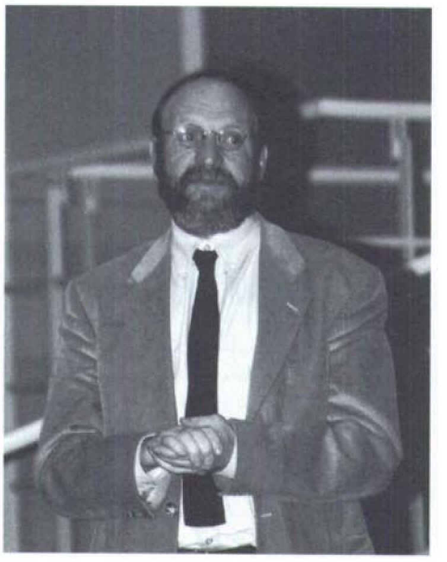
ties of the lanthanide complexes to be influenced that he and his group had synthesized. The goal of these studies is to obtain intelligent materials for applications such as switches.

Prof. Claude Piguet, University of Geneva, demonstrates the use of lanthanides complexes in material sciences.

Closing Remarks

It was obvious to everyone at the symposium that there was a lot more to the science presented than can be covered in any one lecture. But as the goal of this symposium had been to present a cross-section of chemistry in Swiss academia there was not the time to go more into the details. However it was impressive to see during this one-day meeting how knowledge in one field was used and applied in a completely different context by another speaker. Lanthanide complexes *e.g.* appeared twice, once as the cutting 'head' in the lecture of Prof. Häner and then in the lecture of Prof. Piguet in their applications for material science. The goal of this symposium to show the breadth and the interconnectivity of today's research in chemistry was certainly achieved.

The day ended with an warm welcome pronounced by Mr. *Jean-Daniel Perret*, representing the University in the Canton of Neuchâtel, who described the importance of the University for the Canton and who then invited all the participants to profit from the apéritif offered by the Canton to the participants. The day hopefully convinced the participants that chemistry in Swiss academia is healthy, but also that the Society is full of life, so that it is worthwhile for chemists to be or to become members of our Society.



Jean-Daniel Perret, the representative of the University of Neuchâtel, welcomes all the speakers and participants to Neuchâtel.

Chimia 55 (2001) 463–465

ISSN 0009–4293

4th Lausanne Conference on Bioorganic Chemistry, March 8/9, 2001

Institute of Organic Chemistry, University of Lausanne

For the fourth time, the Lausanne scientific core community, augmented by a considerable number of regular scientific guests, focused interest onto topics in bioorganic chemistry. Highly ranked speakers from Europe and overseas accepted invitations, and allowed younger scientists to participate and communicate interactively. And again *Manfred Mutter*, who together with *Pierre Vogel* and *Gabriele Tuchscherer* organized the meeting, welcomed a particularly large and eager audience of well over 200 scientists in an auditorium generously decorated with forsythia.

'Molecular Recognition' is the keyword for a long-standing endeavor of Prof. *François Diederich*, ETH Zürich, to understand host-guest interactions at a high level of molecular perception. This endeavor is by no means confined uniquely to the ivory tower of purely academic research, but perfectly well suited to shape up pharmaceutical research programs. By means of two examples of a fruitful collaboration with F. Hoffmann-La Roche Ltd., the design of thrombin inhibitors as well as bisubstrate inhibitors of the (*S*)-adenosylmethionine (SAM)-dependent enzyme catechol O-methyltransferase (COMT), he convincingly demonstrated the power of rational drug design. This process is, of course, the more promising, the more structural information on a particular receptor is available, preferably at the resolution of an X-ray structure. By thoughtful computer-assisted design, the extent of structural information can be complemented, and the convergence of a lead-finding process further enhanced when taking into consideration first-order determinants of intermolecular interactions such as multiple hydrogen-bonding, aromatic stacking, edge-to-face interactions or fluorophobic/fluorophilic effects.

As Prof. *Franz P. Schmidtchen* of the TU München explained in the following lecture, co- or posttranslational decoration of peptides and proteins with non-proteinogenic moieties like saccharides,

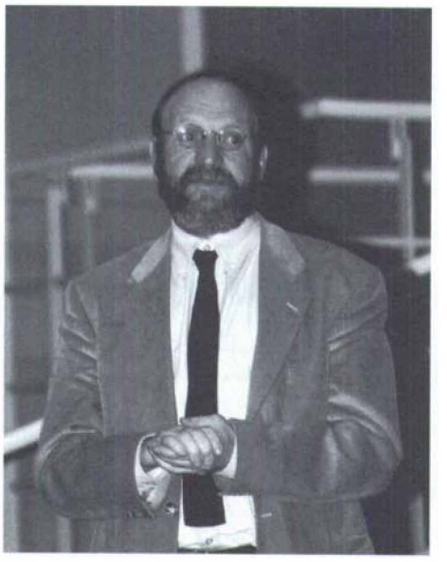
ties of the lanthanide complexes to be influenced that he and his group had synthesized. The goal of these studies is to obtain intelligent materials for applications such as switches.

