

## 31st Euchem Stereochemistry Conference

Bürgenstock, April 28–May 4, 1996

The 31st incarnation of the Euchem Stereochemistry Conference brought together 131 participants from all over the world, both from academia as well as industry. This year's program covered, as in previous years, a wide variety of topics reflecting the diverse interests of the conference president, *F. Diederich* (ETH-Zürich, Switzerland). It spanned the range from enzyme mechanism elucidation and supramolecular architecture to combinatorial chemistry and natural product synthesis. The conference was held, in a long-standing tradition, at the Bürgenstock hotel complex, situated high above the Vierwaldstätter See in a magnificent surrounding that, unfortunately, could only be appreciated during the few periods of drought. Here, the vice president, *S.V. Ley* (University of Cambridge, England), as usual in charge of the weather, could not quite perform to the expectations of the participants. They in turn were especially pleased by the attendance of former president *G. Ourisson* (Université Louis Pasteur, Strasbourg, France) as guest of honor. In one of the many traditions of this symposium, the participation of numerous young European scientists was made possible by the generous support of the European Science Foundation (Strasbourg) and the Swiss National Science Foundation as well as contributions from industry.

The first day of the conference already tied together a series of marvellous lectures from various fields. In the opening lecture entitled 'Neocarzinostatin: A New Mechanistic Puzzle and a Synthetic Problem Solved', *A.G. Myers* (California Institute of Technology, Pasadena, USA) presented the total synthesis of the neocarzinostatin (NCS) chromophore aglycon and the recently solved X-ray crystal structure of the native protein-NCS complex which provided important insight to the mechanism of activation. In view of the inherent instability of this DNA-binding enediyne antibiotic the effort put into its total synthesis is all the more impressive. Shifting gears, *R. Ghadiri* (Scripps Research Institute, La Jolla, USA) in his talk focused on 'Peptide Architecture: From Form to Function'. His design of cyclic peptides consisting of alternating D- and L-amino acids allowed the self-assembly of nanotubular structures very similar, although on a small-



F. Diederich  
(the President)

er scale, to the protein coat of tobacco mosaic virus. The functionalization of individual peptide rings by alkenyl side chains made it possible to stabilize these structures by covalent bond formation after self-assembly. Other functional groups were used to modulate hydrophobicity of such tubes, to form trans-membrane ion channels, to mimic ligation processes on nanotubular templates, or even to construct models of helix bundle metalloproteins.

In late afternoon on Monday as well as on Tuesday, Thursday, and Friday, a two part poster session took place which gave the many younger participants the opportunity to present their work. The high quality as well as the quantity of the posters reflects the special emphasis that conference president *F. Diederich* has given this part of the proceeding. The evening lecture on Monday was presented by *J.-A. Stubbe* (Massachusetts Institute of Technology, Cambridge, USA). She described mechanistic findings on ribonucleotide reductases of different origins. Using site-directed mutagenesis, isotope labeling, and a series of substrate analogs, a concise picture of the multi-step reduction process was revealed. Although far from complete – especially the mechanism of transposition of the initially formed radical center to the active site remains unclear – these important studies have already led to the development of nucleoside analogs of potential clinical use.

On the second day, *D.A. Dougherty* (California Institute of Technology, Pa-

sadena, USA) continued the protein theme in his lecture 'Physical Organic Chemistry on the Brain' dealing with the mechanism of activation of nicotinic acetylcholine receptor (nAChR). His interest in nAChR, a prototype ligand-gated ion channel, obviously was spurred by possible  $\pi$ -cation interactions knowing that the agonist binding site contains many aromatic amino acids and that acetylcholine is a positively charged neurotransmitter. Mapping essential amino acids within the active site by site-directed mutagenesis has so far not led to a complete understanding of acetylcholine binding. But the introduction of unnatural amino acids at the gate has yielded a structural model for receptor assembly. *J.S. Siegel* (University of California, San Diego, USA) then took the audience back to synthetic organic chemistry grounds with his 'Stereochemical Variations on the Sphere'. Starting from the synthesis of cyclophanes as a molecular description of a sphere, the sphere was reduced to its parts, exemplified by corannulene. Through functionalization of the rim of these hemispheres, different basket- and sphere-like molecules could be created. Further graphical simplification of the sphere led to rings and from there to non-planar graphs which found correspondence in the synthesis of a *Kuratowski* cyclophane. We then gained insight to Icelandic mythology when presented an entertaining history of the *Borromean* rings, three rings intertwined in



