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From Solar Cells to Nanoparticles and Lots of Organic Synthesis in Between: The 48th Bürgenstock Conference

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conference report · nanoparticles · solar cells · synthetic methods

We were roughly 120 attendees at this year's Bürgenstock conference, and we enjoyed the now traditional cocktail of high-profile lecturers hailing from many subfields of the molecular, materials, and life sciences. What makes the "Bürgenstock experience" arguably unique is the willingness of all participants to look beyond their own horizons and seek inspiration from the paths chosen by colleagues from diverse subdisciplines. This readiness comes across in the animated discussions that often go on for half an hour or more after the lectures have finished, and involve ten to fifteen questions.

In her choice of invited speakers, the President of this year's meeting, Luisa de Cola (Strasbourg and Karlsruhe), demonstrated an admirable command over the international scene of confirmed and emerging leaders in their fields. The meeting was opened on Sunday night by Michael Grätzel (Lausanne) whose research since 1988 has simply revolutionized the field of low-cost solar-panel design. At that time, the field was wholly taken by surprise by the efficiency in light conversion achieved by a nanoporous TiO_2 matrix covered with an appropriate organic dye, an efficiency truly competitive with semiconductor-based cells. To this day, dye-sensitized solar cells ("Grätzel cells") continue to grow in their impact on our daily life, and earned Grätzel a position among the five most-cited chemists. Monday's program started with Jeffrey Hubbel (also from Lausanne) who captivated us with his interest in the understanding of tissue regeneration. His group's efforts include the immobilization of growth and adhesion factors on fibrin (and even wholly artificial polymers) by electrostatic forces or enzyme-induced covalent binding. Such materials are then used to elicit the growth of new tissue in vivo, and thereby to either study fundamental phenomena such as angiogenesis (the growth of blood vessels) or to induce wound healing and bone regeneration. Two of his bioactive materials are currently undergoing clinical testing.

After a typically animated discussion, the stage was taken by Heather Maynard (Los Angeles), who was a postdoctoral researcher in Hubbell's laboratory and has now developed a promising research program in the stabilization of delicate proteins by enclosing them in covalently bound artificial polymers. Her choice in using numerous copies of trehalose, an unusual disaccharide, as a constitutive monomer component on a polymer and coupling multiple copies to a model protein, lysozyme, proved very successful. In a more recent development, her group made headlines with the use of a heparin-mimicking sulfonate-displaying polymer that effectively stabilizes bFGF, a prominent but inherently fragile growth factor, against a number of stresses where the unmodified protein degrades. After a relaxing pause of four hours, the day continued with the first of two poster sessions. Here, established researchers blend in perfect ease with younger colleagues in the display of their recent research results, and both groups receive extensive attention by all participants, old and young.

The daily dinner is held in a magnificent hall of the venue (the Seehotel Waldstätter Hof), where illustrious members of Europe's nobility and even a few crowned heads dined a long time ago, and where in 1908, Winston Churchill may likely have purred terms of endearment into the ears of his newly wed bride during their honeymoon stay. The evening's lecturer, Dennis P. Curran (Pittsburgh), was introduced by Scott Denmark (Urbana-Champaign), who gave away Curran's avowal that "tonight we will see some real organic chemistry". Indeed, our speaker convincingly demonstrated that one can elucidate the highly monotonous stereopatterns of certain complex natural products with the development of new synthetic routes; these make use of the fantastic separation power of his "Fluoroflash" chromatographic technique when the analytes bear fluorocarbon tags of different lengths (difluoromethylene groups).