Prof. Claude Piguet, University of Geneva, demonstrates the use of lanthanides complexes in material sciences.

Closing Remarks

It was obvious to everyone at the symposium that there was a lot more to the science presented than can be covered in any one lecture. But as the goal of this symposium had been to present a cross-section of chemistry in Swiss academia there was not the time to go more into the details. However it was impressive to see during this one-day meeting how knowledge in one field was used and applied in a completely different context by another speaker. Lanthanide complexes *e.g.* appeared twice, once as the cutting 'head' in the lecture of Prof. Häner and then in the lecture of Prof. Piguet in their applications for material science. The goal of this symposium to show the breadth and the interconnectivity of today's research in chemistry was certainly achieved.

The day ended with an warm welcome pronounced by Mr. *Jean-Daniel Perret*, representing the University in the Canton of Neuchâtel, who described the importance of the University for the Canton and who then invited all the participants to profit from the apéritif offered by the Canton to the participants. The day hopefully convinced the participants that chemistry in Swiss academia is healthy, but also that the Society is full of life, so that it is worthwhile for chemists to be or to become members of our Society.



Jean-Daniel Perret, the representative of the University of Neuchâtel, welcomes all the speakers and participants to Neuchâtel.

Chimia 55 (2001) 463–465

ISSN 0009–4293

4th Lausanne Conference on Bioorganic Chemistry, March 8/9, 2001

Institute of Organic Chemistry, University of Lausanne

For the fourth time, the Lausanne scientific core community, augmented by a considerable number of regular scientific guests, focused interest onto topics in bioorganic chemistry. Highly ranked speakers from Europe and overseas accepted invitations, and allowed younger scientists to participate and communicate interactively. And again *Manfred Mutter*, who together with *Pierre Vogel* and *Gabriele Tuchscherer* organized the meeting, welcomed a particularly large and eager audience of well over 200 scientists in an auditorium generously decorated with forsythia.

'Molecular Recognition' is the keyword for a long-standing endeavor of Prof. *François Diederich*, ETH Zürich, to understand host-guest interactions at a high level of molecular perception. This endeavor is by no means confined uniquely to the ivory tower of purely academic research, but perfectly well suited to shape up pharmaceutical research programs. By means of two examples of a fruitful collaboration with F. Hoffmann-La Roche Ltd., the design of thrombin inhibitors as well as bisubstrate inhibitors of the (*S*)-adenosylmethionine (SAM)-dependent enzyme catechol O-methyltransferase (COMT), he convincingly demonstrated the power of rational drug design. This process is, of course, the more promising, the more structural information on a particular receptor is available, preferably at the resolution of an X-ray structure. By thoughtful computer-assisted design, the extent of structural information can be complemented, and the convergence of a lead-finding process further enhanced when taking into consideration first-order determinants of intermolecular interactions such as multiple hydrogen-bonding, aromatic stacking, edge-to-face interactions or fluorophobic/fluorophilic effects.

As Prof. *Franz P. Schmidtchen* of the TU München explained in the following lecture, co- or posttranslational decoration of peptides and proteins with non-proteinogenic moieties like saccharides,

lipid membrane anchors, prosthetic groups, exotic amino acids or others is essential for biological function. Whereas modern genetic engineering tools allow expression of site specifically mutated protein targets to a high degree of the investigators intent, subsequent steps in protein maturation are much less amenable to directed molecular design incentives. Nevertheless, the bio-organic chemist can forge nature's effector principles to his own demands: Enzymatic steps involving reverse proteolysis by the thiol aminodipeptidase Cathepsin C or the restriction endopeptidase IgA-Protease, followed by N-Myristoyl-Transferase (NMT) acting on fatty acyl CoA analogs. Ultimate chemical bioconjugation exploiting palladium phosphane catalyzed C–C cross-coupling reactions in mild aqueous solution were discussed and showed that modern bio-organic chemistry has definitely paved the way to protein engineering.