R. Ghadiri



J.S. Siegel



J.S. Moore



F.A. Quiocho



R.R. Schmidt

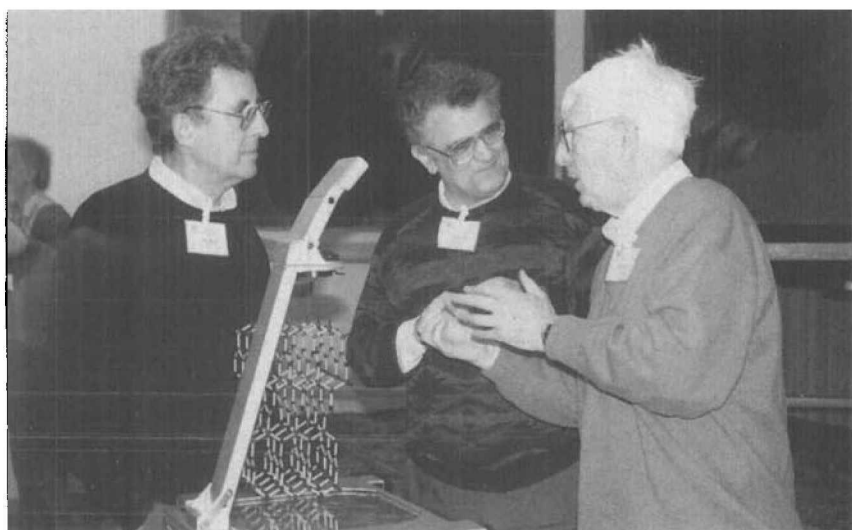


W.C. Still

the same way as the olympic rings, again illustrated by a synthetic target.

The second day was brought to a conclusion by *B. Meijer* (Eindhoven University of Technology, The Netherlands) who described studies on 'Dendrimers and Supramolecular Polymer Chemistry'. The poly(propylenimine) dendrimers he described are created by the high yield *Michael* addition of acrylonitrile to polyfunctional amines. Having optimized the heterogeneously catalyzed reduction of the terminal nitrile groups he discussed the formation of molecular boxes by capping the end groups of an early generation dendrimer with sterically demanding substituents. In the presence of guest molecules, such as dyes, inclusion complexes may be formed. Alternatively, the end groups may be derivatized by hydrophilic moieties thus forming molecular inverse micelles and by using chiral dendrimer building blocks asymmetrically shaped objects can be built up. The evening ended with a lively discussion of the term cryptochirality following a comment by *J. Dunitz* (ETH-Zürich, Switzerland).

On Wednesday morning the lectures remained in the area of supramolecular chemistry. *J.S. Moore* (University of Illinois, Urbana-Champaign, USA) described his research on 'Modular Chemistry, Molecular Architecture, and Functional Materials'. The design goal was to define crystalline hosts held together by H-bonds or metal-ligand binding that have stable compartments. Within these compartments it should then be possible to study the dynamics of guest inclusion and guest exchange. The realization revolved around hexagons built from benzoic acids at the corners linked by ethynyl bridges. In a different approach, dicyano-substituted biphenyls or symmetric tricyanobenzene in conjunction with silver(I) and a non-coordinating counterion were used to create marvelous crystalline networks of stacked and interlocked aromatic rings. An aromatic supermolecule was also the focus of *A. Hirsch* (Universität Erlangen, Germany) in his talk 'Regioselective Addition Reactions and Framework Modifications of Buckminsterfullerene (C<sub>60</sub>)'. C<sub>60</sub> easily undergoes various addition reactions but is hard to oxidize. By carefully controlling the sequence of addition reactions pentafunctionalized buckyballs were obtained that allowed the regioselective oxidation and subsequently the opening of the carbon framework. This may potentially lead to the specific synthesis of inclusion compounds and open ways to fullerene-based materials with tailor-made physical properties.



H.-B. Bürgi

M. Lahav

J. Dunitz



F. Diederich

J.-A. Stubbe

After the first sunshine of the week during the afternoon hours, we could enjoy an excellent concert organized by *K. Müller* (*F. Hoffmann-La Roche AG*, Basel, Switzerland) according to the suggestions of the conference president. The *Aura Ensemble* (Basler Sinfonieorchester, Switzerland) and *Paul Lamaze* (Basler Sinfonieorchester, Switzerland) masterfully interpreted a string quartet by *Mendelssohn* and the quintet for clarinet, two violins, viola, and violoncello by *Mozart*.