Tuesday began with a lecture that filled many of us with awe. We were witnessing a true master at work. Most of us were of course aware of the historic Meerwein–Ponndorf–Verley and Oppenauer reactions. But the force of the profound vision of Michael Krische (Austin, Texas) slowly dawned on us when he described many carbon–carbon bond-forming reactions catalyzed by his new transfer-hydrogenation catalysts. These transition-metal complexes can be fed directly with a masked version of the aldehydic electrophile—an alcohol. In a development bordering on the improbable, Krische demonstrated

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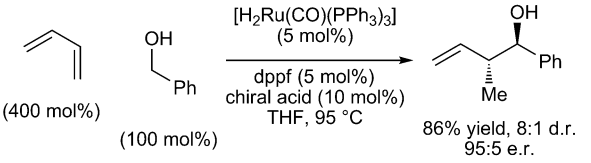
that an appropriate hydrogenation catalyst can mobilize an alcohol's content of molecular hydrogen, thereby setting the aldehyde free, and then proceed to catalyze the reductive coupling of the aldehyde with unsaturated reactants of a wide variety [Eq. (1)]. The high value of the products of course requires them to be formed with high stereoselectivity, and Krische furnished us with numerous examples. But the many cases where his group succeeded in using petrol-based bulk chemicals such as butadiene, and even methanol(!), as starting materials for these reactions must have put a gleam into the eyes of the many participants from industry. Krische closed by reporting on how his procedures have resulted in cutting the number of steps of routes to well-known complex natural products almost by half.



(1)

The stage was then taken by Véronique Gouverneur (Oxford), who described the astonishing recent expansion of the field of fluorination of organic molecules, whether on the level of a single fluorine atom or that of a trifluoromethyl group, and then proceeded to outline her group's own contributions. Positron emission tomography (PET) imaging is today highly appreciated by pharmaceutical industry for the evaluation of drug candidates in cell-receptor-displacement assays in small animals and even in humans. The use of PET tracers carrying a radioactive fluorine nuclide (^{18}F) is particularly popular. Gouverneur made us aware to what extent newly developed smooth fluorination schemes can stimulate PET imaging, and thus boost the entire drug discovery process. The methodologies elaborated by Gouverneur's group, including the establishment of CF_3 groups bearing one radioactive fluorine atom, proceed under mild conditions, and are thus amenable to more delicate substitution patterns. They promise to furnish a plethora of fluorinated versions of known drugs, and in particular also new drug candidates explored by the pharmaceutical industry. The day was closed by the traditional musical concert in lieu of an evening lecture. Luisa de Cola took the initiative to invite a young talented vocal artist from Italy (Pilar), who was accompanied by two male instrumentalists. She sang modern, jazz-type songs, and with her beautiful voice and body language, as well as her sometimes burlesque imitations of human passions, charmed all of us, and outright enchanted some of us!

Wednesday's first speaker, Christoph Weder (Fribourg), took us back into the realm of polymers and materials from Sunday's and Monday's program, but this time by combining them. How? By compression molding of dried blends of two polymer solutions at 80 °C. One of the components is often a synthetic polymer equipped with various effector substituents. The other is "nanocellulose" that has been identified by Weder's group in a simple marine organism that can be easily harvested from many of the world's leisure harbors. This nanocellulose is composed of stiff fibers and confers on its composite materials properties such as mechano-, water, and light responsiveness. Weder showed us movies that beautifully demonstrated the change in the materials' form, including scratch-healing(!), or a change in its fluorescence in response to an external stimulus.

The morning's second speaker, Gianluca M. Farinola (Bari), discussed three of his remarkably diverse global projects with us. His group has obtained a chiral polymer that distinguishes the two enantiomers of citronellol with a sensitivity three orders of magnitudes higher than any previously reported polymer and still one order of magnitude better than the human nose. But his success in the preparation of a potent hybrid photosynthetic system is proof of particular motivation. This procedure required his group of collaborators to produce sufficient quantities of the simplest light-harvesting protein and equip it with a tailored organic dye by site-specific conjugation. Farinola closed with yet another remarkable attempt to create hybrid structures, but this time with a biomaterial, the elaborate microporous silica structures formed by the thousands of different diatom species (microscopic algae, see Figure 1) populating our waterways.

