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Conference Report

# Functional Biosupramolecular Systems

## 40th CUSO Summer School, Aug. 23–27, 2009

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*Abstract:* This year, the CUSO Summer School in Organic Chemistry celebrated its 40th anniversary. With a coinciding 450th anniversary, it was organized by the University of Geneva. The focus was on large molecules and supramolecules that are synthesized from scratch, have interesting functions, and address lessons from nature.

**Keywords:** CUSO Summer School in Organic Chemistry · University of Geneva

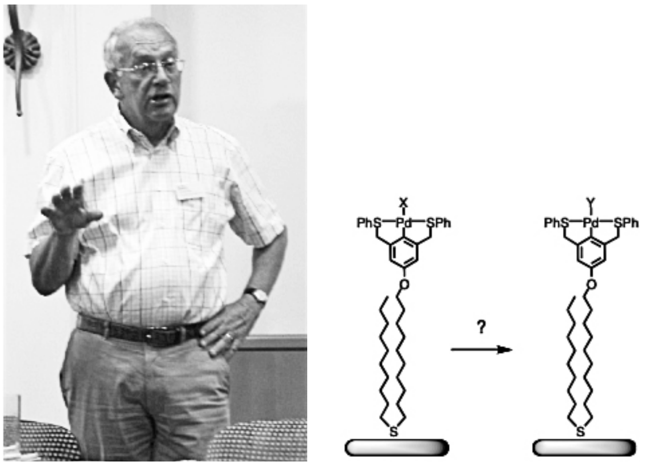

Fig. 1. David Reinhoudt, talking about molecular printboards and how to perform reactions at the single-molecule level on gold surfaces.

The 40th CUSO Summer School in Organic Chemistry was held during the last week of August 2009. Coinciding with the 450th anniversary of the University of Geneva, this special event was chaired by *Damien Jeannerat* and *Stefan Matile* from that University. The location was Villars-sur-Ollon, a beautiful village surrounded by the Alps, overlooking the Rhône Valley and with the eminent Mont Blanc as spectator. In this quiet and inspiring atmosphere 68 chemists from all over the world joined efforts to celebrate the 40th anniversary of the meeting. This year, it focused on the creation and properties of supramolecular functional architectures, an area of chemistry that attracts much current attention in the scientific community. Thus, the need to make accessible and improve the knowledge in this area of chemistry is important, especially for young scientists. For this purpose, five of the most important leaders in this field were invited to talk about their views and perspectives on the topic.

The opening lecture by ***David Reinhoudt*** from the University of Twente, started with a very simple question: What do we need to place research at the top level? The answer to this question could differ among different individuals. Some will answer that you need money, some that you need good and creative people, others will reply that you will need the best facilities. But the common and ultimate answer is that you need a dream. In fact, at some point a scientist should ask himself: What is the problem that I want to solve? In the case of David Reinhoudt, this dream was to understand molecules at the molecular level and to manipulate them to build self-assembly of noncovalent nanostructures in a controlled fashion.[1] In his first lecture, he explained the possibility of performing chemical reactions with a single molecule through the confinement of these molecules using self-assembled monolayers on gold surfaces (Fig. 1). He also described the use of noncovalent interactions for the synthesis in solution of large supramolecular aggregates, as an example for the preparation of non-covalent artificial receptors using melamine lattice. A particularly exciting feature in this section was the use of melamine-modified calixarenes for the synthesis of double rosettes and their ability to form enantiomerically pure hydrogen-bonded assemblies.

In his second lecture, David Reinhoudt focused on the design of molecular printboards and how this methodology could be employed for the 3D fabrication of devices such as an organic field effect transistor. Finally, he mentioned the new techniques developed in his laboratories for the immobilization of biomolecules using either supramolecular approaches or covalent chemistry such as imine and click chemistry.

The audience of the CUSO summer school was very lucky and extremely pleased to have the opportunity to attend the two spectacular lectures from ***Takuzo Aida*** from the University of Tokyo.[2] He delivered an amazing firework on creativity in organic chemistry, showing first the capability of iron complexes capped with dendrimers to mimic iron proteins. These dendrimers could then be used for the transport of molecular oxygen without degradation of the entrapped precious gas. Next he explained how aryl ether dendrimers could be employed for the preparation of devices that emit white light. When the dendrimer is alone the emitted light is coloured blue, but when coordinated with the suitable transition metal it changed, for example to green with $Tb^{3+}$ and to red with $Eu^{3+}$. It was possible to combine all these together to get white emission because the presence of the dendrimer prevented the undesired interactions of the three different fluorophores in solution.

