Hello All!

RE: BOS 2016, RIGA, Latvia: THE OPENING, THE CHEMISTRY, THE FINALE

The Opening (Sunday, July 3, 2016)

- To what appeared to be the almost complete participation of attendees, Victor Sniečkus provided a short ppt history of BOS, 2000- 2016.
- Three lectures followed (see below) and a marvellous reception in the artistic atrium where we heard, for example: "hello, how are you, haven't seen since um…", good to see you again, we haven't met since ummm…, you are from University, company X, oh, do you know chemist Y? Of course, we are in the same department, lab!".

The Opening Ceremonies (Monday, July 4, 2016)


J. Pesti, J. Duncia, E. Butkus, V. Sniečkus

- We (Peteris Trapencieris, Eugenijus Butkus, Jaan Pesti, Victor Sniečkus, but sadly, without Jonas Dunčia) did our normal trilingual greeting which you will find in the "Welcome" page of the Program and Abstract booklet.


P. Trapenceris

- Peteris gave additional words on the venue (National Library of Latvia) and emphasized thanks from all of us to InnovaBalt for tremendous support of BOS 2016.
- There followed a rousing, well prepared, and thoughtful presentation by OJĀRS SPĀRĪTIS, the President of the Latvian Academy of Sciences. Among his points was the value of science in modern day, the need for support of research, and the progress of the Latvian Institute of Organic Chemistry.


V. Sniečkus

- And, finally, Sniečkus rose to give a more detailed history of Latvia, its culture and its language, the history of BOS (and lectures of 7 Nobelists), and ended with thanks to Peteris, Ieva, and Vita, and staff and **Let the Riga 2016 BOS begin!**

The Chemistry

- To amplify the comments in the BOS 2016 RIGA APRES 1 file, our committee were fortunate to gather chemists which, combined, gave us the following themes:
    - Synthetic method discovery and development (*Glorius, Schunk, Shenvi, Turks, Mykhailiuk, Stoltz, Maulide, Aav, Blum, Dalby, Cikotiené, Reisman, Nicewicz, Echavarren).* For key literature, see their abstracts.
        - "I want to discover" proclaimed Frank *Glorius*, drawing parallel to Columbus with a ppt portrait of his landing in the West Indies by Vanderlyn. Fran k set forth his group's efforts on mechanistic insight which led to matrix screening technologies allowing the discovery of new catalytic reactions.


F. Glorius, A. Echavarren

        - Following the "room for improvement" dictum, Stefan *Schunk* presented a literature-to-lead success story on an opiate agonist chemotype. (See also below).

- "Nature is not very organized… for drug development" reads Ryan *Shenvi's* abstract from which he proceeded to demonstrate how fundamental knowledge of functional groups (isonitrile), reactions (Sc-based), and new FG combinat ions leads to abbrevviations of total synthesis – jadiferin from toxic principle *Illicium verum.* One key reference: *Natural Product Repts.* **2016**, 535, the journal of the RSC which presented Ryan a young investigator award.


R. Shenvi

- The honor of being the Latvian speaker for BOS 2016 was given to Maris who demonstrated the theory and practice of SO_2 as a reagent and solvent. In ongoing work in his group, Maris showed the utility of this "reagent" for reactions of aziridines, and the Ritter the Ene reactions, among other applications.


M. Turks

- From the university-industry based Pavel *Mykhailiuk* flowed a series of F-containing compounds, some strained, other potentially conf ormationally biased. We learned that there are 50 patents on 4-CF_3-piperidine, that photochemistry can be done on kg scale in flow, and that F-diazoalkanes are handlable materials. Fundamental research in service of practical ends is the byline of Pavel's work. (See also below).


P. Mykhailiuk

- New reactions in service of natural product total synthesis was superbly demonstrated by several examples, in particular, the historic target, quebrachamine was conquered in fresh new chemistry in the delivery by Brian *Stoltz* who was introduced by his colleague, Sarah Reisman (and see below for the inverse).
- Giving credit where due (Leon Ghosez), Nuno *Maulide* painted a canvas of aza-allene, sulfoxonium ion, benzyne, and oxindole chemistries for our view. He reminded, with some embarrassment to the BOS comm ittee, that he was present at BOS 2004, when still a student. This will cause the committee to scan all lists of participants in the future!


