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# Focal Point: Third Swiss COST Chemistry Symposium

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*Abstract:* Over a hundred scientists attended the third Swiss COST Chemistry workshop in Basel last October 2002. The scientific programme consisted of some sixty posters illustrating Swiss participation in COST programmes, and ten invited lectures which progressed from small molecule synthesis, *via* catalysis and diagnostics to chemistry in biological systems.

**Keywords:** Catalysis · COST Chemistry · Enzymes · European collaboration · Synthesis

The COST organisation provides an efficient framework for encouraging collaboration between European laboratories, and Swiss chemists have been participating in COST since its creation. The vitality of Swiss COST activity was clearly shown by the contributions at the third COST symposium which brought together all groups participating in COST actions together with a number of invited speakers. It was clearly impossible to represent all actions, and the lecture programme therefore concentrated on a few selected themes, beginning with modern synthetic methods, followed by the introduction of small molecules into biological systems, and concluding with the study of chemistry within biological systems.

The symposium began with a brief presentation of the current status of COST by Dr. *Eva Klaper* of the Federal Office of Education and Science (Bern). After some doubts, it is now certain that the COST programme will continue in the sixth framework programme of the European union. However there will be some changes, notably in the organisation of the scientific secretariat which will be organised in collaboration with the European Science Foundation, but which will remain in Brussels.

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## Session 1

The first session was devoted to **modern aspects of synthesis**, and began with Prof. *Philippe Renaud* (University of Bern) whose lecture covered new synthetic reactions using radicals, and more specifically the use of radical reactions to form carbon–nitrogen bonds. He illustrated the advantages of radical methods and presented the various approaches he has developed, notably for carboazidation of alkenes. His lecture concluded with the application of radical methods to the synthesis of alkaloids under mild conditions.

In the second lecture Prof. *Martyn Poliakoff* (University of Nottingham, GB) gave a fascinating view of the development of supercritical fluids as reaction media from the viewpoint of green chemistry. Supercritical fluids offer an alternative to environmentally unfriendly solvents, and allow greater control over reactivity by control of pressure and temperature: solubility for example, depends strongly on the pressure. Supercritical fluids are also ideally suited to continuous flow rather than batch processes. Among the examples treated were hydroformylation, hydrogenation (now scaled up to industrial scale) and oxidation using molecular oxygen which is completely miscible with supercritical water.

Prof. *Peter Chen* (ETH Zürich) presented his work on new high-throughput methods for catalyst screening using electrospray mass spectrometry. Although many homogeneous catalysts are now well characterized, industrial catalysts are often poorly defined mixtures in which only a part is catalytically active. Identification of the active species should allow much lower catalyst concentrations, with, in polymerisation reactions, a correspondingly lower level of catalyst retained in the polymer. Mass spectrometry may be used to identify the active members of a mixture (or library) of catalysts, for example by the characterization using mass spectrometry of the high molecular weight intermediates in a polymerisation reaction. He concluded his talk by discussing the possibility of using gases in the reaction chamber of the mass spectrometer to separate ions by their mobility.

Prof. Peter Chen (ETH Zürich) looking for intermediates in catalysis.

The synthetic session ended with a discussion by Prof. *Jean-Claude Chambron* (University of Burgundy, Dijon) of chirality in complex systems, especially topologically non-trivial molecules. A chemically achiral molecule such as *meso*-tartaric acid has in fact only two achiral conformations. Restriction of intramolecular motion can

lead to formally *meso* species which are never achiral, and in which two enantiomeric forms interconvert without passing through an achiral intermediate, in the same way that peeling off a right-handed rubber glove will lead to a left-handed one without ever passing through an achiral form. If one was allowed to stretch and bend bonds, without changing the topology, then achiral intermediates could be formed. However topologically more complicated species may show different behaviour, and he presented the case of a catenane which is chemically achiral but which can only be drawn with a chiral structure.

Prof. Roger Alberto does some rapid synthesis.