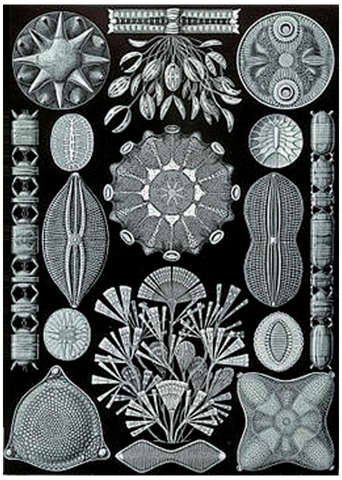


Figure 1. Ernst Haeckel's rendering of diatoms (1904).

After a free afternoon, we met up again in the evening to listen to Huw Davies (Atlanta), who made us feel his passion for functionalization reactions of unactivated or barely activated C–H bonds, still considered a "holy grail" in the 1990s, as I can vividly remember. But what really sets this gifted chemist apart from the rest of us is his praiseworthy drive to unite his colleagues in the same field with the common objective of pooling each others' insights and recent advances to result in a higher synergy between them. He thus began his talk by explaining his initiative that resulted in the foundation of the CCHF (Center for Selective C–H Functionalization) funded by the NSF (USA). Without further ado, Davies then led us into the world of rhodium and iridium catalysts that manage to stereoselectively insert carbenes from diazo precursors into a variety of aliphatic and aromatic C—H bonds, including plain adamantane.

After a good night's sleep, we were up for a morning of chemical biology. Nicolas Winssinger (Geneva) taught us the interest in powerful tagging schemes for the discovery of high-affinity ligands of protein targets. He successfully employed short PNA (peptide nucleic acid) tags as a robust means to encode organic molecular building blocks in fusion reactions that give rise to highly diverse libraries. He also alerted us to commercialized array technologies that became available only recently and that allow chemists to quickly carry out high-throughput screening of minute amounts of library members. In the quest for high-affinity ligands, his group learned to appreciate the significant differences in binding capacity brought about by only slight variation of spacer length between building blocks. The morning's second speaker, Tom Muir (Princeton) shared with us his exploits in chromatin research, a hot topic in biology labs throughout the world. He stressed his extra motivation that is drawn from the perspective to tackle many terrible diseases if one were to better understand the posttranslational modification of chromatin proteins and thus cell differentiation. As a peptide chemist by origin, his efforts led to the discovery of a small peptide that effectively inhibits gene silencing by a lysine-methylating enzyme. Such tools are of utmost importance to understand epigenetics, and Muir made a convincing case for continuing with low-throughput classic biochemistry approaches in parallel with high-throughput modern genomic and proteomic methods.

The late afternoon involved a second round of about 20 posters, and many lively discussions ensued. In the evening, Viola Vogel (Zurich), a biophysicist by training, gave her talk entitled "the art of making and breaking a bond". But what sort of bond? In fact, it is the bond between a live cell, bacterial or eucaryotic, and its environment that was meant. Its understanding is absolutely essential as mechanical forces exerted onto cells are an additional dimension of functional regulation of these cells. And these bonds implicate adhesion proteins that are drawn or compressed out of their equilibrium structures (Figure 2). Vogel pointed out to us the total lack of attention to such structures over those contained in well-known structural databases today. She also made us appreciate a fact almost overlooked when chemists consider the strength of the cooperative effect in peptidic β-sheet formation: they argue in terms of calories and thermodynamic stability, while Vogel does so in terms of mechanical stability. This was illustrated with the example of a zipper that can be easily torn apart when pulling on the opposite ends facing one another, but not so for the ends at the distal extremities of the zipper.