The morning session on Thursday was opened by protein crystallographer *F.A. Quijcho* (Baylor College of Medicine, Texas, USA). Not sure about the scope and program of the conference, he ended up presenting three different topics. In his first lecture 'Structural Basis of Stereospecificity of an Enzyme (Adenosine Deaminase) and a Phosphate Receptor for Active Transport' detailed structural information on substrate-binding of adenosine deaminase, a zinc-containing enzyme present in all mammalian cells was described. By using various analogs of adenosine he also gave a detailed account on the enzyme mechanism. In the second part of this talk, the differences in binding modes of two bacterial phosphate- and sulfate-binding proteins were mapped. By popular request, he agreed to additionally present the work on carbohydrate recognition on Friday afternoon. *D. Lilley* (University of Dundee, England) then discussed the 'Folding of Branched Nucleic Acids: Recognition and Catalysis'. By using the experimentally straightforward technique of gel mobility assays he investigated the role of metal binding to the cores of three- and four-way junctions in nucleic acids. These structures, important in double-stranded DNA recombination and RNA secondary structure formation, display distinct structural transformations upon

metal-binding. These, in turn, have consequences on the recognition by specific proteins or – in the case of ribozymes – on catalytic activity.

The evening was devoted to small molecules again. *H. Bock* (Universität Frankfurt, Germany) in his entertaining lecture 'What Crystallizes How and Why? Static Aspects of Molecular Self-Organization from Single-Crystal Structure Data' covered the whole array of intermolecular forces in the solid state. The examples mentioned for cation solvation, H-bonding, charge-transfer complexes, and *van der Waals* interactions relied on elegantly designed experiments and represented true craftsmanship.

Friday brought a densely packed program of four lectures and the last day of the poster presentations. *M. Shibasaki* (University of Tokyo, Japan) in his lecture 'Catalytic Asymmetric Synthesis Using Heterobimetallic Complexes' first described the use of lanthanide-alkali metal complexes with substituted binaphthols in nitroaldol reactions. Through careful optimization of the reaction conditions and a proper choice of lanthanides, very high diastereo- and enantioselectivity could be achieved. Switching to catalytic asymmetric *Michael* additions required the substitution of the central atom in these complexes for aluminum. Further development eventually lead to catalysts for tandem *Michael*-aldol reactions. *R.R. Schmidt* (Universität Konstanz, Germany) discussed 'New Aspects of Glycoside Bond Formation'. Cell surface interactions with a variety of functionally different proteins involve carbohydrate recognition. In order to investigate these interactions efficient glycoside syntheses have to be developed. After a short demonstration of the versatility and efficiency of the acetimidate method, the use of anomeric phos-

phite-triesters in the synthesis of various  $\alpha$ -glycosides was assessed paving the way for the synthesis of a wealth of oligosaccharide conjugates. As mentioned above, *F.A. Quijcho* (Baylor College of Medicine, Texas, USA) continued the sugar-theme in the afternoon by speaking on 'Protein-Carbohydrate Interactions'. By comparing the active sites of three highly specific carbohydrate-binding proteins, a general motif for carbohydrate recognition emerged based on specific and cooperative H-bonding networks and stacking with aromatic amino acid side chains.

On the final evening, *W.C. Still* (Columbia University, New York, USA) described recent contributions from his laboratories to the ever more important field of combinatorial chemistry. The ingenious method of labeling solid supports with a binary chemical tag was applied to the screening of short peptide libraries for binding to a variety of hosts. The symposium was then summed up in a unique lecture by *K. Müller* (*F. Hoffmann-La Roche AG*, Basel, Switzerland). His humorous review bridging the world of small to medium sized molecular structures and solid support beads left no one in the audience unmoved. The meeting was closed after a few entertaining thoughts on the creation of chemistry advisors by guest of honor *G. Ourisson* (Université Louis Pasteur, Strasbourg, France).

The 32nd EuChem Conference on Stereochemistry will take place at the Bürgenstock resort from April 4th to May 3rd, 1997, under the presidency of *S.V. Ley* (University of Cambridge, England).

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