Takuzo Aida also introduced the concept of morphology-dependence of the photochemical properties in dendrimer porphyrins, showing how energy migrates very efficiently over the continuous dendritic array to enhance the probability of energy transfer to the porphyrin core.

Another outstanding example on creativity in chemistry concerned original work his group developed on ‘secret ink’, consisting of phosphorescent paper which is erasable and rewritable with tuneable ‘confidentiality’ being controlled by the kinetics and the thermodynamic self-assembling events during writing and after reading. He also described his recent success in the synthesis of a new class of molecular glues, which bear multiple guanidinium ions as sticky ends that could be used to adhere to proteins and stabilize protein assemblies.

The second lecture of Takuzo Aida focused on ATP-responsive biological nanomachines such as the chaperonin-mediated stabilization and the ATP-triggered release of semiconductor nanoparticles. As another key topic, molecular scissors were introduced (Fig. 2). Molecular scissors represent an example of nanomachines, devices composed of different parts that interact in a controlled fashion to produce coupled motion. An azobenzene moiety was connected to the two cyclopentadienyl rings of a ferrocene, each in turn conjugated to a Zn-porphyrin. The two porphyrins can host a 3,3'-bis-isoquinoline, in a stable asymmetric conformation of its twisted rings. Irradiation with UV light promotes *cis-trans* isomerization of the azobenzene moiety, which in turn brings about a relative reorientation of the ferrocene rings, pushing the porphyrins closer together, so that a different twisting of the bis-isoquinoline rings is forced. Interestingly, the time scale of the azobenzene isomerisation (ns), of the ferrocene ring 'rotation' (μs) and of the bis-isoquinoline isomerisation (ms) is significantly different, suggesting a multistep process of decomplexation, isomerisation and recomplexation.

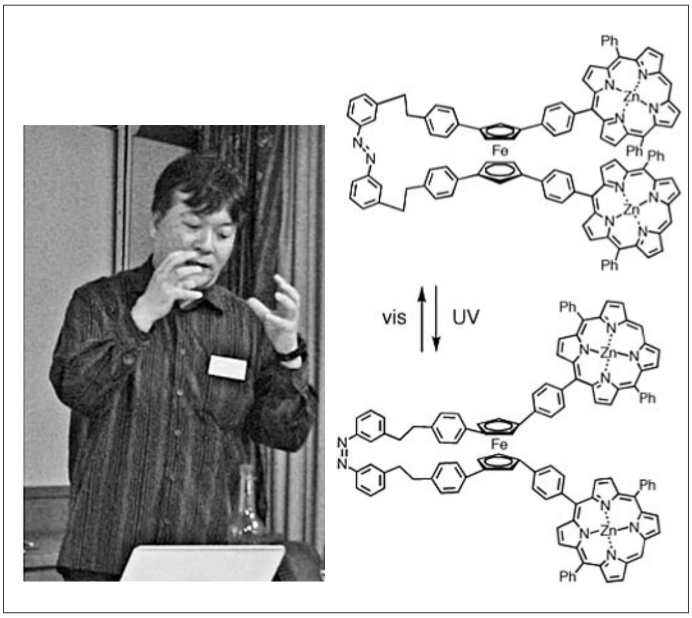

Fig. 2. Takuzo Aida talking about molecular scissors that operate with light.

At the end of his two stunning talks, Takuzo Aida described the results recently achieved in his laboratories regarding new conductive hexabenzocoronene nanotubes and their application in optoelectronic devices, including photovoltaics. He closed by discussing the preparation of a new stretchable organic light-emitting diode display, using printable elastic conductors.

Fullerenes could not be ignored in a meeting on biosupramolecular chemistry. For this reason, the organizing committee invited ***Jean-François Nierengarten*** from the University of Strasbourg, who is one of the most important specialists in this field.[3] He gave three outstanding lectures of exceptional educational value, covering a wide range of research regarding $C_{60}$. This included synthetic methodology, photophysical studies, properties and possible applications of $C_{60}$-dendrimers. He started with the contributions from his research group in the synthesis of dendrimers composed of porphyrins and fullerenes and the study of electron transfer reactions in these architectures. He highlighted that fullerene is a superb electron acceptor but it could also behave as energy acceptor, and therefore the energy transfer could quench the desired photoinduced charge separation in the system. A very elegant solution to overcome this obstacle was to attach fullerene acceptors moieties closer to the porphyrin donor using imidazole coordination chemistry.