Abasic lesions within DNA occur as a result of electrophile induced depurination in the course of spontaneous mutations, irradiations, alkylations or enzymatically as a first step in DNA repair processes. Prof. *Jean Lhomme*, University of Grenoble, France, in his own compelling way presented studies in molecular recognition involving the abasic site. Thereby a purine residual substitute is coupled to an acridine type intercalator *via* a spermidine-like unit, which has a high minor groove and phosphate affinity and seems to contribute to the overall stability of the complex. Molecular design of intercalator heads as well as linker dimensions are of crucial importance to efficient DNA binding. Footprinting and NMR-studies demonstrated the precise targeting of the abasic site, whereas a series of derivatives were designed to exert proven AP-nuclease activity.

The second day's sessions were opened by Prof. *Manfred Reetz*, Max-Planck Institut für Kohlenforschung, Mülheim, Germany, concisely illustrating the value of test-tube evolution in the creation of enantioselective enzymes for organic transformations. Instead of testing a large number of chiral ligands as required for enantioselective transition metal catalysis, the chiral determinant offered by enzymes can be shaped by directed molecular evolution of a given weakly selective enzyme. For the process presented by Reetz, random mutagenesis combined with an efficient screening system for rapid identification of enantioselective mutants is essential for success. As an example, the *ee*-value of only 2% of a lipase from *Pseudomonas aeruginosa* could be increased to over 90% by the evolution method. The result of this approach deserves well being compared to the results obtained *via* the generation of catalytic antibodies, where the cell's own variation principle is elegantly exploited, however restricted to the class of surface active immunoglobulin fragments.

Biomolecular recognition of DNA as well as of protein receptors by miniature protein mimetics was subsequently highlighted by *Alanna Schepartz*, Professor of chemistry at Yale University, USA, in a most original approach to stabilize the α-helix. By joining a polyproline stretch reminiscent of proline rich regions in the avian pancreatic peptide to the DNA recognizing N-terminal helix of the well-known yeast transcription factor GCN4, the DNA binding free energy of the latter was enhanced by more than 3 kcal/mol. The polyproline motif has been shown to fold to the α-helical part of the mini-protein in its extended all-*trans* polyproline II conformation, whereby the backbone carbonyl groups are more exposed to interact in intra- as well as intermolecular H-bonding or aprotic dipolar contacts. Not surprisingly, but highly significant towards therapeutic goals, variants of this miniature protein bearing essential residues of the amphipathic p53 monohelical transactivation domain proved highly effective in binding to their receptor, notably the MDM2 oncogenic protein.

Is DNA a carrier of electric charge? A convincing wealth of positive evidence to this long-standing question was presented by Prof. *Bernd Giese* from the University of Basel. His major field of investigation, the chemistry of radicals, predestines him to this sort of objective. And his answer to the above question is 'Yes' – but only if DNA is already charged itself: injection of a positive radical charge to (and the expulsion of an electron from, respectively) a guanine base residue makes all guanines carriers of charge, even in aqueous environment. Charge transport along distances of more than 50 bases has been detected, and it is proposed that such transfer reactions occur *via* a hopping mechanism relayed by purine residues. Charge transport through DNA over long distances not only propagates or delocalizes 'oxidative stress' along the molecule, but also features DNA as an interesting molecule for nanoelectronics.

The Friday afternoon session block was opened by an enthusiastic account by *Andrew D. Miller*, Director of the Imperial College Genetic Therapies Centre (GTC), London, not only of his newly inaugurated Institute, but also of his research team's progress towards non-viral vector systems for gene therapy applications. Cationic liposomes were formulated from a cationic lipid called 'cytofectin' and a neutral co-lipid such as dioleoyl L-α-phosphatidyl ethanolamine (DOPE). Such molecular vectors form the basis for a successful delivery of lacking or depleted genes, for instance of the cystic fibrosis transmembrane conductance regulator (CFTR) gene to the lungs of cystic fibrosis transgenic mice. The developed chemical transfection vectors owe their efficacy first to their ability to neutralize, condense and encapsulate nucleic acids, and secondly to the buffering capacities of the weakly basic amine groups ($pK_a < 8$) allowing release of the gene into the cytosol after transfection. Miller always wanted to embark on projects which went beyond pure chemistry, and the presented methodology is certainly a way to practice chemistry at its own frontiers.

Another approach towards gene therapeutic drugs was presented by Prof. *Peter E. Nielsen*, University of Copenhagen and Pantheco A/S, Denmark, who put into evidence the broad scope of the pseudopeptide DNA mimetic PNA (peptide nucleic acid). This unique constitution has not only a high potential within the antisense RNA context, but is tailored to bind to double stranded DNA as well. Interference with translation and transcription is therefore equally possible, the latter particularly well by complexation of double stranded DNA in AT-rich target regions. Due to its high chemical stability and bioavailability, PNA has already passed a number of important hurdles on the way of its recognition as a gene regulating antibacterial drug with modular targeting properties.

