis of a variety of simple heterocycles (isoquinolines, pyridines). Thus, diphenyl sulfoxide was used for metal-free arylation reactions. Prof. N. Maulide group has shown that sulfoxide can play important role in sigmatropic rearrangements as well. The other two surprises came from his very professional piano play at the Culture palace *Ziemeļblāzma* (Nordic Lights) and on the Steinway instrument at the closing ceremony of the BOS-2016 conference.

Interesting aspects of supramolecular chemistry were presented by the young chemistry professor **Riina Aav** (Tallinn University of Technology, Estonia). Prof. R. Aav group is working on hemicucurbiturils and investigating their structures, synthesis, and possible applications in host-guest interactions.

Prof. **Suzanne Blum** (University of California, Irvine, USA) has family roots from Latvia, because her grandgrandfather came from Liepaja, a city on the western sea coast of Latvia. She started her research career as an undergraduate student in Prof. Edwin Vedejs group at the University of Michigan. Prof. S. Blum group now has performed significant mechanistic studies of borylation reactions in several types of heterocycles (indoles, furans, isoxazoles). They have described the first catalytic aminoboration and oxyboration of olefins and applied these tools to the synthesis of valdecoxib.

Elegant process chemistry was presented by Dr. **Stephen Dalby** (Merck, Rahway, USA). He showed examples of multi-kilogram scale asymmetric synthesis used to produce the antiviral agent Letermovir. The most interesting part of the synthesis was asymmetric aza-Michael reaction featuring a phase-transfer-catalyzed step for which the catalyst was specifically optimized.

The most biologically oriented investigation was presented by Prof. **Sheng Ding** (University of California, San Francisco, USA) who has focused his efforts on stem cells. Reprogramming of somatic cells by chemical signals relies on the development of small molecule agents. The first step is identification of small molecules acting by suitable mechanisms, followed by sequential combination of these small molecules. Prof. S. Ding group was investigating epigenetic mechanisms by using synthetic and natural (a triterpenoid – ursolic acid) compounds and achieved remarkable results in their work toward stem cell reprogramming.

Prof. **John Sutherland** (MRC Laboratory of Molecular Biology, Cambridge, UK) surprised the audience with an original approach to the study of origin of life. The main starting information came from earlier publications by Eschenmoser. His adventures in geochemistry were aimed at answering several fundamental questions: What sort of chemistry occurred on the young planet Earth? How did DNA arise? Prof. J. Sutherland group has experimentally obtained and published the first results on cyanosulfidic photoredox chemistry. They have discovered that chemical recycling is crucial for simplifying complex mixtures.

Natural product synthesis has been the main research area of Prof. **Sarah Reisman** (California Institute of Technology, USA) group. The complexity of linear and spatial structures and the availability of synthetic methods always determine the choice of natural product targets for synthesis. Thus, ryanodol was synthesized in 13 steps, ryanodine in 20 steps, and anhydroryanodol in 13 steps. Every complex route of synthesis included some newly developed synthetic steps, such as Ni-catalyzed asymmetric reductive coupling and Cu-catalyzed tryptophan arylation.

Prof. **Inga Čikotienė** (Vilnius University, Lithuania) is advancing the synthesis of heterocyclic compounds (5-nitrosopyrimidines, benzoisoxazoles, naphthyridines, furopyrimidines, pyranopyrimidines) and their transformations. The title of her presentation was "From curiosity to development of new synthetic methods". Her approach has been to carefully investigate every new and unpredicted product in order to find the mechanism of transformation.

Organic photoredox catalysis was the main method featured in the presentation by Prof. **David Nicewicz** (University North Carolina, Chapel Hill, USA). This method was applied in various forms – single electron transfer catalysis, intermolecular hydroamination, and Newman–Kwart rearrangement. Another topic of presentation was aromatic CH functionalization, particularly the *para*-selective direct CH-amination reactions.

Biosynthetic transformations of natural products have served as the main research direction at Prof. **Emily Balskus** (Harvard University, USA) laboratory. New enzymatic transformations have produced secondary metabolites that are of great interest. Among the unusual structural motifs obtained were cylindrocyclophanes, coronatines, and bartolosides, and the redox enzymes used included ferritin-like diiron carboxylates and diiron halogenases.

Reactivity prediction and ligand library design were the main topics covered in the presentation by Dr. **Per-Ola Norrby** (AstraZeneca, Sweden) presentation. The researchers at AstraZeneca have performed 1 million experiments for reaction selectivity screening with various ligands with the aim of catalyst optimization.

The last presentation was given by Prof. **Antonio Echavarren** (Institute of Chemical Research of Catalonia, Spain) on gold catalysts for natural product synthesis of various complexity. His research group has developed new cascade reactions for gold-catalyzed alkyne activation to construct new cyclic molecules (acenes). Heterocycles further presented in the lecture mainly were based on indole (lundurine C, grandilodine C) and lactone (rumphellaone A) subunits.

The BOS-2016 conference in Riga was very successful from all the aspects – excellent speakers with interesting discussions after every lecture, active poster sessions, wide social program, and a perfect venue of the conference at the Latvian National Library. The main financial issues were covered by generous support from EU 7th FP project InnovaBalt. The tradition of *Balticum Organicum Syntheticum* (BOS) conferences will continue, and we will meet again after two years in Tallinn, Estonia.

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