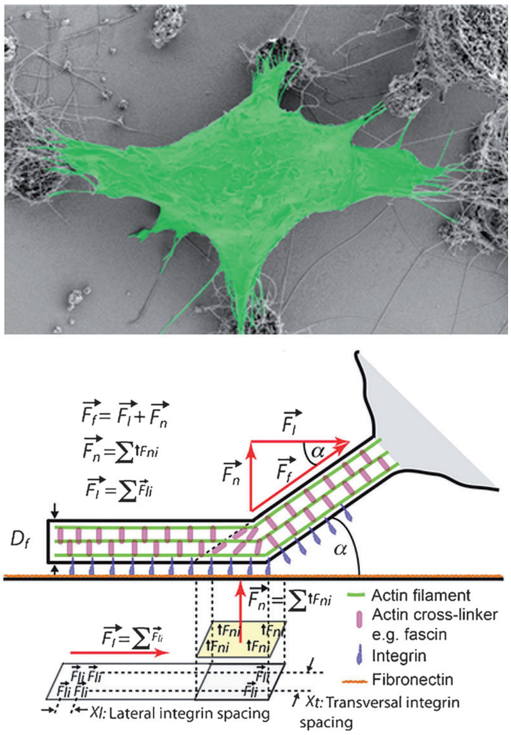


Figure 2. Top: A fibroblast under stress, bonded to engineered nanowires; bottom: distribution of the forces exerted on an integrin protein involved in adhesion.

Antonio M. Echavarren (Tarragona, Spain), the President of next year's Bürgenstock Conference, introduced the two speakers on Friday morning. The first lecturer, Jun-ichi Yoshida (Kyoto, Japan), is the inventor of "flash chemistry". It distinguishes itself from batch chemistry (flasks) by the use of a micromixing chamber and a microreactor in the form of a looped steel line. Mixing times must be much shorter than reaction times. We were then stunned by the fine control one can gain over product distribution if one were to shorten reaction times to only tenths of seconds and mixing times to half a millisecond(!). Yoshida demonstrated the fantastic power of flash chemistry with the example of the controlled capture of short-lived species such as organolithium intermediates or glycosyl ions, but also with the example of living polymerizations leading to remarkably low polydispersities. But what really topped all this was our realization, helped by the speaker, that microreactor does by no means imply microscale. In fact one can simply run the reaction at high flow speeds and short residence times in order to scale up to industrial proportions!

Last, but by no means least, Bruno Chaudret (Toulouse) reported on his ground-breaking work in the preparation of metallic nanoparticles. He repeatedly emphasized (and apologized for) his "culture" of an inorganic chemist. The major technological advance of his work consists in the use of cyclooctadiene and cyclooctatriene transition-metal complexes that can be converted under much smoother reactions conditions than are typical in the field. This is brought about by destabilizating the complexes by hydrogenation (the audience has already been made receptive to the benefits of smooth hydrogenation reactions thanks to the talk by Michael Krische). Chaudret made a persuasive case for exploiting these particles even for organic synthesis (catalysis), but their remarkable quality and shape diversity also bodes well for more traditional nanoparticle applications. He was publicly lauded by the guest of honor, Professor Reinhoudt (Enschede), for the refreshing effect that his topic had on a meeting that continues its tendency to be somewhat organic-chemistry-weighted despite its well-established, and well-received(!), ambition to cover all aspects of modern chemical research.

The traditional closing ceremony was expertly handled by members of the Organizing Committee. It served to thank first and foremost the president, Luisa de Cola, for her personal investment in the success of the 48th Bürgenstock conference, which greatly benefited from her warm and discrete ways that allowed things to flow naturally and in an uninhibited manner. Secondly, all members of the hotel team were thanked for their display of remarkable responsibility and welcome and for their care of all the needs of the attendees. Lastly, Antonio Togni (Zurich) was announced as Vice-President for 2014, and will preside over the conference in 2015. It should not be left unmentioned that the meeting saw itself threatened by seriously competing events, that is, two Champions League semifinals. It speaks for the quality of this year's meeting that few succumbed to the temptation.