Does chemistry always have to deal with the explicit making and breaking of bonds? Prof. *Ernest Giralt* from the University of Barcelona, Spain, definitely put aside old-fashioned ideas about the principle task of chemistry: by the impressive paradigm of virus capside protein he put forward the principles of molecular recognition by non-covalent interactions leading to self-assembly. Innumerous examples found in nature are waiting to be emulated by creative chemists. In particular, the N-terminal domain of maize γ-zein presents an interesting proline rich aggregation nucleating sequence, which was elaborated into the synthetic $(VHLPPP)_8$ oligopeptide. This polyproline type II helical unit self-assembles on graphite surfaces, forming

amphipathic monolayers with diameters of 1.2 nm measured by atomic force microscopy. Organized domains of nanofibrils with larger diameter could as well be imaged, whereby incorporated terminal cysteine to cystine crosslinking was mandatory to determine relative orientations of monolayers – making and breaking of bonds remains suitable to get more insight even within a project on self-assembly!

The concluding lecture given by *Laura L. Kissling*, Professor of Chemistry and Biochemistry at Wisconsin-Madison, USA, was a vivid and lucidly presented tour d'horizon on the tuning of cellular responses by chemical ligands. Starting from a view of the cell surfaces across the living kingdoms – from the most simple surface sensitive organisms like *Dictyostelium*, over bacteria which can change direction of their movements according to nutrient concentrations, to higher organisms which react through their immune response on external stimulus, the major principles found in nature like reduction of dimensionality or multivalency through the presence of several receptor units can be perceived. In particular, Kissling's research group focuses on the exploitation of multivalency through the generation of multivalent ligand arrays *via* the ring-opening metathesis polymerization (ROMP) reaction. Carbohydrate recognition epitopes were varied systematically, as well as the downregulation of cell-surface L-selectin by multivalent ligands studied, a protein involved in the inflammatory response.

Our way of introductory **poster sessions** through three minutes microtalks for each poster presented found general appreciation. The facettes were indeed very broad this year, treating themes like charge transport through DNA *via* radical intermediates, step-by-step solid support synthesis of 3'-peptidyl-RNA, *in vitro* selection of novel DNA repair enzymes, non-linear optics to study DNA oligonucleotides in water solution as well as proteins adsorbed at liquid/liquid interfaces, investigation of biomolecular hydration through radiation damping in NMR, cross-correlations for the characterization of hydrogen bonds and CSA tensors, resolving contradictions between overdetermined NMR cross-correlation rates, linear heptapeptides containing epimerization prone phenylglycines as potential intermediates in vancomycin biosynthesis, topological templates stabilized by defined β-turn types as surface mimetics of ICAM-1, a prototype template X-ray structure, new leads as inhibitors of glycosidases, regio- and diastereoselective photocyclizations in amino acids and peptides, chemoselective synthesis of glycopeptides as mimics of carbohydrate recognition function, isolation and characterization of urobilinogenoidic chlorophyll catabolites, synthesis of oligo(3-hydroxyalkanoates) for probing the role of hydrogen-bonding in the formation of helices by β-peptides, pseudoprolines in drug design through the example of cyclosporin c derivatives, targeting a bioactive *cis* conformation in the v3 loop of HIV-1, models for Zn dependent methyltransferases, directed molecular evolution of cytochrome c peroxidase, topological and functional study on gene delivery and cell trafficking by non-viral LMD vectors, chemical approach towards the understanding of DNA interstrand crosslink repair, selection of new sequence specific DNA-binding zinc finger domains, and many more which would deserve further mention.

Tendencies this year proved to be more bio-oriented, and this tendency seems only partially related to the choice of lecturers – hard-core 'organic' chemists are addressing more and more objectives within chemical biology, some even use the methods of enzymology or natural variational principles to solve classical chemical problems. As is emerging at dawn of the third millennium, the two major challenges of modern chemistry will be perceived on one side in chemical biology, on the other in materials science. Both areas will flourish on the grounds of supramolecular assembly and oligomerization – principles evolved in nature for gaining supercritical size sufficient for significant function.

Concluding remarks by Professor Mutter humorously relayed the charge of inspiration along the contiguous chain of lectures – a process which was facilitated by its generation at the beginning of the conference. Greatly rewarded and exhilarated by the presentations from our eminent scientific guests, all participants were reassured of the lasting value of this conference and its real potential to establish as a major event in the field in Switzerland. The organizers look forward to being 'in charge' again at the next 'Lausanne Conference on Bioorganic Chemistry' to take place in early March 2003.

Christian Lehmann
Institute of Organic Chemistry
University of Lausanne