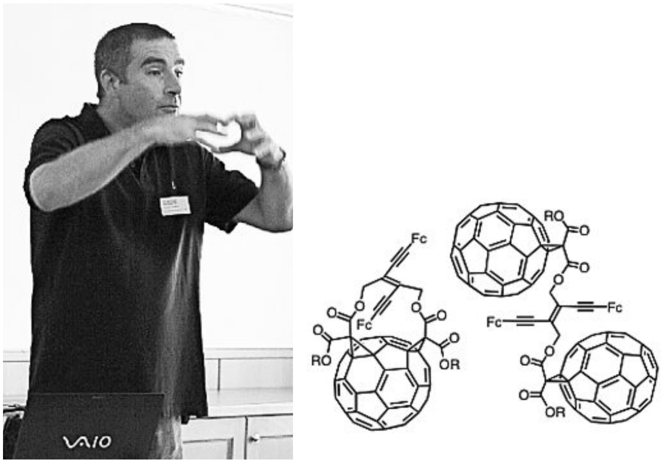

Fig. 3. Jean-François Nierengarten talking about the combination of fullerene acceptors with donors such as ferrocene (Fc).

Jean-François Nierengarten then moved on to fullerene-substituted bis(ferrocenylethynyl) derivatives (Fig. 3). He explained how the intramolecular interactions of the $C_{60}$ units with the π-conjugated bridge could modulate the strength of the electronic interactions between the two redox centers. An interesting part of his lecture was the description of the first system containing a luminescent Ir(III) cyclometallated species and a functionalized $C_{60}$. He described the synthesis of these compounds and the energy transfer process from iridium to the $C_{60}$ triplet state that leads to phosphorescence of the fullerene. An attractive topic for concluding his three enriching lectures was the synthesis and electrochemical properties of fullerene-nanoclusters. In these nanoclusters, up to 24 $C_{60}$ units were placed around a hexaphenylbenzene core. The key step in the synthesis was a cobalt-catalyzed cyclotrimerization of bis(aryl)alkyne fullerodendrimers.

The use of supramolecular chemistry and self-assembling interactions has been proved to be of critical importance when studying the biochemistry involved in membrane transport and ion channels. To expand the audience's background in this field, ***Jeffrey Davis*** from the University of Maryland, College Park, was invited to the 2009 CUSO summer school.[4] Jeffrey Davis explained significant issues concerning this topic in a very didactic and clear-cut way. This included the self-assembly of lipophilic nucleosides, synthetic ion channels formed by nucleobases, anion selective transport across membranes and new artificial lipids designed to form large pores (Fig. 4).

In the beginning of his first lecture, he described some of the supramolecular structures that have been built using guanine self-assembly. These synthetic G-quartet systems could be used as a model for understanding the assembly in DNA and RNA, and they also have potential impact on sensor development, materials science, and nanoscience. He highlighted the diverse functions that can arise from these interesting supramolecular assemblies such as synthetic ion channels, dynamic gels, liquid crystals, hydrogels, noncovalent polymers, nanomachines, molecular electronic devices, biosensors, therapeutic aptamers and catalysts. As an interesting example he remarked the ability of cations but also anions to control the structure and stability of G-quartets and the complementary isoG-quintets in solution.

His second lecture was more focused in membrane biochemistry where he underscored the value and importance of finding new ways to control the transport of anions across lipid membranes. The development of efficient synthetic systems that could mediate this process may provide new ways to treat diseases such as cystic fibrosis. In this respect, he showed his

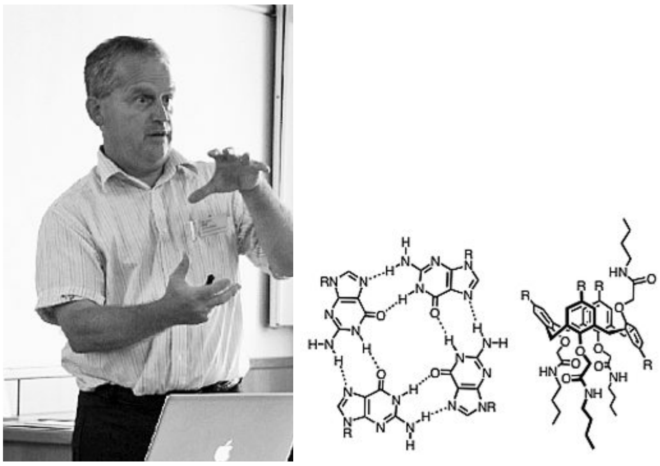

Fig. 4. Jeffrey Davis on G-quartets and calixarenes to transport cations and anions, respectively.