N. Maulide and admirers

- From Tallinn University of Technology and the Estonian BOS 2016 speaker came Riina *Aav* with the topic of… stop, lick your lips in order to say… hemicurbiturils. The synthesis, dynamic character, chiro-optical properties, and inclusion complexes of these barrel-shaped molecules was provided. There appears to be a bright future for the curbiturils as sensors, in catalysis, and nanomachines. These *molecules are never still, host and guest, never at rest.*
- Like Emily Balskus, Suzanne *Blum*, was searching for her Lithuanian (and possibly Latvian) roots. In chemistry, Suzanne searches with great success how to aminoboronate and oxyboronate C=C bonds and then finds application in indole and furan synthesis. Never to be forgotten, after her lecture, are the bond strengths of the B-O (130 kcal/mol) and B-N (<100 kcal/mol) bonds.
- For a comment on Stephen *Dalby's* lecture, delivered in beautiful Queen's English, please see below, dear reader.

- Sarah *Reisman,* introduced by her Caltech colleague, Brian Stoltz by memorable words, “there is only one Caltech and… there is only one Sarah Reisman”, played molecular lego on some horrendously complex synthetic targets, including ryanodol, a landmark in natural product synthesis first conquered by the Canadian Pierre Deslongchamps. Here, Sarah put expediency (starting material pulegone) and modern methods (e.g. Pauson-Khan) to successful execution.
- Inga *Čikotienė* showed how a plan for certain results can lead to the unexpected which leads to new method development, something that synthetic chemists like to have happen more often. The canvas painted by Inga shows her to be a heterocyclic chemist par excellent, achieving new methods for numerous classes of heterocycles, including isoxazoles, carbazoles, and pyrimidines and their annulated heterocyclic systems.
- I noted David *Nicewicz* and Professor *Makosza* engaged in friendly conversation… but in English. One of the originators of organic photoredox catalysis, David began by relating how the cyanobacteria photoredox system can provide inspiration to synthetic chemists. With a solid mechanistic viewpoint, he laid the physical foundation for excellent photoredox catalysis (e.g. organic dyes) using a $22 blue LED flood light from Amazon, and then provided anti-Markovnikov hydrofunctionalization, cycloaddition, arene C-H functionalization transformations based such rationale. For his most recent review, see *Chem. Rev*. **2016** ASAP (96 pp).
- The students in Antonio *Echavarren’s* laboratories in Tarragona, Spain literally have a golden touch. We brought the BOS 2016 to a close with a display of gymnastics of Au catalysis for the construction of complex natural products, sometimes in surprising abbreviated paths.


A. Echavarren, N. Maulide

- Many of the above took medium to bold jumps into total synthesis as already mentioned above (*Glorius, Shenvi, Stoltz, Reisman, Echavarren*).
- To take a breadth and conclude from the above, *synthesis was alive and well in BOS 2016.*
- Right from our opening lecture by Frank Glorius, it was clear that organic synthesizers were giving considerable attention to biological activity, enzymatic reactions, nature of biological processes (*Glorius, Shenvi, Reisman, Stoltz*).
- The impact of biology or, in the modern terminology “chemical biology” and “systems chemistry” (simple chemical systems capable of self-replication), is evident to all of us: whether we are facing the announcement of the discovery of the details of the sequence of a gene that gives insight to (one of the) cancers, the finding that is an initial encouraging sign to understand the tangled proteins that lead to Alzheimer’s, will stem cell research give us ultimate solutions to some diseases, or the surprise that some mushrooms can activate singlet oxygen to give the brightness of luciferin (in the dark!). Addressed by our speakers (*Nielsen, Sutherland, Ding, Balskus*) were questions of the following type:
    - Were PNAs (peptide nucleic acids) before RNA, now that we know that it was before DNA or, on more common grounds, *What is Life?* The title of the book by Addy Pross with the subtitle of *How Chemistry becomes Biology,* a pithy book from OUP, 2012 written by an originally trained organic chemist. Furthermore,

how is Cu(I)-Cu(II) photoredox chemistry involved in prebiotic feedstock molecule generation? These themes raised in various fundamental reactions easily understood by synthetic chemists was raised by *Nielsen* and *Sutherland* with an appreciation that breakthroughs in our understanding of the title of Pross' book are looming. For deeper browsing, Nielsen: *Org. Biomol. Chem*. **2014**, 6901; Sutherland: *Science*, **2016**, 1075.