## Session 2

The second session concentrated on **introduction of small molecules into biological systems**. Dr. *Enzo Terreno* (University of Torino) discussed the use of lanthanide complexes, especially of gadolinium, in magnetic resonance imaging (MRI). He reviewed the requirements for efficient extracellular contrast agents, and the strategies to obtain efficient relaxivities. Most of the currently used contrast agents attain only a few percent of the theoretical maximum, largely because of the short rotational correlation times of the molecules used. Binding to larger molecules such as albumin offers a route to greater efficiencies. The excellent spatial resolution of MRI makes it an interesting potential tool for sensors, but it suffers from low sensitivity. This may be treated by increasing the number of paramagnetic ions in each sensor molecular unit. It would also be interesting to produce sensors which were responsive to the environmental conditions such as pH, $pO_2$, metabolite concentration, *etc.* Chemical Exchange Saturation Transfer (CEST) agents using lanthanides other than gadolinium show great promise for this, and have been used to measure pH and lactate concentration.

Prof. *Roger Alberto* (University of Zürich) stayed in the field of imaging in his lecture on the preparation of technetium compounds such as $[Tc(OH_2)_3(CO)_3]^+$. This precursor is used for the combination of $^{99m}Tc$ with various targeting biomolecules such as peptides for imaging various diseases. Given the short half-life of $^{99m}Tc$ and the need for preparation directly in the clinics, syntheses must be highly efficient both in terms of yield and time, as well as being compatible with biological media. He reviewed a variety of synthetic procedures developed to satisfy these demands, from simple technetium complexes to complexes bound to biomolecules.

The final speaker in this session, Prof. *Gerard van Koten* (Debye Institute, Utrecht University) adopted a different approach: rather than bind small molecules to biomolecules in order to study the latter, he uses the biomolecule to tune the property of the small molecule. Thus catalytically active species can be anchored to biomolecules. Solubility and catalytic activity are maintained, but the size of the biomolecule–catalyst complex is such that it may be retained by membrane filtration, offering a combination of the advantages of homogeneous and heterogeneous catalysis. He illustrated his talk with examples of an anchored 'pincer' type platinum complex as a sensor for $SO_2$, and catalysis of Michael addition by a pincer palladium complex bound to an enzyme simply by attaching an inhibitor of the enzyme to the back of the catalytically active complex. Prof. van Koten, who is the current chairman of COST chemistry, concluded his lecture by underlining the many possibilities for exchange of young scientists between different laboratories offered by the COST programme.

Prof. Martyn Poliakoff (left) is supercritical about Prof. van Koten's pincers (right).

## Session 3

The third session was dedicated to **chemical reactions in biological systems**, and more specifically in enzymes. Prof. *Wolf-Dieter Fessner* (Technical University of Darmstadt) discussed carbohydrate chemistry: nature shows a huge variety of carbohydrates, generated from a relatively small number of monomers. The chemist can envisage the generation of libraries of carbohydrates, many not found in nature, by suitable combination of monomers. His strategy uses well-characterised enzymes, (particularly glycoside forming glycosidases and C–C forming aldolases) obtained by overexpression in *E. coli*, to effect specific linkings. Successive use of different enzymes leads to libraries of carbohydrates, usually differing only in the stereochemistry at the carbon centres. For such reactions stereoselective preparation of precursors is not necessary because the use of pairs of diastereomeric substrates only enhances the accessible product stereodiversity.

Prof. *Horst Vogel* (Ecole Polytechnique Fédérale de Lausanne) presented new technologies for studying the reactions of G-protein-coupled receptors. Membrane proteins represent some 40% of the human genome, but structural data are much rarer than for other proteins. The G-protein-coupled receptors are a particularly important family of membrane proteins and react to a broad range of stimuli such as light, neurotransmitters, and hormones. One technique involves attaching the membrane containing the receptor to a sensor surface and monitoring the interaction of activated receptors with signalling molecules using surface sensitive techniques, for example, surface plasmon resonance spectroscopy. A second approach requires the extrusion of the receptors in vesicles, which are then localised in microarrays produced by micro-contact printing, and studied by fluorescence correlation microscopy.

Prof. *Jean-Louis Reymond* (University of Bern) returned to two aspects of the study of enzymes. He discussed the search for catalytic activity in peptide dendrimers as an alternative to folded peptide chains, and showed that catalytic activity is indeed observed in dimers (formed by S-S bridges between cysteines) of dendritic hexapeptides. The second subject concerned the classification of enzymes, and the assessment of their relative activities and stereoselectivities. A new assay using an array of different substrates allows the rapid screening of many enzymes and allows a fingerprinting of the enzyme, highlighting the differences and similarities of different enzymes.

Apart from the lectures, more than 60 posters from 15 of the 23 actions now running in COST chemistry were presented. With well over a hundred participants, and animated discussions during the coffee and lunch breaks, the COST programme clearly showed its vitality.