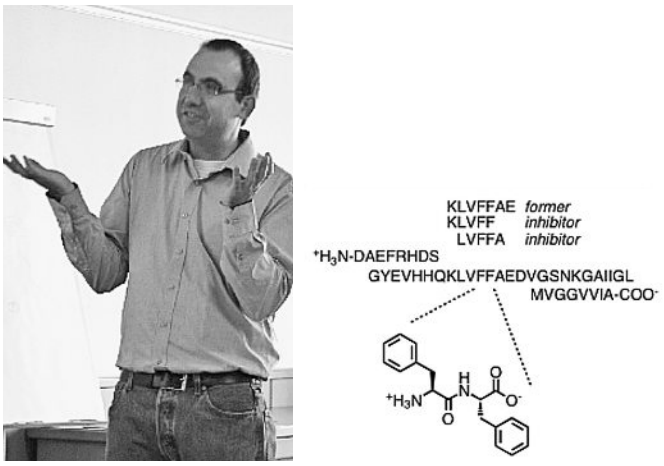

Fig. 5. Ehud Gazit talking about peptide self-assembly in neurodegenerative diseases and nanotechnology.

results with synthetic calixarenes that could be used to enable or inhibit transmembrane chloride transport. Continuing with this subject, he highlighted the significance of the bicarbonate ion, which is transported across biomembranes *in vivo* by membrane-bound proteins. However, not much is known about the structure of these proteins, although malfunction of bicarbonate transport leads to diseases such as cystic fibrosis, heart diseases and infertility. Therefore, he decided to study this transport trying to develop new bicarbonate carriers. He found that 'small' molecules such as the natural product prodigiosin and synthetic analogues could facilitate the chloride–bicarbonate exchange process typically mediated by the membrane proteins.

It was then the turn of ***Ehud Gazit*** from Tel Aviv University.[5] He described to the audience his journey through the amyloid fibers research. It was really interesting to notice how this valuable but simple idea could originate infinitive possibilities not only related to medicinal problems (Alzheimer's disease, Parkinson's disease, type II diabetes, prion disorders) but also for the preparation of new and attractive nanomaterials.

In the first part of his lectures, he underscored that the key step in amyloid formation is the transition of a protein from its native structure to a β-sheet arrangement. Therefore the introduction of a β-breaker moiety, aminoisobutyric acid (Aib), in the short recognition motif of an artificial peptide leads to a significant inhibition of the aggregation of amyloid fibers. During his research in this field, Ehud Gazit identified three different peptide sequences that could mediate the formation or inhibition of the amyloid fibers. The structural motifs were as follows KLVFFAE (formation), KLVFF and LVFFA (inhibition). The fact that the repetitive unit in all of them was diphenylalanine (FF) pushed forward the careful examination of this very simple motif (Fig. 5).

The results of this study were fantastic and ended up with the observation of the self-assembly of this short dipeptide into discrete and stiff nanotubes. Moreover the reduction of ionic silver within the nanotubes followed by enzymatic degradation of the peptides afforded nanowires with a long persistence length. In his third and last lecture, Ehud Gazit showed the multiple and original applications of these FF-nanotubes such as self-assembled platforms for electrochemical biosensing, the preparation of self-cleaning glass, and as a new material for teeth implants. The suggestion from the audience to combine these properties for the invention of self-cleaning teeth was received with applause.

In summary, the summer school provided a broad overview on current fundamental research efforts towards functional biomimetic architectures, which pave the way for fascinating applications in nanofabrication, solar cells, optoelectronics and biosensing. The organized mountain hikes and other possibilities to restore energy in the afternoon were a warmly accepted opportunity to aid in digesting the ample lunch buffets as well as the morning lectures, such that most participants were starving for the evening lectures and poster sessions. To break the ice and to stimulate discussions among the participants, the organizers came up with the idea to confer each evening a 'Question-of-the-Day Award', which went to *Erin Sheepwash* from Lausanne (Sunday), *Marc Creus* from Basel (Monday), *Guillaume Duvanel* from Geneva (Tuesday), *Piero Geotti-Bianchini* from Bern (Wednesday) and *Jens Peter Hermes* from Basel (Thursday). The speakers were pleased about the success of this idea and admitted that they have never experienced a conference with such lively discussions. This prompted the organizers to additionally acknowledge the persistent contributions of *Ruud van Deursen* (Bern) and *Andreas Hennig* (Geneva). The highly stimulating atmosphere during the whole conference also extended into the poster session discussions, which were despite (or because) the late hour so lively that the organizers had to interfere, switch off the lights and lock the conference halls at midnight.