- Can we better understand the molecular mechanisms that control stem cell fate and function and even manipulate them? Can we differentiate, control, promote survival of stem cells by small molecules. Ding very insightfully addressed this topic of hopeful dimensions.

- The chemical factories of microorganisms produce molecules whose complexity is still a daunting experience for chemists undertaking total synthesis. DNA sequencing has now allowed us to obtain microbial genomes which are leading to opportunities to discover new enzymes that will change, at least in part, the way that we syntheticers make molecules. An enthusiastic, no, I don't hesitate to say, upbeat lecture from *Balskus* placed us in a position of knowledge and appreciation of the upward path of this field as applied in biocatalysis and metabolic engineering. She is literally a microbial miner.

o Leaving, arguably, the best for the end, Industrial chemistry in various lessons to be learned was presented (*Schunk, Mykhailiuk, Dalby, and Norrby*). Thus, some of the highlights (to me) were:

- Serendipity is found in industrial settings as demonstrated by following (rather than garbaging) an unexpected Pictet-Spengler reaction in the area defined by the need of new analgesics of better quality than morphine (*Schunk*)
- The F-atom in various forms (CF_3, CHF_2, and F itself) pervades the current journals. Facts: 20% of drugs and 30% of agrochemicals are ^{19}F compounds. The comment by Seebach in an *Angew.* article on the state of organic synthesis "when there is an F in the molecule, expect a completely different reaction result" may be worth storing in the mind by those that are making F-containing molecules either to demonstrate a new method or to find how its lipophilic properties affect bioactivity. A tour de force lecture by *Mykhailiuk* showed where we stand and raised, appropriately, numerous questions.
- *Dalby*, with great zest, showed us where we stand on multi-kilo processes and yet reminded us mechanistic understanding is crucial to an economic synthesis. S_NAr, as (hopefully) taught to our undergraduates, was THE key reaction. We were led through the steps: med chem → process chem → engineering/regulation to the commercial product. There was excellent displays of aza-Michael catalysis, cinchonidine-based PTC (with the master of this area sitting in the front row), and Bronsted acid catalysis for us to enjoy. It must be added, I vowed to renew my weak biology knowledge after listening to Stephen and to read further the cited Cornforth (*Chem. Brit*. **1975**, 432) and Mencken (see below) quotes
- We will always remember Per-Ola *Norrby* for the lecture on the impact of computational chemistry on reactions which we use routinely (π-allyl complexes)

but understand only superficially. To test, I urge you to ask someone how many forms of Pdacac there are. But, and I counted, there is no question that Per-Ola is the winner of largest number of questions asked for BOS 2016… and maybe for all BOSes: I counted 27 questions, which is 1.5 questions/speaker.