The high quality of the posters and of the accompanying discussions was acknowledged by conferring poster prizes to *Torsten Peterle* (*OBC* Award, Basel, 'Benzylthioether stabilized gold nanoparticles: toward novel hybrid superstructures'), *Rupali Shivapurkar* (*OBC* Award, Geneva, 'An automatic titration device for the determination of chemical constants using 2D NMR. Applications to the determination of $pK_a$s in complex mixtures'), *Dirk de Bruyn Ouboter* (Basel, 'Suitable applications of self-assembled peptide beads'), *François Otis* (Laval, 'Synthesis and characterization of multiple crown helical peptides having ion channel properties'), and *Guillaume Journot* (Neuchâtel, 'Synthesis, structure and complexation of calix[4]pyrroles: towards novel macrocycles').

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[1] a) K. D. Schierbaum, T. Weiss, E. U. T. van Veizen, J. F. J. Engbersen, D. N. Reinhoudt, W. Göpel, *Science* **1994**, *265*, 1413; b) D. N. Reinhoudt, M. Crego-Calama, *Science* **2002**, *295*, 2403; c) L. J. Prins, F. De Jong, P. Timmerman, D. N. Reinhoudt, *Nature* **2000**, *408*, 181; d) H. Xu, X. Y. Ling, J. van Bennekom, X. Duan, M. J. W. Ludden, D. N. Reinhoudt, M. Wessling, R. G. H. Lammertink, J. Huskens, *J. Am. Chem. Soc.* **2009**, *131*,

797; e) D. I. Rozkiewicz, B. J. Ravoo, D. N. Reinhoudt, *Langmuir* **2005**, *21*, 6337; f) J. M. Spruell, b. A. Sheriff, D. I. Rozkiewicz, W. R. Dichtel, R. D. Rohde, D. N. Reinhoudt, J. F. Stoddart, J. R. Heath, *Angew. Chem., Int. Ed.* **2008**, *47*, 9927.

[2] a) M. Enomoto, T. Aida, *J. Am. Chem. Soc.* **2002**, *124*, 6099; b) D. L. Jiang, T. Aida, *J. Am. Chem. Soc.* **1998**, *120*, 10895; c) K. Okuro, K. Kinbara, K. Tsumoto, N. Ishii, T. Aida, *J. Am. Chem. Soc*. **2009**, *131*, 1626; d) D. Ishii, K. Kinbara, Y. Ishida, N. Ishii, M. Okochi, M. Yohda, T. Aida, *Nature* **2003**, *423*, 628; e) T. Sekitani, H. Nakajima, H. Maeda, T. Fukushima, T. Aida, K. Hata, T. Someya, *Nat. Mat.* **2009**, *8*, 494.

[3] a) F. Nastasi, F. Puntoriero, S. Campagna, S. Schergna, M. Maggini, F. Cardinali, B. Delavaux-Nicotc, J.-F. Nierengarten, *Chem. Commun*. **2007**, 3556; b) T. M. Figueira-Duarte, V. Lloveras, J. Vidal-Gancedo, A. Gégout, B. Delavaux-Nicot, R. Welter, J. Veciana, C. Rovira, J.-F. Nierengarten, *Chem. Commun*. **2007**, 4345; c) U. Hahn, M. Elhabiri, A. Trabolsi, H. Herschbach, E. Leize, A. Van Dorsselaer, A.-M. Albrecht-Gary, J.-F. Nierengarten, *Angew. Chem., Int. Ed.* **2005**, *44*, 5338; d) U. Hahn, E. Maisonhaute, C. Amatore, J.-F. Nierengarten, *Angew. Chem., Int. Ed.* **2007**, *46,* 951.

[4] a) J. T. Davis, G. P. Spada, *Chem. Soc. Rev*. **2007**, *36*, 296; b) X. Shi, J. C. Fettinger, J. T. Davis, *Angew. Chem., Int. Ed.* **2001**, *40*, 2827; c) J. L. Seganish, P. V. Santacroce, K. J. Salimian, J. C. Fettinger, P. Zavalij, J. T. Davis, *Angew. Chem., Int. Ed.* **2006**, *45*, 3334; d) J. T. Davis, P. A. Gale, O. A. Okunola, P. Prados, J. C. Iglesias-Sanchez, T. Torroba, R. Quesada, *Nat. Chem.* **2009**, *1*, 138.

[5] a) S. Golead, E. Gazit, *Angew. Chem., Int. Ed.* **2004**, *116*, 4133; b) C. Soto, *Nat. Rev.* **2003**, *4*, 49; c) R. Meital, E. Gazit, *Science* **2003**, *300*, **625**; d) M. Reches, E. Gazit, *Nat. Nanotechnol*. **2006**, *1*, 195; e) M. Yemini, M. Reches, J. Rishpon, E. Gazit, *Nano Lett.* **2005**, *5*, 183.