- **Finale**
  - If you have read the above, you will appreciate fully, with less or more of a laugh than Artis and I had in the process of the preparation, the attached ppt titled by the name of the speaker (ppt entitled Lecturers).
  - As tradition holds, the major event of the Closing Ceremonies is the presentation of *Poster Prizes*. 146 posters were posted with care and fun (see website photos). As also seen from website, attendance was high and discussion was animated. As seen from the various addresses, the BOS committee is happy that chemistry is budding in Europe and the Baltic States. We hope the posters gave students the opportunity to test their presentation skills (engaging a questioner for a few minutes is an art) and receive questions (which they could answer) and comments for future work. The students who walked to the stage clearly were pleased with their success and, of course, the achievement of fine chemistry. The Thieme Prizes winners, presented by Jaan Pesti, were:
    - Artis Kinēns, Latvian Institute of Organic Synthesis, PO-054 for his work on chiral DMAP catalysts (made, to my great pleasure, by D*o*M)(or was it for PO-057) artis@osi.lv
    - Sandra Kaabel, Tallinn University of Technology, PO-043, PO-044, PO-125 (misukune oli? Vabandust, ma ei naenud) for either hemicucurbiturils as neutral hosts, or triazole-based halogen bond donor synthesis, OR hemicucurbituril inverted types sandra.kaabel@ttu.ee
    - Aurelija Urbanaitė, Vilnius University, PO-130 for the synthesis of pyrroles from in situ generated alkyinylcyclopropyl imines aurelija.urbanaite@chf.vu.lt
    - Elisabeth Speckmeier, University of Leipzig, PO-112 for photoredox type deoxygenative synthesis of α-aryl ketones Elisabeth.Speckmeier@uni-leipzig.de

  and the unrevealed judges then very enthusiastically decided that the RSC Prize, judicated by James Anson, also be awarded to Sandra Kaabel.

- A few words of "wish you good chemistry and thank you for attending" from *Peteris*, an enthusiastic "Tere tulemast Tallinnal" = welcome to Tallinn" for BOS 2018 from Margus *Lopp*, via ppts (*look for website soon*) and the traditional wrap up of speakers from *Viktor*. Will you give me the pleasure of your comments on the best and the worst of the attached ppts prepared by Artis. The following key words may help:
    - Glorius: Munster is a capital city of bicycles in the world
    - Schunk: pain, oh, pain
    - Shlenk: aside from chemistry, he gave us the art of George Seurat and embedded the S_N2 inversion of Paul Walden by the umbrella.
    - Turks: SO_2 is a gas but does it have an odor?
    - Mykhailiuk: bomb squad needed. Perhaps rather sick humor in current times.
    - Nielsen: it takes superb detective work to detect double strands
    - Maulide: I always take care to dress according to the country I lecture in

        - Aav: a barrel of beer metaphor for hemicucrbiturils
        - Blum: Breaking Bad… B-O bonds
        - Dalby: modification of Mencken quote
        - Ding: today biology research raises questions for all of us
        - Čikotienė: beautiful angles, smile
        - Balskus: mining of the molecular type
        - Norrby: holds the record for # of questions asked at a BOS conference at 29
        - Echavarren: since initiating Au chemistry, Prof. Echavarren does not need to apply for grants
- **And finally, Viktor's comments**
    - We learned a great deal of forefront organic chemistry
    - We were exposed to the interface of chemistry and biology… or biology and chemistry, if you wish ☺
    - The joy of learning by the speakers, the participants, the poster presenters, one and all was evident and is best described by the scintillating photos – Congratulations to the photographer: who focussed, picked, zoomed, and shot. Please visit: http://www.boschem.eu/
    - Likewise, in spite of various languages cultures, and backgrounds, there was obvious joy in the interaction created by BOS
    - We of the BOS committee – Eugenijus, Jaan, the absent Jonas Duncia, and Viktor express our gratitude to Peteris, Ieva, Vita, Duce, Artis, and definitely others whom we did not get to know as well for a conference to be placed in the annals of BOS: you made it happen, thank you.
    - Of course, to the participants and attendees: without you, there would be no BOS. Veni, vidi, vici… or maybe better cognosci.
    - It remains to say, once more, Loodame, et näeme Tallinnas (10th BOS).
- **And finally, finally**,
    - An exposition of the piano artistry of Nuno Maulide in ~ 5 minutes of a well known piece of Bach...or was it Beethoven? ... with instructive comments on how to enrich our listening experience in music listening. In 2014 Vilnius BOS, we had Negishi-Kobayashi Japanese melodies, now we had a recital, so what will it be in 2018 Tallinn? Kohtumiseni Tallinnas kahe aasta pärast! Uz drīzu tikšanos Tallinā .... pēc diviem gadiem! Matysime jus Taline po dvejų metų!